

Case Studies in Brain Dosimetry for Internal Emitters

Is More Biokinetic Detail Needed for Epidemiology?

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ICRP's biokinetic treatment of systemic (absorbed) radionuclides

- Systemic biokinetic models generally are element specific
- Typically the systemic biokinetic model for an element explicitly depicts only a small number of dosimetrically important tissues
- Remaining tissues and fluids are aggregated into a pool called *Other tissue*
- Activity in *Other tissue* is assumed to be uniformly distributed

ICRP treatment of brain for internal emitters

- Typically, brain is included in *Other tissue* because it is rarely a major repository for a radionuclide
- Brain is addressed explicitly in systemic biokinetic models for a few elements with elevated uptake by brain, for example:
 - Nitrogen as ammonia (ICRP Pub. 53)
 - Copper (ICRP Pub. 30)
 - Manganese (ICRP OIR series)
 - Mercury (ICRP OIR series)

Growing interest in brain dosimetry for internal emitters

- The U.S. Million Worker Study is estimating brain doses and evaluating dementia, Alzheimer's, and other brain diseases as possible adverse effects of ionizing radiation
- Also, NASA is interested in adverse effects of alpha dose on brain as a limited but perhaps informative analogy of behavioral and cognitive effects of galactic cosmic ray exposure on astronauts

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- Development of Models for Brain Dosimetry for Internally Deposited Radionuclides (2018 – 2020):
 - Richard Leggett (Chair, ORNL)
 - Sergei Tolmachev (Vice Chair, USTUR)
 - Maia Avtandilashvili (USTUR)
 - Keith Eckerman (ORNL, retired)
 - Gayle Woloschak (NWU)

Purpose of this study

- We are investigating potential improvements in brain dose estimates for internal emitters resulting from *explicit* rather than *implicit* biokinetic treatment of brain (and improved dosimetric treatment – but focus here is on biokinetics)
- *Explicit treatment* of brain for an internal emitter means its systemic biokinetic model contains compartments and transfer rates specifically representing brain kinetics
- *Implicit treatment* of brain means brain is part of *Other tissue*

