USTUR - 0382-15

United States Transuranium and Uranium Registries

Annual Report

April 1, 2012 - March 31, 2014

College of
Pharmacy
WASHINGTON STATE UNIVERSITY

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Compiled and Edited

Stacey L. McComish and Sergei Y. Tolmachev

January 2015

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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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Inside This Report

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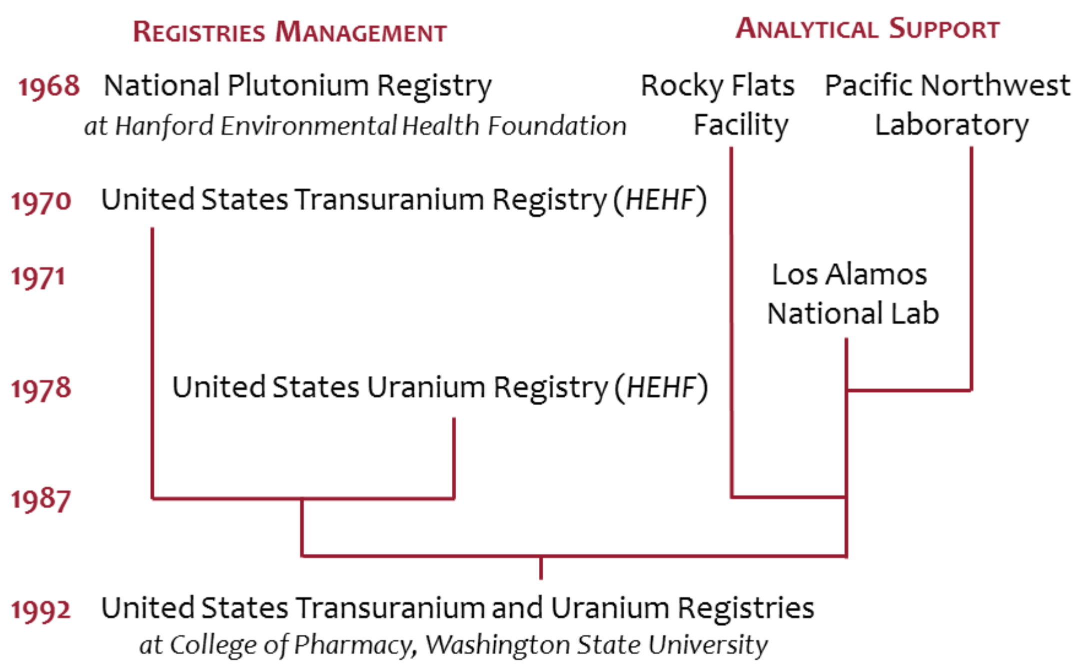
Foreword

Richard E. Toohey, *Chair, Scientific Advisory Committee*

The mission of the United States Transuranium and Uranium Registries (USTUR) is to gather and analyze actual human data to improve radiation protection of workers exposed to plutonium and other nuclear-weapons-related isotopes. The Registries began as the National Plutonium Registry in 1968 at the Hanford Environmental Health Foundation (HEHF) to follow workers with documented intakes of plutonium and other actinide isotopes to identify any adverse health effects. The name was changed to the U.S. Transuranium Registry in 1970, and the U.S. Uranium Registry was established in 1978 as a parallel but separate study. The two Registries were administratively joined in 1992 and moved to the Washington State University Tri-Cities campus in Richland, WA.

Because we cannot directly measure radiation doses received from radioisotopes inside the body, we use mathematical models to describe where they are deposited, how long they stay there, and how rapidly they are excreted, all of which enables us to calculate the radiation doses workers receive from intakes. However, these models are largely based on animal data, and one of the goals of the Registries has been to improve these models by using data from human exposures. To a large extent, this goal has been accomplished. For example, data from the Registries led to a significant change in the predicted retention of ^{241}Am in the liver. Brand-new data from the Registries will very likely lead to a model for retention of radioactivity in the lungs if it was inhaled in an acidic form, causing chemical damage to lung tissue. This lung damage model did not even exist when the Registries began. Clearly, continued collection of human data will still be important to improve dosimetry models in the future.

However, new research in radiobiology is pointing



towards a new mission for the Registries to support fundamental scientific investigations of the connections between radiation exposure and cancer formation. The Department of Energy has sponsored a research program for about the last 10 years to investigate the biological effects of radiation at the cellular, and even sub-cellular level. That is, what really happens within a cell that is exposed to radiation, and how do those changes in the cell lead to the formation of a cancer? Again, much of the data used has been from animal experiments, but new collaborative programs between USTUR and DOE and University laboratories will use human tissue samples from the Registries to compare with animal data. This project, which was undreamed of when the USTUR was established, is just one more example of the invaluable national scientific resource that the USTUR has become. There is no doubt that at some time in the future, USTUR data will lead to scientific insight into a problem that does not even exist today.

Despite up-and-down funding levels, the entire Scientific Advisory Committee considers the USTUR to be not merely an important, but an irreplaceable scientific resource for the nation and the world to continue improvement of radiation protection for all workers. Of course, none of this would be possible without caring and compassionate donations of Registrants and their families, and we feel that helping to protect current and future workers from radiation is the best thank-you that the USTUR can offer.

Financial Report

Margo D. Bedell-Parker, *Fiscal Specialist I*

On April 1, 2012, the USTUR began a new 5-year grant cycle (April 1, 2012 – March 31, 2017). The originally requested budget to manage and operate the Registries in FY2013 - FY2017 was $6,048,665. It was directed by U.S. Department of Energy that only $4,500,000 will be allocated for the USTUR in FY2013 – FY2017, resulting in a flat $900,000 annual budget.

To accommodate the reduced budget, two administrative positions, Fiscal Technician II and Office Assistant II, were eliminated during FY2013, and replaced by a Fiscal Specialist I position in FY2014. (See organization charts in Appendix A.)

Total FY2013 – FY2014 (April 1, 2012 – March 31, 2014) research program funding sources were:

Federal Resources

Grant

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

Manage and Operate the United States Transuranium and Uranium Registries

DE-HS0000073

- FY2013
Amount awarded: $900,000
Period: April 1, 2012 – March 31, 2013

- FY2014
Amount awarded: $900,000
Period: April 1, 2013 – March 31, 2014.

Total funding granted by DOE/HS-13 to WSU/COP/USTUR from April 1, 2012 until March 31, 2014 was $1,800,000.

External Funding

Grant

Public Health England (UK)/Epidemiological Studies of Exposed Southern Urals Population (SOLO) project (EU)

Microdistribution and Long-Term Retention of $^{239}Pu(NO_3)_4$ in the Human Respiratory Tract

GA249675

Amount awarded: $20,992
Period: October 1, 2012 – April 31, 2013.

Operating budget

Operating expenses for FY2012 were overspent by $29,687. This amount was carried forward into FY2013, leaving a budget of $870,313 out of the DOE awarded $900,000 grant. With the PHE/SOLO award of $20,992, the USTUR net operating budget for FY2013 was $891,305. Operating expenses for FY2013 were $913,286 resulting in $21,981 overspending. This amount was carried forward into FY2014, giving net operating budget of $878,019 out of $900,000 awarded grant. With the reduction of the USTUR personnel, and less than expected number of donations in FY2014, operating expenses were maintained at $878,000. Thus, FY2014 was completed with a zero balance.

Grant Administration

Submitted

A grant proposal to study plutonium binding in the upper airways of the human respiratory tract was submitted to the Pacific Northwest National Laboratory (PNNL) as part of the DOE Project 2.4 Mayak Worker Dose Reconstruction, of the Joint Coordinating Committee on Radiation Effects Research (JCCRER) collaboration. The requested budget was $50,000 for a one-year grant period: October 1, 2013 – September 31, 2014. Grant was funded on February 20, 2014.

During FY2013 – FY2014, the USTUR submitted two grant proposals to Washington State University (WSU). One was a 2013 New Faculty Seed Grant proposal: "Uncertainty Analysis on Lung Doses for the US Nuclear Workers" with a requested budget of $24,799. The second was grant proposal for 2014 International Research Travel Award (IRTA) sponsored jointly by WSU's Office of International Programs and the Office of Research. Requested budget was $4,267. These proposals were not funded.

No-cost Extension

The USTUR received a no-cost time extension from Public Health England for the GA249675. The request extended the contract period from May 1 to July 30, 2013.

FY2015 Grant Renewal Proposal

On January 22, 2014, a grant renewal proposal to manage and operate the United States Transuranium and Uranium Registries and the associated National Human Radiobiology Tissue Repository (NHRTR), in FY2015 (April 1, 2014 – March 31, 2015) was submitted to the Department of Energy Office of Domestic and International Studies (DOE/HS-13) through the WSU's Office of Grant and Research Development (OGRD). The total amount requested for the FY2015 was $900,000.

Reporting Requirements Met

Eight quarterly progress reports for the federally funded grant (DE-HS0000073) and one technical report for the externally funded grant (GA249675) were distributed on a timely basis to sponsoring agencies during the period April 1, 2012 – March 31, 2014. FY2011 – FY2012 annual report (USTUR-0344-12) for the federally funded grant (DE-FG06-92EH89181) was published and mailed to over 200 scientists nationally and internationally.

Registrant Statistics

Stacey L. McComish, *Associate in Research*

As of March 31, 2014, the Registries had a total of 877 Registrants in all categories (Table 1). Of that number, 62 were living and 345 were deceased. The 62 living Registrants included 8 individuals who were registered for eventual whole-body donation, 48 for partial-body donation, and 6 for 'Special Studies,' i.e., a bioassay study with no permission for autopsy. There were also 470 Registrants in an inactive category, which includes those lost to follow-up and those whose voluntary agreements were not renewed.

Registrant Renewals

The USTUR renews agreements with active Registrants every five years, to ensure that they still wish to participate in the program. The renewal process, along with the annual Registrant newsletter (Appendix B), also serves to maintain USTUR contact with all living Registrants. During this fiscal period, thirty-two Registrants renewed, eleven were placed in the inactive category, one changed from inactive to a potential partial-body donor, and two new Registrants joined the program.

Table 1. Registrant Statistics as of March 31, 2014

Total Living and Deceased Registrants:	407
Living Registrants:	**62**
Potential Partial-body Donors:	48
Potential Whole-body Donors:	8
Special Studies:	6
Deceased Registrants:	**345**
Partial-body Donations:	298
Whole-body Donations:	42
Special Studies:	5
Inactive Registrants:	**470**
Total Number of Registrants:	877

Registrant Deaths

The USTUR was notified of ten Registrant deaths. Three were whole-body donors and seven were partial-body donors. Autopsies of partial-body donors were performed near the municipality where the Registrants passed away, and tissues were sent to the USTUR laboratory for radiochemical analysis.

Case 0272: This partial-body donor's primary intake was an inhalation of plutonium; however, he also received a contaminated acid burn that resulted in a smaller intake. The Registrant died as a result of a fall.

Case 0343: This whole-body donor worked with both plutonium and uranium during the course of his career. He had two possible intakes of plutonium. One was indicated by a positive urine sample and the other by high airborne concentrations at his workplace. He died from bronchial carcinoma of the lung.

Case 0636: This partial-body donor's primary intake was an inhalation of insoluble ^{239}Pu. Two years later, the Registrant was thought to have inhaled soluble ^{238}Pu. Work site staff estimated that the committed effective dose equivalent for these two intakes was 55 mSv (5.5 rem). The Registrant died from mesothelioma.

Case 0691: This partial-body donor was exposed to ^{238}Pu, and work site personnel estimated that he inhaled a total of 1.33 kBq (36 nCi) from five separate incidents. The Registrant died from mesothelioma.

Case 0743: This partial-body donor was involved in several minor incidents involving wounds and workplace contamination; however, they did not result in confirmed intakes. At the time of his retirement, work site personnel estimated that this Registrant had 56 Bq (1.5 nCi) of ^{239}Pu in his lungs. He died from heart disease.

Case 0757: This whole-body donor worked with plutonium for about 1½ years and with uranium for about 2½ years. No exposure incidents were documented. A urine sample collected 40 years after his radiation work contained a small, but detectable amount of ^{239}Pu. The Registrant died from respiratory failure.

Case 0803: This partial-body donor was primarily exposed to fission products. A significant autopsy finding was asbestosis.

Case 0804: This whole-body donor worked with plutonium for 37 years. The Registrant died from heart disease, and chronic renal failure likely contributed to death.

Case 0814: This partial-body donor worked in the nuclear field for 34 years, and was employed at several US DOE laboratories. A previously-analyzed surgical specimen contained a low, but measurable, amount of plutonium. He died from pulmonary thromboembolus.

Case 0861: This partial-body donor worked with plutonium, americium, uranium, and radium over the course of seven years. He inhaled approximately 333 Bq (9 nCi) of plutonium.

Longevity Statistics

The average age of living whole- and partial-body Registrants was 79 years and 81 years, respectively. Figure 1 shows how the living Registrants and their ages were distributed among the various DOE work sites. Figure 2 shows the number of donations per calendar year. The average age at death for USTUR's 335 deceased Registrants was 68 years.

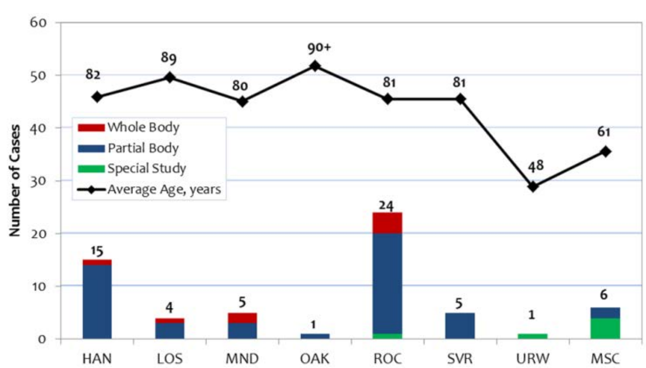


Fig. 1. Number of living Registrants and average age by work site: HAN – Hanford, LOS – Los Alamos, MND – Mound, OAK – Oak Ridge, ROC – Rocky Flats, SRS – Savannah River, URW – Uranium Workers, MSC – Miscellaneous.

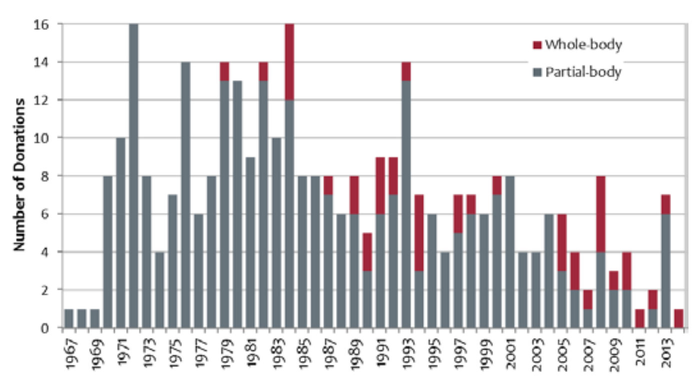


Fig. 2. Number of whole- and partial-body donations per calendar year.

Health Physics Database

Maia Avtandilashvili, *Research Associate*

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.

Data Entry

The USTUR currently holds the documents containing health physics and bioassay records for the 42 whole-body and 298 partial-body Registrant tissue donors. Starting in 2012, the USTUR adopted the following strategy for the health physics database population:

- The most recent donation is given the highest priority and is completed immediately
- Whole-body cases are given higher priority than partial-body donations and are completed based on specific worksite: Rocky Flats, Los Alamos, Hanford, *etc*.
- Partial-body cases are processed on a routine basis when all whole-body cases are completed
- In special circumstances, priority is given to specific case(s), which are subjects of particular scientific interest.

Since the expansion and restructuring of the USTUR's internal health physics database in 2008, standardization of health physics records and bioassay data was completed for a total of 83

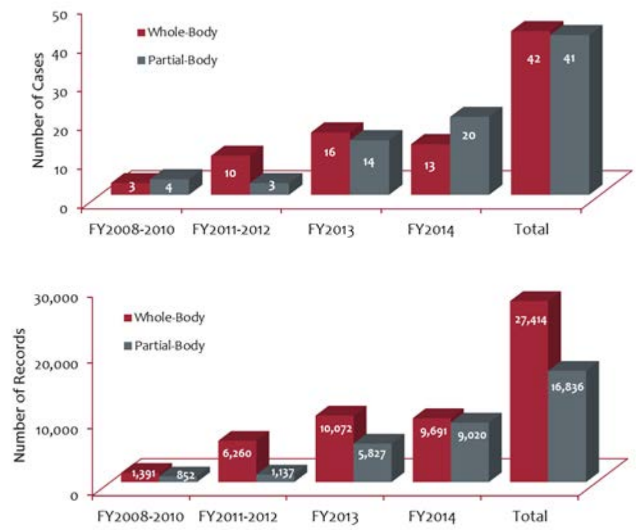


Fig. 3 FY2014 progress and overall status of the USTUR health physics database.

USTUR donations: 42 whole-body (all whole-body cases) and 41 partial-body (10% of all partial-body cases). In total, 44,250 health physics records have been entered into the database.

Figure 3 shows the FY2008 - FY2014 progress and the overall status of the health physics database as of March 31, 2014.

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 4.

