2011 SAC Recommendations and 2012 Overview

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"Learning from Plutonium and Uranium Workers"

UNITED STATES TRANSURANIUM AND URANIUM REGISTRIES
established 1968

WASHINGTON STATE UNIVERSITY
World Class. Face to Face.

July 20, 2011

- 2011 Scientific Advisory Committee Meeting
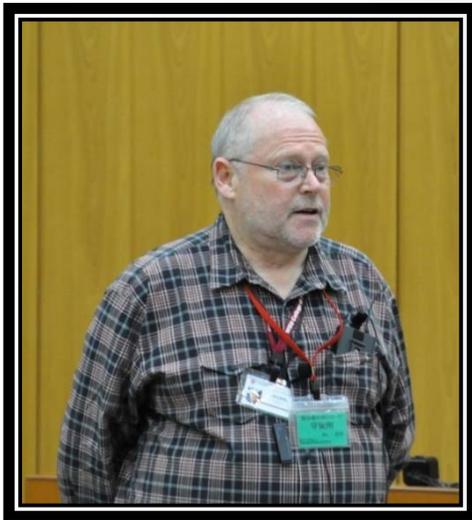
Anthony Clive James

(May 14, 1943 – July 20, 2011)

USTUR Core Functions (DOE)

- Accepting and processing future Registrant donations.

- Completing radiochemical analysis of previous Registrant donations.

- Completing the development and population of USTUR databases.

2011 SAC's Recommendations

- Following the 2011 Annual Meeting, the SAC made 10 specific recommendations/ comments.

Recommendation #1

- The USTUR needs to focus DPTA research on the possible effectiveness of removing Pu from the liver.

Collaboration with Karlsruhe Institute of Technology
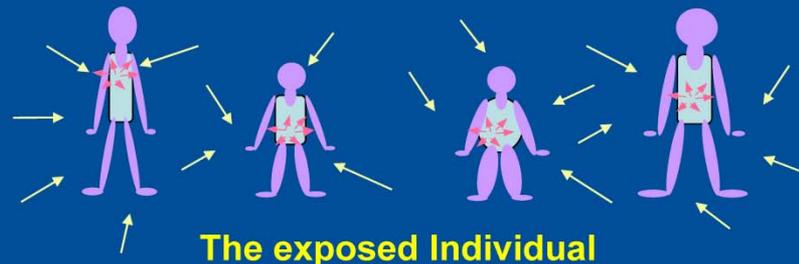
Dr. Bastian Breustedt

Research on Chelation Therapy

Recommendation #2

- Biokinetic modeling support may be needed in order to address the use of data and medical management issues. This specifically involves maintaining professional contact with Dr. Alan Birchall, U.K., to conduct biokinetic modeling of USTUR data.

New Faculty/SOLO Project

Dr. Maia Avtandilashvili
Dr. Alan Birchall

New USTUR Member

- Dr. Maia Avtandilashvili (Research Associate)
  - ✓ PhD from Idaho State University (2011)
  - ✓ Standardization of Exposure Records and Bioassay Data – Health Physics Database
  - ✓ USTUR Case Analysis (IMBA)

HPA/SOLO Project

- Grant from Health Protection Agency (UK) "*to quantify the fraction of the initial deposited activity which is still retained in the upper airways due to binding (f_b), taking account of particle transport from the deep lung; and characterize the deposited activity in terms of its particulate or diffuse nature in bronchial epithelium, lung parenchyma and lymph nodes.*"

- Period: October 1, 2012 – July 30, 2013.

- Budget: €16,000 ($20,992) – Funded.

Recommendation #3

- Care needs to be given to time prioritization so that USTUR staff do not "burn out," and in order to continue the quality work that the USTUR is currently conducting.

Tasks Prioritizations

Maia Avtandilashvili, Stacey McCord

Sergei Tolmachev

Recommendation #4

- The USTUR should continue the emphasis on recruiting new donors. *New donors would increase the number of available subjects and provide fresh tissues that can be preserved in different ways to obtain the best possible data.*

What is the Mechanism?