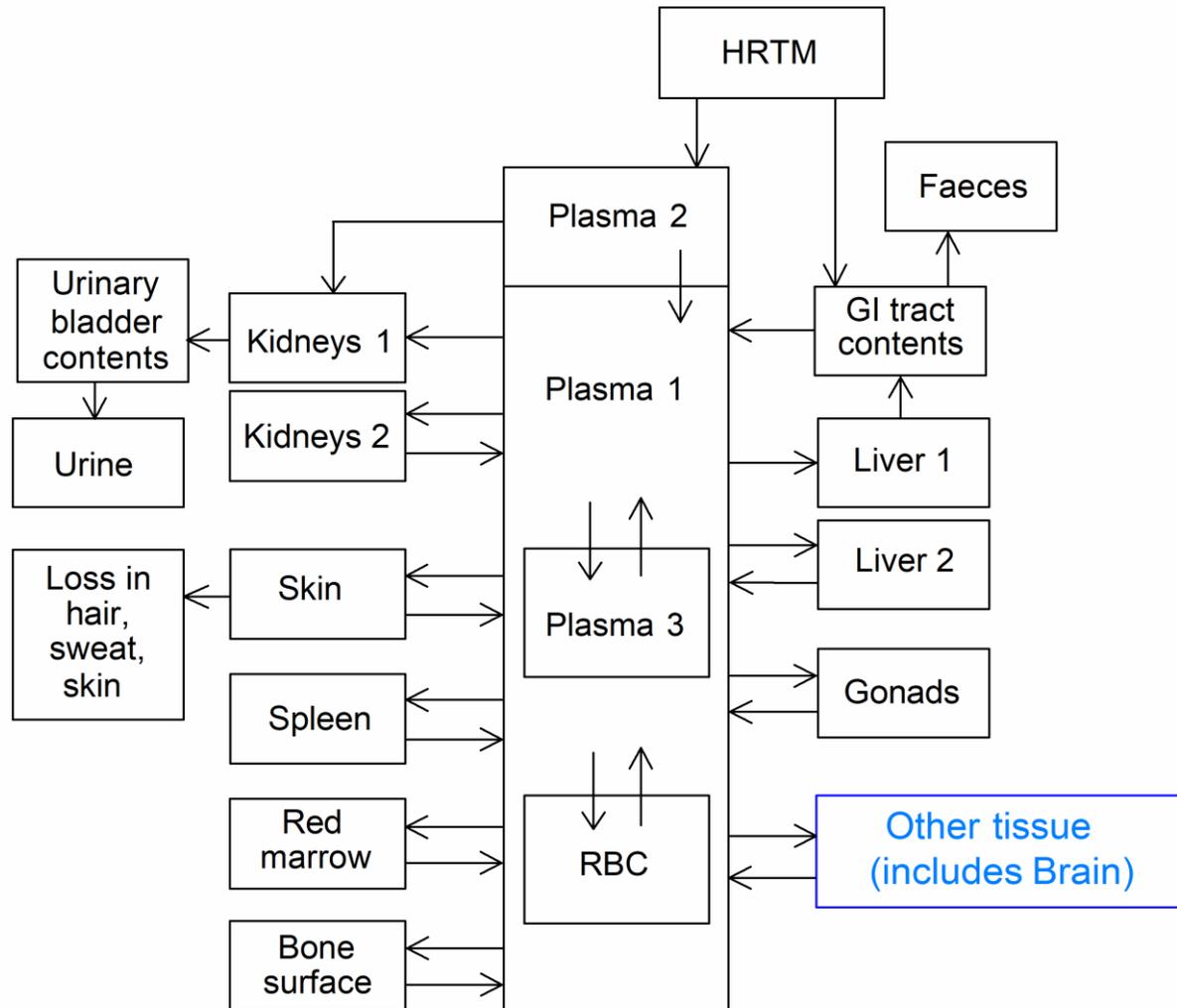
Study design

- We selected several elements for which brain kinetics can be modeled reasonably well
- For a selected radioisotope of each element we compared two derived injection dose coefficients for brain, using ICRP Pub. 133 (2016) dosimetry and two versions of the latest ICRP systemic model for occupational intake of the radionuclide:
 1. with brain contained implicitly in *Other tissue* (in most cases this is just the unmodified ICRP model)
 2. with an explicitly modeled brain pool

Example: Po-210

- The ICRP's biokinetic model for systemic polonium (Po) was updated in ICRP Publication 137, 2017 (Part 3 of the Occupational Intake of Radionuclides or OIR series)
- In the Po model, brain is included implicitly in *Other tissue*, which is represented by a single compartment