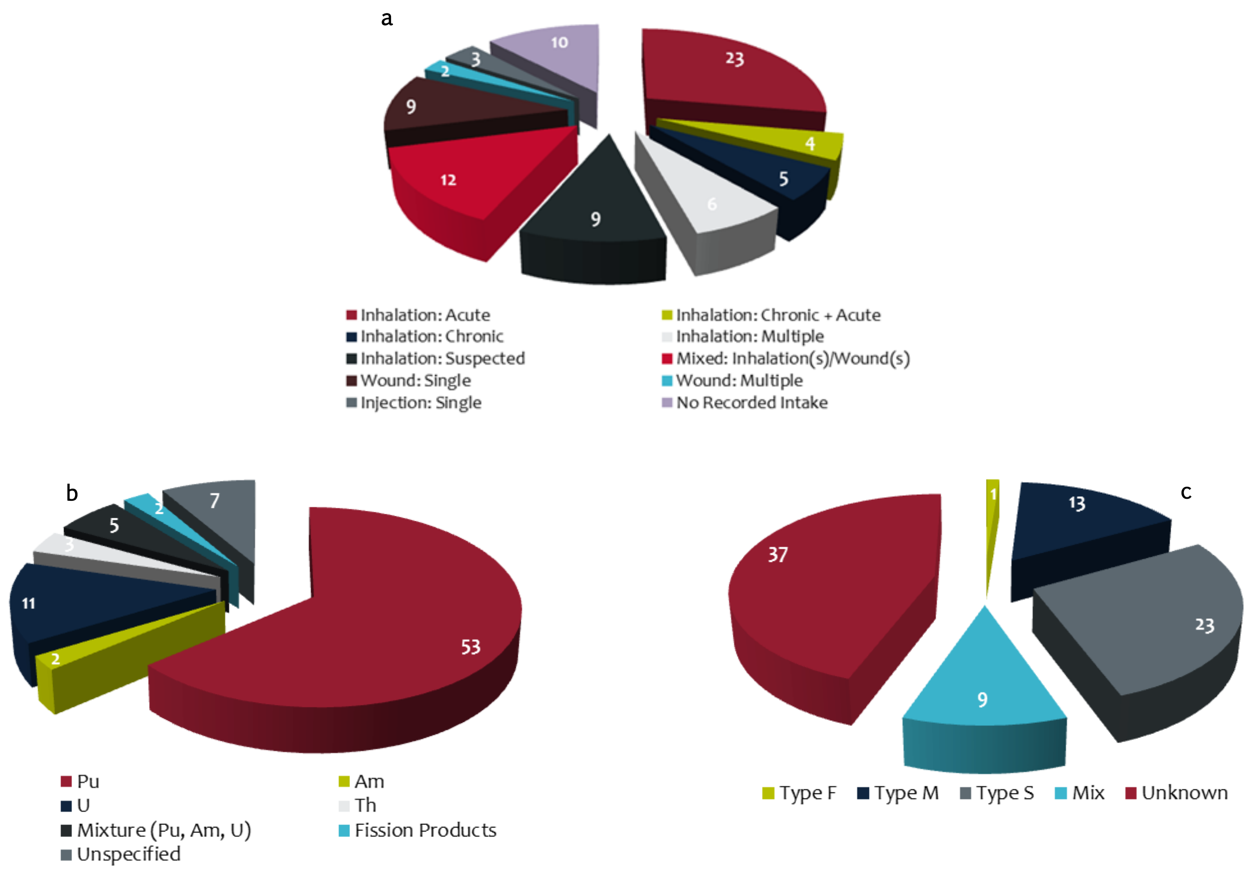


Fig. 4. Summary statistics of the health physics database: completed cases by (a) intake; (b) primary radionuclide; (c) material type.

NHRTR National Human Radiobiology Tissue Repository

Stacey L. McComish, Associate in Research

NHRTR activities focused on: (i) tissue prosection, consisting of dissection and hygienic packaging; (ii) THEMIS (the information management system) inventory of the processed tissues; and (iii) THEMIS inventory of acid solutions.

Tissue Prosection

During the current reporting period, 10 whole- and 38 partial-body donations were dissected (Table 2). Tissues from another ten cases that had previously been classified as fully dissected were also identified and vacuum packaged. Processed cases included both recent donations and archival tissues from past donations (e.g. tissues from the left side of the body that were saved for future research). The Registrants' deceased dates ranged from 1984 to 2013.

THEMIS Inventory

To date, 13,879 samples have been inventoried using THEMIS database. Sixty-seven percent of the samples were USTUR tissues, 25% USTUR acid solutions, 3% miscellaneous USTUR, and 5% non-USTUR samples. Non-USTUR samples included reagents, National Institute of Standards and Technology (NIST) standards, radium dial painter tissues, acid solutions from LANL population studies, etc. Of the 13,879 samples, 2,118 were subsamples (Table 3).

Table 2. Whole- and partial-body cases

Whole Body			
0205 (1984)	0242 (1987)	0757 (2012)	1007 (1991)
0208 (1984)	0259 (1989)	0804 (2013)	
0213 (1984)	0706 (1992)	1001 (1989)	

Partial Body			
0270 (2002)	0331 (2000)	0636 (2012)	0861 (2013)
0271 (2002)	0334 (2004)	0640 (1992)	0991 (2004)
0272 (2013)	0371 (1992)	0691 (2013)	1015 (1995)
0274 (1996)	0379 (1996)	0709 (2000)	1016 (1992)
0279 (1998)	0427 (1994)	0719 (1998)	1025 (1993)
0281 (1993)	0441 (1993)	0727 (2001)	1052 (1993)
0285 (1997)	0445 (2003)	0743 (2013)	1065 (2000)
0302 (1998)	0492 (1993)	0803 (2013)	
0306 (2000)	0511 (1993)	0814 (2013)	
0318 (1997)	0526 (1993)	0841 (1994)	

Table 3. Inventoried NHRTR samples

Tissue Type	Parent	Sub-sample	Total
Frozen Soft Tissue	4,487	465	4,952
Frozen Bone	4,180	64	4,244
Acid	2,174	1,250	3,424
Fixed	141	175	316
USTUR Misc.	159	38	197
Non-USTUR	620	126	746
Total	11,761	2,118	13,879

Parent samples best represent the number of unique tissues available at the USTUR; therefore, the following discussion excludes subsamples. Forty-one whole-body and 100 partial-body cases have been inventoried. On average, whole-body cases have 194 ± 106 samples per case and partial-body cases have 30 ± 27 samples per case. Figure 5 displays the distribution of tissue types among USTUR tissues and acid solutions, respectively. The tissues are predominantly frozen bones and soft tissues; however, formalin fixed samples are also included. The five most frequent tissue types in the miscellaneous category were circulatory, nervous, urinary, hepatic, and genital. Skeletal samples were most abundant. This results from both the large number of bones in the human body, as well as the dissection protocol. Typically, long bones were dissected into four samples that were inventoried as unique parent samples.

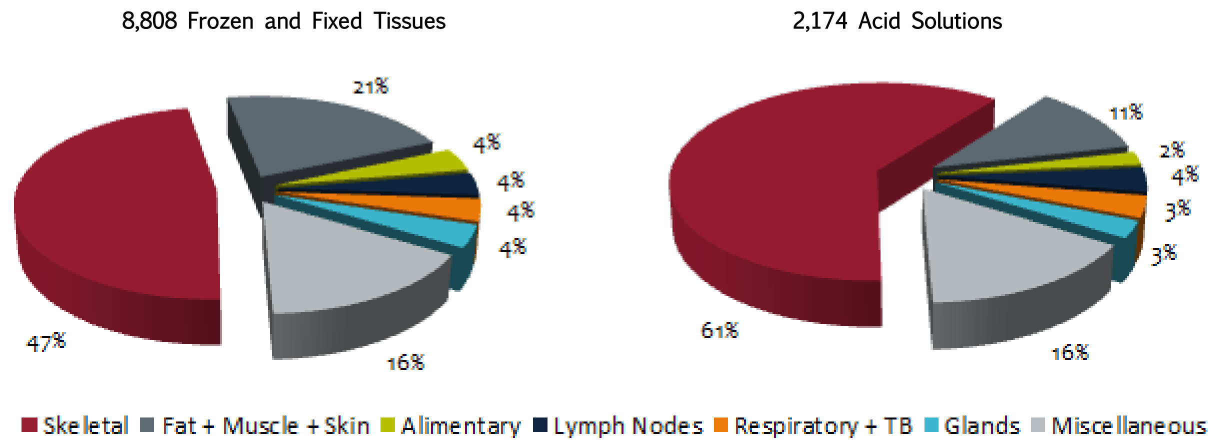


Fig. 5. Frozen and formalin-fixed tissues, including soft tissues and bone, by tissue type (left). Acid-digested (acid solutions) tissues by tissue type (right). *TB = tracheobronchial.*

Planchet Inventory

The USTUR houses thousands of planchets on which americium or plutonium was electrodeposited in preparation for alpha spectroscopy counting. In March 2014, the USTUR commenced inventorying these planchets. During that month, 554 planchets from 28 partial-body donations were entered into an Excel spreadsheet. About half of the planchets, 51%, contained americium and about half, 49%, plutonium. The excel inventory contained information such as the date when the planchets were counted, the activity of tracer that was added, and the amount of plutonium or americium that was detected on each planchet. Once all samples have been entered into the Excel spreadsheet, the information will be transferred to the THEMIS database.

Radiochemistry Operation

Sergei Y. Tolmachev, *Director/Principal Radiochemist*

In FY2013 – FY2014, Radiochemistry Group activities were mainly focused on radiochemical tissue analyses.

Personnel

During FY2013 (April 1, 2012 – March 31, 2013), the Radiochemistry Group was fully staffed; the staff included Ms. Elizabeth Thomas (Laboratory Technician I), Mr. Fredrick Miller (Laboratory Technician Level III), and Dr. Sergei Tolmachev (Principal Radiochemist). Mr. Miller retired from the USTUR/WSU in December 2013 (FY2014), and Ms. Thomas was promoted to Laboratory Technician II in March 2014. This results in two full time equivalent (FTE) technical personnel support for FY2013 and 1.67 FTE for FY2014.

Tissue Sample Analysis

During FY2013 - FY2014, 625 tissue samples, including 268 bones and 357 soft tissues from 22 donations, were processed and analyzed in-house and at external laboratories. Of 625 samples, 338 were analyzed for plutonium (^{238}Pu, $^{239+240}$Pu), isotopes, and americium (^{241}Am), and 287 for uranium (U). All Pu/Am samples were analyzed at the USTUR using α-spectrometry (AS), while U samples were sent to external laboratories for ^{234,235,236,238}U isotopic or total U measurements by inductively coupled plasma mass spectrometry (ICP-MS).

Whole-body Donations

A total of 417 tissue samples, including 205 bones and 212 soft tissues from 10 USTUR whole-body donations, where Registrants were exposed to Pu (6 cases) and U (4 cases), were analyzed. Analyzed cases were: Case 0269 (died 1994; 13 samples), Case 0456 (2009; 33), Case 0503 (1994; 14), Case 0635 (2000; 2), Case 0679 (1997; 4), Case 0680 (1998; 2), Case 0740 (2010; 44), Case 0745 (2005; 55), Case 1007 (1991; 35), Case 1010 (2006; 38), Case 1031 (2010; 34), and Case 1060 (2008; 143).

Case 0269 was analyzed as a part of Public Health England (UK)/Epidemiological Studies of Exposed Southern Urals Population (SOLO) project (EU). For the details, see the "Bound Plutonium in Human Lungs" section below.

Bone samples from cases 0635, 0679, and 0680 were analyzed to complete the data set for a USTUR study that estimated the total skeleton activity based on the analysis of a limited number of bones. For more details, see "From a Single Bone to Total Skeleton" section below.

Samples from cases 1007, 1010, 1031, and 1060 were analyzed for uranium by ICP-MS through external laboratories.

Digested tissue samples (acid solutions) from Case 1007 were sent to Laval University Radioecology Laboratory (Quebec, Canada). Cases 1010 and 1031 were analyzed at the ICP-MS facility at Northern Arizona University (Flagstaff, AZ). Case 1060 was analyzed at the Bioassay Laboratory at AREVA NP (Richland, WA) as a part of the USTUR-AREVA collaborative study on uranium biokinetics.

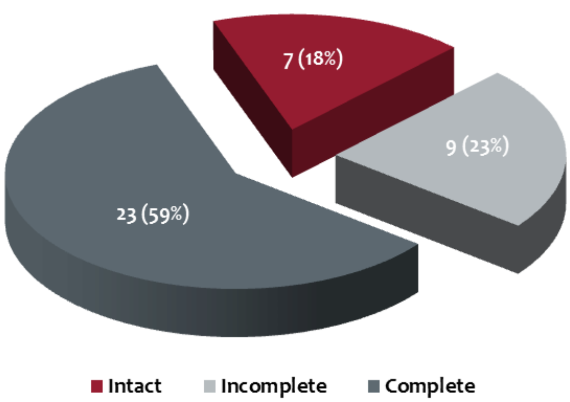
Partial-body Donations

A total of 208 tissue samples, including 63 bones and 145 soft tissues from 12 USTUR partial-body donations, where Registrants were exposed to Pu (11 cases) and U (1 case) were analyzed during FY2013 – FY2014. Analyzed cases were: Case 0375 (died 2002; 26 samples), Case 0412 (2005; 4), Case 0511 (1993; 1), Case 0691 (2013; 43), Case 0709 (2000; 1), Case 0785 (2008; 32), Case 0803 (2013; 17), Case 0814 (2013; 26), Case 0861 (2013; 21), and Case 1063 (2005; 37). Case 1063 was analyzed for ^{234}U, ^{235}U, ^{238}U concentrations and $^{234}U/^{238}U$, $^{235}U/^{238}U$ atom ratios at the ICP-MS facility at Northern Arizona University (Flagstaff, AZ).

Radiochemistry Status Changes

As of March 31, 2014, the USTUR had received 42 whole- and 298 partial-body donations, including receiving 3 new whole- and 7 new partial-body donations during FY2013 – FY2014. Figures 6 and 7 summarize overall radiochemical analysis status of all previous whole- and partial-body donations as of the beginning of FY2013 and the end of FY2014.

Cases are categorized as 'Intact,' 'Incomplete,' or 'Complete,' where 'Intact' denotes that no tissue samples have been analyzed, 'Incomplete' typically denotes that a selected sub-set of 10 – 15



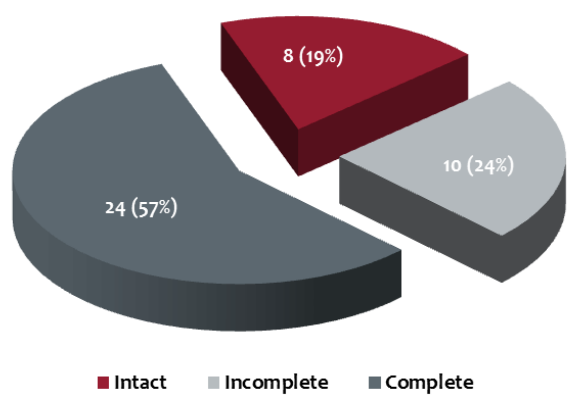
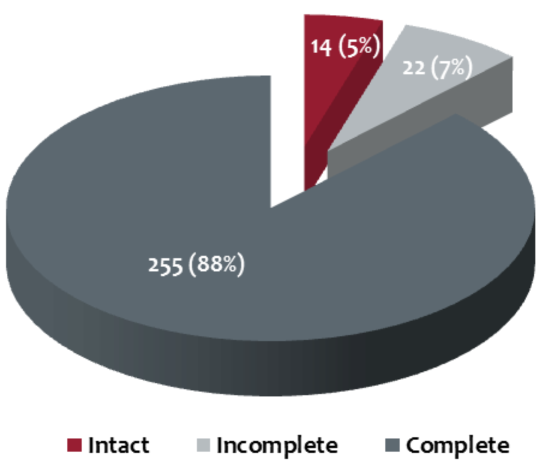


Fig. 6. Radiochemical analysis status for whole body donations: as of April 1, 2012 (left); and as of March 31, 2014 including 3 new donations during FY2013 – FY2014 (right).



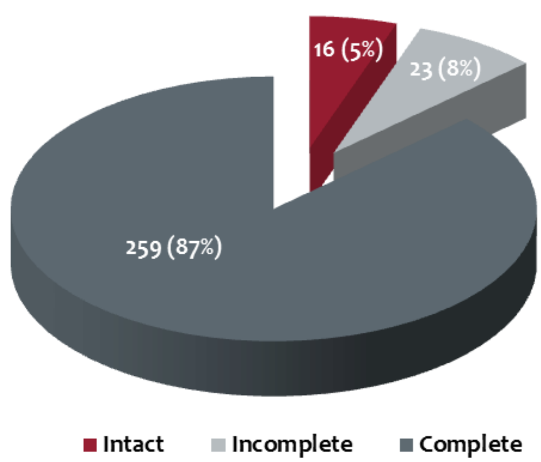


Fig. 7. Radiochemical analysis status for partial body donations: as of April 1, 2012 (left); and as of March 31, 2014 including 7 new donations during FY2013 – FY2014 (right).

tissues was analyzed or case analysis is in progress, and 'Complete' denotes that a full selection of tissue samples was analyzed and results were reported.

Table 5 summarizes changes in radiochemical analysis status during FY2013 – FY2014 for individual cases.

Table 5. FY2013 – FY2014 progress of radiochemical analysis

Case No	Year of Donation	Status Change	
Whole-Body			
0456	2009	Intact	Incomplete
1010	2006	Intact	Incomplete
1054†	1992	Intact	Incomplete
1060	2008	Incomplete	Complete
Partial Body			
0375	2002	Intact	Complete
0691	2013	Intact	Incomplete
0785	2008	Intact	Complete
0803	2013	Intact	Complete
0814	2013	Intact	Incomplete
0861	2013	Intact	Incomplete

†- no analyses were performed; digested tissues were found.

Student Involvement

Stacey L. McComish, *Associate in Research*

Eighteen WSU Tri-Cities nursing students have assisted at USTUR autopsies. Pictured above are Scott Roberts and Jessica Harper before Case 0757 autopsy.

Students from our community and abroad have benefited from unique educational opportunities at the USTUR. Students from WSU's environmental sciences program, Idaho State University's (ISU) health physics program, and Gent University (UGent), Belgium, have published and/or presented USTUR-related research during this reporting period. In addition, the USTUR has a vibrant collaborative relationship with the WSU Tri-Cities nursing program.

WSU Tri-Cities Nursing Program

Autopsy Assistants

Since 2010, 18 WSU Tri-cities nursing students have assisted with local USTUR autopsies. This mutually beneficial arrangement gives students the opportunity to observe an autopsy, and it provides the USTUR with extra hands to weigh and package tissues removed during the autopsy. Students are extremely grateful for this educational opportunity, and there is never a lack of volunteers.