Stacey McCord/Sergei Tolmachev

Opportunities to Recruit

- Contact through DOE.

- Professional communications.

- Communication with 'inactive' Registrants.

- Publishing information in Homesteader's newsletter(s).

New Registrants in 2011 - 2012

- Case 0820 (whole-body) - through DOE.
- Case 0587 (partial-body) – 'reactivation'.

✓ *In contact with Savannah River Site Dosimetry Group to recruit potential Registrant with ^{238}Pu wound.*

Recommendation #5

- The goal of the Registries should continue to be expanded beyond solely radionuclide exposures by evaluating effects from chemicals, asbestos, beryllium, and smoking to give support to what the USTUR is doing.

Collaboration with Laval University

Prof. Dominic Larivière

Beryllium Detection by ICP-MS

ORIGINAL PAPER

Detection of beryllium in digested autopsy tissues by inductively coupled plasma mass spectrometry using a high matrix interface configuration

Dominic Larivière · Mélodie Tremblay ·
Myriam Durand-Jézéquel · Sergei Tolmachev

Limit of Detection = 3 pg g^{-1}

Table 3 Concentration of Be in digestate and wet tissues from several USTUR cases measured by ICP-MS—see attached tables

Tissue/organ description	Donation type	Time of exposure[a], y	Weight, g		^{9}Be concentration	
			Tissue	Solution	Solution, pg g^{-1}	Tissue, µg kg^{-1}
Case 0262						
Lung (L)	WB	8	433.5	400.1	227±7	0.210±0.006
LN Peribronchial			18.1	300.0	373±4	6.18±0.07
Femur (R) MS			155.8	600.0	4±1	0.015±0.003
Case 0425						
LN Hilar	WB	23	6.5	177.1	300±3	8.17±0.08
Femur (R) MS			95.4	507.2	19±1	0.101±0.005
Case 0706						
Lung (R)	WB	6	389.7	1075.6	1326±6	3.66±0.02
LN Pulmonary			2.1	325.0	382±2	59.11±0.3
Hair			14.8	232.8	18.4±0.4	0.289±0.005
Femur (R) MS			133.7	653.9	825±4	4.03±0.02
Case 0720						
Lung (R)	WB	23	606.1	500.0	126±2	0.104±0.002
LN Hilar (R)			4.0	427.3	969±16	103.5±1.7
LN Paratrechial			6.9	100.0	4928±54	71.4±0.8
Femur (R) MS			124.3	558.5	21±1	0.094±0.004
Case 0744						
Lung (R)	WB	3	60.3	166.2	9.0±0.1	0.025±0.001
LN Pulmonary			1.4	250.0	1427±17	255±3
Femur (R) MS			155.6	813.9	19±4	0.10±0.02
Case 0817						
Lung (R)	PB	38	313.0	997.2	25.6±1.5	0.082±0.005
Femur (R) MS			162.6	933.1	27.7±1.3	0.159±0.007
Case 1002						
Femur (R) MS	WB	27	146.7	600.0	8±1	0.033±0.004

R right side, *L* left side; *MS* middle shaft; *WB* whole body; *PB* partial body
[a] Self-reported years of exposure

Beryllium in Human Body

Beryllium Particulates and Their Detection
October 1-4, 2012 - Denver, CO

USTUR-0340-12A

Beryllium in a Human Body: USTUR 0706 Case Study

Sergei Y. Tolmachev[†], Stacey L. McComish[†] and Dominic Larivière[‡]

[†]U.S. Transuranium & Uranium Registries, Washington State University, Richland, USA
[‡]Department of Chemistry, Laval University, Quebec, Canada