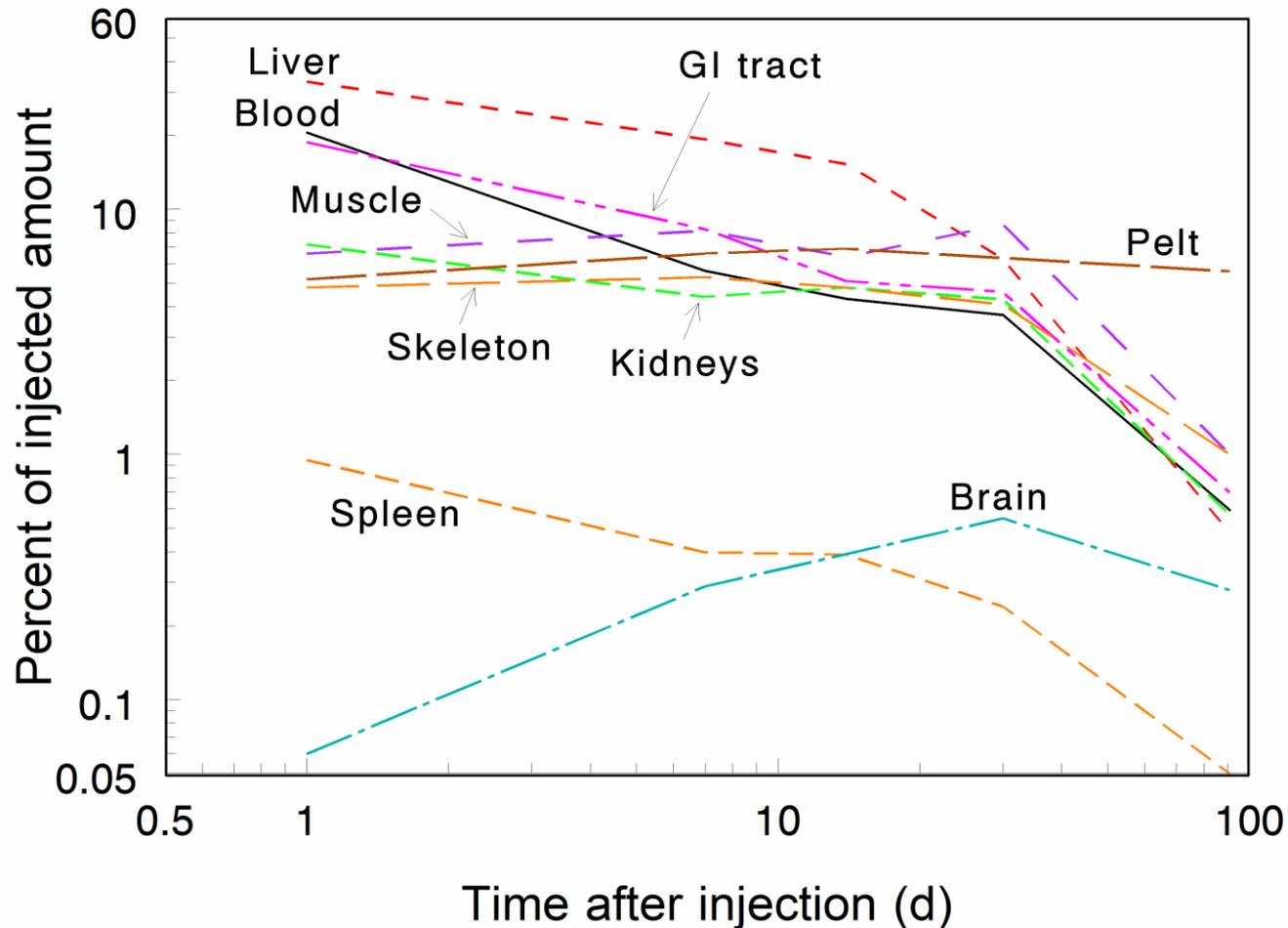
ICRP's biokinetic model for systemic Po (Pub. 137, 2017)



Data on brain kinetics of Po

- Accumulation of Po in brain at known times after intake has been observed in laboratory animals and in a human subject who was poisoned with ^{210}Po
- The activity concentration in the human subject was higher in brain than in some other soft tissues including muscle and skin
- Best available data for modeling time-dependent brain kinetics of Po may be for baboons (Cohen *et al.*, 1987, NYU studies)