Student Employees

In 2010, a nursing student expressed interest in working at the NHRTR, and became the first of many nursing students to work as laboratory assistants. These students worked closely with the USTUR prosector, Florencio Martinez, to assist with dissections, vacuum package tissues, and inventory samples. Mr. Martinez is an excellent teacher, who willingly explains both the anatomical and pathological aspects of the tissues they work with. For example, diseases such as atherosclerosis are pointed out. The students arrive equipped with a solid training in anatomy and physiology, and have become an instrumental part of the tissue and acid solution inventory process at the laboratory.

Graduate Student Project

In 2013, Becky Phillips – from the WSU Graduate College of Nursing, Family Nurse Practitioner Program – performed a 45-hour clinical research project at the USTUR as a part of her master's degree program. Ms. Phillips assisted during the dissection of a plutonium worker's lung into the ICRP 66 lung model's three thoracic compartments (*BB*, *bb*, and *AI*). These samples were analyzed to determine their plutonium content, and the results were used to study the long-term binding of soluble plutonium in the lung.

Gent University, Belgium

In 2010, a M.S. research project began at UGent. Ms. Eva Vergucht focused on the application of synchrotron radiation x-ray fluorescence (SR-XRF) spectroscopy to study elemental bio-imaging of actinides and other stable elements. In support of this research, the USTUR provided six formalin-fixed samples, including lymph nodes and a lung sample. Ms. Vergucht discovered that SR-XRF is a potential tool for quantification of uranium and transuranium elements in human tissues. Such results could contribute to further refinement of dose assessment methods for these internal emitters as a basis for reliable epidemiological studies, risk projection, and credible standards for radiological protection. Ms. Vergucht successfully defended her MS thesis in 2011, and presented her research at the 2012 European conference on X-Ray Spectroscopy (EXRS) in Vienna, Austria.

Presentation

Vergucht E, Izmer A, De Samber B, Vekemans B, Appel K, Tolmachev S, Vincze L, Vanhaecke F. Elemental imaging of actinides in human tissues using LA-ICP-MS and SR micro-XRF. European Conference on X-Ray Spectroscopy (EXRS), Vienna, Austria, June 18-22, 2012.

Idaho State University

In 2006, the USTUR entered into a collaborative relationship with Idaho State University (ISU). Initially, the USTUR funded one Ph.D. Student; however, due to a reduction in DOE funding, the subcontract was discontinued in 2008 and two no-cost extensions were granted to carry forward unspent funding until 2010. As a product of this collaboration, four Ph.D. and three M.S. degrees were awarded. Two of the doctoral degrees were awarded during this reporting period.

Seven papers were published based upon USTUR data. Former USTUR director, Dr. Anthony C. James, was a co-author on two of the publications, and the remaining five were published independently of the USTUR.

Doctoral Degrees

George Tabatadze. USTUR Case 0102 voxel phantom for external gamma-ray detector response simulation. Defended in August 2012.

Majid Khalaf. A new leg voxel model in two different positions for simulation of the non-uniform distribution of ^{241}Am in leg bones. Defended in December 2012.

Peer Reviewed Publications

USTUR Publications

Avtandilashvili M, Brey R, James AC. Maximum likelihood analysis of bioassay data from long-term follow-up of two refractory PuO_2 inhalation cases. *Health Phys.* 2012; 103(1): 70-79.

Weber SN, Brey RR, James AC. Reevaluation of USTUR plutonium wound Case 0262 using Bayesian methodology and new data. *Health Phys*. 2012; 103(3): 286-300.

USTUR Associated Publications

Fallahian NA, Brey RR, Tivis RD, Piland NF, Simpson DR. Cancer deaths and occupational exposure in a group of plutonium workers. *Health Phys*. 2012; 102(4): 443-452.

Tabatadze G, Brey R, Kramer GH, Capello K, Meldrum DJ. Reevaluation of ^{241}Am content in the USTUR Case 0102 leg phantom. *Health Phys*. 2013; 104(1): 9-14.

Khalaf M, Brey R, Meldrum J. A new leg voxel model in two different positions for simulation of the non-uniform distribution of ^{241}Am in leg bones. *Health Phys.* 2013; 104(1): 51-56.

Khalaf M, Brey RR, Derryberry D. Evaluation of ^{241}Am deposited in different parts of the leg bones and skeleton to justify in vivo

measurements of the knee for estimating total skeletal activity. *Health Phys.* 2013; 104(1): 57-62.

Avtandilashvili M, Brey R, Birchall A. Application of Bayesian inference to the bioassay data from long-term follow-up of two refractory PuO_2 inhalation cases. *Health Phys.* 2013; 104(4): 394-404.

Uncertainties in Lung Doses: Pilot Study

Maia Avtandilashvili, *Research Associate*

In this pilot study, selected USTUR cases were analyzed using a Bayesian approach and Monte Carlo simulation methodologies to obtain the best estimates of the lung dose and calculate the associated uncertainties as expressed by Bayesian posterior probability distributions.

Background

For nuclear workers, inhalation is the most significant pathway of internal contamination. The lung as the initial deposition site for inhaled material is the main target organ from a radiological standpoint. Hence, accurate assessment of absorbed doses to the respiratory tract tissues is an important basis for better understanding of health effects of inhaled radionuclides and obtaining more reliable estimates of cancer risks from exposure to radioactive aerosols. Quantifying uncertainties in lung doses is, therefore, of great significance for further use in epidemiologic studies. However, up until now, in most of the published epidemiology studies, the internal dose estimates are usually point values provided without uncertainties.

Bayesian analysis methods are widely used in internal dosimetry and enable one to calculate uncertainties in dose estimates, as well as in biokinetic models expressed as posterior probability distributions (Figure 8) by incorporating all prior knowledge on the exposure scenario (material type, particle size, model parameters etc.).

Recently, Puncher *et al*[1] published the results of Bayesian uncertainty analysis conducted for the epidemiology study of European radiation workers. The authors estimated lung doses from occupational exposure to plutonium for a large group of UK workers, along with the associated uncertainties.

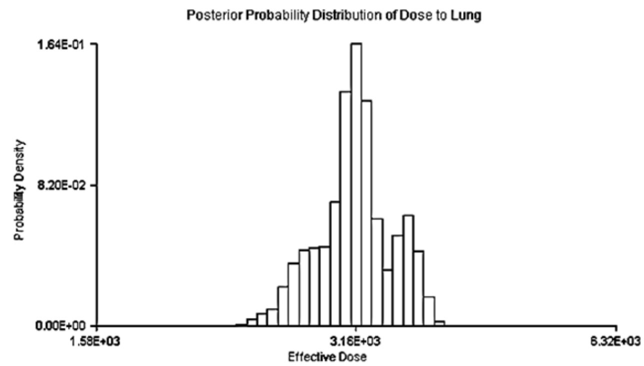


Fig.8. Bayesian posterior probability distribution.

The concept of a hyper-model, where some of the model parameters were represented by the probability distributions instead of having fixed values, was employed for this analysis. In order to account for the strong dependence of deposition, retention and excretion of incorporated radioactive material on its physico-chemical characteristics and metabolic behavior, two types of plutonium material (nitrates and oxides) were investigated separately and the corresponding sets of model parameters were derived. The results of this study indicated the need for further research to better determine the estimates of the critical model parameters as the bases for reliable dose estimates for workers.

Study Population

Since its establishment in 1968, the USTUR received 42 whole-body and 298 partial-body donations. Most of the USTUR Registrants had a number of different exposure incidents involving inhalation, ingestion, and wound intakes, with

Table 6. Pilot study cases

Solubility	Chemical Form	Cases	Worksite	$^{239/240}Pu$ in Lungs, Bq
Type M	$Pu(NO_3)_4$	3	HAN, LOS	0.3 – 4
Type S	'High Fired' PuO_2	5	RFP	730 – 7,500

inhalation being the most common pathway. As of January 1, 2014, tissue samples from a total of 279 (out of 340) USTUR donors were analyzed. The range of $^{239/240}Pu$ concentrations in lungs spans about 8 orders of magnitude (≤0.0001 to 7,200 Bq kg^{-1}). Post-mortem tissue analysis results combined with detailed work history, radiation exposure, medical and industrial hygiene records form a powerful dataset that is used to evaluate and improve biokinetic models.

Methods

In FY2014, the USTUR staff completed a pilot intramural study on uncertainty analysis in lung doses for a small group of donors exposed to air-borne plutonium in different chemical forms. Eight cases with a single, well-defined inhalation intake were selected (Table 6).

Case histories including exposure details, bioassay data, and autopsy tissue analysis results were reconstituted in IMBA Professional Plus® files for biokinetic calculations. The Weighted Likelihood Monte-Carlo Sampling (WeLMoS) method, as implemented in IMBA Uncertainty Analyzer software tool[2,3], was applied to these data to quantify the lung doses, and calculate the associated uncertainties expressed by Bayesian posterior probability distributions. Prior probability distributions of the critical model parameters (Table 7) were selected based on the most up-to-date information available in the literature and expert judgment.

Results

Full posterior probability distributions of lung doses and model parameters were generated with 10,000 input parameter vector realizations. The effect of using autopsy tissue analysis results combined with bioassay monitoring data was examined (Table 8).

This evaluation demonstrated that using autopsy data significantly affected the dose assessment results and in the case of insoluble material, substantially increased the lung dose estimates. Hence, the doses from inhaled plutonium oxides obtained based on exclusively urine data may be underestimated. The results of this study were presented at the 11th International Conference on the Health Effects of Incorporated Radionuclides in Berkeley, CA on October 13-17, 2013.

Future Work

The USTUR team is now seeking funding opportunities to expand this pilot study into a full-scale study of the entire USTUR population. A joint research proposal titled "Uncertainty Analysis on Lung Doses for US Nuclear Workers" to be submitted for external funding in collaboration with the scientists from Department of Toxicology, Centre for Radiation, Chemical and Environmental Hazards, Public Health England (UK) is currently under preparation.

This research project will quantify uncertainties in lung dose estimates for all USTUR donors, and derive probability distributions of the critical biokinetic model parameters.

Table 7. Prior probability distributions of ICRP human respiratory tract model parameters

Particle Transport		Absorption to Blood		
Parameter	Prior Distribution	Parameter	Prior Distribution	
			Nitrate†	Oxide‡
INT_{Dep}	LN(0.37; 2)	f_r	LN(0.17; 2)	U(0.001; 0.02)
ALV to bb, d^{-1}	LN(0.0027; 3)	s_r, d^{-1}	LN(1; 4)	U(0.1; 10)
INT to LN_{TH}, d^{-1}	LN(0.00003; 3)	s_s, d^{-1}	LN(0.0012; 2.3)	U(0.000001; 0.0001)
K_{PT}	LN(1; 1.73)	f_b§	Tr(0; 0.08)	n/a

† Taken from Puncher *et al*[1)]
‡ Taken from Avtandilashvili *et al*[(4)]
§ s_b = 0 (fixed).

Table 8. Posterior probability distributions of equivalent lung doses (mSv)

Case No	Years Post-Intake	Urine Data Only		Bioassay† + Autopsy Data‡		Median Dose Ratio
		Median Dose	GSD	Median Dose	GSD	
Nitrate						
0224	14	395	2.51	230	1.49	0.58
0631§	66	525	2.16	190	2.03	0.37
0795	42	130	2.46	48	1.46	0.37
Oxide						
0028	5	3,410	2.22	9,830	1.27	2.88
0036	6	3,350	2.53	5,050	1.24	1.51
0202	18	6,680	2.64	60,810	1.13	9.10
0407§	43	8,800	3.12	20,920	1.15	2.38
0821	28	5,110	2.66	7,000	1.28	1.37

† Urine for nitrates; Urine and in vivo lung counts for oxides
‡ Pu activity in lungs, liver, skeleton
§ Autopsy data: skeleton for Case 0631; lung and skeleton for Case 0407.

Results of the study will be used to test and validate the upcoming revisions to the ICRP biokinetic models and recommendations and, critically, to support application of these models in ongoing epidemiology studies of former plutonium workers in Russia and the UK, among others.

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Bound Plutonium in Human Lungs

Christopher E. Nielsen, *PhD Student, Washington State University*

Sergei Y. Tolmachev, *Associate Research Professor, Washington State University*

The distribution of plutonium activity concentration in lung tissues was investigated in this study. The results of this work provide key information on the extent of plutonium binding in the upper airways of the human respiratory tract.

Introduction

The USTUR whole-body donation (Case 0269) involved a single acute inhalation of an acidic $Pu(NO_3)_4$ solution in the form of an aerosol 'mist'. The estimated intake was ~58 kBq. At the time of death (38 years post-intake), ~2% of total body activity still remained in the lungs. A detailed description of the case was previously published(1).

Tissues from the respiratory tract of Case 0269 were analyzed for this study. This case is one of three cases available at the USTUR where individuals were exposed to soluble Pu through single acute inhalation.

Experimental Methods

In this study, the left lung from USTUR Case 0269 was dissected based on ICRP 66 Human Respiratory Tract Model (HRTM) and radiochemically analyzed for plutonium isotopes.

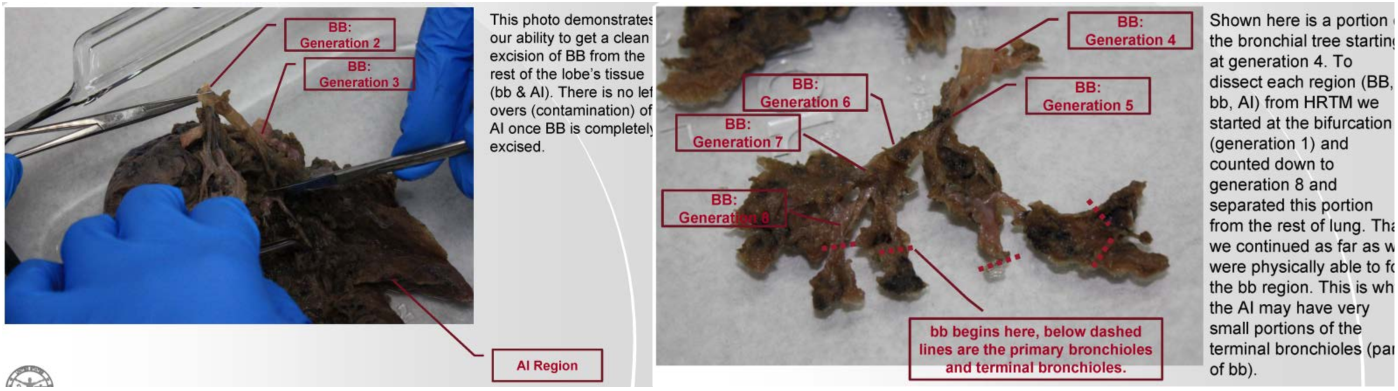
ICRP 66 HRTM divides the lung in three major compartments: bronchial (*BB*); bronchiolar (*bb*), and alveolar interstitial (*AI*). Anatomically, the *BB* compartment includes the trachea, main bronchi, and bronchi; *bb* – bronchioles, and *AI* – alveolar duct and alveoli(2). Such dosimetric compartment structure is different from general anatomical structure where the lung is divided by lobes: superior, middle or lingular, and inferior. Each of the lobes contains all three dosimetric compartments – *BB*, *bb*, and *AI*. Thus, careful dissection of each lobe to separate *BB*, *bb*, and *AI* regions is important. Clear separation of three dosimetric compartments from each other is crucial. It is expected that plutonium activity concentration in *BB* region is an order of magnitude lower compared to that in bb, where it is lower compared to *AI*. Thus, incomplete dissection will cause cross contamination leading to false results in plutonium activity concentration measurements, especially if tissue from *AI* region is present in *BB*.

Alpha spectrometry (AS) was primarily used for $^{239+240}Pu$ and ^{238}Pu measurements.

Tissue Dissection

Originally taken at autopsy (1994), the left lung of Case 0269 was frozen and stored at -30 ˚C. In 2010, it was dissected in three anatomical lobes; each lobe was preserved in 10% buffered formalin.

In this work, the superior, lingular, and inferior lobes of the left lung were dissected into *BB*, *bb*, and *AI* compartments. A new set of surgical instruments was used each time to avoid potential tissue cross contamination. The dissection was performed by Mr. Florencio Martinez (USTUR), assisted by Mr. Chris Nielsen (WSU College of Arts and Sciences employed by Pacific Northwest National Laboratory), and Ms. Becky Phillips (MS student WSU College of Nursing).



Dissection of left lung from Case 0269 based on ICRP 66 Human Respiratory Tract Model compartment structure.

Through dissection, we were able to achieve: (i) *BB* excised with no contamination by *AI* region; (ii) *bb* has very little if any *AI* contamination; (iii) *AI* region is pure with some terminal bronchioles (part of *bb*), which were too small to excise, and infiltrated along the pleura.

Separated tissues from *BB*, *bb*, and *AI* regions of each lobe were submitted for radiochemical analysis.

In total, ten tissue samples including tissues from *BB*, *bb*, and *AI* regions of the left lung, larynx, trachea, left bronchus, hilar fat, parabronchial lymph nodes (LN), pulmonary LN, and tracheabronchial LN were prepared for radiochemical analysis.

Radiochemical Analysis

The actinide tissue analysis methods used at the USTUR were described elsewhere[3].

Plutonium Analysis by Alpha Spectrometry

Plutonium analysis by AS was performed by the USTUR in Richland, WA using standard operation protocol, routinely used for actinide determination in human tissue samples. All USTUR's standard operation procedures are available at http://www.ustur.wsu.edu/PolicyProcedures/RadChemProcedures.html

Seven samples from the respiratory tract, including half of the larynx and trachea; the right (R) lung; the pulmonary (R), mediastinal, and tracheobronchial lymph nodes (LN); and blood were analyzed by the USTUR in 1996.

