

NCI Workshop on Dosimetry of Systemic Radiopharmaceutical Therapy (SRT): Pb-212 Research at the University of Iowa

Michael Schultz, Dave Bushnell, Yusuf
Menda, Stephen Graves, Mark Madsen

Ongoing $^{212}\text{Pb}/^{203}\text{Pb}$ Theranostic Projects at Iowa

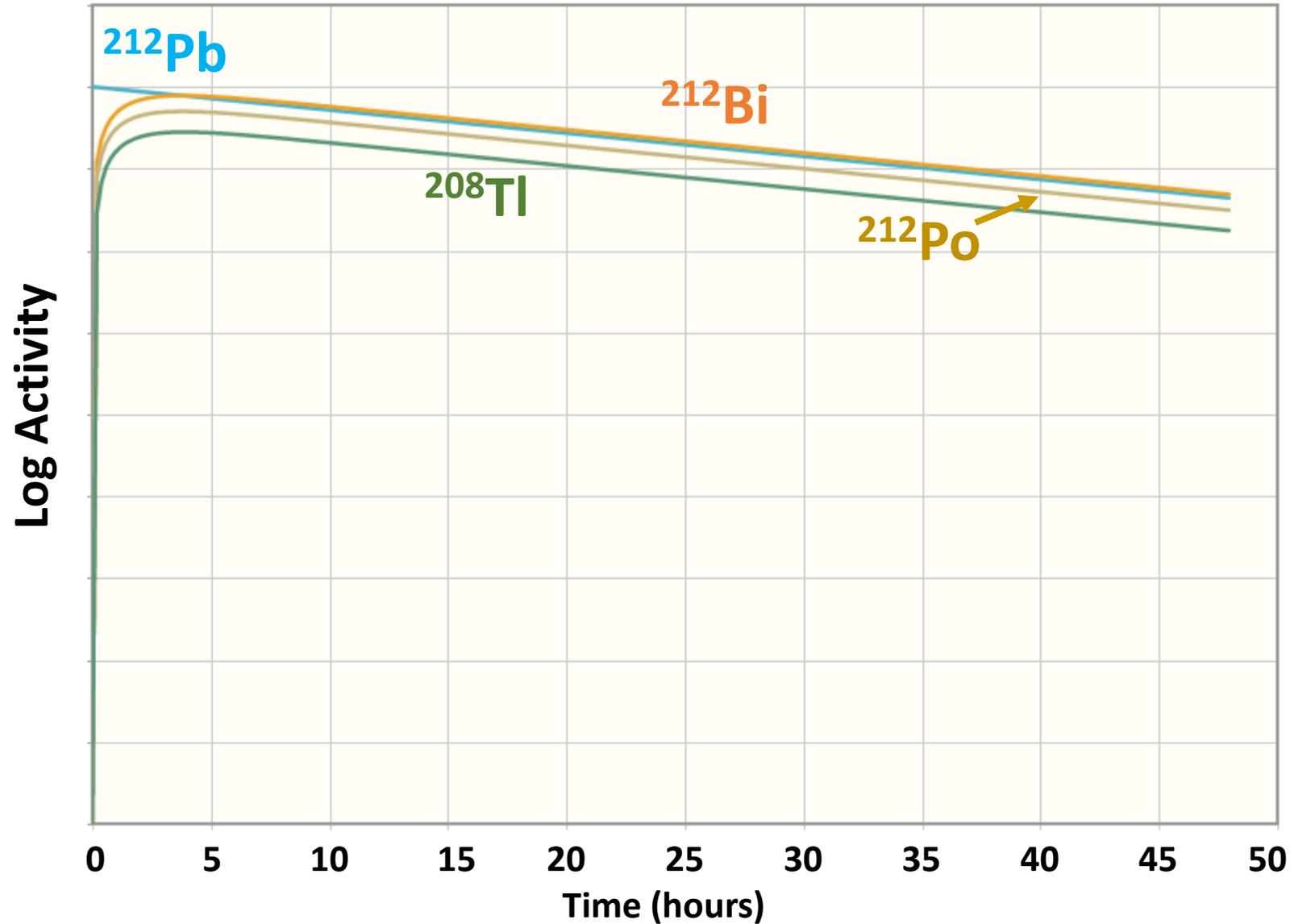
Projects in clinical development

- Neuroendocrine tumors
- Prostate Cancer
- Metastatic Melanoma
- Pediatric Brain Tumors