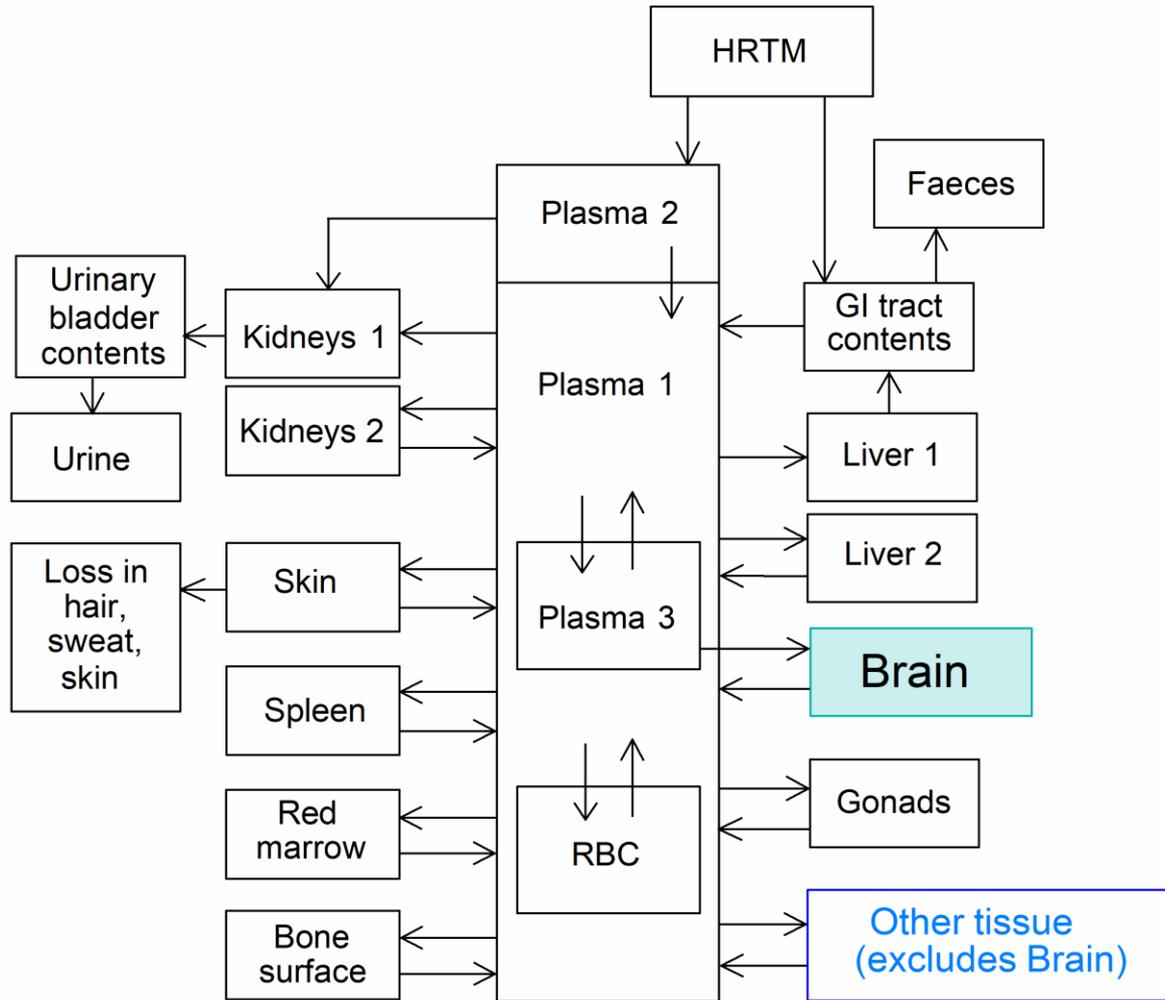
Retention (%) of intravenously administered ^{210}Po in baboon tissues (NYU studies)