Fourteen samples, henceforth referred to as the separation batch were submitted for Pu analysis. These included ten soft tissues and three formalin samples that contained tissue debris from the original superior, lingular, and inferior lobes, plus a method blank. Prior to radiochemical analysis, all samples were dry ashed at 450 °C, followed by wet ashing with mixture of concentrated HNO_3 – H_2O_2, and treatment with HF. After dry/wet ashing, resulting residues were re-dissolved in 6 M HCl and solution aliquots were taken for further analyses. For quality assurance and quality control (QA/QC) of the actinide separation, internal QA/QC sample (spiked with ^{240}Pu) and blank sample (6M HCl) were added to the separation batch. Plutonium isotopes $^{239+240}$Pu and ^{238}Pu were radiochemically separated from sample matrices and isolated from interfered actinides (U, Am, Th) using vacuum-assisted extraction chromatography technique. Separation was performed with 1-ml TEVA® – DGA® chromatographic resin cartridges on vacuum box system. A standard electrodeposition technique

BB tissues *bb* tissues *AI* tissues

USTUR Case 0269: Dissected BB, bb and AI tissues from left lung prepared for radiochemical analysis.

was used to prepare a counting α-source (planchet) for $^{239+240}$Pu and ^{238}Pu activity measurement by AS. Prepared planchets and instrumental background were counted for 600,000 seconds.

Table 9 summarizes results of the 1996 and 2013 $^{239+240}$Pu and ^{238}Pu radiochemical analyses carried out by the USTUR[4]. The $^{239+240}$Pu and ^{238}Pu activities were decay-corrected to the day of donation (1994).

Table 9 Results of plutonium isotope analysis by AS in tissues from USTUR Case 0269

Tissue/Organ	Sample weight, g	Activity concentration†, Bq kg^{-1} $^{239+240}$Pu	Activity concentration†, Bq kg^{-1} ^{238}Pu	Activity Ratio ^{238}Pu/$^{239+240}$Pu, Bq Bq^{-1}
Larynx (right part)‡	31.30	31.7 ± 0.5	0.61 ± 0.04	0.019 ± 0.001
Larynx (left part)§	18.11	42.1 ± 0.3	0.78 ± 0.03	0.018 ± 0.001
Larynx (whole)		*35.5 ± 0.3*	*0.67 ± 0.03*	
Trachea (right part)‡	8.40	10.5 ± 0.3	0.20 ± 0.05	0.019 ± 0.005
Trachea (left part)§	7.52	7.4 ± 0.1	0.15 ± 0.02	0.020 ± 0.003
Trachea (whole)		*9.0 ± 0.2*	*0.17 ± 0.03*	
Lung (right)‡	641.90	23.9 ± 0.3	0.40 ± 0.02	0.017 ± 0.001
Lung (left, dissected)§				
Bronchus	7.78	11.1 ± 0.1	0.23 ± 0.02	0.021 ± 0.002
Other bronchial airways (*BB*)	69.54	27.3 ± 0.2	0.51 ± 0.02	0.019 ± 0.001
Bronchiolar airways (*bb*)	26.35	28.9 ± 0.2	0.54 ± 0.02	0.019 ± 0.001
Alveolar-interstitium (*AI*)	274.31	22.8 ± 0.2	0.45 ± 0.01	0.020 ± 0.001
Total left lung		*23.8 ± 0.1*	*0.46 ± 0.01*	
Thoracic lymph nodes (right)‡				
Tracheobronchial LN	0.65	36.5 ± 1.3	0.47 ± 0.30	0.013 ± 0.008
Mediastinal LN	0.87	28.0 ± 0.9	0.24 ± 0.33	0.009 ± 0.012
Pulmonary LN	0.65	29.4 ± 2.3	0.89 ± 0.73	0.030 ± 0.025
Total right LN_{TH}		*30.9 ± 0.9*	*0.50 ± 0.27*	
Thoracic lymph nodes (left)§				
Tracheobronchial LN	0.35	13.4 ± 0.8	0.22 ± 0.16	0.017 ± 0.012
Parabronchial LN	1.09	13.4 ± 0.4	0.19 ± 0.06	0.014 ± 0.005
Pulmonary LN	1.70	44.7 ± 0.7	0.87 ± 0.09	0.019 ± 0.002
Total left LN_{TH}		*30.4 ± 0.4*	*0.56 ± 0.06*	

† Total propagated uncertainty (1σ)
‡ Analyzed in 1996; James et al (2007)
§ Analyzed in 2013. Tolmachev et al (2014, in preparation)

Funding

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Uranium Distribution in Man: A Reprise

Ronald L. Kathren, *Professor Emeritus, Washington State University*

Sergei Y. Tolmachev, *Associate Research Professor, Washington State University*

In the Annual Report for October 1, 1995 to September 30, 1996, the USTUR published the first report of measured natural uranium concentrations in two whole-body donors(1). This initial preliminary report was essentially a tabulation of measured uranium concentrations in the several hundred samples of soft tissues and bones from USTUR Cases 0213 and 0242, Caucasian males aged 68 and 78 years respectively, who were whole body donors to the Registries. These cases had no known occupational or other than natural environmental exposure to uranium, and both were long-time residents of the same geographic area (Los Alamos, NM) and thus likely to be representative of elderly Caucasian males in that area and of equilibrium levels of environmental uranium. Case 0213 had a history of 20 pack-years of cigarette smoking and died from lung cancer at age 68; Case 0242 was a nonsmoker who died from coronary artery disease at age 78.

As reported previously, evaluation of the data was limited to a preliminary examination of uranium tissue concentrations and indicated, not unexpectedly, that the primary depot for uranium in the body was the skeleton and, somewhat unexpectedly, that uranium was widely distributed throughout the soft tissues as a whole. Soft tissue concentrations ranged over about an order of magnitude and averaged about 0.5 μg kg^{-1} with the exception of the thoracic lymph nodes, which showed concentrations more than an order of magnitude greater than most of other soft tissues. An unexpected observation not evaluated or discussed was that uranium concentrations in the thoracic lymph nodes of the case with a smoking history were significantly lower than those of the nonsmoking cohort. The latter case also showed a possible anomalously high concentration of uranium in the thyroid which also begs further analysis. Although there was considerable variation of uranium concentration among individual bones and bone samples, concentrations in bone averaged about 4 μg U kg^{-1} of wet weight.

Although the tissue uranium concentration data from these two cases were never published in the peer reviewed literature nor indeed fully evaluated in depth, nonetheless, they have been referenced in important publications relating to uranium toxicity and biokinetics, including the National Research Council study of risks of depleted uranium to military personnel(2) and the ATSDR toxicological profile for uranium(3), as well as topical publications in the peer reviewed literature, indicative of the utility of these data. Accordingly, the USTUR has undertaken to evaluate the results of the tissue analyses of uranium from the two cases with an eye towards publication in the peer reviewed literature. The laboratory analytical results have been reviewed and quality-assured, and the process of systematically evaluating and comparing the analytical results from these two cases is in progress. To provide some indication of the validity and applicability of the ICRP models and Reference Man data, comparison will also be made with the results from the already published evaluation of USTUR Case 1002, an elderly Caucasian male, whole-body donor with a documented history of uranium exposure and intake[4] , as well as ICRP Reference Man data and the relatively recent study of element content in adult Chinese males[5], as well as the more limited data from existent empirical postmortem tissue concentrations reported in the open peer reviewed literature.

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From a Single Bone to Total Skeleton

Sergei Y. Tolmachev, *Research Associate Professor, Washington State University*

Estimation of total skeletal actinide (Pu, Am, U, Th) activity is an important task to support biokinetic modeling and dose assessment.

Introduction

Typically, a limited number of bones is collected at autopsies, and the total skeletal actinide activity is calculated using several approaches with various degrees of precision. Availability of actinide radiochemistry data from skeleton analyses from whole-body donations provides a unique scientific opportunity to validate current algorithms or develop new ones. Recently, the USTUR was involved in the validation of an algorithm developed at the South Ural Biophysics Institute (SUBI) in Ozyorsk, Russia[1]

Using data from skeletal analyses of four (4) whole-body donations, the USTUR published a paper suggesting that the patella can be conveniently used to estimate total actinide skeletal activity[2]. The patella is one of a few bones analyzed as the entire sample (no subdivision for radiochemistry analysis) and can be easily collected at the autopsy from routine (partial) donations. Lynch *et al.* estimated that 0.66±0.09% (n=3) of total $^{23+240}$Pu skeletal activity (activity in right and left patella/total activity in skeleton) was deposited in patellae, assuming longitudinal (left/right) symmetry of the skeleton and identical Pu activity concentration expected in left and right patella.

Methods

Data on ^{238}Pu and $^{239+240}$Pu radiochemical skeleton analysis from fifteen (15) USTUR whole-body cases: 0193 (primary exposure to $^{239+240}$Pu), 0208 ($^{239+240}$Pu), 0212 ($^{239+240}$Pu), 0213 ($^{239+240}$Pu), 0259 (^{238}Pu), 0262 ($^{239+240}$Pu), 0269 ($^{239+240}$Pu), 0425 ($^{239+240}$Pu), 0635 ($^{239+240}$Pu), 0680 ($^{239+240}$Pu), 0682 (^{238}Pu), 0706 ($^{239+240}$Pu), 0720 ($^{239+240}$Pu), 0744 ($^{239+240}$Pu), and 0769 ($^{239+240}$Pu) were revised and the total skeletal Pu activities were calculated using a standardized approach. The plutonium deposition coefficient (K_{dep}) in a single (analyzed) patella for ^{238}Pu and ^{239,240}Pu was calculated for each of 15 cases as:

$$K_{dep} = \text{Activity in Patella/Activity in Total Skeleton}$$

Typically, only the right patella is analyzed at the USTUR. This approach eliminates uncertainties associated with left/right skeletal asymmetry (weight of the left patella is not necessary equal to that of the right). The assumption of Pu concentration equality in the left and right patella was used by Lynch *et al.*

Results

The average (± standard deviation) patella K_{dep} for ^{238}Pu ($^{238}K_{dep}$) and $^{239+240}$Pu ($^{239}K_{dep}$) isotopes was calculated to be 0.37±0.14% and 0.33±0.12%, respectively. A paired t-test revealed no significant statistical difference between $^{238}K_{dep}$ and $^{239}K_{dep}$ (n=15, p=0.3332). Individual $^{238}K_{dep}$ and $^{239}K_{dep}$ were combined (K_{dep}) and treated as a single data pool (n=30). The average patella K_{dep} for plutonium was calculated to be 0.35±0.13% with relative standard deviation (RSD) of 37.9%. With this simple approach, total plutonium skeletal activity can be estimated based just on patella analysis (single bone analysis) within 40% uncertainty.

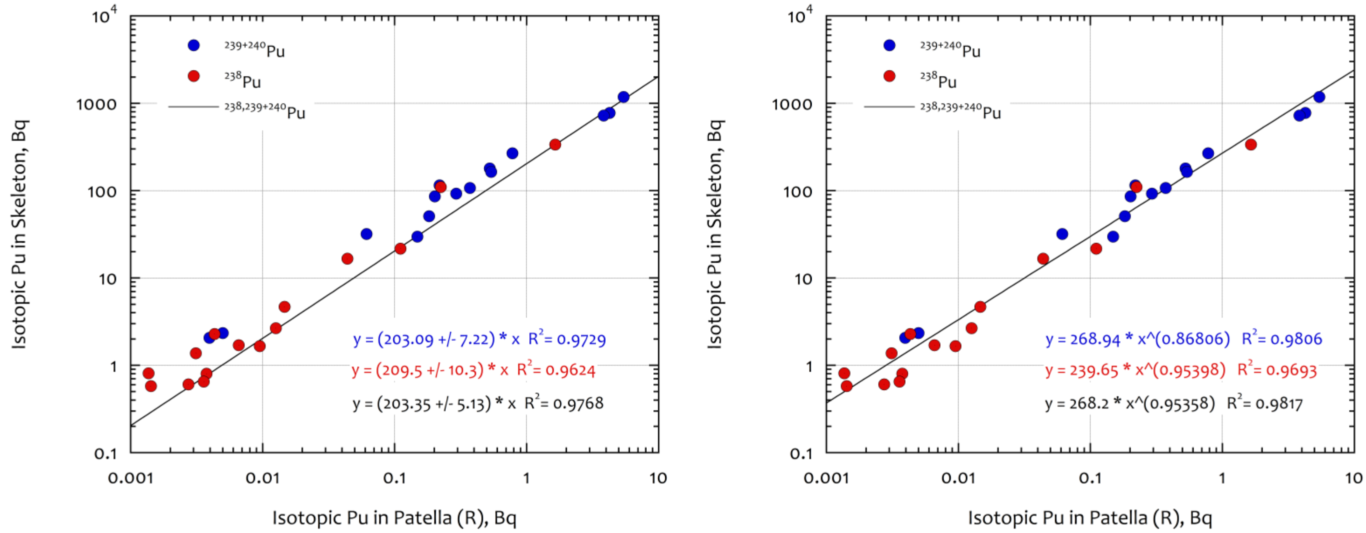

Fig. 9. Linear zero fit (left), and power fit (right) model regression for plutonium activity in skeleton vs patella.

Conclusions

Linear zero fit, $y=ax$, and power, $y=ax^b$, models were proposed to calculate total plutonium activity in the skeleton based on plutonium activity measured in a right patella bone (Fig. 9). By eye, the power model fits the data better compared to the linear zero one ($^{238,239+240}$Pu line). It should be noted that linear zero fit model is a particular case of power fit model (b = 1). Leave-one-out cross-validation (LOOCV) method will be used to compare the two models.

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1. Suslova KG, Orlova IA, Burikova EA., Sokolova AB, Salamatova VY, Tolmachev SY and Miller SC. MWDS 2013: Estimation of plutonium skeletal content from limited autopsy bone samples from Mayak PA workers. *Radiat Prot Dosim.* In Preparation; 2014.

2. Lynch TP, Kathren RL and McInroy JF. Macrodistribution of plutonium and americium in four human skeletons. *J Radiol Prot.* 8: 67-76; 1988.

2012 Advisory Committee Meeting Report

Stacey L. McComish, *Associate in Research*

Sergei Tolmachev, *Director*

The 2012 Annual Scientific Advisory Committee (SAC) meeting was held September 7-8 at Anthony's at Columbia Point, Richland, WA.

2012 Meeting Attendees

Advisory Committee

William Hayes, *Chair/Radiochemistry*
Robert Bistline, *Occupational Health*
Herman Gibb, *Epidemiology*
Kathryn Meier, *University/Ethics*
Richard Toohey, *Health Physics*
Timothy Ledbetter, *Ethics, Incoming Member*

Department of Energy

Joey Zhou, *Program Manager*

USTUR Staff

Sergei Tolmachev, *Director*
Stacey McComish, *Associate in Research*
Maia Avtandilashvili, *Research Associate*
Fredrick Miller, *Laboratory Technician III*
Elizabeth Thomas, *Laboratory Technician I*
Margo Bedell-Parker, *Fiscal Technician*
Julie Blumenkranz, *Administrative Assistant*
Florencio Martinez, *Prosector*

WSU College of Pharmacy

Gary Meadows, *Associate Dean*

Invited Guests

William Bair, *PNNL Retired*
Antone Brooks, *WSU/PNNL Low Dose Program*
Darrell Fisher, *PNNL*
Ronald Kathren, *WSU Professor Emeritus*
William Morgan, *PNNL Low Dose Program*
Christopher Nielsen, *PNNL/WSU PhD Student*
Paul Stansbury, *WSU/Dade Moeller*
Dan Strom, *Battelle*
Next-of-Kin, *Family Representative*

Unable to Attend

Roger McClellan, *SAC, Toxicology*

Presentations

2011 SAC Recommendations & 2012 USTUR Overview - Tolmachev, S.Y.

The SAC's recommendations from the 2011 meeting, and the way the USTUR addressed each recommendation, were presented. Additional 2012 activities were also summarized. These included topics such as: the new FY2013-17 grant cycle, a visit from a Russian scientist from the Southern Urals Biophysics Institute (SUBI), and recent publications.

Administrative & Financial Developments - Parker, M.

The FY2012 expenditures, FY2013-17 budget, and the new 5-year grant cycle were explained. The cost of facilities leases, personnel changes, and the number of full-time equivalent (FTE) personnel that are supported by the current $900,000 grant were also discussed.

USTUR Statistics & Registrant Correspondence - McComish, S.L.

Changes in the number of deceased, living, and inactive Registrants were summarized. The reason for these status changes and/or a brief summary of each individual's exposure were provided.

Health Physics Database: Standardization of Exposure Records and Bioassay Data - Avtandilashvili, M.V.

The health physics data entry forms were described. Progress toward entering Registrant exposure records into the USTUR's health physics database was summarized by intake type, contaminant, and solubility class.

National Human Radiobiological Tissue Repository - McComish, S.L.

During the past year, 2,595 samples have been logged into THEMIS. These were summarized by sample type. Progress toward logging in frozen tissue samples, and the procedures for re-packaging acid solutions were described in greater detail.

2012 Radiochemistry Progress Report - Miller, F.

Operation of the radiochemistry laboratory was described. Topics included building maintenance and modification, laboratory equipment, method development, and sample processing and analysis.

USTUR/PNNL Collaboration - Morgan, W.

Chris Nielsen's master's thesis and anticipated PhD research on the microdistribution of plutonium nitrate in the lungs of beagle dogs and former workers were summarized. The value of the USTUR was emphasized, as was the usefulness of data and materials from historic beagle dog studies.

Progress toward a Graduate Certificate Program in Radiation Protection - Stansbury, P.

A graduate certificate program in radiation protection is being developed at WSU Tri-Cities. The timeline, core competencies, and coursework associated with this program were summarized.

USTUR Donor Family Perspectives - Next-of-Kin

The son of one of our Registrant donors summarized his father's work history, exposure, and health concerns. He also provided feedback from a family perspective on what the USTUR is doing well and where the USTUR has room for improvement. An extremely valuable discussion on how the USTUR can better communicate with Registrants and their next of kin followed.

Research & Operation Plan for FY 2013 - Tolmachev, S.

The 2013 goals for radiochemical analyses, entry of exposure data into the health physics database, development of a radiochemistry database, NHRTR tissue and acid solution inventory, and scientific collaborations were presented.

Research & Operation Plan for FY2014 - Tolmachev, S.Y.

The FY2014 budget, and goals for radiochemical analyses, entry of exposure data into the health physics database, NHRTR tissue and acid solution inventory, and scientific collaborations were presented.

