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Latent Bone Modeling Approach to Estimate Plutonium Activity Concentration in Human Skeleton

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Background

- Plutonium is a bone seeker
- Most of USTUR Registrants had plutonium intakes
- For 19 whole-body cases, right side of the skeleton (up to 90 bones) was analyzed for plutonium
- For 266 partial-body cases, only a selected number of bones (2 to 8) were analyzed for plutonium
- A long time practical research question: *how to estimate skeletal plutonium concentration (C_{skel}) from a selected number of bones?*



Estimation of Plutonium in Human Skeleton from Selected Number of Bones

- Published USTUR's studies

- Lynch TP, Kathren RL, McInroy JF. Macrodistribution of plutonium and americium in four human skeletons. *Journal of Radiological Protection* 8 (2): 67–76 (1988)
- Hall CA. Estimation of skeletal deposition of plutonium and americium from a selected bone subset. MS Thesis, Washington State University (1997)
- Filipy RE, Alldredge JR, Hall CA, McInroy JF, Glover SE, Qualls S. Estimation of actinide skeletal content in humans based on bone samples collected at autopsy. *Health Physics* 84 (1): 34–45 (2003)
- Matthews T. Estimation of skeletal plutonium and americium content from bone samples taken at autopsy. MS Thesis, Idaho State University (2009)
- Tolmachev SY, Avtandilashvili M, Kathren RL. Estimation of total skeletal content of plutonium and ²⁴¹Am from analysis of a single bone. *Health Physics* 117 (2): 202–210 (2019)



Linear Regression Approach

- *Assumption:* Linear relationship between plutonium concentration of a bone (C_{bone}) or bone group and the total skeleton plutonium concentration ($C_{\text{bone}}/C_{\text{skel}}$)
 1. Single bone linear model ('best bone'): $C_{\text{skel}} = r \times C_{\text{bone}}$
 2. Group bone linear model: $C_{\text{skel}} = r \times (\sum_{i=1}^n C_{\text{bone}, i})/n$
 3. Multiple linear model: $C_{\text{skel}} = a_1 \times C_1 + a_2 \times C_2 + \dots + a_n \times C_n$



Limitations of Multiple Linear Regression (MLR) Approach

- A previous USTUR study using MLR approach
 - Filipy RE, Alldredge JR, Hall CA, McInroy JF, Glover SE, Qualls S. Estimation of actinide skeletal content in humans based on bone samples collected at autopsy. Health Physics 84 (1): 34–45 (2003)

Eight (8) whole-body cases were analyzed at the time

- General limitations:
 - Multicollinearity (highly correlated independent variables)
 - Sample size (case-to-variable ratio)
 - Result in imprecise and unstable estimates of the model parameters



Multicollinearity: Correlation Matrix

- Commonly collected at autopsy bone samples: vertebral body, rib, sternum, patella, femur middle shaft (MS), and clavicle

Bone [†]	Vertebra	Rib	Sternum	Patella	Femur MS	Clavicle
Vertebra	1.00					
Rib	0.98	1.00				
Sternum	0.98	0.96	1.00			
Patella	0.95	0.94	0.94	1.00		
Femur MS	0.93	0.90	0.96	0.97	1.00	
Clavicle	0.97	0.96	0.99	0.96	0.98	1.00

[†] data from 19 whole-body tissue donations



Principal Component Regression (PCR)