^{203}Pb as an Imaging Surrogate for ^{212}Pb

- The downstream daughters of ^{212}Pb , in particular ^{208}Tl have high energy gamma rays (2.6 MeV) that make imaging challenging.
- ^{203}Pb is a better imaging alternative
 - Halflife: 52 hours
 - Gamma Ray Emissions
 - 279 keV (81%)
 - 401 keV (3.4%)
 - 681 keV (0.75%)
- Assuming comparable labeling, the activity of a ^{212}Pb agent at a given time point is equal to the activity measured for the ^{203}Pb agent multiplied by the ratio of the decay factors:
 ^{212}Pb activity at time T = ^{203}Pb activity at time T x $\exp(-0.693 \cdot T/10.6) / \exp(-0.693 \cdot T/52)$

^{212}Pb Decay Series Radionuclide Equilibrium



Single Time Point Derivation



^{212}Pb DOTATOC Simulation Parameters

k2: **0.075** based on 10.6 h physical half life and 75 hour biological half time in the kidneys.

c: **1** based on considerations from ^{90}Y DOTATOC experience

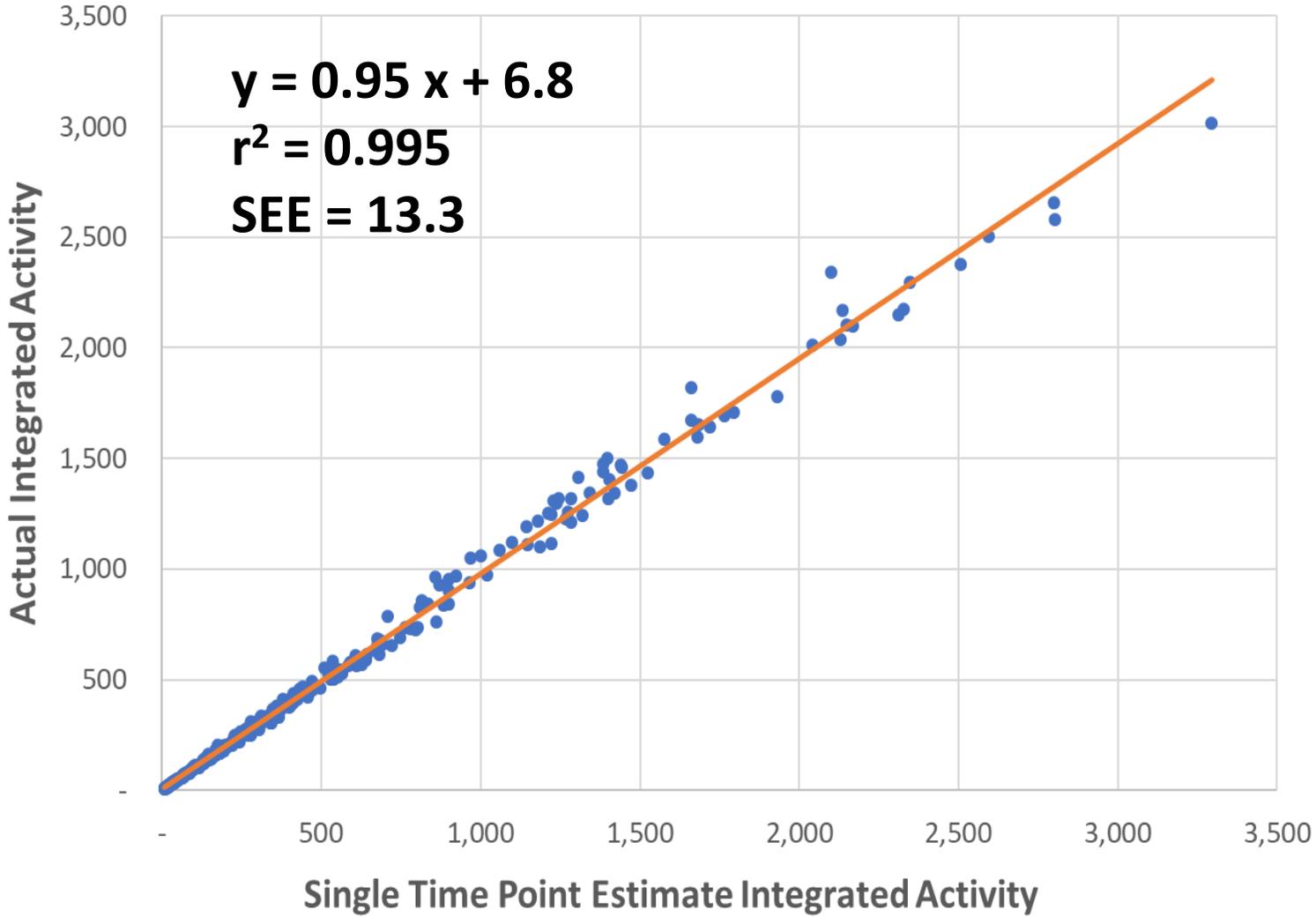
a: **3** based on 10.6 h physical half life and 4 hour biological half time in the kidneys.