In order to study the distribution and biokinetics of beryllium (Be) in a human body, Be concentrations were measured in autopsy tissue samples taken from a USTUR whole-body donor (Registrant). The Registrant self-reported chronic exposure to Be for 6 years during his work within the U.S. DOE complex. Beryllium was analyzed in 114 acid-digested tissue samples by inductively coupled plasma mass spectrometry (ICP-MS) using a high matrix interface configuration. With an ICP-MS detection limit of 0.003 μg kg^{-1} of solution, Be was measured in 100 digested tissue samples (acid solutions). The Be concentration in human tissues ranged from 0.007 (brain) to 50.8 (pulmonary lymph node) μg kg^{-1} of wet tissue. The Be concentrations in the lung, liver, and skeleton were found to be 3.65 ± 0.02, 10.2 ± 0.1 and 2.84 ± 0.01 μg kg^{-1}, respectively. It was found that Be in human body primarily accumulated in the skeleton, followed by deposition in the liver and lungs. The lung:liver:skeleton ratio of total Be content in the organs was estimated to be 1:4:7. Currently, the USTUR retains frozen tissues and acid solutions from additional 5 whole-body donors who were potentially exposed to Be in the workplace.

Collaboration with Tetra Tech Sciences

Dr. Herman Gibb

Mesothelioma Study

- A grant proposal titled: "Proportionate Mortality Ratio Analysis of the United States Transuranium and Uranium Registries" was submitted to DOE.

- The requested budget was $52,105. The grant was not funded.

- The work was still carried out by USTUR and Tetra Tech Sciences personnel.

- Results will be presented by Dr. Herman Gibb.

Recommendation #6

- A Data Quality Objective (DQO) document needs to be prepared to address how laboratories (outside and inside the Registries) will be required to report data as well as minimum quality assurance (QA) requirements and documentation.

Recommendation #7

- An emphasis for future direction should be on cellular and molecular radiobiology using fresh tissue samples to investigate gene expression or other effects in exposed workers.

Collaboration with PNNL

Mr. Chris Nielsen

Dr. William Morgan

Immunohistochemistry and Real-Time PCR Analysis

- Analysis - to determine genetic and inflammatory response pathways following plutonium exposure:

  ✓ Possible pathways - tissue injury, apoptosis, and gene expression modifications.

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

- RT-PCR - to quantify the expression of chemokine/cytokine regulatory genes thought to be involved in inflammation and carcinogenisis:

  ✓ BCL-2, CASP-3, FASL, IL4, IL8 and TGFß-1.

Immunohistochemistry of Lungs

A. Trichrome staining collogen fiber increased in sub-pleural regions.

B. Elastic staining for elastic fibers. Increases in elastic fiber in areas of visceral pleural and arterial walls.

C. TGFβ1 antibody staining. TGFβ1 signaling indicated in brown. TGFβ1 receptors are overexpressed under pleural pulmonary parenchyma, regions of interstitial fibrosis, and epithelium cells of AI.

