66th Annual Meeting of the Health Physics Society
Phoenix, Arizona, July 25–29, 2021

Latent Bone Modeling Approach to Select Best Combination of Bones for Estimating Plutonium Activity Concentration in Human Skeleton

Sergei Y. Tolmachev[1], Maia Avtandilashvili[1], Joey Y Zhou[2]

[1] United States Transuranium and Uranium Registries, College of Pharmacy and Pharmaceutical Sciences, Washington State University

[2] Office of Domestic and International Health Studies, U.S. Department of Energy

College of Pharmacy and Pharmaceutical Sciences
Washington State University

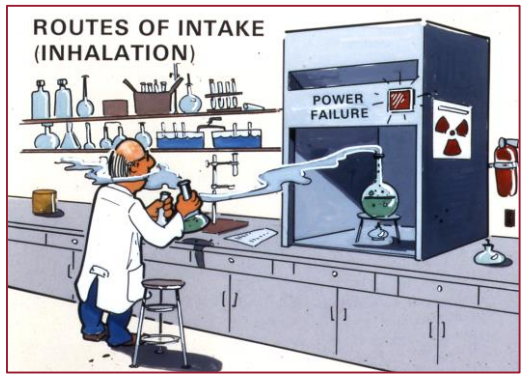
Office of Environment, Health, Safety and Security

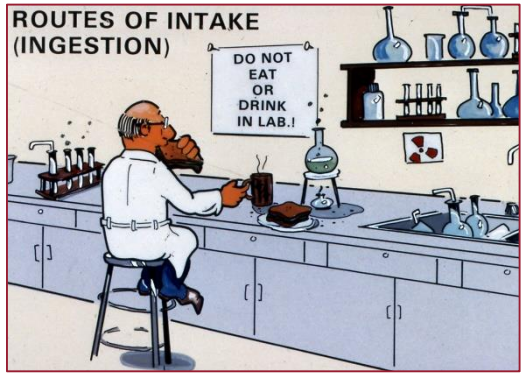
USTUR-0585-21A

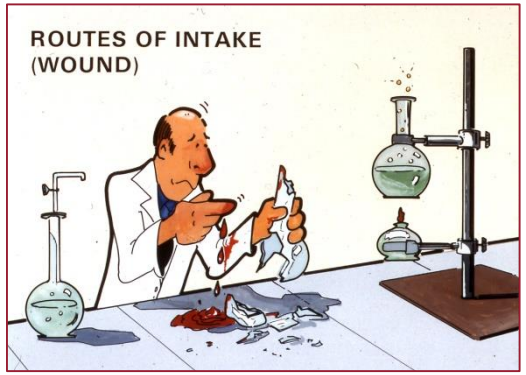
USTUR Bone Series

- WAM-C.4 08:45 Comparison of Two Methods to Estimate Skeletal Plutonium Concentration from Limited Sets of Bones
- WAM-C.5 09:00 Latent Bone Modeling Approach to Estimate Plutonium Activity Concentration in Human Skeleton
- WAM-C.6 09:15 Effect of Osteoporosis on Latent Bone Models to Estimate Plutonium Activity Concentration in Human Skeleton
- WAM-C.7 09:30 Uncertainty Evaluation of Skeleton Plutonium Activity Concentration Estimated from a Latent Bone Model
- WAM-C.8 09:45 Latent Bone Modeling Approach to Select Best Combination of Bones for Estimating Plutonium Activity Concentration in Human Skeleton