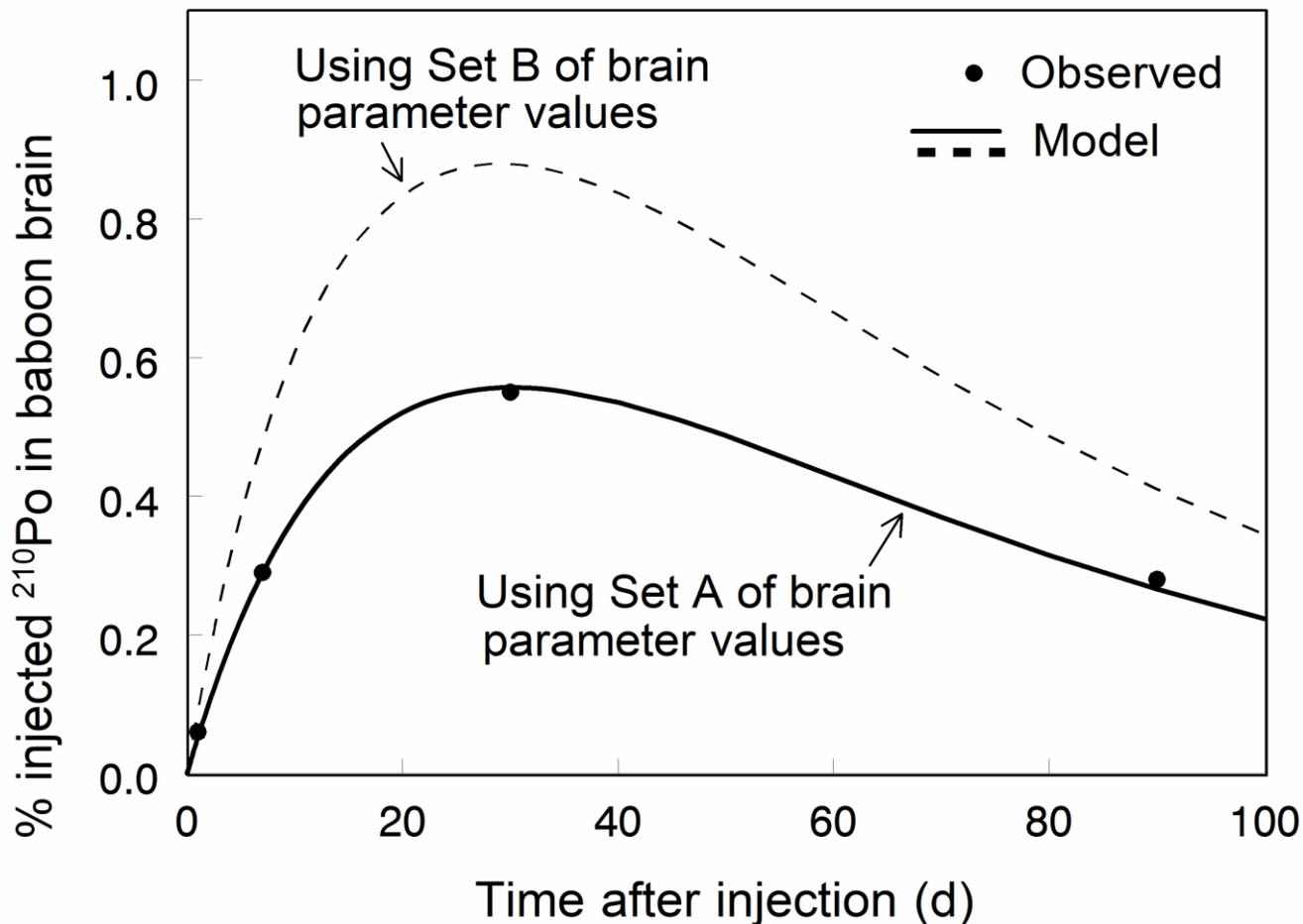
Addition of brain to Po model

- We added a brain compartment to the ICRP's biokinetic model for systemic Po
- Two sets of parameter values were developed to describe brain kinetics:
 - Set A: This set of parameter values (deposition fraction and removal half-time) was derived as a fit to data for baboons and was not adjusted for application to humans
 - Set B: This set consists of the removal half-time from Set A, but the deposition fraction for brain in Set A was increased by 70% in view of the roughly 70% larger brain size in humans (relative to total-body size)

Model structure for Po with explicitly depicted brain



Predictions of modified ICRP model (with explicit brain) compared with baboon data