D. TGFβ1 antibody staining in control human lung tissue. Negative expression of TGFβ1.
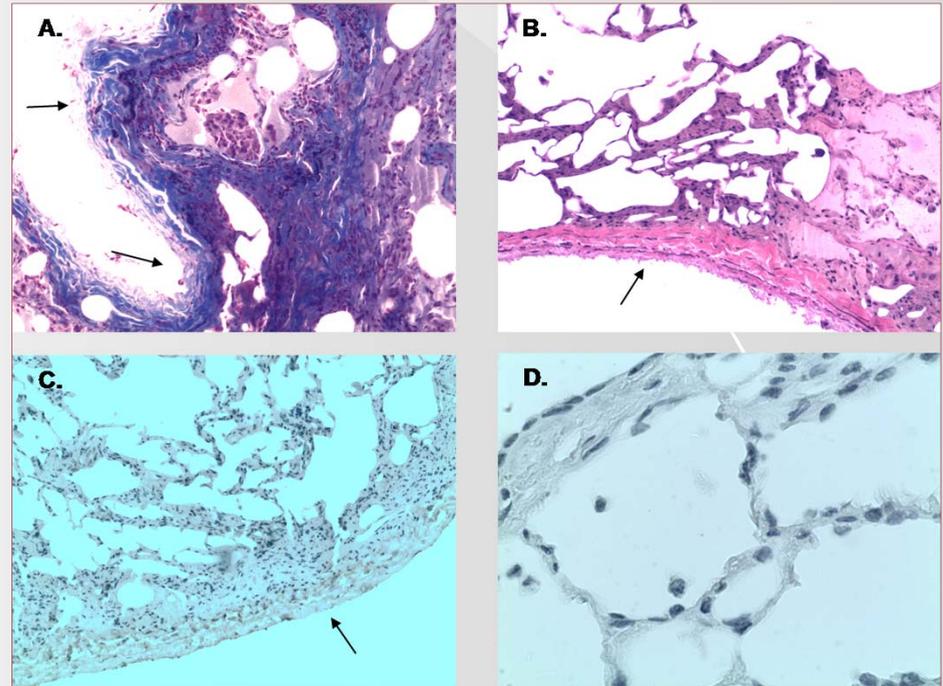
Quantification of Apoptosis and Cytokine Regulatory Genes
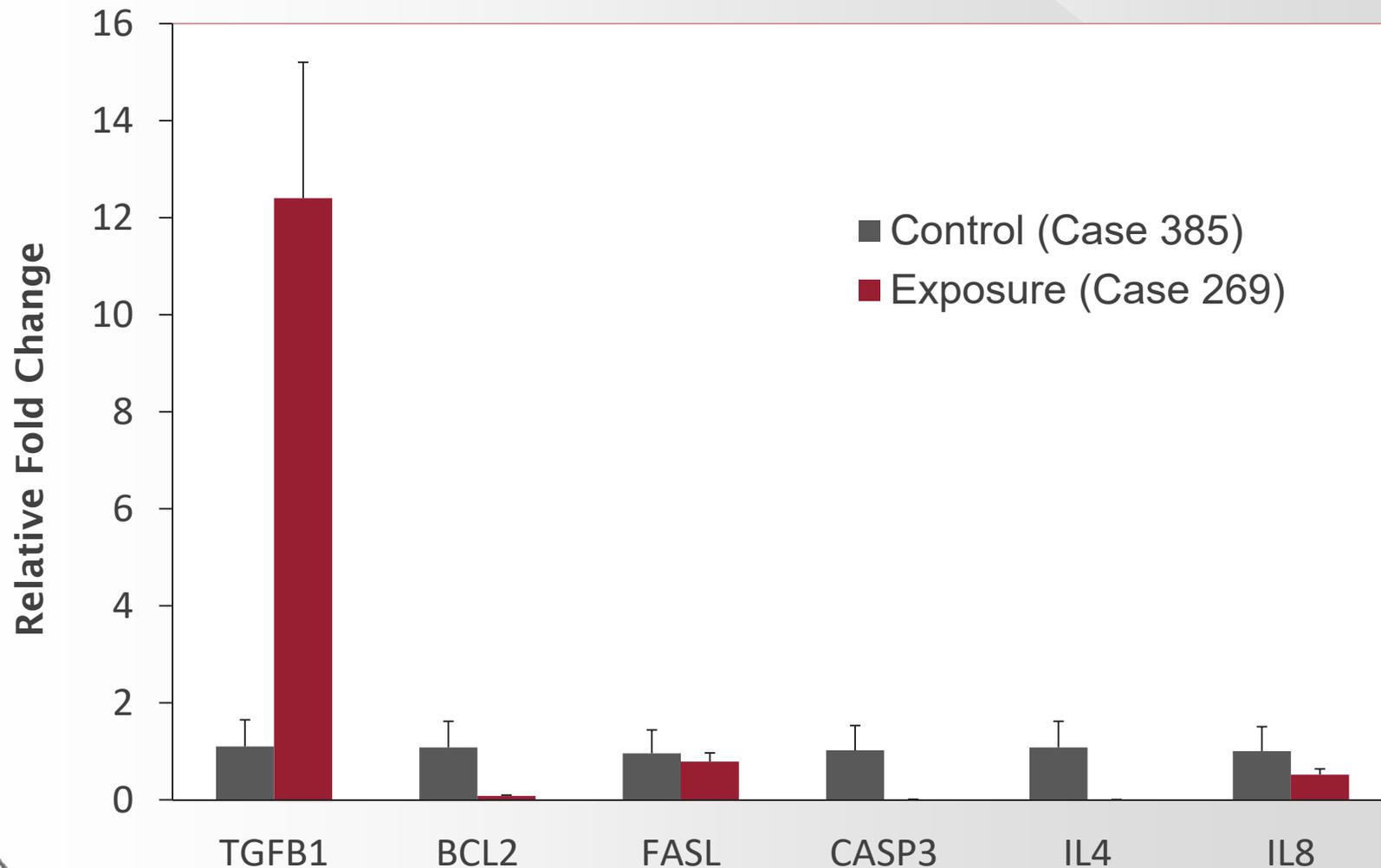
Recommendation #8