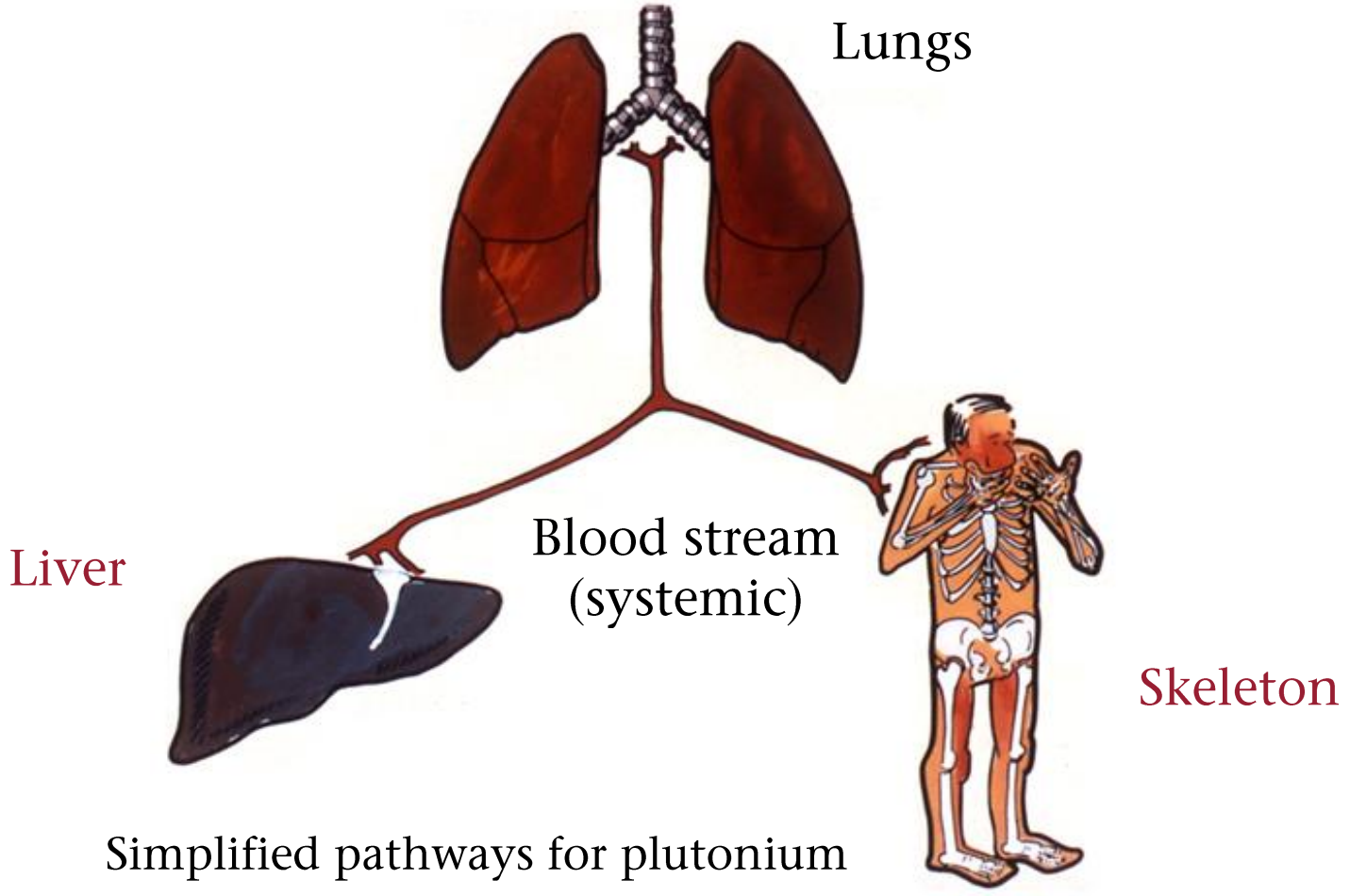
Why Plutonium in the Skeleton?







- Plutonium is a *bone-seeker*



Simplified pathways for plutonium

Total Plutonium in Skeleton: Analysis of Selected Bones

$$A(\text{Bq}) = W(\text{kg}) \times C_{\text{skel}}(\text{Bq kg}^{-1})$$

- Assuming W is known, $A \rightarrow f(C_{\text{skel}})$. How do we estimate C_{skel}?