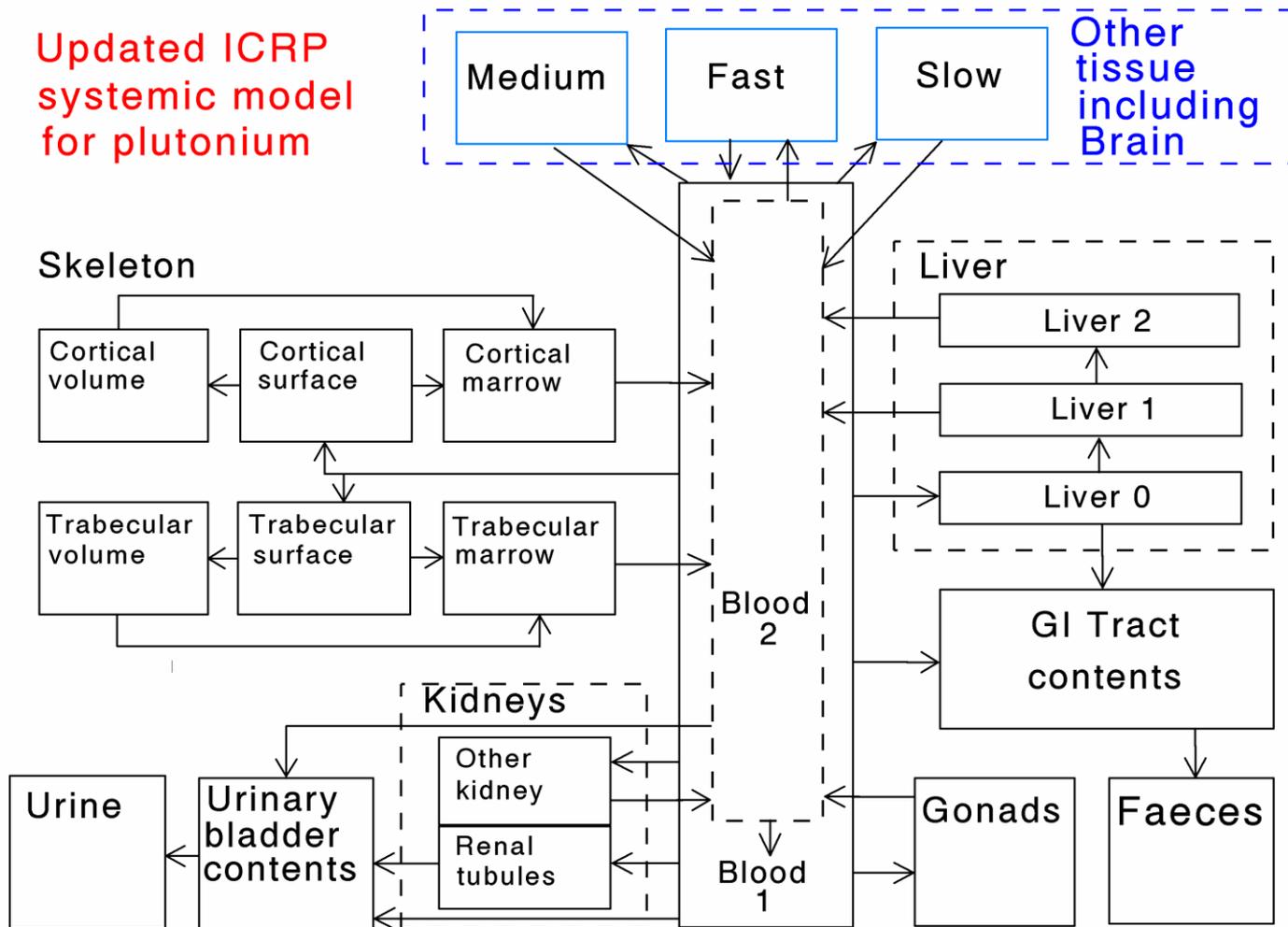
Results for Po-210

- The modified ICRP model with Set A of parameter values for brain yields 1.3 times higher dose to brain than the Pub. 137 model for Po
- The modified ICRP model with Set B of parameter values for brain yields 2.0 times higher dose to brain than the Pub. 137 model

Example: Pu-239

- The ICRP's biokinetic model for systemic plutonium (Pu) is updated in Part 4 of the OIR series (upcoming)
- As in previous ICRP models for Pu, brain is included implicitly in *Other tissue*
- In the Pu model, *Other tissue* consists of three compartments representing fast, moderate, and slow removal back to blood