- DOE and WSU should continue working on a documented arrangement for long-term storage and ownership of samples. *Resolution of this matter would free the USTUR from concern over such issues.*

Who Owns the Materials?

Sergei Tolmachev/ Joey Zhou

Recommendation #9

- A plan for the long-term disposition of digested samples needs to be developed. This plan needs to consider future research needs and investigate options for disposal.

Full Inventory of NHRTR

Sergei Tolmachev/Stacey McCord

Storage Area: Acid Solutions

10,000+ dissolved tissue samples are available for future research

Repackaging of Acid Solutions

Re-packaging shelter

Inside the shelter

Corrugate plastic box

Absorbent mat

Paraffin wax-sealed bottles

Ready to be boxed

THEMIS Inventory and Storage

Electronic inventory of the acid samples

New storage area

Recommendation #10

- External dosimetry and other compiled data need to be maintained in the database.

Improvement of the Health Physics Database Interface

Stacey L. McCord

New Features – External Dose

New Features – Chemical Exposure

New Features – Asbestos Risk

2012 Activities Overview

From McCord to McComish

July 14, 2012, Tri-Cities
Our Congratulations to Stacey and Colin!

2012 Overview

- Management and Operation
- In-house Radiochemistry
- Intramural Research Project
- Extramural Collaborations
- Professional Activities/Services
- Presentations/Publications

Management Changes

- Department of Energy Changes
  - ✓ New 5-y grant cycle: April 2, 2013 – March 31 2017 (FY2013 – 2017). FY2012 was 6 months.
  - ✓ Starting in FY2013, granted funds are directly allocated from DOE HQ in DC to the WSU/COP instead of being routed through the DOE Consolidated Business Center in Cincinnati.

- College of Pharmacy Changes
  - ✓ Non-departmental research units are reporting through the College's Associate Dean of Graduate Education and Scholarships.

FY2013 – 2017 Grant Proposal

- New 5-y grant proposal to manage and operate the USTUR was submitted to DOE/HS-13.

- Period: April 1, 2012 – March 31, 2017 (FY2013 – 2017)

- Requested budget: $6,048,665.

- The FY2013 – 2017 requested budget was almost the same as that proposed for FY2010 – 2015: $6,016,096.

- Revised FY2013 – 2017 budget: $4,500,000

USTUR Organization Structure

College of Pharmacy
Gary Meadows
Associate Dean for Graduate Education & Scholarship

† Half time
‡ Part time (Contractor)

Scientific Advisory Committee

William Hayes, *Chair*
Robert Bistline, *Occupational Health*
Herman Gibb, *Epidemiology*
Roger McClellan, *Toxicology*
Kathryn Meier, *University/Ethics*
Richard Toohey, *Health Physics, Radiobiology*

USTUR Research Center
Director, Principal Investigator
Sergei Y. Tolmachev, PhD
Associate Research Professor