A PMR and PCMR Analysis of Radiation and Mesothelioma in the United States Transuranium and Uranium Registries - Gibb, H.

The background, methods, and results of a collaborative study carried out by the USTUR and Tetra Tech Sciences were presented. This study was conducted to investigate the unusually high incidence of mesothelioma among USTUR Registrants, and had been accepted for publication in the American Journal of Public Health.

2012 Recommendations and Comments

Following discussions involving only the SAC members, several recommendations and comments were proposed.

Recommendations

1. Improve communication with Registrants and their families.
2. Improve the recruitment of new donors.
3. Modify the prioritization plan for radiochemical analyses such that older tissue samples are of a higher priority.
4. Provide radioanalytical progress reports that show the backlog, types of samples, and percentage of progress toward eliminating the backlog.
5. Promote and report on USTUR data users: external users
6. Establish Data Quality Objective (DQO) requirements. Specifically, address quality assurance requirements, required records, data maintenance and archiving, and "raw data" availability (data sources provided).
7. Continue to develop research collaboration.
8. Expand academic involvement with College of Pharmacy Dean and WSU. Incorporate graduate students and continue involvement with the Certificate Program in Radiation Protection.
9. Encourage progress toward understanding of the ownership of USTUR samples.

General Comments

1. Excellent progress on the Radiochemistry and Health Physics databases.
2. Excellent collaboration with PNNL and others.
3. High productivity was achieved on constrained funding.
4. The USTUR staff are self-motivated, qualified, and capable.
5. Continue developing mechanisms for being a resource for other research.
6. 2012 SAC Annual Meeting was very useful, and better than teleconferences.

SAC Membership

William Hayes' second 3-year term on the advisory committee was due to expire on September 30, 2012. He chose to continue his service on the SAC for another three-year term; however, he stepped down as the Chair. Dr. Richard Toohey was chosen to be the new SAC Chair.

2013 Advisory Committee Meeting Report

Richard E. Toohey, *Chair, Scientific Advisory Committee*

The 2013 Annual Scientific Advisory Committee (SAC) meeting was held September 6-7 at the Courtyard Marriott Hotel in Richland, WA.

The USTUR SAC met in Richland to review the progress of the Registries' programs and recommend some possible directions for the Registries to pursue. There are basically three considerations to keep in sight: first, the human aspects of the Registries, namely continuing contact and information exchange with Registrants and their families; second, the scientific contributions of the Registries; and third, the future prospects for the Registries. New SAC member Rev. Tim Ledbetter of the Tri-Cities Chaplaincy, who is a recent member of the DOE Central Institutional Review Board (IRB) that oversees research involving human subjects, brings an important perspective on the human aspects to the SAC.

Dr. Danny Talbot, the Chief of Staff at WSU-Tri-Cities noted that the Registries are an important component of the main emphasis of WSU-TC, namely science, technology, engineering and math (STEM) education, with emphasis on engineering. The goal is to build a program to attract students and meet the needs of the local scientific community. WSU-TC will be supporting the health sciences campus at Spokane with programs in pre-medical and biological sciences, which offer more collaborative opportunities for the Registries. SAC member Dr. Kay Meier has a new position as Associate Dean for Graduate Education in the College of Pharmacy, which has consolidated in Spokane. Dr. Andrea Lazarus, Assistant Vice President for Research in the College of Pharmacy, further described the Spokane initiative, where the College of Nursing and programs in medical sciences, health policy and administration, and criminal justice are now located. The Registries offer an opportunity for research and training for both undergraduate and graduate students in the biokinetic behavior of radionuclides, closely related to both biological and pharmacological sciences. Dr. Joey Zhou, the DOE program manager for the Registries, stated that although these are difficult budget times, USTUR was not targeted for a reduction in funding. In addition, another long-standing issue has now been resolved, in that DOE has decided to accept ownership of the Registries' tissue samples, relieving WSU of fiscal responsibility for the eventual disposal of these materials.

USTUR Director Dr. Sergei Tolmachev then described the overall progress of the Registries during the last year. Some concerns had been raised by family representatives that communications from the Registries were overly technical, to the point of being difficult to understand. Consequently, the 2013 newsletter was less technical and written in a simpler language; it featured an article by a SAC family representative, whose late father worked at Rocky Flats and was a USTUR donor. The newsletter was sent to 70 Registrants and 112 families. SAC member Tim Ledbetter will assist Registries staff in developing more family-friendly communications. Similarly, the results letter will be simpler, and the radioactivity levels of a donor's tissues will be compared to the average levels of all Registrants. In fact, 3% of Registrants have tissue contents that are at background levels of ^{239}Pu, indicating little or no workplace exposure. Recruitment of new Registrants is largely passive, relying on direct contacts, DOE contractors, and the work sites, plus through the Homesteader's newsletter, distributed to Rocky Flats retirees. Active recruitment would need permission from the IRB, DOE agreement, and extra funding. However, it is not clear how useful recruits from the current workforce would be, because typically their intakes are lower than intakes that occurred during the height of the Cold War. Some accident cases involving contaminated wounds would be valuable to test the new wound model developed by the National Council on Radiation Protection and Measurements.

Reduction in the backlog of samples to be analyzed is still a priority: the Registries need to focus on whole-body donors and older cases to ensure that a ratio of analyses of old (1992-2005) to new (2006 and later) cases remains at 1 to 3. Data quality objectives have been established and a quality implementation plan is in place and underway as resources allow. Mr. Fred Miller is an experienced International Standards Organization auditor and trained in advanced quality management methods.

Research use of USTUR data continues around the world, including the South Urals Research Institute in Russia and the EURADOS consortium of the European Union. There are 8 active international research collaboration programs currently in place. Academic involvement with WSU continues: College of Nursing students participate in clinical research and the autopsy program for whole-body donors. The WSU-TC graduate certificate program in Health Physics is scheduled to begin in the fall of 2013, and has acquired four alpha spectroscopy units. Chris Nielsen, a graduate student working on the retention of soluble plutonium in the respiratory tract for his Ph.D. in Earth & Environmental Sciences took a full-time job, and will complete his degree in the future. A €16,000 (approx. $21,000) grant from the U.K. Health Protection Authority (now Public Health England) has been completed, and year two of the DOE grant to WSU to operate the Registries is funded at $900,000.

There were six new Registrant donations this year, including one whole-body donor. Radiochemical analyses were performed on 132 soft tissue and 187 skeletal samples from 8 whole-body and 2 partial-body donors. All samples from a partial-body donor are analyzed, but samples from a whole-body donor are selected for analysis to provide adequate data for family information. A typical whole-body donation is comprised of 150 samples. Of a total of 297 partial-body donors, 256 are completed, and of 40 whole-body donors, 22 are completed. Whole-body donor case 1031 is of particular scientific interest: this worker was exposed to low-enriched (0.85%) uranium hexafluoride (UF_6), and there were higher-than-expected concentrations of uranium in brain tissue; this crossing of the blood-brain barrier by uranium may be due to the inhalation of nanoparticles, and may shed some light on excess brain cancers noted in Oak Ridge uranium workers.

Margo Bedell-Parker then discussed the Registries' budget situation. There was a deficit of $22,000 carried over to FY2014 (April 1 to March 31). New Budget Planner software has been acquired, and the Year 2 operating budget is $883,000. The quarterly funding from DOE is $225,000, and for the first 6 months, the Registries are $7,000 under budget. Facilities and administrative charges are $164,000 per year, with an increase for office rent, but none for lab space. The grant supports 6.5 full-time equivalent (FTE) personnel. The A.C. James Scholarship fund will provide assistance to a WSU student who is pursuing a degree in the natural sciences and technology.

Stacey McComish presented the Registrant statistics: there are 62 live and 325 deceased male, and 2 live and 12 deceased female Registrants. The average age of living Registrants is 82 and the average age of Registrants at death is 69. Two Registrants were changed to inactive status; new forms are sent every 5 years, and Registrants who do not respond to the renewal paperwork are placed in inactive status. In FY2013, 15 Registrants renewed, and 27 renewals are going out in December. There are also 7 special studies of individuals who are not full USTUR Registrants, but have provided exposure data, e.g., urinalysis results, or a biopsy sample. Dr. Maia Avtandilashvili then discussed progress on the health physics (HP) database: data from only 5 whole-body donors remain to be entered, but data from 300 partial-body donors still need to be entered.

Stacey McComish presented an update on the National Human Radiobiology Tissue Repository (NHRTR): 11,900 samples have been entered in the THEMIS database, of which 74% are tissues, 19% acid solutions, and 7% were non-USTUR samples; the latter include radium worker samples from Argonne, reagents, blanks, QC samples, and the Los Alamos population samples collected by Dr. Jim McInroy.

Fred Miller discussed laboratory operations: a change from 2 mL to 1 mL TEVA-TRU-DGA ion-exchange resin cartridges provided significant cost savings while still meeting QA requirements.

Chris Nielsen discussed his thesis research on lung retention of soluble plutonium: case 269 was a chemical operator with an inhalation of 58 kBq of plutonium nitrate, of which 1.3% remained in the lung, contrary to expectations. Parameters for the so-called “bound compartment” of the human respiratory tract model (HRTM) had not previously been established, but this case indicates that it contained 0.4% of the intake; this doubles the estimated lung dose.

Tristan Hay presented data on the Joint Collaborating Center for Radiation Effects Research effort on dosimetry for workers at the MAYAK Production Association in the former Soviet Union. There are 26,000 workers under study, and they are now looking further at the bound fraction in the lung; two more USTUR cases are available for analysis and the work is supported by $50,000 from DOE. This effort demonstrates the importance of the USTUR archived tissue collection, and this analysis is vital for proper epidemiological risk assessment.

Dr. Paul Stansbury discussed the WSU-TC graduate certificate in health physics; he has been assured FY2013 funding ($100,000) is coming. This program is supported by the DOE joint workforce restructuring effort. Courses will start in the fall of 2014, but the program still needs approval from the WSU faculty Senate. Instruments include a 20% HPGe gamma spectrometer, Ludlum hand-held detectors, a laser power meter, 3 laptops, 1 desktop, 2 oscilloscopes, and tools. The program will use the alpha spectrometry lab located at USTUR for 1-2 weeks per year, and the lab will be available otherwise for USTUR use. The text is “Radiation and Modern Life” by Alan Waltar, and will be supplemented with student research and presentations. The certificate requires 12 credit hours, and the program hopes to use WSU distance learning features.

Dr. Avtandilashvili then presented more data on the UF_6 case: USTUR case 1031 is one of the cases described in Kathren & Moore 1986 ("Acute Accidental Inhalation of U: a 38-Year Follow-up" Health Phys. 51: 609-619.) The Registrant received a single acute inhalation of UF_6 during an explosion. Urine samples on days 2-18 ranged up to 0.51 mg d^{-1}, indicating about 1 mg U g^{-1} kidney, or 330 times the no adverse effects level. Post mortem analysis by ICP-MS of 33 tissue samples showed enriched U in the lungs, so the material was not inhalation Type F as UF_6 is assumed to be. There was 20 times the activity in lymph nodes as in lung tissue, suggesting that the material behaved as an insoluble particulate. The best estimate is that the intake of 80 mg U comprised 87% Type F and 13% Type S material, possibly a uranium oxide. This case had a kidney retention level 100 times that of the standard model. A significant difference in the transfer rates between plasma and kidney is needed to explain this measurement. These data will be re-analyzed with a revision of the HRTM bound compartment and Bayesian methods. This case demonstrates the importance of long-term follow-up of exposed persons for biokinetic modeling. The results will be compared to the plutonium nitrate inhalation case.

Dr. Tolmachev then described the research and operations plan for FY2014. The goals are to analyze 400 samples, with a whole-body to partial-body case and old to new donations each at a ratio of 1:3. Efforts will continue on DQO, QA/QC planning and implementation. Data entry will continue, and quantitative goals for record entry in the HP database and THEMIS may be set. The emphasis for data entry will be on new donations, complete whole-body, and expedited partial-body cases. The Registries will estimate their total radioactive materials holdings, and WSU will seek to modify grant language to include ownership description of the samples.

A question arose if funds would be more valuable for recruiting new Registrants than for reinstating inactive Registrants, especially those who were dropped in the 1990's. Dr. Bistline stated he has lists of Rocky Flats Registrants and can use the Homesteader newsletter for contact information.

Stacey McComish raised a question if samples should be accepted from the next-of-kin of deceased workers who are not current, but may be former Registrants, but for whom there are typically no exposure data. Inactive status records were not transferred to WSU in 1992. The SAC felt that if there is evidence of previous registration (e.g., a wallet card), the Registries should accept the samples regardless of intake/dose criteria. However, sample input soon will exceed analytical capacity, if it has not already. Consequently the Registries should look at possible sources of capital funding to expand laboratory capacity.

Dr. Joey Zhou then discussed the research on mesothelioma in the Registries' population. Because the population is self-selected and relatively small in size, it has limitations for epidemiologic research. Dr. Zhou pointed out that the research did not consider the disease coding change for mesothelioma over the timeframe of the study, resulting in overestimation of proportionate mortality ratios [reducing the PMR from 62.4 to 11.7]. However, it is apparent that death from mesothelioma is elevated.

The SAC then met in Executive Session to discuss the presentations and formulate recommendations for the Registries' staff and subsequently returned to open session to provide comments to the staff.

All of the staff presentations were very well done and informative, and the Registries have made good progress over the past year in completing analyses, populating the databases, and have been responsive to the SAC's recommendations. Analyses have been prioritized and the staff are of uniformly high quality and productivity. There has been significant improvement in the newsletter and other communications with Registrants, demonstrating improved sensitivity to the donors and their families. Research collaborations with other programs continue to be very fruitful. The findings on the long-term retention of uranium and plutonium in the lung if inhaled as acidic compounds is very important for improving the respiratory tract model used in radiation protection. Data on the retention of radionuclides in the lymph nodes may also be very important to help explain the incidence of lymphomas in uranium miners. Although the Registries are not epidemiological studies in themselves, they can definitely provide information on what effects to look for in radiation epidemiology and radiobiology research. The Registries' scientific output is extremely impressive for the funds available.

The SAC made the following recommendations:

1. Continue further prioritization of sample analyses, and set goals for the number of analyses (> 400) to be performed annually. In addition, improve the secure storage of samples.

2. Continue data entry efforts, establish annual goals for data entry, and commit to completing data entry by the end of the current 5-year grant period.

3. Complete DQO documentation and implementation.

4. Search for and retrieve available records to reconstitute the Registrant list as fully as possible.

5. Investigate new avenues for former worker communication and recruitment.

6. Consider the feasibility of obtaining Registrants' work histories.

7. Continue, and if possible, expand academic involvement with WSU COP and the Health Sciences campus in Spokane, as well as the science and engineering undergraduate programs at WSU-TC and the graduate certificate program in radiation protection.

8. Improve DOE HSS awareness of the USTUR through presentations at EFCOG meetings and interactions with site medical directors for donor recruitment. The Registries can also serve as a resource for scientific data on other hazardous exposures, such as asbestos and beryllium.

9. Demonstrate the importance of USTUR by publicizing the number of publications and their importance.

10. Continue scientific presentations at national and international meetings as funding permits.

11. Continue outreach efforts to Registrants, and investigate efforts to locate and re-enroll inactive Registrants.

12. Continue international collaborations such as with EURADOS and the Mayak project.

13. Encourage staff to mine the data, think outside the box, push the boundaries, and consider the implications of Registries data for radiation protection and radiobiology.

R. E. Toohey

Richard E. Toohey, Ph.D., CHP
SAC Chair

Professional Activities/Services

During FY2013 – FY2014, the USTUR staff was actively involved in professional and academic activities nationally and internationally.

Academic Activities

WSU Graduate Certificate Program in Radiation Protection

The USTUR's Director, Dr. Sergei Y. Tolmachev continued to serve on the advisory committee for the WSU Graduate Certificate Program in Radiation Protection at the Tri-City (TC) Campus. This two-year course of study will educate students on key topics in radiation protection, preparing them to be technicians in health physics and related fields. A layout of teaching courses and practical laboratories for the Environmental and Internal Dosimetry class, developed by Dr. Tolmachev, was accepted by WSU/TC.

Graduate Student Visit

Dr. Maia Avtandilashvili was contacted by Ms. Veronica Ruiz, an MS student at the Physics Department of WSU. Ms. Ruiz expressed her interest in conducting graduate research to pursue a PhD degree in Health Physics. She is a Fulbright scholar from El Salvador.

In 2013, Ms. Ruiz visited the USTUR office and discussed the research opportunities for her PhD study with Dr. Avtandilashvili, Ms. McComish, and Dr. Tolmachev. She was given a tour to the USTUR facilities and provided with information on the on-going research projects conducted by the USTUR team.

Adjunct Professor Appointment

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

International Committees and Meetings

Expert Group on Fukushima Dose Reconstruction

Dr. Sergei Y. Tolmachev was invited by National Institute of Radiological Sciences (NIRS, Japan) to attend a second expert-group meeting on reconstruction of early internal dose after TEPCO Fukushima Daiichii Nuclear Power Plant accident. Due to his busy schedule, Dr. Tolmachev was not able to accept the invitation. The meeting was organized and sponsored by NIRS, and held on January 27, 2013 in Tokyo.

IRPA Societies Admission and Development Committee

Dr. Sergei Y. Tolmachev became a member of the International Radiation Protection Association Societies Admission and Development Committee (IRPA SADC). The Committee has nine volunteer members from six countries and is chaired by Dr. Roger Coates (Society for Radiological Protection, UK).

Editorial and Ad-hoc Review Services

Japanese Journal of Health Physics

Dr. Sergei Y. Tolmachev has been appointed to serve a 3rd term as a member of the Editorial Board for the Japanese Journal of Health Physics (JJHP) from August 2013 to July 2015.

International Journal of Radiation Biology

Dr. Maia Avtandilashvili was invited to provide scientific expertise as an *ad-hoc* reviewer to the International Journal of Radiation Biology. One paper was reviewed by Dr. Avtandilashvili.