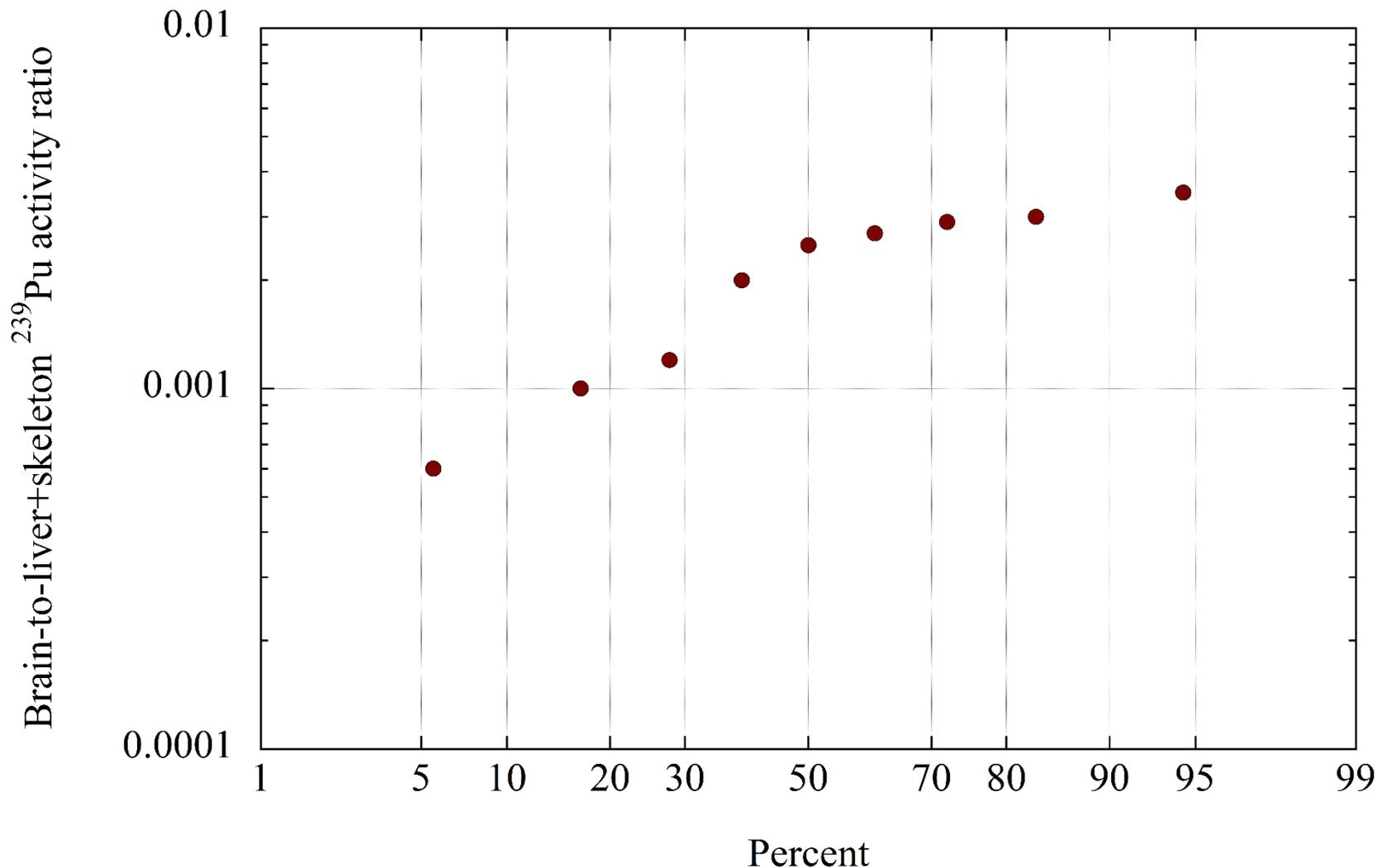
Updated ICRP's biokinetic model for systemic Pu (OIR Part 4, upcoming)