Relationship between plutonium concentration of a bone (C_{bone}) or bone group and the total skeleton plutonium concentration (C_{skel}):

1. Arithmetic (or mass-weighted) average: $C_{\text{skel}} = (\sum_{i=1}^{n} C_{\text{bone},i})/n$
2. Single bone linear model ('best bone'): $C_{\text{skel}} = r \times C_{\text{bone}}$
3. Group bone linear model: $C_{\text{skel}} = r \times (\sum_{i=1}^{n} C_{\text{bone},i})/n$
4. Multiple linear model: $C_{\text{skel}} = a_1 \times C_{\text{bone,1}} + a_2 \times C_{\text{bone},2} + \ldots + a_n \times C_{\text{bone,n}}$

- Latent bone model (LBM): $C_{\text{lb1}} = a_1 \times C^*_{\text{bone,1}} + a_2 \times C^*_{\text{bone,2}} + \ldots + a_n \times C^*_{\text{bone,n}}$

where C_{lb} – latent bone concentration
$C^*_{\text{bone,n}}$ – n-bone standardized concentration

Total Plutonium in Skeleton: Analysis of Half Skeleton

…at the United States Transuranium and Uranium Registries (USTUR):

- Bone samples collected post-mortem from ***whole-body*** tissue donors – individuals with known uptake of plutonium (≥2 nCi)
- All bones from the *right side* of the skeleton and *odd* ribs and vertebrae are radiochemically analyzed (A_{right}); each C_{bone} is calculated. For *even* rib and/or vertebra, C_{bone} is estimated as average of adjacent *odd* ribs and/or vertebrae
- To reduce uncertainty in A_{skel} estimation – no assumption on skeleton bilateral symmetry is made: $A_{skel} \neq A_{right} \times 2$
- Activity in the *left side* (A_{left}) is estimated as a sum of (measured) C_{bone} × autopsy (measured) weight of a 'matching' bone
- Total activity, $A_{skel} = A_{right} + A_{left}$ and 'true' concentration, $C_{skel} = A_{skel}/W_{skel}$
- C_{skel} is a mass-weighted average of the entire skeleton

USTUR Motivation

- Estimate plutonium (and americium) activity in skeleton for 232 ***partial-body*** donors, where only 2 to 8 bone samples were collected at autopsy and radiochemically analyzed
- Optimize number of radiochemical analyses for C_{skel} estimation

Material and Methods

- Data from 19 whole-body tissue donors to the United States Transuranium and Uranium Registries (USTUR) were used
- Latent variable (bone) modeling was performed using Principal Component Regression (PCR)
- Relative standard error (RSE) was used as a criteria to compare latent bone models for C_{skel} estimation

$$RSE = \sqrt{\frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{(n-p-1)}}$$

- Reduction of RSE was investigated in terms of (i) bone structure type and (ii) number of analyzed bones
- Best bone (group of bones) selection was performed for 14 'healthy' cases using six bone samples, those are most commonly collected and radiochemically analyzed at the USTUR