Margo Bedell-Parker, AAS
Fiscal Technician II

Manager Laboratory Operations/Research
Sergei Y. Tolmachev, PhD
Principal Radiochemist

Manager Logistic Operations/Research
Stacey L. McCord, MS
Associate in Research (Health Physics)
Maia V. Avtandilashvili, PhD
Research Associate (Health Physics)

USTUR Radiochemistry Laboratory
Fredrick L. Miller, BA
Laboratory Technician III
Elizabeth M. Thomas, BS
Laboratory Technician I

Julie Blumenkranz, AAS, †*Office Assistant II*

Minh Pham, BS, ‡*IT Support*
Mariya Tolmachova, MA ‡*Technical Editor*

Extramural Projects/Collaborations/Education
USTUR/NHRTR "Work for Others"
(Externally Funded)

National Human Radiobiological Tissue Repository
(NHRTR)
Florencio T. Martinez, ASCP, †*Med. Tech., Prosector*
Daniel J. Selove, MD †*Consultant Forensic Pathologist*

In-House Radiochemistry

- Personnel:
  - ✓ New Lab Tech I   Elizabeth M. Thomas
  - ✓ Total, FTE   2 (EMT, FLM)

- Activities:
  - ✓ Tissue sample ashing/digestion/dissolution (microwave/hot-block)
  - ✓ Optimization of electrodeposition procedure
  - ✓ Updating of SOPs
  - ✓ Upgrading α-spectrometry system
  - ✓ Actinide Analysis by ICP-MS at NAU

Improvements in Sample Preparation

RRMC
Radiobioassay & Radiochemical Measurements Conference

RRMC 2012
Fort Collins, Colorado
October 29 - November 2, 2012

USTUR-0339-12A

Application of Microwave-Assisted Techniques for Human Tissue Samples Preparation for Actinide Analysis

F. L. Miller, E. M. Thomas, S. Y. Tolmachev

United States Transuranium and Uranium Registries, College of Pharmacy, Washington State University, 1845 Terminal Drive 201, Richland, WA 99354, USA

This paper describes the application of microwave-assisted drying and digestion procedures using an Anton Paar Multiwave 3000 microwave system (MW3000), equipped with a Rotor DRY1 (RD1) for drying, and a Rotor 8 (R8) for digestion.

'Best Bone' Project
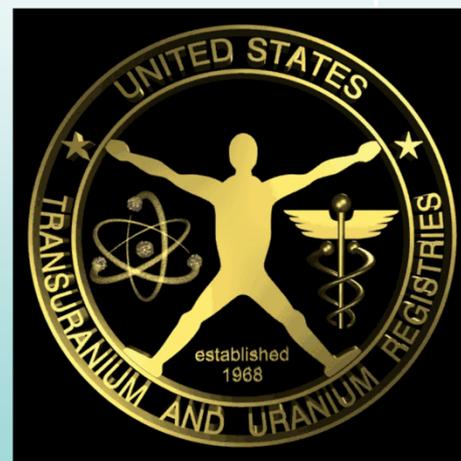
Goal – Task – Benefits

- Goal: *Precise estimation of skeleton content based on a limited number of bone analyses (partial-body donor, biopsy.)*

- Task: *Define the 'best bone' (or group of bones) for the estimation of total actinide content in the skeleton.*

- Benefits: *Reduction of uncertainties when estimation actinide content from partial-body analyses. Optimization (reduction) of number of bone samples in whole-body analysis.*

Whole- *vs* Partial-Body Analysis

Type	Skeleton	Number of Samples	
		Collected	Analyzed
Whole Body	Axial	110	62
	Limbs	70	50
Partial Body	Total	5 - 7†	5 - 7

† - ribs, clavicle, patella, sternum, vertebrae, femur (MS)

It Is Not a New Task

- McInroy *et al* (1985, HPJ): *analysis of half of the skeleton. Single case analysis.*

