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USTUR Studies: An Update



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*“Learning from Plutonium
and Uranium Workers”*

Outline

- Bound Fraction (HPA/PNNL/USTUR)
- 'Best' Bone (USTUR)

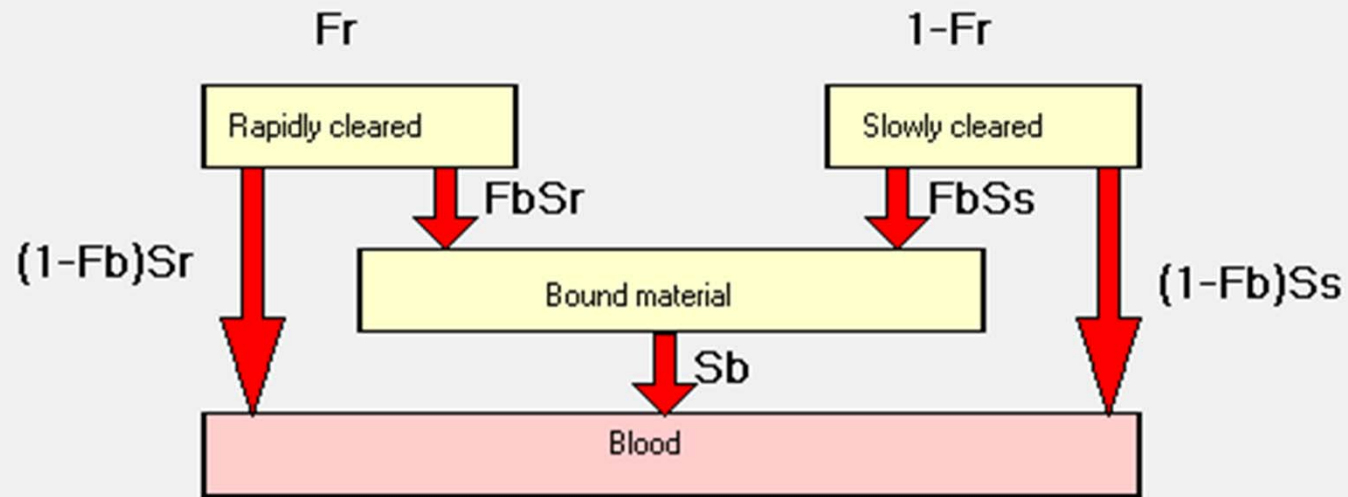


HPA/SOLO Project

- 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.



Testing HRTM Absorption Model



Fraction dissolved rapidly: Fr

Rapid rate: Sr

Slow rate: Ss

K_{Fb}

Fraction to bound state: Fb

Uptake rate from bound state: Sb

ICRP default assumption: $f_b = 0$



USTUR Whole Body Case 0269

- Acute inhalation of $^{239}\text{Pu}(\text{NO}_3)_4$ aerosol mist
- Chelated
- 31 y of follow-up measurements
- Died 38 y after intake
- $^{239,240}\text{Pu}$ activity in body organs, Bq
 - ✓ Lungs & LNTH 26.9
 - ✓ Liver 937.0
 - ✓ Skeleton 1197.0



Case 0269: Analysis of Intake

- IMBA Expert™ USDOE-Edition
- Exclude data affected by chelation
- Maximum likelihood fit to:
 - ✓ Urinary and fecal excretion data
 - ✓ Total Pu Lung/LNTH activity measured at DOD
- Results:
 - ✓ Intake ≈ 58 kBq
 - ✓ AMAD ≈ 2 μm
 - ✓ GI absorption fraction, $f_1 \approx 0.0005$
 - ✓ $f_r \approx 0.09$, $s_r \approx 110$ d⁻¹, $s_s \approx 0.02$ d⁻¹
 - ✓ **Bound fraction, $f_b \approx 8\%$**
 - ✓ $s_b \approx 0.0002$ d⁻¹

James et al (2007) RPD.



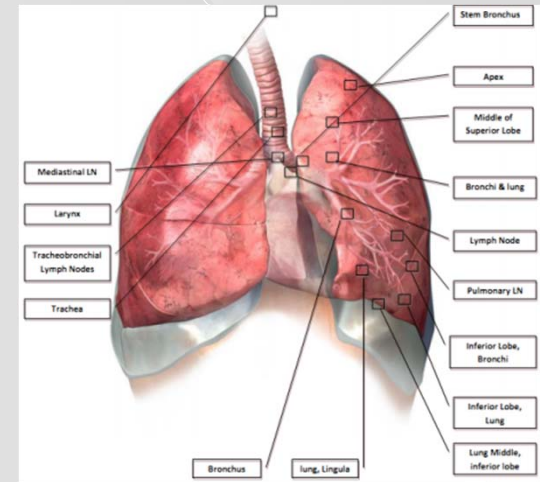
M.S. Project (WSU/PNNL)

Christopher E. Nielsen



Microdistribution and Long-Term Retention of $^{239}\text{Pu}(\text{NO}_3)_4$ in the Respiratory Tract of USTUR Registrant 0269

- Techniques:
 - ✓ Autoradiography
 - ✓ Immunohistochemistry
 - ✓ Real-time PCR analysis
- Summary:
 - ✓ Non-uniform distribution in lung
 - ✓ No observable ^{239}Pu associated with bronchi
 - ✓ Sub-pleural scarring and fibrosis of alveolar septa (~79%)
 - ✓ Plutonium and cigarette residues sequestered in fibrotic scar tissues



Nielsen et al (2012) Cancer Res.