USTUR Bone Dataset

Pu exposure

Whole-body

19 cases

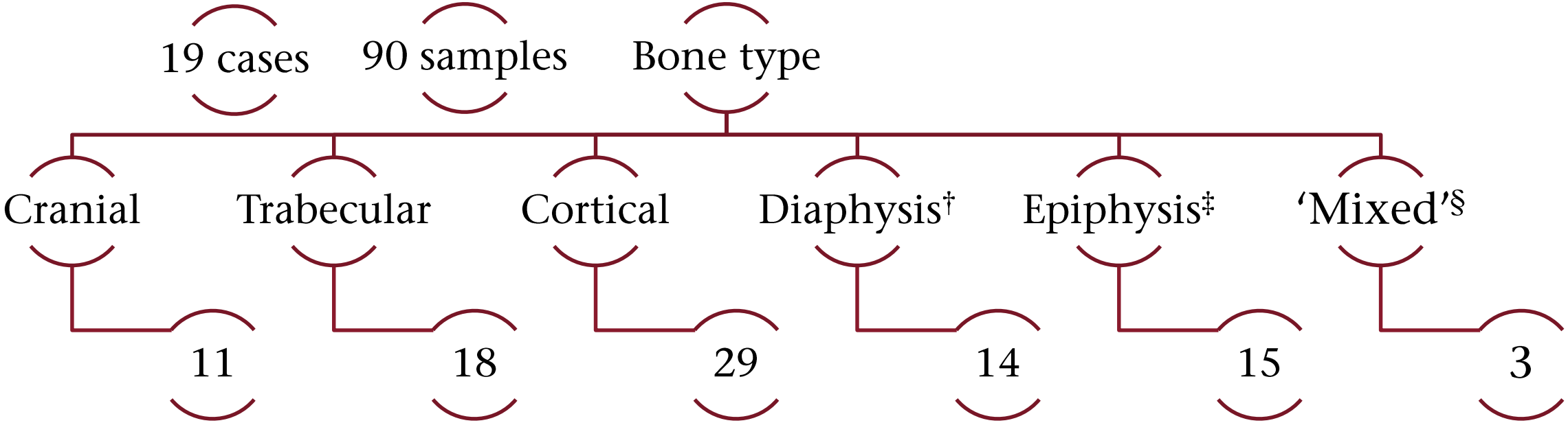
× 90 samples

'Healthy': 14

Osteoporotic: 5

- Age: 73.8 ± 10.4 (54 – 90) y
- A_{skel}: 9.0 – 1,183.8 Bq
- C_{skel}: 0.9 – 122.3 Bq kg^{-1}