Journal of Radioanalytical Nuclear Chemistry

Dr. Sergei Y. Tolmachev was invited to provide scientific expertise as an *ad-hoc* reviewer to the Journal of Radioanalytical Nuclear Chemistry. One paper was reviewed by Dr. Tolmachev.

Professional Affiliations

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

- Health Physics Society (USA)
- Japan Health Physics Society (Japan)
- Society of Nuclear and Radiochemical Sciences (Japan)
- European Radiation Dosimetry Group (EURADOS), Working Group 7 (WG7) on Internal Dosimetry (EU).

Publications/Presentations

The following manuscripts and presentations were published or presented during the period of April 2012 to March 2014. The names of USTUR faculty are underlined. Previous manuscripts and abstracts are available on the USTUR website at:

www.ustur.wsu.edu/Publications/index.html

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

Published

USTUR-0317-11

Avtandilashvili M, Brey R, James AC. Maximum Likelihood Analysis of Bioassay Data from Long-term Follow-up of Two Refractory PuO_2 Inhalation Cases. *Health Phys*. 103 (1): 70-79; 2012.

USTUR-0317-11A

Avtandilashvili M, Brey R, James AC. Maximum Likelihood Analysis of Bioassay Data from Long-term Follow-up of Two Refractory PuO_2 Inhalation Cases. (Abstract) *Health Phys*. 103 (2): S80-S81; 2012.

USTUR-0324-12A

Breustedt B, McCord S, Tolmachev S. Biokinetic Modeling of Chelation Therapy for ^{241}Am – USTUR Case 0846. (Abstract) *Health Phys*. 103 (2): S80; 2012.

USTUR-0328-12

Weber S, Brey RR, James AC. Reevaluation of USTUR Plutonium Wound Case 0262 Using Bayesian Methodology and New Data. *Health Phys*. 103 (3): 286-300; 2012.

USTUR-0336-12

Nielsen CE, Wilson DA, Brooks AL, McCord SL, Dagle GE, James AC, Tolmachev SY, Thrall BD, Morgan WF. Microdistribution and long-term retention of $^{239}Pu(NO_3)_4$ in the respiratory tracts of an acutely exposed plutonium worker and experimental beagle dogs. *Cancer Research*. 72: 5529-5536; 2012.

USTUR-0325-12

Larivière D, Tolmachev S, Kochermin V, Johnson S. Uranium Bone Content as an Indicator of Chronic Environmental Exposure from Drinking Water. *J Environ Radioact*.. 121: 98-103; 2013.

USTUR-0323-12

Avtandilashvili M, Brey R, Birchall A. Application of Bayesian Inference to the Bioassay Data from Long-term Follow-up of Two Refractory PuO_2 Inhalation Cases. *Health Phys*. 104 (4): 394-404; 2013.

USTUR-0326-12

Gibb H, Fulcher K, Nagarajan S, McCord S, Hoffman H, Fallahian NA, Tolmachev S. A PMR and PCMR Analysis of Radiation and Mesothelioma in the United States Transuranium and Uranium Registries. *Am J Public Health.* 103: 710-716; 2013.

USTUR-0344-12

Parker M, Tolmachev SY. United States Transuranium and Uranium Registries Annual Report: October 1, 2010 – March 31, 2012. United

States Transuranium and Uranium Registries; USTUR-0344-12, Richland, WA 2013.

USTUR-0346-13

McComish SL, Tolmachev SY. United States Transuranium and Uranium Registries 2013 Newsletter, Issue 19. College of Pharmacy, Washington State University, Richland, WA. Mailed June 2013.

USTUR-0353-13

Gibb H, Fulcher K, Nagarajan S, McCord S, Hoffman H, Fallahian NA, Tolmachev S. Respond to "Incorrect Analyses of Radiation and Mesothelioma." *Am J Public Health. 104(2): e1-e2; 2014.*

USTUR-0354-13

Zhou J. Incorrect analyses of Radiation and Mesothelioma. *A J Public Health. 104(2): e1; 2014.*

USTUR-0351-13

Nielsen CE, Wang X, Robinson R, Brooks AL, Lovaglio J, Patton K, McComish SL, Tolmachev SY, Morgan WF. Carcinogenic and Inflammatory Effects of Plutonium-Nitrate Retention in an Exposed Nuclear Worker and Beagle Dogs. *Int J Radiat Biol.* 90: 60-70; 2014.

Presented

May 2012

USTUR-0332-12A

Lopez MA, Breustedt B, Balashazy I, Blanchardon E, Berard P, Bravo B, Broggio D, Castellani CM, Cruz-Suárez R, Davesne E, Doerfel H, Etherington G, Fojtik P, Franck D, Fritsch P, Giussani A, Gregoratto D, Guilmette R, Hofmann W, Huikari J, Hurtgen C, Kramer GH, Li C, Li WB, Malatova I, Marsh JW, Marzocch O, McCord S, Molokanov A, Nogueira P, Nosske D, Puncher M, Oeh U, Ruhm W, Saizu M, Peixoto-Teles P, Tolmachev SY, Vrba T. EURADOS Network on Internal Dosimetry. Poster presentation at the 13th International Congress of the International Radiation Protection Association (IRPA), Glasgow, Scotland, UK, May 13-18, 2012.

July 2012

USTUR-0324-12A

Breustedt B, McCord S, Tolmachev S. Biokinetic Modeling of Chelation Therapy for 241Am – USTUR Case 0846. Podium presentation at the 57th Annual Meeting of the Health Physics Society, Sacramento, CA, July 21-26, 2012.

USTUR-0317-11A

Avtandilashvili M, Brey R, James AC. Maximum Likelihood Analysis of Bioassay Data from Long-term Follow-up of Two Refractory PuO_2 Inhalation Cases. Podium presentation at the 57th Annual Meeting of the Health Physics Society, Sacramento, CA, July 21-26, 2012.

USTUR-0335-12A

Khalaf M, Brey R, Tolmachev S. A New Leg Voxel Model in Two Different Positions for Simulation of the Non-Uniform Distribution of ^{241}Am in Leg Bones. Poster presentation at the 57th Annual Meeting of the Health Physics Society, Sacramento, CA, July 21-26, 2012.

August 2012

USTUR-0337-1A

McComish SL, Avtandilashvili M, Tolmachev SY. The United States Transuranium and Uranium Registries (USTUR). Poster presentation at the WSU College of Pharmacy Research and Scholarship Day, Spokane, August 14, 2012.

USTUR-0338-1A

Avtandilashvili M, McComish SL, Tolmachev SY, James AC. Maximum Likelihood Analysis of Refractory PuO_2 Inhalation Cases. Poster presentation at the WSU College of Pharmacy Research and Scholarship Day, Spokane, August 14, 2012.

October 2012

USTUR-0331-12A

McCord SL, Nielsen CE, Avtandilashvili M, Parker M, Miller FL, Thomas EM, McLain DJ, Morgan W F, Tolmachev SY. The U.S. Transuranium and Uranium Registries: a Unique Human Data Resource. Poster presentation at the 58th Annual Meeting of the Radiation Research Society, San Juan, Puerto Rico, September 30 – October 3, 2012.

USTUR-0333-12A

Nielsen CE, Wilson DA, McCord SL, Brooks AL, Dagle GE, James AC, Tolmachev SY, Morgan WF. An Analysis of the Microdistribution and Long-Term Retention of $^{239}Pu(NO_3)_4$ in the Respiratory Tracts of an Exposed Plutonium Worker and Experimental Beagles. Poster presentation at the 58th Annual Meeting of the Radiation Research Society, San Juan, Puerto Rico, September 30 – October 3, 2012.

USTUR-0343-12A

Tolmachev SY, Nielsen CE, McComish SL, Avtandilashvili M. The U.S. Transuranium and Uranium Registries: Research Update. Podium presentation at the European Dosimetry Group (EURADOS) Working Group 7 on Internal Dosimetry, Budapest, Hungary, October 1-3, 2012.

USTUR-0340-12A

Tolmachev SY, McComish SL, Larivière D. Beryllium in a Human Body: USTUR 0706 Case Study. Podium Presentation at the 4th International Symposium on Beryllium Particulates and Their Detection, Denver, CO, October 1-4, 2012.

USTUR-0327-12P

Gibb H, Fulcher K, Nagarajan S, McCord S, Hoffman H, Fallahian NA, Tolmachev S. A PMR and PCMR Analysis of Radiation and Mesothelioma in the United States Transuranium and Uranium Registries. Poster Presentation at the American Public Health Association (APHA) 140th Annual Meeting, San Francisco, CA, October 27 - 31, 2012.

USTUR-0339-12A

Miller FL, Thomas EM, Tolmachev SY. Application of Microwave-Assisted Techniques for Human Tissue Samples Preparation for Actinide Analysis. Podium Presentation at the 58th Annual Radiobioassay and Radiochemical Measurements Conference (RRMC), Fort Collins, CO, October 28 – November 2, 2012.

March 2013

USTUR -0355-13P

Gibb H, Fulcher K, Nagarajan S, McCord S, Hoffman H, Fallahian NA, Tolmachev S. A PMR and PCMR Analysis of Radiation and Mesothelioma in the United States Transuranium and Uranium Registries. Podium Presentation at the 2013 Department of Energy (DOE) Occupational Medicine Workshop and Webinar, March 18-19, 2013.

October 2013

USTUR -0352-13P

McComish SL, Tolmachev S.Y. Biodosimetry of Plutonium Workers. Podium Presentation at the European Radiation Dosimetry Group (EURADOS) Working Group 7 on Internal Dosimetry, Bologna, Italy, October 1-3, 2013.

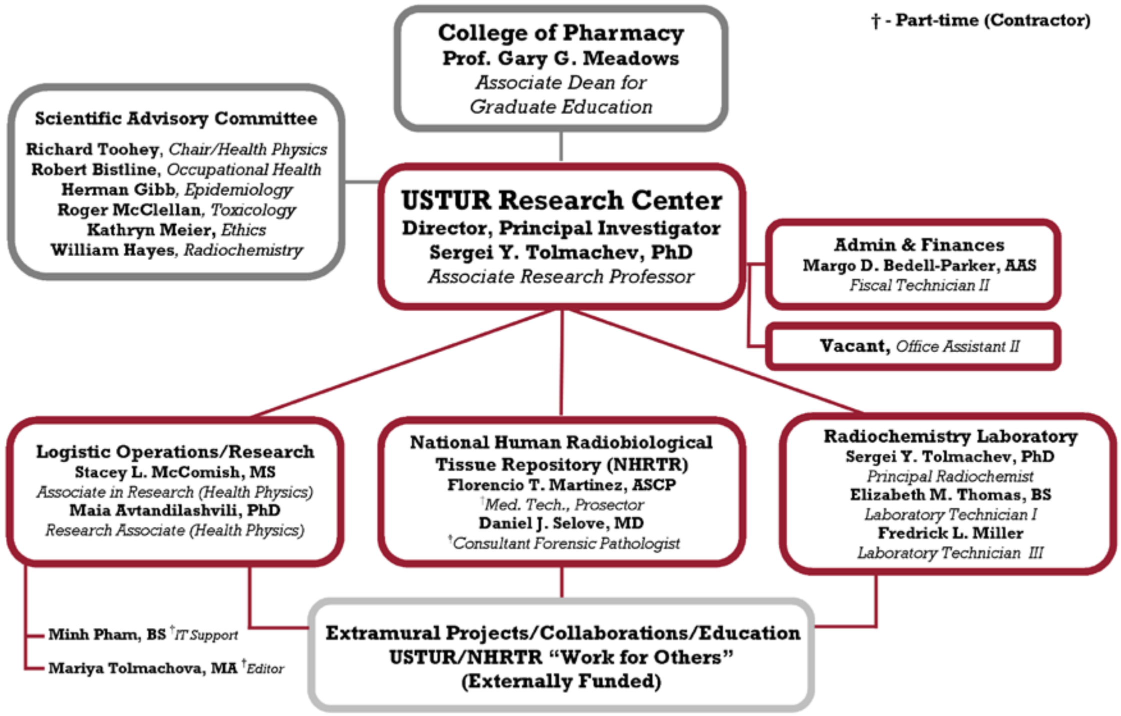
USTUR-0347-13A

Avtandilashvili M, McComish SL, Tolmachev SY. USTUR Case Study on Accidental Exposure to Uranium Hexafluoride. Podium presentation at the 11th International Conference on the Health Effects of Incorporated Radionuclides, Berkeley, CA, October 13-17, 2013.

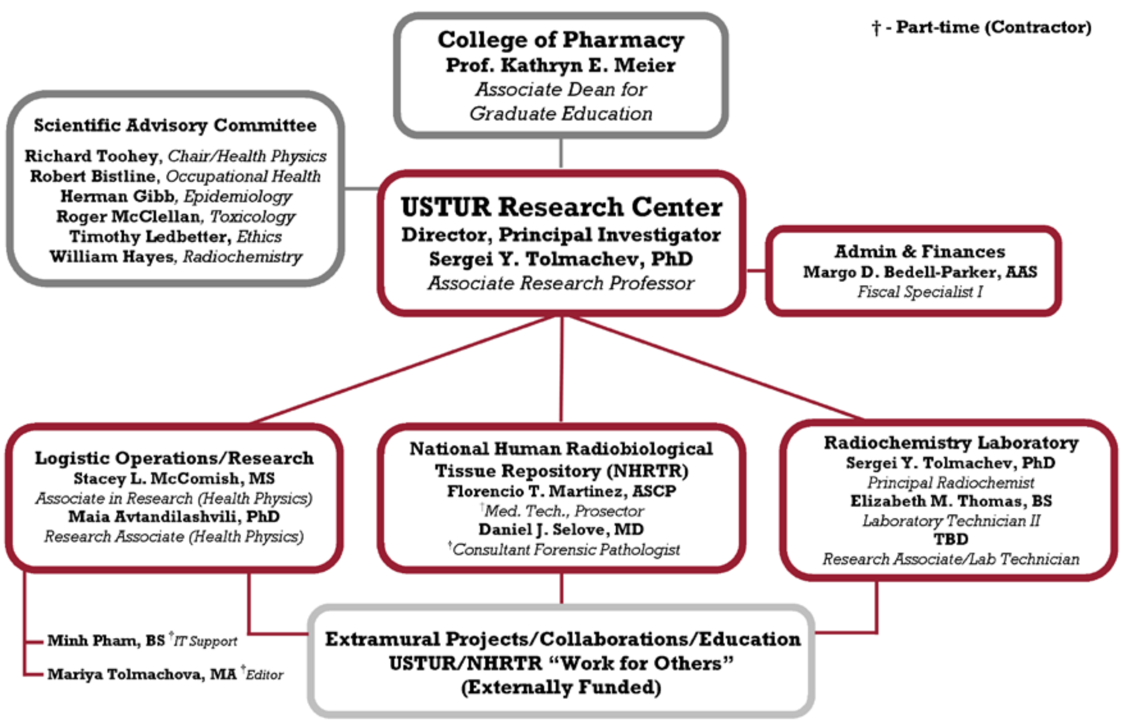
USTUR-0348-13A

Avtandilashvili M, McComish SL, Tolmachev SY. Uncertainty Analysis on Lung Doses for U.S. Nuclear Workers. Poster presentation at the 11th International Conference on the Health Effects of Incorporated Radionuclides, Berkeley, CA, October 13-17, 2013.

Appendix A



USTUR Research Center organization structure as of March 31, 2013.



USTUR Research Center organization structure as of March 31, 2014.

Appendix B

June 2013 USTUR-0346-13, Issue 19

USTUR Newsletter

Direct from the Director

It is my pleasure to have this opportunity to keep in touch with you and provide you with our recent updates.

Previously, our readers used to receive this newsletter around the Christmas/New Year holidays; now, it is almost summer. This is because the beginning of our fiscal year was changed from October to April. Thus the holiday season has become very busy with preparing new grant proposals. As such, you can expect to receive future Registrant newsletters during late spring or early summer. As a side note, our grant proposal was successfully submitted to the DOE. For the current 5-year grant period, we were awarded 4.5 million, which is lower than the 6 million we requested. We wish our request had been granted; however, given our hard financial times, receiving this substantial amount is advantageous and we will do everything in our power to spend the allocated funds with the utmost benefit for the Registries.

Now I would like to proceed to scientific as well as practical affairs, providing you with several highlights.

First, I would like to welcome our new Scientific Advisory Committee Chairman – Dr. Richard Toohey and our new radiochemist – Ms. Elizabeth Thomas. With Ms. Thomas' arrival, I look at radiochemistry with redoubled optimism – now we have two radiochemists on board.

In March, the 2012 USTUR Annual Report was published; it includes our progress reports from October 2010 to March 2012. This report was widely distributed nationally and internationally. You can download it from our website or call to request a copy.

In addition, I would like to emphasize the publication of papers on such topics as mesothelioma and radiation, and validation of the plutonium lung model in leading international journals.

You will read about these highlights and more in this newsletter. This year, following recommendations from our Scientific Advisory Committee – who stated that our language was too scientific, we made all efforts to write in plain, clearly understandable language. We hope our attempts were successful.

To conclude, I want to underscore that all of our accomplishments could happen only because of our donors – without our Registrants, nothing would be possible.

Best wishes,

Sergei Y. Tolmachev

Inside this Issue

A Note from Our New Scientific Advisory Committee Chair

I am very pleased and honored to be the new chair of the Scientific Advisory Committee for the USTUR. Dr. Tolmachev appointed me as the health physics representative to the SAC last year, and at our meeting in September, Bill Hayes decided to step down as Chair after several very productive years of leading the SAC, and the committee elected me to replace him. Although relatively new to the SAC, I have been very involved with the programs of the USTUR over the years, and I spent a sabbatical year in 1993-94 at the USTUR as Associate Director, compiling data on USTUR Case 246, the Hanford americium accident victim, and produced five scientific articles that were published in Health Physics journal. I began my career as an internal radiation dosimetrist at Argonne National Laboratory, working on the follow-up study of the radium watch dial painters from the 1920's; although that program was terminated, all the records and tissue samples were transferred to the USTUR, where they are still maintained.