Examples of data on Pu accumulation in brain

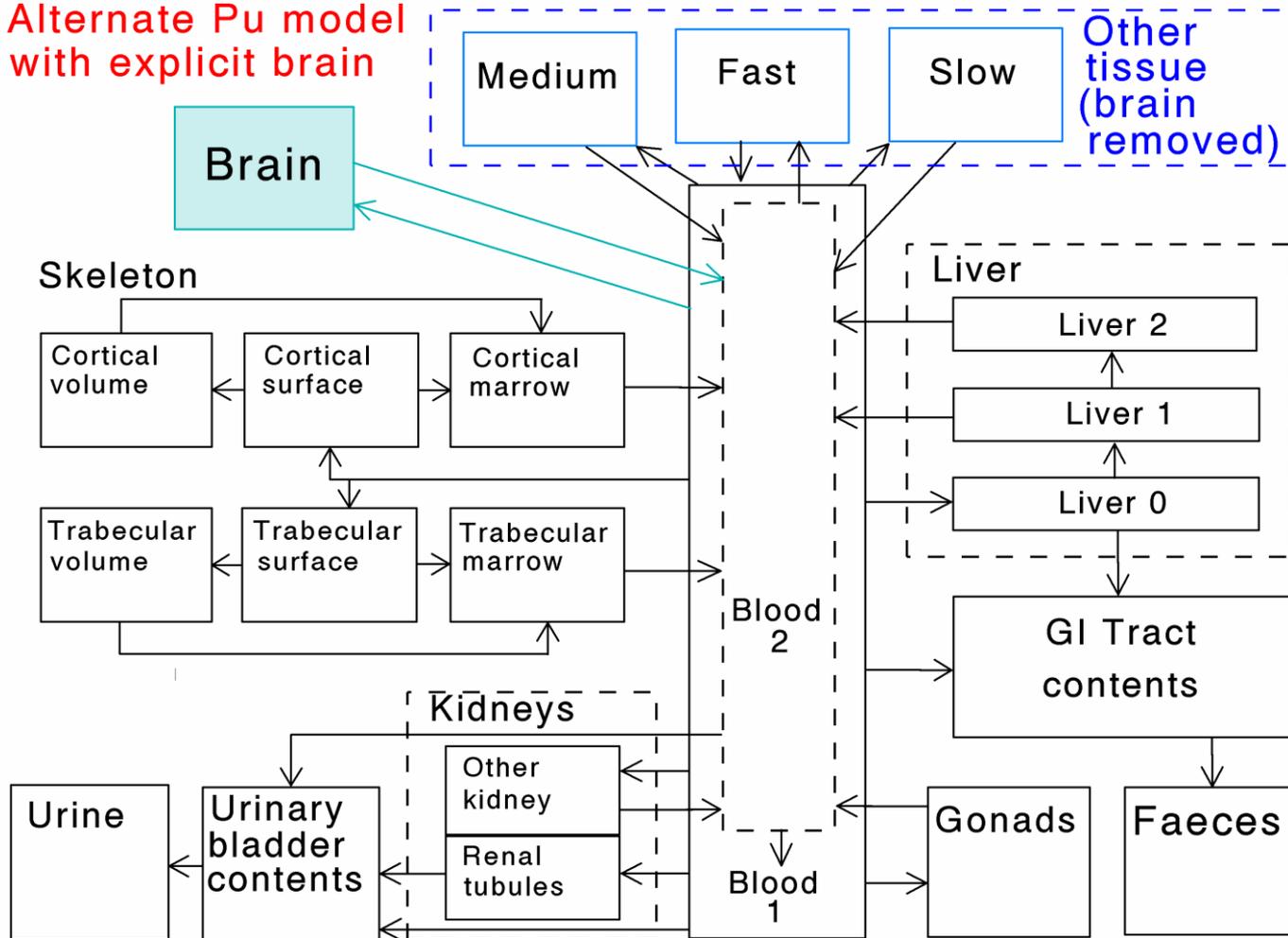
- Data for dogs indicate central activity ratio *Brain-to-(Liver + Skeleton)* of about 0.0013 at 2 - 4 weeks post intravenous injection
- USTUR data for Pu workers indicate central activity ratio *Brain-to-(Liver + Skeleton)* of about 0.002 at 18 - 64 years post intake

USTUR data on relative contents of ^{239}Pu in Brain and Liver + Skeleton



Model structure for Pu with explicitly depicted brain

Alternate Pu model with explicit brain



Results for Pu-239

- Brain dose based on Pu model with explicit brain is 0.96 times brain dose based on latest ICRP model with brain contained in *Other tissue*

Summary of results for all radionuclides examined to this point

Radionuclide	Ratio of dose estimates for brain Explicit Brain : Implicit Brain
Manganese-54	1.7
Cesium-134	1.5
Mercury-203 (vapor)	1.4
Lead-210	1.4 ^a (3.3 ^b)
Polonium-210	1.7 ^c
Plutonium-239	0.96

^aDoes not address lower chain members

^bIncludes contribution of Bi-210 and Po-210 progeny

^cAverage of ratios for two different explicit brain models

Conclusions

- Biokinetic data for several elements suggest that brain has slower uptake but longer retention than most other soft tissues
- Based on cases examined so far, it appears that implicit treatment of brain as part of *Other tissue* is more likely to underestimate than overestimate brain dose
- Based on cases examined so far, the brain dose estimates based on an explicitly modeled brain are on average about 40% (75%) larger than estimates based on a model in which brain is implicitly contained in *Other tissue*
- For a large portion of the periodic table, brain-specific data may be too sparse to allow explicit modeling of brain kinetics with much confidence