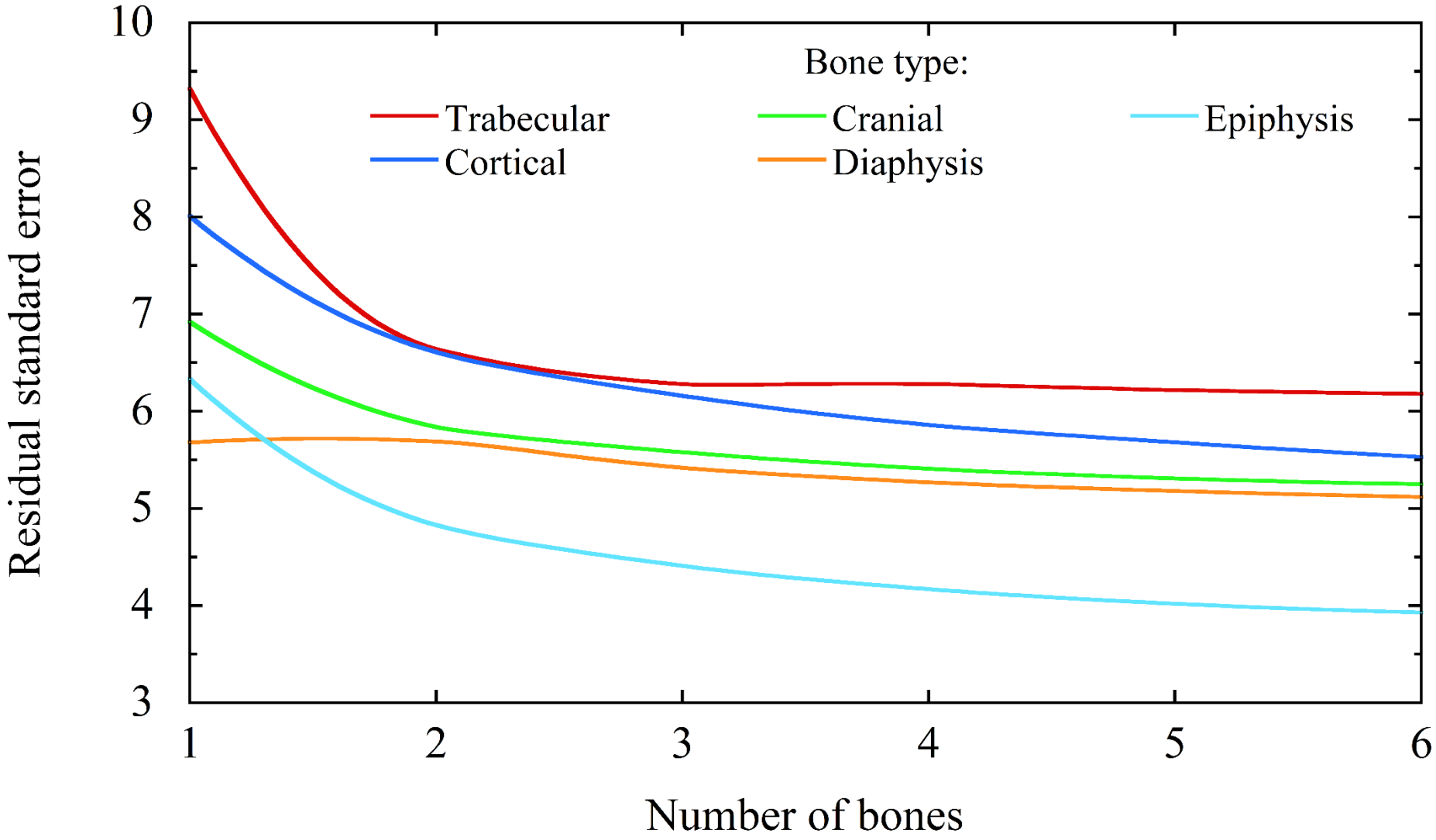
Dataset: Bone Type



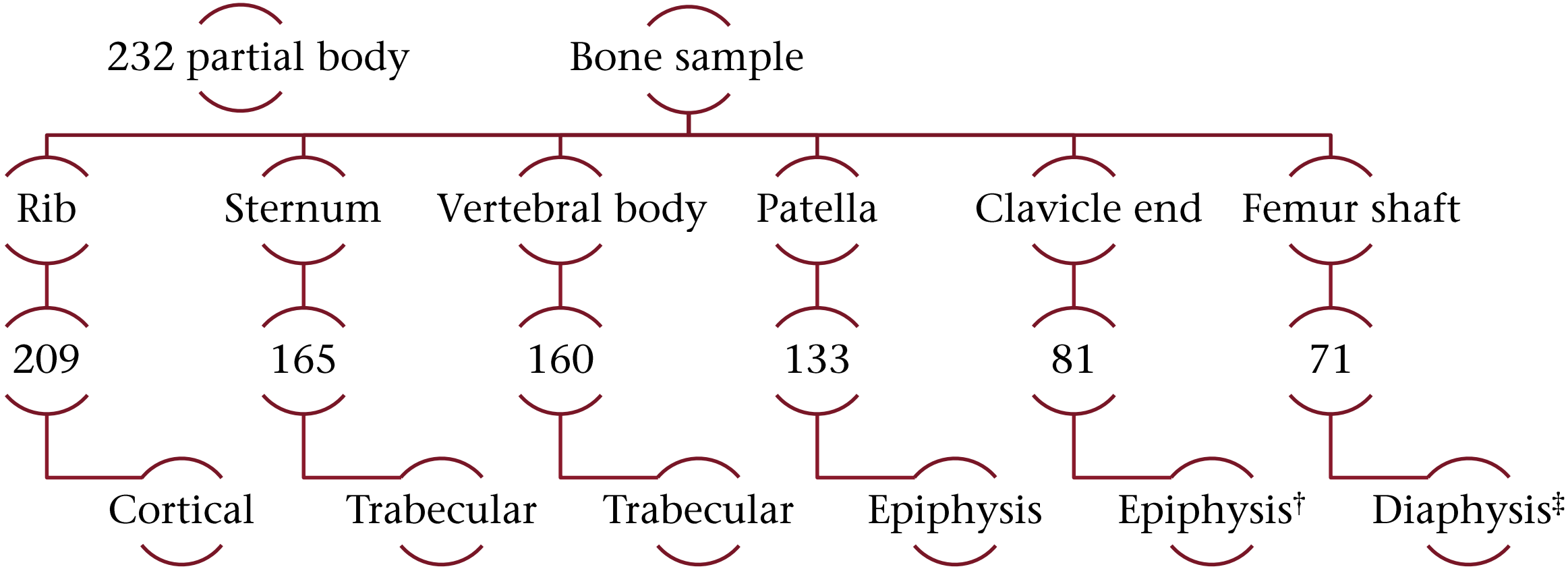
† - shafts of the long bones
‡ - ends of the long bones + patella
§ - cervical vertebra #1 whole, patella, hand and wrist, foot and ankle

Comparison of Bone-Type-Specific Latent Bone Models

– All 19 Cases –



Commonly Collected and Analyzed Bone Samples



† - ends of the long bones + patella
‡ - shafts of the long bones

LBM: 'Best' Bone Combinations

- LBMs were built for all possible combinations from 6 (n) commonly collected at autopsy and radiochemically analyzed bone samples