I am very excited to be able to assist the USTUR as it evolves from its original mission, which was to gather actual human data to improve the mathematical models we use to calculate the radiation doses workers receive from intakes of radioactive materials, to a new mission to support fundamental scientific investigations of the connections between radiation exposure and cancer formation. The Department of Energy has sponsored a research program for about the last 10 years or so investigating the biological effects of radiation at the cellular, and even sub-cellular level, that is, what really happens in a cell that is exposed to radiation, and how do those changes in a cell lead to the formation of a cancer. Much of the data used has been from animal experiments, but a new collaborative program between the USTUR and Battelle Pacific Northwest National Laboratory will use human tissue samples from the USTUR to compare with the animal data. This project, which was undreamed of when the USTUR was established, is just one example of the invaluable national scientific resource that the USTUR has become. Another project is the work of SAC member, Dr. Herman Gibb, on mesothelioma in USTUR Registrants. Mesothelioma is a type of lung cancer previously thought to be caused only by exposure to asbestos, but Dr. Gibb's work is indicating that radiation also may have a role in causing this disease, another new finding from the USTUR data.

Despite the current fiscal belt-tightening in Washington, D.C., the funding for the USTUR seems to be secure for at least the near future, and all of us on the SAC look forward to continuing the USTUR's record of scientific excellence. Of course, none of this would be possible without the caring and compassionate donations of Registrants and their families, and we feel that the development of new scientific data resulting in improvements in radiation protection of workers is the best thank-you that the USTUR can offer.

~*Richard E. Toohey*

2

Scientific Advisory Committee Meeting

The USTUR has an independent Scientific Advisory Committee (SAC) that meets annually to review the program activities and progress. Last year, this meeting was held September 7-8 in Richland, WA. It was attended by Advisory Committee members; USTUR faculty and staff; Department of Energy representative, Joey Zhou; WSU Associate Dean of Graduate Education & Scholarship, Gary Meadows; and a donor's son as a next-of-kin representative. Major feedback from the 2012 meeting includes:

Comments

- High productivity was achieved on limited funding
- Excellent collaborations with non-USTUR scientists.

Recommendations

- Improve communication with Registrants and their families

2012 SAC Members

Richard Toohey (chair) - *Health Physics*
Robert Bistline - *Occupational Health*
Herman Gibb - *Epidemiology*
William Hayes - *Radiochemistry*
Kathryn Meier - *Ethics & Academic Community*
Roger McClellan (unable to attend the meeting) - *Toxicology*

Q&A

What are the benefits of involving students in USTUR research?

Today's students will become tomorrow's radiation protection professionals. Investing our scientific resources in their education is an investment in the safety of future nuclear workers! As an added benefit, students are able to conduct cutting edge research at little or no added cost to the USTUR, thus stretching our limited grant funding further.

Graduate Research

The USTUR contains a wealth of materials that provide graduate students with meaningful data for dissertation topics relevant to radiation protection. We desire to share our unique dataset with students and to provide feedback that will help shape them into leading scientists.

ISU Health Physics

In 2006, The USTUR initiated a collaboration with Idaho State University (ISU), Pocatello, ID to share USTUR data with students who have an interest in the field of internal dosimetry.

As a product of this collaboration, four Ph.D. and three M.S. degrees were awarded, five students published seven papers, and one student (Maia Avtandilashvili) was hired by the USTUR.

WSU Environmental Sciences

In last year's newsletter we mentioned the work of PNNL employee/WSU student, Chris Nielsen, who studied the distribution of plutonium in a Registrant's lungs 38 years after it was accidentally inhaled. He found that the plutonium had congregated into localized areas of the pleura. Often the plutonium was found in parts of the pleura that had black residue from cigarettes. These findings were recently published in a leading journal, Cancer Research.

A Donor Family's Perspective

My father was a tissue donor to the USTUR. Involved in a significant incident in 1957, he was exposed to plutonium through simultaneous ingestion, inhalation, and injection. It was an unprecedented event at the time, and the long-term effects of this exposure were unknown. Although he certainly did not seek the notoriety, nevertheless he became the subject of scientific study and monitoring from that day on.

In the 1970's, my father was approached by the site physician to consider becoming a tissue donor for the Registry. I remember there was a fair amount of discussion within the family about signing up for the program; however, it was a decision in which he was adamant. He felt strongly that the experience, his exposure and subsequent treatments, needed to be documented and studied to further the understanding of both short and long term health effects. Additionally, those results needed to be shared with those who found themselves in situations similar to his due to their own exposures.

It was a difficult time for the family when he passed away in 2008; however, we knew the importance of his decision to him, and we notified the USTUR. Thankfully, the process of the donation was virtually transparent, with the USTUR staff taking care of all the details. That was a tremendous relief to us at a time of profound grief.

The USTUR has been instrumental in validating exposure models used for routine and accident dosimetry protocols. Research is continuing into new analytical laboratory processes that will refine and validate the accuracy of current dose assessment techniques. Other studies are looking at beryllium exposure analysis and a possible connection between plutonium exposure and the incidence of mesothelioma. Many other research projects are ongoing as well.

I encourage Registrants and their families to become aware of, and involved in, the USTUR activities. The USTUR's website contains links to many published reports of research involving Registrants. I would also recommend reading the Annual Report for an overall summary of ongoing USTUR activities. Although I might not understand much of the technical information presented, as a family member, I am reassured that meaningful scientific contributions continue to be made through the tissue donation of the Registrants, including my father.

The decision to donate to the USTUR is a highly personal one, and I'm sure each individual has his or her own reasons for doing so. As a son, I am proud of the decision my father made. As a second generation nuclear worker, I am thankful and appreciative of the contribution, not only of my father, but of all USTUR donors in making the industry safer through increased understanding of radiation exposure and the resultant health effects.

The USTUR provides a unique resource for scientists worldwide, and it is instrumental in continuing research around the globe. Financial support from the Department of Energy assures continued operation. However, the USTUR would not exist if not for the donations of past and future Registrants.

~Mike

How can I obtain a copy of the Annual Report?

On the web: The Annual Report can be downloaded from our homepage. Look for the red and white picture of the report cover and click "Download Report."

www.ustur.wsu.edu

Give us a call: You can also call us to request the report. We will gladly send a copy to you.

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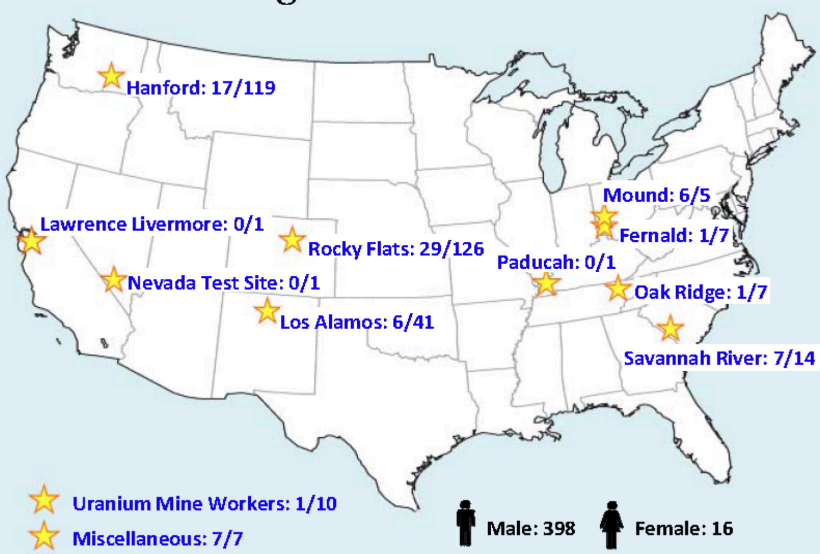
Registrant Statistics



The USTUR has 75 living Registrants. You range in age from 41 to 90+ years, with an average age of 78. Since 1968, the Registries has received tissue donations from 339 nuclear workers and/or uranium miners (average age, 68 y). The U.S. map illustrates the distribution of Registrants by the nuclear site where they worked. The first number represents living Registrants, and the second deceased.

Million Worker Study

The National Council on Radiation Protection and Measurements, with funding from the Department of Energy and the National Cancer Institute, is starting a new large-scale epidemiology study of cancer incidence in workers exposed to radiation. The worker groups to be studied include DOE workers, commercial nuclear power plant workers, medical radiology technicians, military personnel (including "Atomic Veterans" present at nuclear weapon tests), and industrial radiographers. The USTUR Registrants, although a small group compared to the others, will be included in this study because the measurements of radioactivity in their donated tissue samples provide a much better estimate of their internal radiation doses than can be made from their work records. This is one more example of the scientific importance of the data that the Registries gather and maintain.

Hanford Oral Histories

WSU Tri-Cities has partnered with several regional organizations to collect, safeguard, and showcase oral testimonies, so that a lasting legacy of Hanford's heritage may be carried forward for the educational benefit of future generations.

If you worked at Hanford prior to 1963, or knew someone who did, and would like to share your story, please contact the Hanford History Partnership at:

www.ourhanfordhistory.org
(509)372-7306

Please note the USTUR is not involved with the administration of the Hanford History Partnership, and has provided this information because we believe it may be of interest to our Registrants.

Have you **Moved**?

Please give us a call to make sure that we have your current address.

In the **Photo**!

Following the 2012 Advisory Committee meeting Joey Zhou, DOE Program Manager, spent two days visiting the USTUR and discussing operations with our director. Photographed: (back row) Fred Miller, Florencio Martinez, Joey Zhou, Margo Parker, Julie Blumenkranz, Elizabeth Thomas; (front row) Stacey McComish, Sergei Tolmachev, Maia Avtandilashvili.

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U. S. Transuranium and Uranium Registries

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Toll Free: 800-375-9317
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www.ustur.wsu.edu

Note from the Editor

Writing this newsletters has become one of the highlights of my year. I enjoy the opportunity to update you on what is happening at the Registries. If you have any questions about your participation in the USTUR or if you have suggestions as to what you would like to see in next year's newsletter, feel free to give us a call. We always enjoy hearing from our Registrants and their families!

Stacey L. McComish
Associate in Research

smccord@tricity.wsu.edu (email)
800-375-9317 (toll-free)

Appendix C

United States Transuranium and Uranium Registries
College of Pharmacy, Washington State University
2013 Scientific Advisory Committee Meeting
Courtyard Marriott Hotel, Richland, WA
September 6 - 7, 2013

Friday, September 6, 2013

07:45 – 08:30	Breakfast	
08:30 – 08:45	Executive Session (for SAC Members)	R. Toohey, *SAC Chair*
08:45 – 08:55	Welcome & Introductions	S. Tolmachev, *Director*
08:55 – 09:05	WSU/COP & USTUR	A. Lazarus, *COP Asst. Vice Pres.*
09:05 – 09:15	WSU Tri-Cities News	D. Talbot, WSU/*TC Chief of Staff*
09:15 – 09:20	Updates from DOE/HS-13. Guidance for FY2014	J. Zhou, *DOE Manager*
09:20 – 10:10	2012 SAC Recommendations & 2013 USTUR Overview	S. Tolmachev, *Director*
10:10 – 10:30	Administrative & Financial Developments	M. Parker, *Fiscal Specialist*
10:30 – 10:45	Coffee Break	
10:45 – 11:00	USTUR Registrant Statistic	S. McComish, *Asst. in Research*
11:00 – 11:15	Health Physics Database	M. Avtandilashvili, *Research Asst.*
11:15 – 11:30	National Human Radiobiological Tissue Repository	S. McComish, *Asst. in Research*
11:30 – 12:00	Radiochemistry Progress Report	F. Miller, *Chemist*
12:00 – 13:30	Lunch	
13:30 – 13:45	USTUR/PNNL/HPA Collaboration	C. Nielsen, *WSU PhD Candidate*
13:45 – 14:00	USTUR/DOE Mayak 2.4 Project Collaboration	T. Hay, *PNNL*
14:00 – 14:15	WSU Grad Certificate Program in Radiation Protection	P. Stansbury, *WSU/Dade Moeller*
14:15 – 14:40	Uranium Hexafluoride Biokinetic Modeling	M. Avtandilashvili, *Research Asst.*
14:40 – 15:00	Coffee Break	
15:00 – 15:30	Research & Operation: Plan for FY2014	S. Tolmachev, *Director*
15:30 – 16:30	General Discussion: USTUR in 2013 and Beyond	USTUR, DOE, SAC, Guests
17:30 – 18:00	Appetizers and No-Host Reception, at Anthony's Event Center, Billiard Room	
18:00 – 21:00	Dinner, at Anthony's Event Center, Billiard Room	

United States Transuranium and Uranium Registries
College of Pharmacy, Washington State University
2013 Scientific Advisory Committee Meeting
Courtyard Marriott Hotel, Richland, WA
September 6 - 7, 2013

Saturday, September 7, 2013 – SAC, DOE and USTUR Management

07:45 – 08:30	Breakfast	
08:30 – 09:00	'Non-Registrant' Communication	S. McComish, *Asst. in Research*
09:00 – 09:20	Trap in NIOSH/LTAS for Calculating PMR for Mesothelioma: Experience from a USTUR Study	J. Zhou, *DOE/HS-13*
09:20 – 09:30	SAC Membership	S. Tolmachev, *Director*
09:30 – 10:00	SAC Q & A	R. Toohey, *SAC Chair*
10:00 – 12:30	SAC Executive Session	R. Toohey, *SAC Chair*
12:30 – 13:45	Lunch	
13:45 – 15:45	SAC Debriefing	R. Toohey, *SAC Chair*
15:45 – 17:15	Tour to USTUR Laboratory Facility, Richland Airport Return to Marriott, Richland	

Saturday, September 7, 2013 – All

18:30	Hosted Dinner Party – 2407 Swift Blvd, Richland	D. & F. Miller

2013 USTUR Scientific Advisory Committee Meeting Agenda

United States Transuranium and Uranium Registries
College of Pharmacy, Washington State University
2012 Scientific Advisory Committee Meeting
Anthony's at Columbia Point, Richland, WA
September 7 - 8, 2012

Friday, September 7, 2012

08:00 – 08:30	Breakfast	
08:30 – 09:00	Executive Session (for SAC Members)	W. Hayes, *SAC Chair*
09:00 – 09:10	Welcome & Introductions	S. Tolmachev, *Director*
09:10 – 09:15	Changes at WSU/COP & USTUR	G. Meadows, *Associate Dean*
09:15 – 09:25	Report from DOE/HS- 13. Guidance for FY2013- 17	J. Zhou, *DOE Manager*
09:25 – 10:30	2011 SAC Recommendations & 2012 USTUR Overview	S. Tolmachev, *Director*
10:30 – 10:45	Coffee Break	
10:45 – 11:00	Administrative & Financial Developments	M. Parker, *Fiscal Tech.*
11:00 – 11:20	USTUR Statistics & Registrant Correspondence	S. McComish, *Associate in Res.*
11:20 – 11:40	Health Physics Database	M. Avtandilashvili, *Res. Associate*
11:40 – 12:00	National Human Radiobiological Tissue Repository	S. McComish, *Associate in Res.*
12:00 – 13:15	Lunch	
13:15 – 13:45	Radiochemistry Progress Report	F. Miller, *Lab. Tech.*
13:45 – 14:00	USTUR/PNNL Collaboration	W. Morgan
14:00 – 14:15	WSU Certificate Program in Radiation Protection	P. Stansbury
14:15 – 14:30	Family Perspective	M. Simmons
14:30 – 14:45	Coffee Break	
14:45 – 15:15	Research & Operation: Plan for FY 2013	S. Tolmachev, *Director*
15:15 – 16:15	General Discussion: USTUR 2012 and Beyond	USTUR, DOE, SAC, Guests.
18:00 – 18:45	Appetizers and No- Host Reception, Billiard Room	
18:45 – 21:00	Dinner, at Anthony's Event Center, Billiard Room	

Both locations are within walking distance of the Marriott Hotel.

United States Transuranium and Uranium Registries
College of Pharmacy, Washington State University
2012 Scientific Advisory Committee Meeting
Anthony's at Columbia Point, Richland, WA
September 7 - 8, 2012

Saturday, September 8, 2012 – SAC, DOE and USTUR Management

08:00 – 09:00	Breakfast	
09:00 – 09:15	SAC Membership	S. Tolmachev, *Director*
09:15 – 09:45	Mesothelioma Study: Results	H. Gibb, *SAC*
09:45 – 10:30	SAC Q & A	W. Hayes, *SAC Chair*
10:30 – 12:30	SAC Executive Session	W. Hayes, *SAC Chair*
12:30 – 13:45	Lunch	
13:45 – 15:45	SAC Debriefing	W. Hayes, *SAC Chair*
15:45 – 16:45	Tour to USTUR Laboratory Facility, Richland Airport Return to Marriott, Richland	

Saturday, September 8, 2012 – All

18:30	Dinner Party (Catered by Greek Island) - 2455 George Washington Way, Washington Square I Club House, Richland

2012 USTUR Scientific Advisory Committee Meeting Agenda

Appendix D

USTUR-0317-11

Maximum Likelihood Analysis of Bioassay Data from Long-term Follow-up of Two Refractory PuO_2 Inhalation Cases

M Avtandilashvili[1], R Brey[2], AC James[1, 3]

[1]United States Transuranium and Uranium Registries, College of Pharmacy,

Washington State University, Richland, WA, USA

[2]Idaho State University, Health Physics, Pocatello, ID

[3]Posthumous.