Integrated Activity Comparison

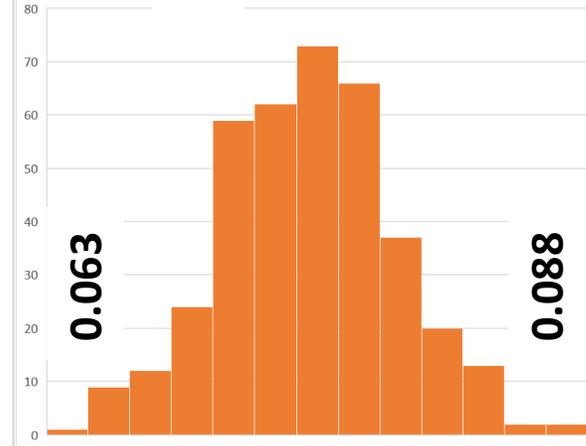
$$y = 0.95x + 6.8$$

$$r^2 = 0.995$$

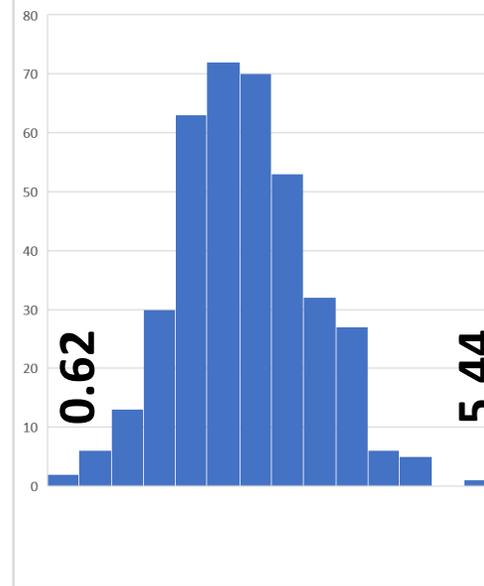
$$SEE = 13.3$$



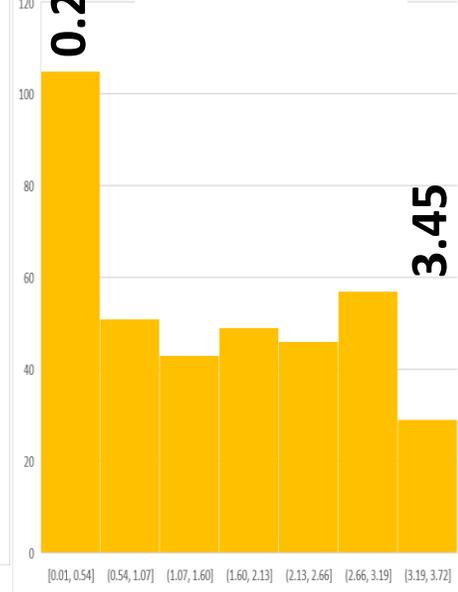
k_2 Histogram



$a = k_1/k_2$



$c = A_1/A_2$



Summary

- The single time point dose approach appears to work well for short-lived radionuclide labels such as ^{212}Pb where the physical half life constrains the clearance rate constants.
- The optimal sample time appears to be approximately 6 hours for ^{212}Pb DOTATOC which is close to the mean life of the fast component.
- If ^{203}Pb labeled agents sufficiently mimic ^{212}Pb agents, then the ^{212}Pb activity at the sample time can be directly calculated by multiplying the ^{203}Pb activity by the ratios of the decay factors (~ 0.76 at $T = 6$ hours).