USTUR Whole Body Case 0631

- Acute inhalation of $^{239}\text{Pu}(\text{NO}_3)_4$ in 1940s
- Worksite estimates
 - ✓ Intake: ~2.3 kBq
 - ✓ Body burden in 1969: ~1.46 kBq
- Not chelated
- Non-smoker
- Died from complications of Alzheimer disease
66 years post-intake



Ph.D. Project (WSU/PNNL)

Christopher E Nielsen



Scoping the Problem

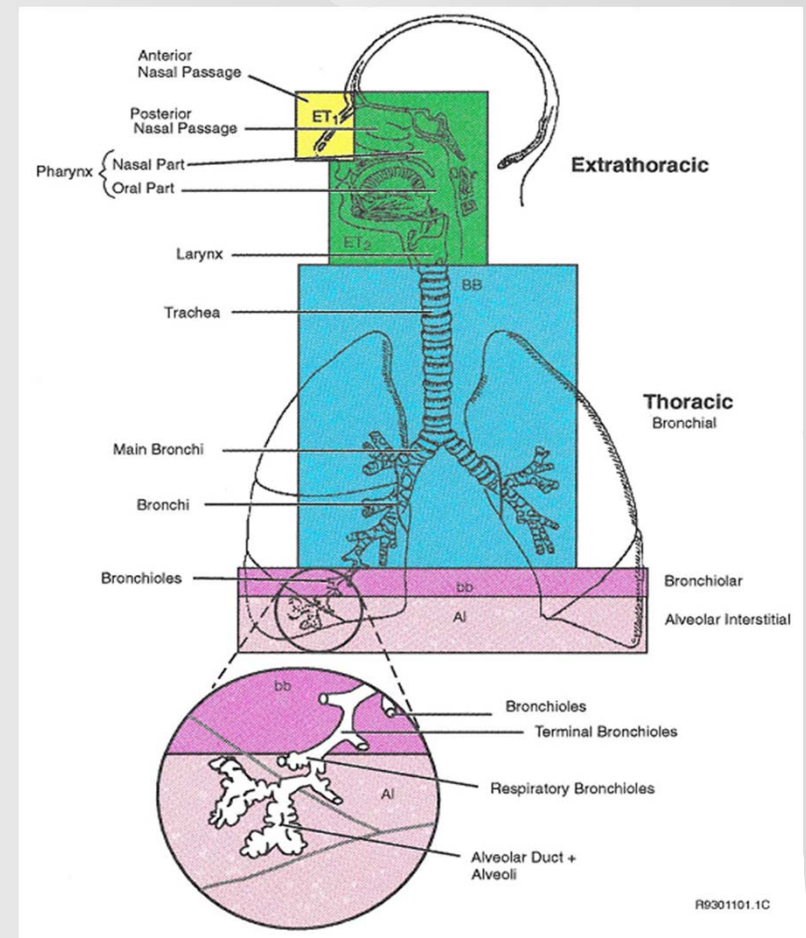
- Radiochemistry results on bone: 5.5 Bq kg^{-1}
- Estimated total skeletal content: 53.7 Bq
- Estimating intake using default ICRP assumptions
 - ✓ Absorption Type M
 - ✓ No bound fraction
- IMBA estimate of intake: $\sim 3.0 \text{ kBq}$
- Activity of Pu in lungs at DOD
 - ✓ $f_b=2\%:$ 21 mBq
 - ✓ $f_b=8\%:$ 85 mBq

Detectable!



Distribution and Quantification

- Autoradiography
- Immunohistochemistry
- Radiochemical analysis
 - ✓ BB
 - ✓ bb
 - ✓ AI
- Biokinetic modeling
- Uncertainty analysis



'Best Bone' Project

WASHINGTON STATE
UNIVERSITY
World Class. Face to Face.

