Preface

Adverse effects of high radiation doses to the brain are well established from studies of radiotherapy-induced brain injury and experimental studies on laboratory animals. Effects include declines in cognitive function and memory. These effects appear to be age- and sex-dependent and brain-region dependent.

Ongoing large-scale epidemiological studies of radiation effects in cohorts with elevated internal or external exposure to radionuclides potentially could establish credible dose-effect relationships for lower levels of brain dose than received in the radiotherapy and animal studies. A limitation of the epidemiological studies, however, is that biokinetic and dosimetric models currently used in radiation protection and dose reconstructions generally include only an implicit brain model, in that the time-dependent activity in the brain is viewed as a uniformly distributed mass fraction of the time-dependent activity in a large portion of the body referred to as *Other* (*i.e.*, all tissues not explicitly identified in the element- specific biokinetic model). Thus, the estimated dose to the brain based on current models generally does not reflect available information on uptake and retention of the element of interest by the brain or its distribution in the brain.

This Commentary examines current information on the accumulation, distribution, and retention of radionuclides in the brain and the extent to which that information can be used to improve estimates of dose to potentially radiosensitive regions of the brain from internal emitters, with emphasis on high linear-energy transfer alpha particle-emitting radionuclides. Dose estimates for the brain based on explicit brain models reflecting best available biokinetic data are compared with estimates based on the brain models typically used in radiation protection and dose reconstruction. The comparisons indicate that predictions of brain doses based on current models for radionuclides may substantially underestimate or overestimate brain dose projections based on an explicit brain model reflecting best available biokinetic data. Potential improvements in dose estimates for the brain based on more detailed dosimetric models of the brain are also examined. Improved estimates of radiation doses to brain based on more realistic biokinetic and dosimetric representations of the brain would be an important step forward in ongoing epidemiologic research aimed at evaluating dementia, Alzheimer's, Parkinson's, motor neuron diseases and cognitive impairment as possible adverse effects of radionuclide depositions in the brain.

This Commentary draws from and builds upon previous NCRP reports on closely related topics, including:

- Report No. 153, *Information Needed to Make Radiation Protection Recommendations for Space Missions Beyond Low-Earth Orbit* (2006)
- Report No. 161 (II), *Management of Persons Contaminated with Radionuclides: Scientific and Technical Bases* (2008)
- Report No. 163, *Radiation Dose Reconstruction: Principles and Practice* (2009)
- Report No. 164, *Uncertainties in Internal Radiation Dose Assessment* (2009)
- Commentary No. 23. *Radiation Protection for Space Activities: Supplement to Previous Recommendations* (2014)
- Commentary No. 24. *Health Effects of Low Doses of Radiation: Perspectives on Integrating Radiation Biology and Epidemiology* (2015)

- Report No. 178, *Deriving Organ Doses and Their Uncertainty for Epidemiologic Studies* (2018)
- Report No. 183, *Radiation Exposures in Space and the Potential for Central Nervous System Effects (Phase II)* (2019)
- Report No. 186, *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment* (2020)

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