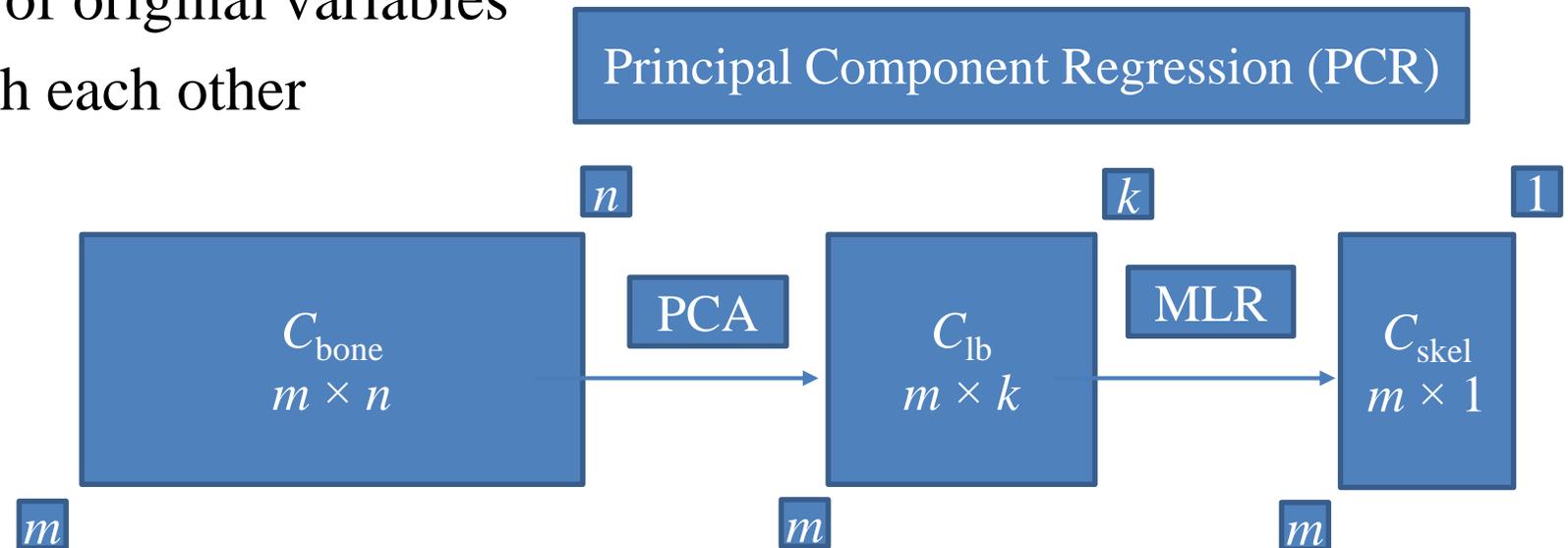
- A regression analysis technique that is based on principal component analysis (PCA)
- In PCR, instead of regressing the dependent variable on the independent variables directly, the principal components of independent variables are used as regressors
- Typically only the first few the principal components used for regression



Principal Component Analysis (PCA)

A statistical technique to reduce the dimensionality of a dataset by finding fewer principal components or latent bones (LB) that are:

1. Preserving maximum possible ‘variability/information’ in original data
2. Linear functions of original variables
3. Uncorrelated with each other





Latent Bone Modeling: Example (I)

- Three (3) most frequently collected bones: rib, sternum, and vertebral body

Bone [†]	²³⁹ Pu concentration Bq kg ⁻¹ wet																			
Rib	6.1	14.2	23.2	60.4	16.6	3.0	4.8	7.6	15.3	14.0	2.1	30.3	35.4	1.4	106.4	44.5	13.7	82.2	6.4	
Sternum	4.7	5.7	17.1	44.8	16.1	2.9	3.2	7.9	7.9	10.5	1.1	22.6	32.7	1.7	117.7	45.8	3.4	52.4	5.4	
Vertebra	6.0	19.0	21.5	58.8	19.5	3.9	4.9	9.6	10.2	14.7	1.8	35.8	40.4	1.7	118.2	58.6	11.9	71.7	9.2	

[†] data from 19 whole-body tissue donations



Latent Bone Modeling: Example (II)