- Lynch *et al* (1988, J. Radiol. Prot.): *defined a group of bones as the best representative of the total skeletal content. Analysis based on 4 whole-body cases.*

- Filipy *et al* (2003,HPJ): *least squares regression analysis based on data from 8 whole-body cases.*

Methodology and Criteria

- Ratio = $\dfrac{\text{Individual Bone Concentration}}{\text{Total Skeletal Concentration}}$

- 'Best bone' = $\dfrac{C_{bone},\ Bq\ kg^{-1}}{C_{skeleton},\ Bq\ kg^{-1}}$ $\rightarrow 1 \pm (TPU \rightarrow min)$

Preliminary Results

Case	Age, y	Osteo-porotic	Primary Nuclide	Cbone /Cskeleton					Variability by Case
				Ribs	Stern.	Vert.	Patella	Clavic.	
0193	62		^{239}Pu	0.77	1.24	1.10	1.21	1.04	1.07±0.19
0208	69		^{239}Pu	0.74	1.29	0.62	1.24	1.00	0.98±0.30
0212	56	no	^{239}Pu	0.74	1.03	0.75	2.06	1.18	1.15±0.54
0213	68	no	^{239}Pu	0.86	1.18	1.06	1.42	0.87	1.08±0.23
0242	77		^{239}Pu	0.68	0.95	0.78	1.28	1.05	0.95±0.23
0259	55	no	^{238}Pu	0.64	0.65	0.63	1.66	0.81	0.88±0.44
0425	83	no	^{239}Pu	1.61	1.10	1.46	0.51	0.99	1.13±0.43
0679	72	yes	^{239}Pu	1.29	0.62	1.13	-----	1.04	1.02±0.29
0720	84	yes	^{239}Pu	0.70	0.71	1.16	0.91	1.22	0.94±0.24
0744	67	no	^{239}Pu	1.2	-----	0.98	1.27	1.00	1.11±0.14
0269	79	yes	^{239}Pu	0.91	1.01	1.01	1.16	1.05	1.03±0.09
0682	71	no	^{238}Pu	1.09	0.80	1.23	1.41	0.67	1.04±0.30
12	70±10	all	Pu	0.94±0.30	0.96±0.24	0.99±0.25	1.28±0.39	0.99±0.15	Variability by Bone

Work in Progress

- Revision of radiochemistry data (skeleton) for 16 whole body cases.

- Calculation of weighted-average actinide skeletal concentration, $C_{skeleton}$, Bq kg^{-1}.

- Calculation of ^{238,239}Pu activity ratio (R) $C_{bone}/C_{skeleton}$ for 6 bones: *rib, clavicle, patella, sternum, vertebrae, femur (MS)*.

- Calculation of 95% CI for R values.

European Radiation Dosimetry Group

- ^{241}Am Skull Measurements Intercomparison

- Coordinator:
  - ✓ Institute of Radiation Protection (Germany)

- Participants:
  - ✓ 13 in-vivo counting laboratories from 11 countries including USA, Canada and China.

- Phantoms used:
  - ✓ BfS Phantom (Germany) - artificial
  - ✓ SÚRO Phantom (Czech Republic) - artificial
  - ✓ USTUR Skull Phantom (USA) – 'natural'