Number		*RSE* range	'Best' bone combination†: smallest *RSE*
bone, k	combination, $C(n, k)$		
2	15	1.096 to 4.888	patella, clavicle end
3	20	0.853 to 2.557	rib, patella, clavicle end
4	15	0.792 to 2.073	rib, patella, clavicle end, femur shaft
5	6	0.970 to 1.382	rib, sternum, patella, clavicle end, femur shaft

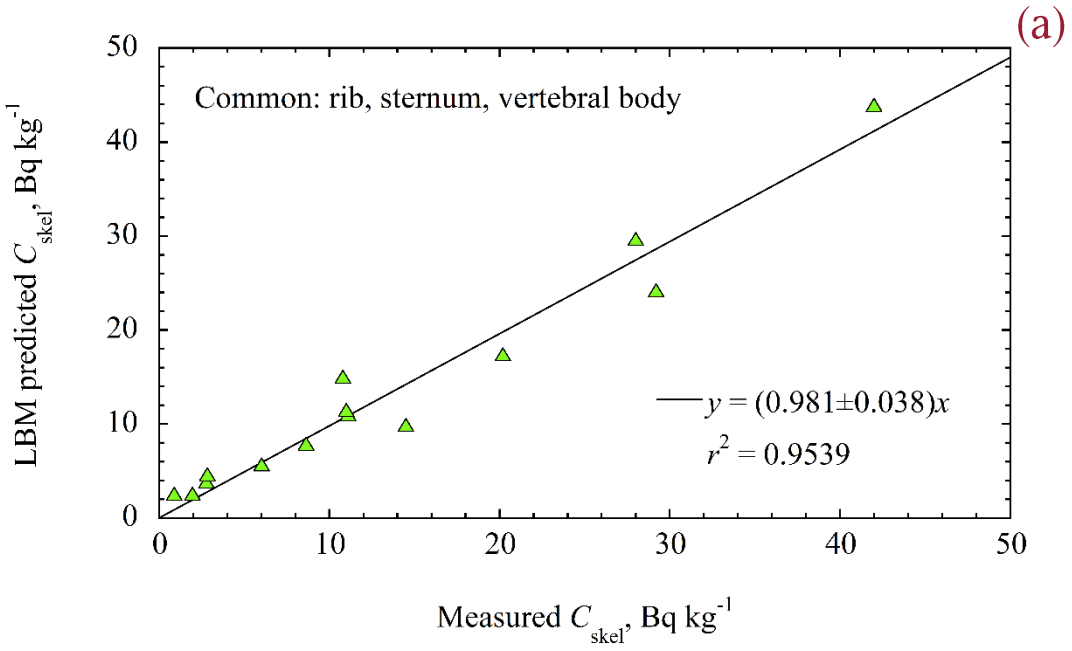
† - 'healthy' group

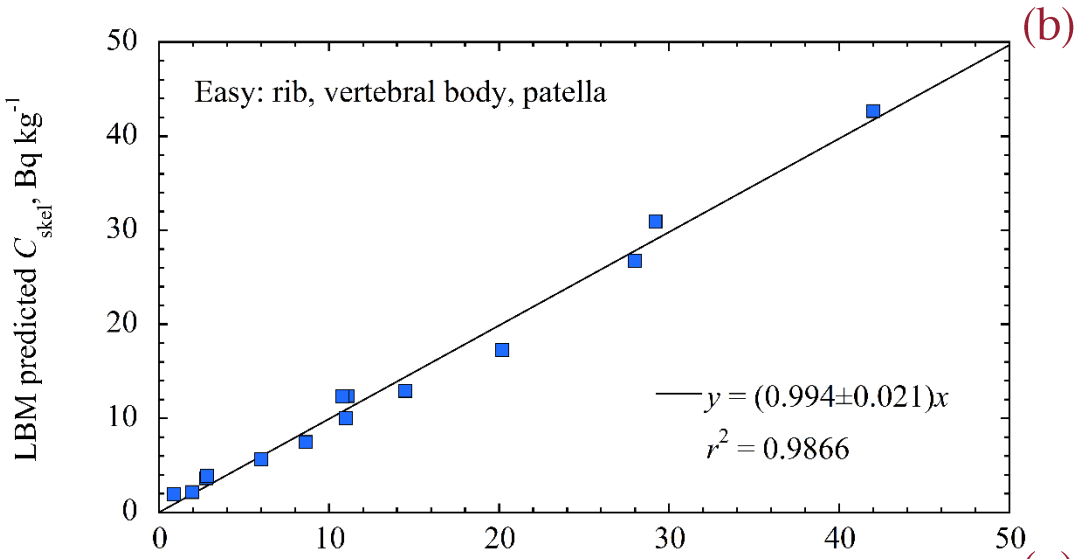
- Combination formula: $$C(n,k) = \frac{n!}{(n-k)!k!}$$