The U.S. Transuranium and Uranium Registries' tissue donors 0202 and 0407 are the two most highly exposed of the 18 Registrants who were involved in the 1965 plutonium fire accident at a defense nuclear facility. Material released during the fire was well characterized as "high fired," refractory plutonium dioxide with 0.32 micrometer mass median diameter. The extensive bioassay data from long-term follow-up of these two cases were used to evaluate the applicability of the Human Respiratory Tract Model presented by International Commission on Radiological Protection in Publication 66 and its revision proposed by Gregoratto et al. in order to account for the observed long-term retention of insoluble material in the lungs. The maximum likelihood method was used to calculate the point estimates of intake and tissue doses and to examine the effect of different lung clearance, blood absorption and systemic models on the goodness-of-fit and estimated dose values. With appropriate adjustments, Gregoratto et al. particle transport model coupled with the customized blood absorption parameters yielded a credible fit to the bioassay data for both cases and predicted the Case 0202 liver and skeletal activities measured post-mortem. PuO_2 particles produced by the plutonium fire are extremely insoluble. About 1% of this material is absorbed from the respiratory tract relatively rapidly, at a rate of about 1 to 2 d^{-1} (half-time about 8 to 16 h). The remainder (99%) is absorbed extremely slowly, at a rate of about 5×10^{-6} d^{-1} (half-time about 400 y). When considering this situation, it appears that doses to other body organs are negligible in comparison to those to tissues of the respiratory tract. About 96% of the total committed weighted dose equivalent is contributed by the lungs. Doses absorbed by these workers' lungs were high: 3.2 Gy to the alveolar-interstitial region and 6.5 Gy to the thoracic lymph nodes for Case 0202 (18 y post-intake); 3.2 Gy to the alveolar-interstitial region and 55.5 Gy to the thoracic lymph nodes for Case 0407 (43 y post-intake). This evaluation supports the Gregoratto et al. proposed revision to the ICRP 66 model when considering situations of extremely insoluble particles.

Health Physics 2012; 103 (1): 70-79

USTUR-0324-12A

Biokinetic modeling of chelation therapy for ^{241}Am – USTUR Case 0846

B Breustedt[1], S McCord[2], S Tolmachev[2]

[1]*KIT-INE, Karlsruher Institut for Technology, Institute for nuclear Waste Disposal, Eggenstein-Leopoldshafen, Germany*

[2]*United States Transuranium and Uranium Registries, College of Pharmacy, Washington State University, Richland, WA, USA.*

Chelation therapy is a method to avert doses after incorporation of actinides. The perturbation of the biological processes cannot be described by the existing biokinetic models. Currently no generic model to describe the perturbation by chelation therapy exists. USTUR Case 0846 was a whole body donor who accidentally inhaled ~67 kBq 241Am, which was first reported in 1967. After confirmation of the intake, he was extensively chelated over 380 wk. Overall 313.5 g DTPA were given in 342 i.v. injections; 57 of them were 0.5 g doses, and 285 were 1 g doses. Virtually all urine was collected during the therapy. The gentleman, who died more than 40 years after the intake, was a whole body donor to the U.S. Transuranium and Uranium Registries (USTUR). Data available at USTUR, including original dosimetry and medical reports, have been analyzed to generate a dataset suitable for thorough biokinetic modeling of the chelation therapy. Based on post-mortem radiochemical tissue analyses, the total skeleton and liver were estimated to contain 30 kBq and 290 Bq of 241Am, respectively. The dataset will be completed when the remaining tissues have also been radiochemically analyzed. These radiochemistry results will provide an insight on the effects of DTPA-chelation therapy and support the biokinetic modeling. The methods used to generate the dataset, and the first steps in the assessment of this case and the development of a biokinetic model of decorporation therapy will be presented.

(Abstract) *Health Physics* 2012; 103 (2): S80

USTUR-0328-12

Reevaluation of USTUR Plutonium Wound Case 0262 Using Bayesian Methodology and New Data

SN Weber[1], RR Brey[1], AC James[2, 3]

[1]*Idaho State University, Pocatello, ID*

[2]*United States Transuranium and Uranium Registries, College of Pharmacy,*

Washington State University, Richland, WA

[3]*Posthumous.*

Skin penetration by radionuclide contaminants serves as a route of entry into the body and may pose a serious health risk to humans depending on the magnitude of intake. The United States Transuranium and Uranium Registry whole body Case 0262 was involved in a wound intake of plutonium at the

Hanford Site. The Registrant died about 33 years later. Results were initially reported in 2007 regarding the deposition and retention of plutonium in various tissues, including the wound site. However in 2009, an additional (previously unrecorded) sample of the wound tissue was located in the National Human Radiobiological Tissue Repository. The new sample was analyzed using inductively coupled plasma-mass spectrometry (ICP-MS), and the results were used to calibrate the measurement of emitted ^{239}Pu x-rays from the original wound tissue sample made in 2007. In the present study, the analysis of ^{239}Pu absorption rates from the wound and axillary lymph node from the initial study is repeated using the additional wound activity data and ICPMS calibration. This new analysis is carried out using the Weighted Likelihood Monte Carlo Sampling (WeLMoS) method and code, which applies Bayesian inference to calculate the posterior probability distribution of intake and wound absorption parameters directly from the observed data and the assumed biokinetic model structure. The resulting central estimates of empirical wound absorption parameters and their associated uncertainties are here compared with the empirical values recommended in NCRP Report No. 156 for plutonium and with the maximum likelihood point estimates derived in the initial study from the Case 0262 data available at the time.

Health Physics 2012; 103 (3): 286-300

USTUR-0336-12

Microdistribution and Long-Term Retention of $^{239}Pu(NO_3)_4$ in the Respiratory Tracts of an Acutely Exposed Plutonium Worker and Experimental Beagle Dogs

CE Nielsen[1], DA Wilson[1], AL Brooks[1], S McCord[2], GE Dagle[3], AC James[4], SY Tolmachev[2], BD Thrall[1], WF Morgan[1]

[1]*Biological Sciences Division, Pacific Northwest National Laboratory, Richland, WA*

[2]*United States Transuranium and Uranium Registries, Washington State University, Richland, WA*

[3]*Retired*

[4]*Deceased.*

The long-term retention of inhaled soluble forms of plutonium raises concerns as to the potential health effects in persons working in nuclear energy or the nuclear weapons program. The distributions of long-term retained inhaled plutonium-nitrate [$^{239}Pu(NO_3)_4$] deposited in the lungs of an accidentally exposed nuclear worker (case 0269) and in the lungs of experimentally exposed beagle dogs with varying initial lung depositions were determined. Autoradiographs of selected histological lung, lymph node, trachea, and nasal turbinate tissue sections were made to determine the location of plutonium within the tissues. These studies showed that both the human and dogs had a non-uniform distribution of Pu throughout the lung tissue. Fibrotic scar tissue effectively encapsulated a portion of the plutonium and prevented its clearance from the body or translocation to other tissues. Alpha radiation activity from deposited plutonium in human case 0269 was observed primarily along the sub-pleural regions while no alpha activity was seen in the tracheobronchial lymph nodes of this individual. However, relatively high activity levels in the tracheobronchial lymph nodes of the beagle dogs indicated the lymphatic system was

effective in clearing deposited plutonium from the lung tissues. In both the human case and beagle dogs, the appearance of bound plutonium within the respiratory tract was inconsistent with current biokinetic models of clearance for soluble forms of plutonium. Bound plutonium can have a marked effect on the dose to the lungs and the potential increase in cancer risk.

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USTUR-0325-12

Uranium Bone Content as an Indicator of Chronic Environmental Exposure from Drinking Water

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Uranium (U) is a ubiquitous radioelement found in drinking water and food. As a consequence of its prevalence, most humans ingest a few micrograms (mg) of this element daily. It is incorporated in various organs and tissues. Several studies have demonstrated that ingested U is deposited mainly in bones. Therefore, U skeletal content could be considered as a prime indicator for low-level chronic intake. In this study, 71 archived vertebrae bone samples collected in seven Canadian cities were subjected to digestion and U analysis by inductively coupled plasma mass spectrometry. These results were correlated with U concentrations in municipal drinking water supplies, with the data originating from historical studies performed by Health Canada. A strong relationship (r_2 = 0.97) was observed between the averaged U total skeletal content and averaged drinking water concentration, supporting the hypothesis that bones are indeed a good indicator of U intake. Using a PowerBASIC compiler to process an ICRP systemic model for U (ICRP, 1995a), U total skeletal content was estimated using two gastrointestinal tract absorption factors (f_1 = 0.009 and 0.03). Comparisons between observed and modeled skeletal contents as a function of U intake from drinking water tend to demonstrate that neither of the f1 values can adequately estimate observed values. An f1 value of 0.009 provides a realistic estimate for intake resulting from food consumption only (6.72 μg) compared to experimental data (7.4 ± 0.8 μg), whereas an f1 value of 0.03 tends to better estimate U skeletal content at higher levels of U (1 - 10 μg L^{-1}) in drinking water.

Journal of Environmental Radioactivity 2013, 121: 98-103

USTUR-0323-12

Application of Bayesian Inference to the Bioassay Data from Long-term Follow-up of Two Refractory PuO_2 Inhalation Cases

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The dominant contribution to the uncertainty in internal dose assessment can often be explained by the uncertainty in the biokinetic model structure and parameters. The International Commission on Radiological Protection (ICRP) is currently updating its biokinetic models, including the Human Respiratory Tract Model (HRTM). Gregoratto et al. (2010) proposed a physiologically-based particle transport model that simplifies significantly the representation of particle clearance from the alveolar interstitial region. Bayesian inference using the Weighted Likelihood Monte-Carlo Sampling (WeLMoS) method is applied to the bioassay and autopsy data from the U.S. Transuranium and Uranium Registries' (USTUR) tissue donors 0202 and 0407 exposed to "high fired," refractory PuO_2 aerosols in order to examine the applicability of the revised model and to estimate the uncertainties in model parameters and the lung doses as expressed by the posterior probability distributions. It is demonstrated that, with appropriate adjustments, the Gregoratto et al. particle transport model can describe situations involving exposure to highly insoluble particles. Significant differences are observed in particle clearance pattern characteristics to these two individuals' respiratory systems. The respiratory tract of Registrant 0202 was most likely compromised by his prior occupational exposure to coal dust, smoking habit, and chronic obstructive pulmonary disease, while donor 0407 was a non-smoker and had no prior history of lung disorder. However, the central values of the particle transport parameter posterior distributions for both cases are found to be still within the 68% probability range for the inter-subject variability derived by Gregoratto et al. PuO_2 particles produced by the plutonium fire were extremely insoluble, with about 99% absorbed into blood at a rate of approximately 4.8×10^{-6} d^{-1} (Case 0202) and 5.1×10^{-6} d^{-1} (Case 0202). When considering this type of plutonium material, doses to other body organs are small in comparison to those to tissues of the respiratory tract. More than 95% of the total committed weighted equivalent dose is contributed by the lungs.

Health Physics 2013, 104(4): 394-404

USTUR-0326-12

A PMR and PCMR Analysis of Radiation and Mesothelioma in the United States Transuranium and Uranium Registries

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Objectives. We examined the relationship between radiation and excess deaths from mesothelioma among deceased nuclear workers who were part of the US Transuranium and Uranium Registries.

Methods. We performed univariate analysis with SAS Version 9.1 software. We conducted proportionate mortality ratio (PMR) and proportionate cancer mortality ratio (PCMR) analyses using the National Institute for Occupational Safety and Health Life Table Analysis System with the referent group being all deaths in the United States.

Results. We found a PMR of 62.40 (P < .05) and a PCMR of 46.92 (P < .05) for mesothelioma. PMRs for the 4 cumulative external radiation dose quartiles were 61.83, 57.43, 74.46, and 83.31. PCMRs were 36.16, 47.07, 51.35, and 67.73. The PMR and PCMR for trachea, bronchus, and lung cancer were not significantly elevated.

Conclusions. The relationship between cumulative external radiation dose and the PMR and PCMR for mesothelioma suggests that external radiation at nuclear facilities is associated with an increased risk of mesothelioma. The lack of a significantly elevated PMR and PCMR for trachea, bronchus, and lung cancer suggests that asbestos did not confound this relationship.

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USTUR-0351-13

Carcinogenic and Inflammatory Effects of Plutonium-Nitrate Retention in an Exposed Nuclear Worker and Beagle Dogs

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Purpose: Plutonium-nitrate has a moderately rapid translocation rate from the lung to blood stream. Previous studies have shown an unexpected retention of soluble plutonium in the beagles and human

case studied here. The inflammatory responses that may be associated with long-term exposure to ionizing radiation were characterized. These pathways include tissue injury, apoptosis, and gene expression modifications. Other protein modifications related to carcinogenesis and inflammation and the various factors that may play a role in orchestrating complex interactions which influence tissue integrity following irradiation were investigated.

Materials and methods: We have examined numerous lung samples from a plutonium exposed worker, a human control, and a variety of plutonium-exposed beagle dogs using immunohistochemistry and quantitative Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR).

Results: The exposed human showed interstitial fibrosis in peripheral regions of the lung, but no pulmonary tumors. Beagles with similar plutonium doses were diagnosed with tumors in bronchiolo-alveolar, peripheral and sub-pleural alveolar regions of the lung. The terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay showed an elevation of apoptosis in tracheal mucosa, tumor cells, and nuclear debris in the alveoli and lymph nodes of the beagles but not in the human case. In both the beagles and human there were statistically significant modifications in the expression of Fas ligand (FASLG), B-cell lymphoma 2 (BCL2), and Caspase 3 (CASP3).

Conclusions: The data suggests that FASLG, BCL2, CASP3 and apoptosis play a role in the inflammatory responses following prolonged plutonium exposure. Utilizing these unique tissues revealed which pathways are triggered following the internal deposition and long-term retention of plutonium-nitrate in a human and a large animal model.

International Journal of Radiation Biology 2014; 90: 60-70

Appendix E

USTUR-0354-13

Incorrect Analyses of Radiation and Mesothelioma

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The recent article, "Analyses of Radiation and Mesothelioma in the US Transuranium and Uranium Registries," by Gibb *et al.*[1] examines seven mesothelioma deaths among a small population of 329 deceased registrants in the US Transuranium and Uranium Registries (USTUR). Using the National Institute for Occupational Safety and Health's Life Table Analysis System with the referent group being all deaths in the United States,[2,3] the study finds a proportionate mortality ratio (PMR) of 62.40 ($P < 0.05$) for mesothelioma, the highest PMR ever observed and more than an order of magnitude higher than any other published studies.[1]

Mesothelioma has been coded as a separate underlying cause of death (C45.0-C45.9) since 1999 when International Classification of Diseases, 10th revision (ICD-10)[4] was implemented. Before 1999, mesothelioma was coded as malignant neoplasm of pleura, unspecified (ICD-9:163.9); malignant neoplasm of bronchus and lung, unspecified (ICD-9:162.9); malignant neoplasm without specification of site (ICD-9:199); and so on. Life Table Analysis System has no death data in the mesothelioma disease category for the United States before 1999[2,5] and therefore does not support PMR analysis for mesothelioma deaths before 1999. More than 80% of USTUR deaths occurred before 1999 including six of seven USTUR mesothelioma cases.[6,7]

Life Table Analysis System calculates PMR as a ratio of weighted sums of the proportion of deaths from a specific cause in the exposed versus the comparable weighted sum in the unexposed (often the US population deaths). Adjustment for age, race, gender, and calendar time is accomplished by stratification and indirect standardization.[2,3] The formula to calculate the PMR is presented below.

(1) $PMR = \Sigma W_i \times P_{i1} \ / \ \Sigma W_i \times P_{i0}$

where the variables are defined as follows:

- P_{i1} = the i^{th} stratum-specific proportion in the observed cohort (the exposed cohort)
- P_{i0} = the i^{th} stratum-specific proportion in the reference population (unexposed population)
- W_i = the i^{th} stratum-specific number of observed deaths in the exposed cohort.

Because all strata before 1999 have zero P_{i0} and only 20% (one fifth) of USTUR deaths contribute the weighted sum of the denominator in the formula, the PMR for mesothelioma by Gibb et al. is greatly overestimated. If one assumes that the age distributions of deceased registrants (who were overwhelmingly White and male) are similar before and after 1999, and the stratum-specific proportions for mesothelioma in the reference populations are the same before and after 1999, the PMR for mesothelioma is a five-fold overestimate.

The USTUR death data are not compatible and therefore should have not been compared with the Life Table Analysis System US death data in the PMR analysis for mesothelioma because there is no specific code for it before 1999. The analyses were conducted incorrectly from the beginning, resulting in an artificially high-reported PMR for mesothelioma. Caution should be exercised when using Life Table Analysis System or similar analytic software for mortality studies in which the rules for coding cause of death are different over the time frame of a study.

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USTUR-0353-13

Gibb et al. Respond

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We thank Zhou for his interest in our study; however, his letter misquotes our article. He states that we reported that our proportionate mortality ratio (PMR) for mesothelioma was "the highest PMR ever observed and more than an order of magnitude higher than any other published studies." We stated that the PMR for mesothelioma was the highest of those in our study. We did not state that it was the highest PMR ever observed. We also did not state that the PMR was an order of magnitude higher than "any other published studies." We stated that the PMR was an order of magnitude higher than that for any occupation reported by McElvenny *et al.*[1]

Zhou claims that the National Institute for Occupational Safety and Health Life Table Analysis System (LTAS; National Institute for Occupational Safety and Health, Atlanta, GA) overestimated the PMR for mesothelioma because 6 of 7 mesothelioma deaths occurred prior to 1999, the year when the International Classification of Diseases, 10th Revision (ICD-10) was implemented. All deaths in our study were coded to ICD10. The LTAS manual does not indicate the program cannot be used if mesothelioma deaths occurred prior to 1999 nor did the program produce error messages when we ran the analysis.

Since our analysis, 11 more deaths have been added to the US Transuranium and Uranium Registries. Mesothelioma was reported to be the underlying cause of one of these deaths and to contribute to another death for which the immediate cause was reported as "pneumonic." Zhou's presumed approach would be to calculate a PMR only for the two post-1998 deaths for which mesothelioma was the underlying cause. Given that only 73 of the deaths in the Registries occurred after 1998, this approach could well produce a PMR for mesothelioma that has confidence limits inclusive of the PMR that we found. Regardless of whether LTAS is used to produce a PMR for mesothelioma using all deaths in the Registries or only deaths occurring after 1998, there is no question that the proportion attributed to mesothelioma is significantly elevated. In addition to those deaths for which mesothelioma was reported to be the underlying cause, one individual was found to have mesothelioma at autopsy (the original cause was reported to be lung cancer), and mesothelioma was reported to be a contributory cause in another death (described above). This means that there are now 10 individuals who had mesothelioma among the 340 workers in the Registries who were occupationally exposed to radiation. By any measure, that is a significant number, and it would be disingenuous to ignore it.

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