In-Vivo Measurement Geometry
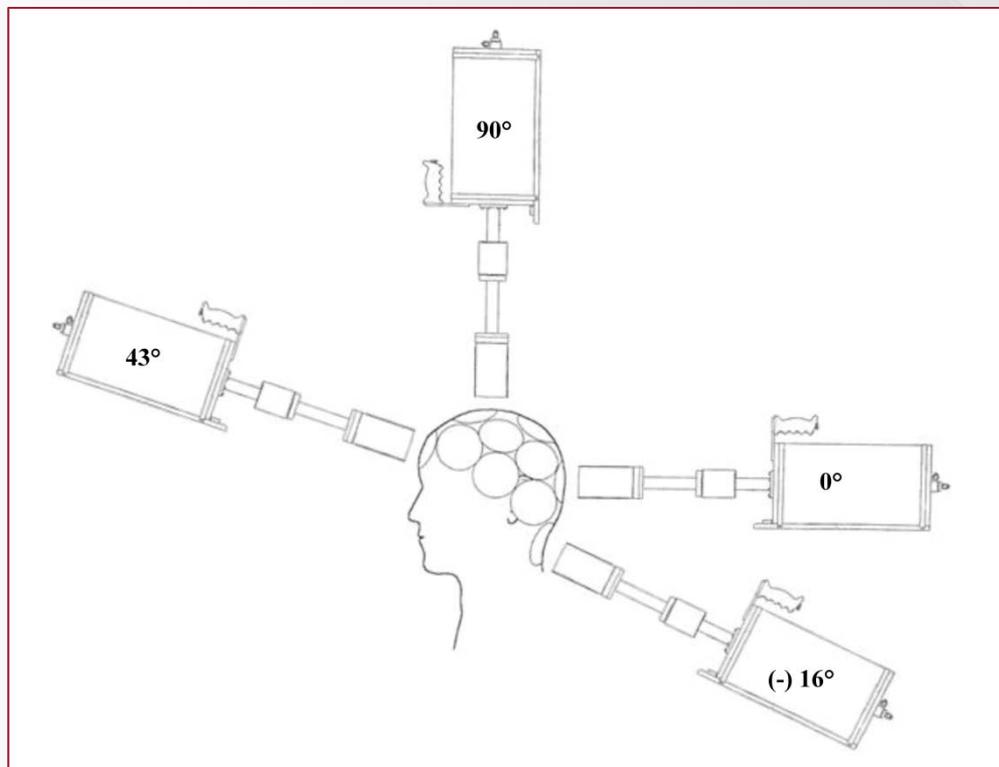
P. Nogueira (2012) "EURADOS ^{241}Am Skull Measurements Protocol"

Visit of Russian Scientist

- July 16-20, 2012, the USTUR hosted Elena Burikova , the Head of the Radiochemistry Group at the Southern Urals Biophysics Institute (SUBI, Ozyorsk, Russia).

- Requested by Mr. Barrett N. Fountos (DOE Russian Health Studies Program) and sponsored by the Joint Coordinating Committee for Radiation Effects Research (JCCRER) Project 2.4.

- Specific interest in microwave (MW) tissue digestion and rapid actinide separation with extraction chromatography on a vacuum-box system (VBS).

During the Visit

In the office

In the lab – separation on VBS

Informal gathering with the USTUR

In the lab - microwave digestion system

Professional Activities/Services

- European Dosimetry Group (EURADOS) WG7 on Internal Dosimetry, *Member*

- Japanese Journal of Health Physics, *Editorial Board Member*

- WSU Graduate Certificate Program in Radiation Protection, *Advisory Board Member*

- WSU MS/PhD Graduate Committee, *Member*

- Department of Chemistry, Laval University (Canada), *Adjunct Professor*

- Radiation Protection Journal, *Ad-hoc Reviewer*

Presentations 2011 - 2012

- Podium
  - ✓ Workshop on Sharing Data and Biomaterials from Radiation Science   1
  - ✓ 57th Annual Health Physics Society Meeting   2

- Poster
  - ✓ IRPA 13th International Congress   1
  - ✓ European Conference on X-Ray Spectrometry   1
  - ✓ 57th Annual Health Physics Society Meeting   2
  - ✓ COP Research & Scholarship Day   2

Publications 2011 - 2012

- Peer-reviewed Journals - Published
  - ✓ Health Physics (0.92)   2
  - ✓ Analytical Bioanalytical Chemistry (3.78)   1
  - ✓ Environmental Radioactivity (1.34)   1

- Peer-reviewed Journals - Accepted
  - ✓ Health Physics   1
  - ✓ Cancer Research (7.86)   1
  - ✓ Am. J. of Public Health (3.93)   1