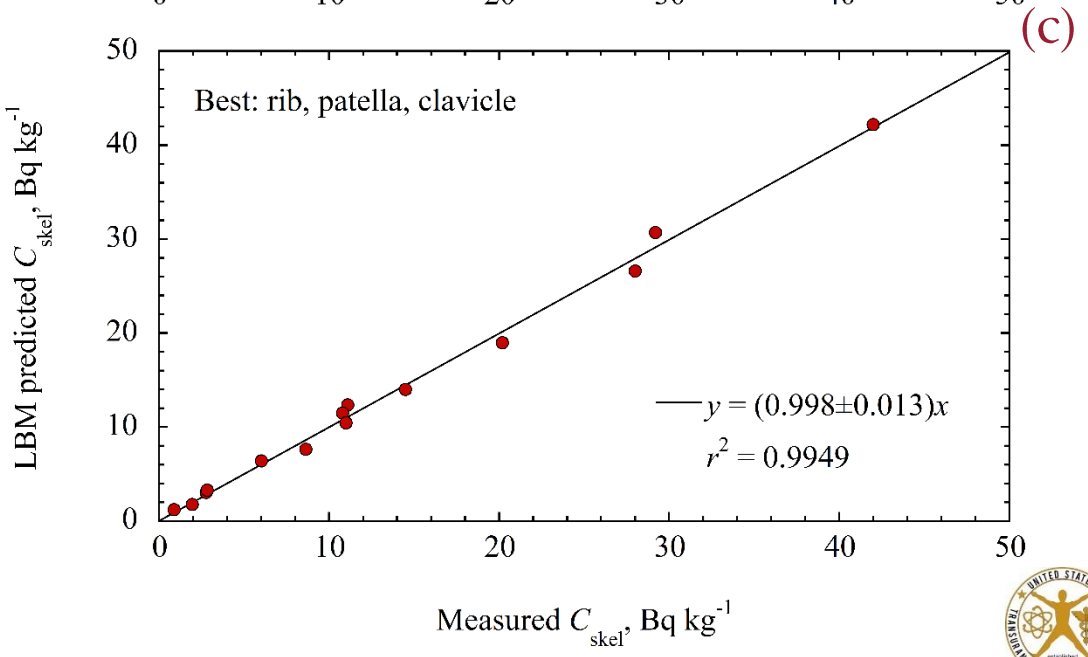
LBM: Comparison of Three-Bone Groups

a. Most common: *rib, sternum, vertebral body* (*RSE* = 2.557)†
b. Easy to collect: *rib, vertebral body, patella* (*RSE* = 1.522)†
c. Best bone: *rib, patella, clavicle* (*RSE* = 0.853)†

† - 'healthy' group (14)







Summary

- Plutonium concentration(s) in the ends of long bones (epiphysis, C_{bone}) most closely estimates plutonium concentration in the total skeleton (C_{skel}) compared to other: *cranial, trabecular, cortical, diaphysis,* and *mixed* bone types used in this study
- Best combinations of 2–5 bone samples were identified from a set of six: *rib, sternum, vertabral body, patella, clavicle end,* and *femur middle shaft* – most commonly collected and analyzed at the USTUR
- *Rib-patella-clavicle* combination was found to be the best for C_{skel} estimation within three-bone group (*RSE* = 0.853); while *rib-sternum-vertebral body* (most commonly collected) combination was the worth (*RSE* = 2.557)