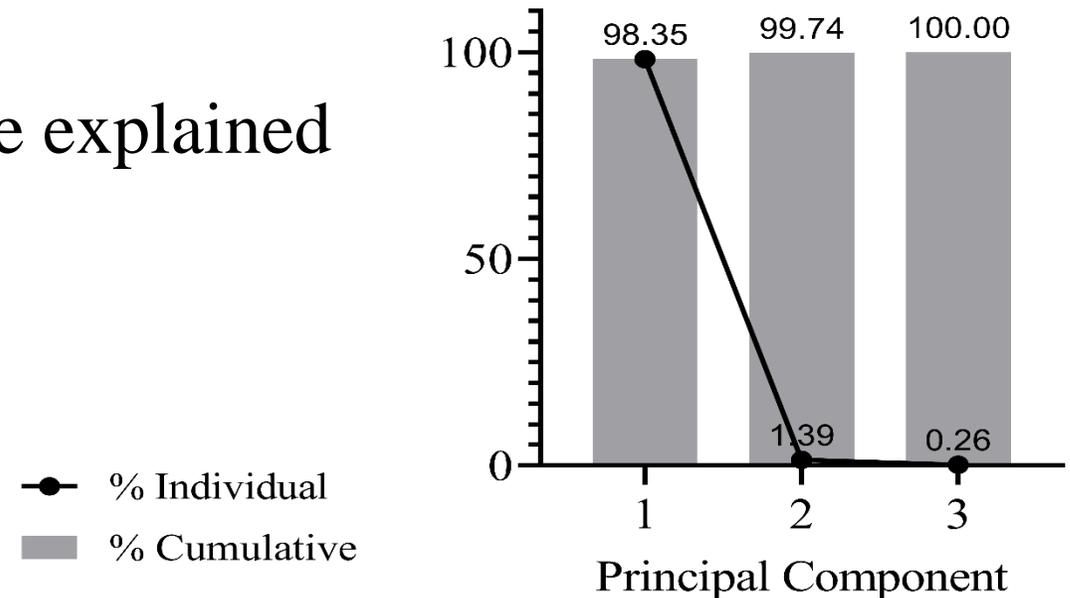
- *Principal Component Analysis* -

$$C_{lb1} = 0.5759 \times C_{rib}^s + 0.5755 \times C_{sternum}^s + 0.5807 \times C_{vert}^s$$

– C_{lb1} : the first *latent bone* concentration

– C_{rib}^s , $C_{sternum}^s$, C_{vert}^s : standardized individual bone concentrations

- In this case, the first latent bone alone explained 98.4% of total variance





Latent Bone Modeling: Example (III)

- *Principal Components Regression* -

- Principal Component Analysis followed by simple linear regression

	^{239}Pu concentration Bq kg ⁻¹ wet																			
C_{lb1}	-1.13	-0.7	-0.24	1.77	-0.43	-1.27	-1.2	-0.96	-0.8	-0.69	-1.36	0.28	0.67	-1.36	5.28	1.47	-0.89	2.6	-1.05	
C_{skel}	6.0	11.1	20.2	42.0	10.8	2.8	2.8	8.6	14.5	11.0	2.0	29.2	28.0	0.9	122.0	65.3	12.2	76.8	9.0	

† data from 19 whole-body tissue donations



An Example of Latent Bone Modeling (IV)

Principal components regression (PCR)

- Estimated total skeleton concentration, $C_{\text{skel}} = 18.0 \times C_{\text{lb1}} + 25.0$
- Model statistics
 - Residual standard error (RSE) = 5.995 ($N_{\text{DF}} = 17$)
 - Adjusted $R^2 = 0.9639$

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



LBM: Selection of Best Combination of Bones (I)

Case†	²³⁹ Pu concentration Bq kg ⁻¹ wet						
	Skeleton	Vertebra	Rib	Sternum	Patella	Femur MS	Clavicle
1	6.02	5.97	6.11	4.72	4.84	5.34	7.50
2	11.10	18.95	14.22	5.65	8.76	8.63	13.97
3	20.20	21.48	23.24	17.09	14.30	17.81	20.15
4	42.00	58.81	60.40	44.79	33.10	28.23	38.57
5	10.80	19.54	16.62	16.14	6.34	12.02	12.31
6	2.79	3.85	3.01	2.87	2.88	2.30	2.68
7	2.84	4.93	4.84	3.20	1.43	2.36	3.32
8	8.64	9.60	7.63	7.90	6.27	7.59	8.44
9	14.50	10.21	15.25	7.87	16.10	17.66	11.06
10	11.00	14.72	13.96	10.53	5.26	9.45	12.30
11	1.96	1.76	2.06	1.12	0.77	1.91	1.85
12	29.20	35.76	30.25	22.58	38.60	36.37	24.23
13	28.00	40.37	35.35	32.66	18.90	21.54	27.63
14	0.90	1.73	1.37	1.71	0.71	0.48	0.97

† - data from non-osteoporotic individuals



LBM: Selection of Best Combination of Bones (II)

- LBM models were built for all possible combinations from 6 (n) commonly collected at autopsy bone samples

Number (k) of bones [†]	Number of combinations	RSE range	Best bone combination
2	15	1.096 to 4.888	Patella, Clavicle
3	20	0.853 to 2.557	Patella, Clavicle, Rib
4	15	0.792 to 2.073	Patella, Clavicle, Rib, Femur MS
5	6	0.970 to 1.382	Patella, Clavicle, Rib, Femur MS, Sternum