Slide 1

European Radiation Dosimetry Group
(EURADOS) WG7 Plenary Meeting
Gent, Belgium, 14-16 September, 2011

From Single Bone Analysis to Total Skeleton Content

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*"Learning from Plutonium and
Uranium Workers"*



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.*



Methodology and Criteria

- Ratio = $\frac{\text{Individual Bone Concentration}}{\text{Total Skeletal Concentration}}$
- 'Best bone' = $\frac{C_{\text{bone}}, \text{ Bq kg}^{-1}}{C_{\text{skeleton}}, \text{ Bq kg}^{-1}} \rightarrow 1 \pm (\text{TPU} \rightarrow \text{min})$



Individual Bone Selection

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



Bone Group Selection

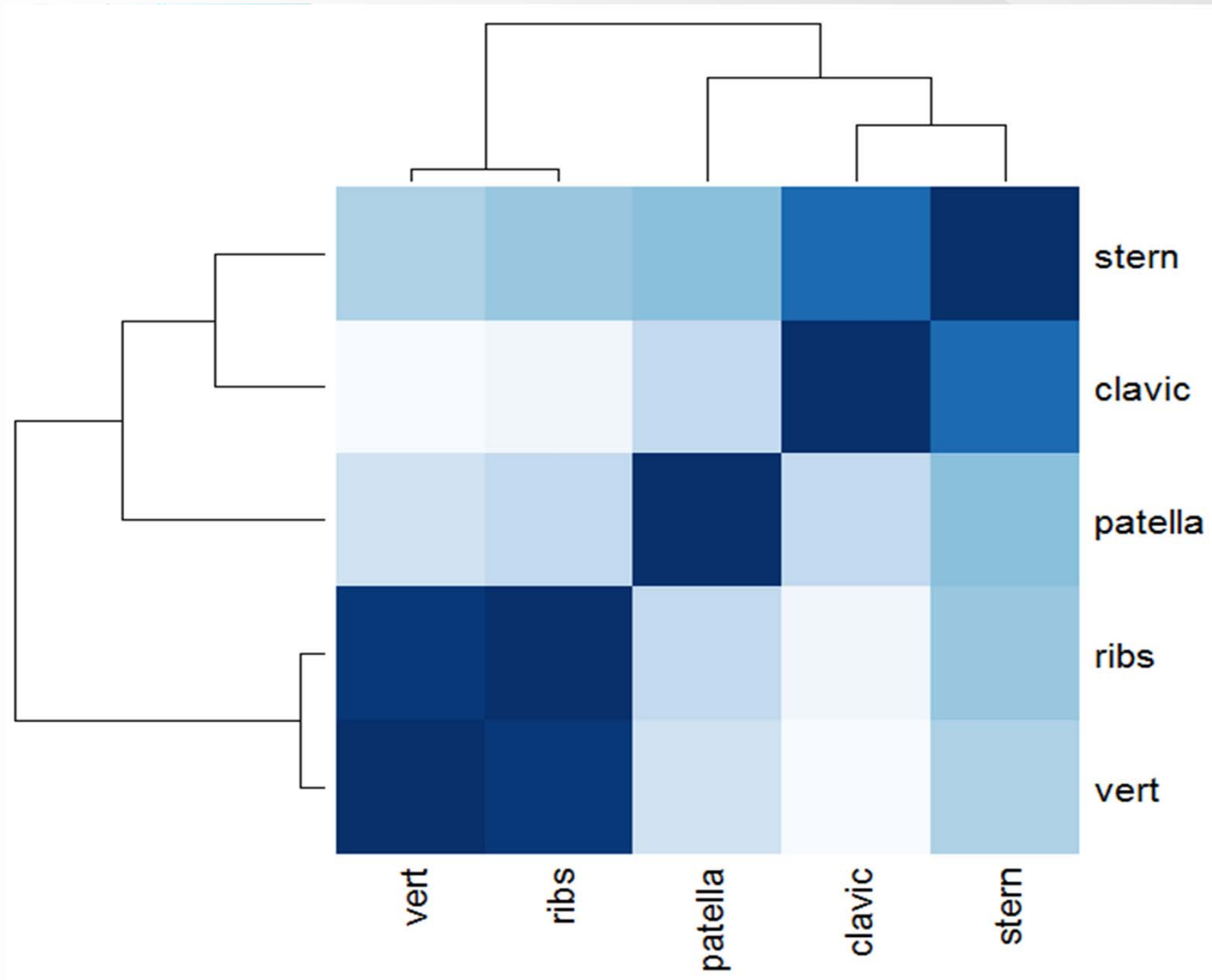
- Objective: *the best linear combination that gives least relative uncertainty*

$$\text{'Best Group'} = \frac{\sum A_i \times C_{bone,i}}{C_{skeleton}} \rightarrow 1 \pm (\text{UNC} \rightarrow \text{min})$$

- Approach: *glmulti* - automated model selection by minimizing Akaike Information Criterion
 $AIC = 2k - 2\ln(L)$, where **k** is the number of parameters of the model, **L** is the maximized likelihood
- Software: *R*



Correlation of Relative Measurements Between the Bones



'Best' Group

- Bones: vertebra, patella clavicle
- Coefficients:
 - ✓ vertebra – 0.340
 - ✓ patella – 0.226
 - ✓ clavicle – 0.373
- Activity Ratio:
 - ✓ $R_{\text{group}} = 0.99 \pm 0.08$
 - ✓ $R_{\text{clavicle}} = 0.99 \pm 0.15$



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) $C_{\text{bone}}/C_{\text{skeleton}}$ for 6 bones: *rib, clavicle, patella, sternum, vertebrae, femur (MS)*.
- Calculation of 95% CI for R values.

