Plutonium in human brain: Is more biokinetic detail needed for dosimetry?

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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:
  ✓ Nitrogen as ammonia (ICRP Publication 53)
  ✓ Copper (ICRP Publication 30)
  ✓ Manganese (ICRP OIR series)
  ✓ Mercury (ICRP OIR series)
Growing interest in brain dosimetry for internal emitters

- **U.S. Million Worker Study:** estimating brain doses and evaluating dementia, Alzheimer’s, and other motor neuron diseases as possible adverse effects of radionuclide depositions in the brain

- **National Aeronautics and Space Administration:** 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 (high Z and high energy ions) exposure on astronauts
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)
• George Sgouros (Johns Hopkins University)
• Gayle Woloschak (Northwestern University)
• Raymond Guilmette (Staff Consultant)
Purpose of this study

To investigate potential improvements in brain dose estimates for internal emitters resulting from *explicit* rather than *implicit* biokinetic treatment of brain (and improved dosimetric treatment)

- *Explicit treatment*: systemic biokinetic model contains compartments and transfer rates specifically representing brain kinetics
- *Implicit treatment*: brain is considered as part of Other tissue
Study design

• Several elements (Mn, Cs, Hg, Pb, Po, U, Pu, Am), for which brain kinetics can be modeled reasonably well, were selected.

• For a selected radioisotope of each element, we compared two derived injection dose coefficients (Sv Bq\(^{-1}\)) for brain, using ICRP Publication 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
  2. with brain *explicitly* modeled
Plutonium-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 of Pu back to blood
Updated ICRP’s biokinetic model for systemic Plutonium (OIR Part 4, upcoming)
Examples of data on Pu accumulation in brain

- Data from dogs indicate central activity ratio \textit{Brain-to-(Liver + Skeleton)} of about 0.0013 at 2 – 4 weeks post intravenous injection
- US Transuranium and Uranium Registries (USTUR) data for Pu workers indicate central activity ratio \textit{Brain-to-(Liver + Skeleton)} of about 0.002 at 18 – 64 years post intake
United States Transuranium and Uranium Registries (USTUR)

- Federal-grant program funded by the U.S. DOE Office of Domestic and International Health Studies (AU-13)
- Operated by College of Pharmacy and Pharmaceutical Sciences at Washington State University under Central DOE Institutional Review Boards (DOE000320)
- Studies biokinetics and tissue dosimetry of uranium and transuranium elements in occupationally exposed individuals
- Faculty and staff:

  ![Faculty and Staff Images]

- Location: Richland, Washington, USA
- Website: www.ustur.wsu.edu
USTUR operation and research: Schematic

**Unique data set**
- Work history
- Medical records
- Exposure records (74 Bq)
- Bioassay measurements
- Tissue analysis results (U, Pu, Am)

**Flowchart:**
- Autopsy
- Tissue collection
- Radiochemical analysis
- Biokinetic modeling
$^{239}$Pu concentration in liver, skeleton, and brain of occupationally exposed individuals

- Liver ($n = 299$): GM = 1.23
- Skeleton ($n = 269$): GM = 0.39
- Brain ($n = 70$): GM = 0.024
Systemic plutonium(americioium) in brain

Brain-to-(liver+skeleton) activity ratio

- $^{239}\text{Pu}$ (n = 38): GM = 0.0018
- $^{241}\text{Am}^*$ (n = 28): GM = 0.0017

* from $^{241}\text{Pu}$ decay

Percent
Alternate biokinetic model for systemic plutonium with explicitly depicted brain

Other tissue (brain removed)

Intermediate turnover (ST1)  Rapid turnover (ST0)  Slow turnover (ST2)

Brain

Skeleton

Cortical volume  Cortical surface  Cortical marrow

Trabecular volume  Trabecular surface  Trabecular marrow

Liver

Liver 2  Liver 1  Liver 0

GI Tract contents

Kidneys

Blood 2

Other kidney  Renal tubules

Blood 1

Gonads  Feces

Urine

Urinary bladder content
# Dose coefficient (Sv Bq\(^{-1}\)) for brain

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Biokinetic model with Implicit brain (A)</th>
<th>Biokinetic model with Explicit brain (B)</th>
<th>Ratio B:A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Am-241</td>
<td>2.80 × 10(^{-5})</td>
<td>3.62 × 10(^{-6})</td>
<td>0.13</td>
</tr>
<tr>
<td>U-234</td>
<td>1.38 × 10(^{-6})</td>
<td>1.11 × 10(^{-6})</td>
<td>0.80</td>
</tr>
<tr>
<td>Pu-239</td>
<td>2.56 × 10(^{-5})</td>
<td>2.45 × 10(^{-5})</td>
<td>0.96</td>
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<tr>
<td>Ra-226</td>
<td>1.87 × 10(^{-7})</td>
<td>3.62 × 10(^{-7})</td>
<td>1.94</td>
</tr>
<tr>
<td>Po-210</td>
<td>3.12 × 10(^{-7})</td>
<td>6.20 × 10(^{-7})</td>
<td>1.99</td>
</tr>
</tbody>
</table>

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

Conclusions

- Where feasible, the brain should be depicted explicitly in biokinetic models used in epidemiological studies addressing adverse effects of ionizing radiation
Acknowledgment
Thank you very much!