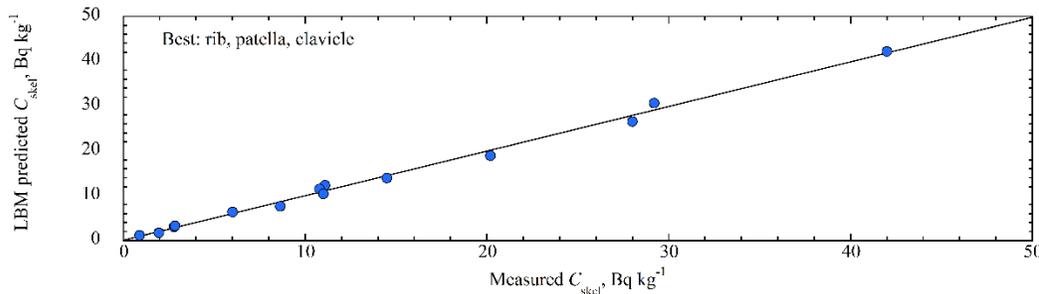
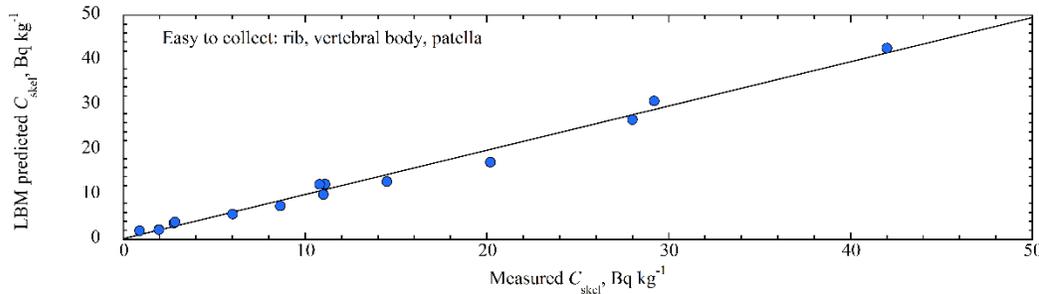
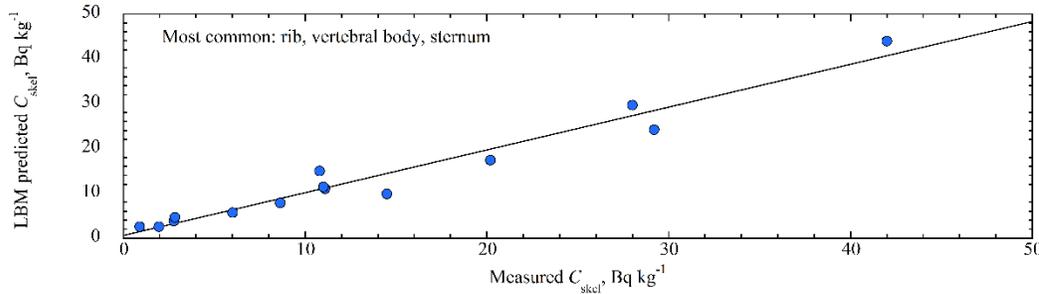
[†] - data from 14 non-osteoporotic individuals

Combination Formula:

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



LBM: Comparison of Three-Bone Combinations



- Most common: *rib, vertebral body, sternum* (RSE = 2.557)[†]

- Easy to collect: *rib, vertebral body, patella* (RSE = 1.522)[†]

- Best: *rib, patella, clavicle* (RSE = 0.853)[†]

[†] - data from 14 non-osteoporotic individuals



Activity Concentration and More...

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

- Zhou JY, Avtandilashvili M, Tolmachev SY. Latent bone modeling approach to estimate plutonium activity concentration in human skeleton
- Tolmachev SY, Avtandilashvili M, Zhou JY. Effect of osteoporosis on latent bone models to estimate plutonium activity concentration in human skeleton
- Tolmachev SY, Avtandilashvili M, Zhou JY. Latent bone modeling approach to select best combination of bones for estimating plutonium activity concentration in human skeleton
- Zhou JY, Avtandilashvili M, Tolmachev SY. Uncertainty evaluation of skeleton plutonium activity concentration estimated from a latent bone model