Uncertain Biokinetic Parameter Considerations in Stochastic Modeling of the Human Respiratory Tract System for Consequence Management Applications: A Comparative Analysis of Uncertain Biokinetic Parameters in the Human Respiratory Tract for an Inhaled Radionuclide

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Purpose: Estimating and reconstructing doses from internalized radionuclides remains a persistent challenge, primarily due to the inability to directly measure the radionuclide body burden resulting from internalized uptakes. Additionally, inhalation as a mode of intake from nuclear or radiological events is recognized as significant, given the prolonged presence of suspended particles in the air post-event. Consequently, the assessment of internal radiation dose exposure relies heavily on mathematical frameworks, particularly biokinetic models, which aim to determine the biodistribution of radionuclides over time post-exposure. For radionuclides inhaled into the body, specialized models have been developed, known as the human respiratory tract model (HRTM). These models have undergone refinement, incorporating deterministic quantities outlined by the International Commission on Radiological Protection (ICRP) in Publication 66 and subsequently updated in Publication 130.

To ensure a comprehensive estimation of inhaled dose, a detailed characterization of the HRTM is imperative. The HRTM encompasses various components, including particle deposition in airways, radioactive decay, systemic biokinetic modeling, and dose estimate. While the ICRP utilizes reference models to establish biokinetic and dosimetric quantities for the computation of dose coefficients, the complexity of inhaled radionuclide metabolism necessitates the utilization of expanded stochastic models. These models must capture a broader range of population-specific variabilities to facilitate accurate dose estimation and reconstruction. Furthermore, uncertainty and sensitivity analyses are indispensable, particularly in consequence management scenarios in which early-phase decisions regarding site-boundary dose estimates and administration of medical countermeasures must be made, incorporating case-specific conditions and individual characteristics.

The aim of this study was to assess the inherent uncertainty and variability in deterministic ^{131}I biokinetic and dosimetry models via inhalation by conducting stochastic analysis using the updated ICRP Publication 130 HRTM.

Method: In the early phase of this study, efforts were focused on implementation of a robust computational method, in Python, for handling the extremely stiff system of ordinary differential equations (ODEs) posed by biokinetic models. Several ODE solving methods, both numerical and algebraic, were investigated subjected to solving biokinetics for inhaled fast clearing (type F) ^{131}I (Figure 1, where Figure 2 illustrates the compartmental model for the ICRP 130 HRTM) (Mate-Kole et. al., 2023). The assessment criterion was based on well converged solution methods, employing numerical amplification factor. Biokinetic solutions for each solving method were compared, and the methods with most converged solutions, having less computational time were chosen for which an in-house dose coefficient code, named REDCAL, is constructed.

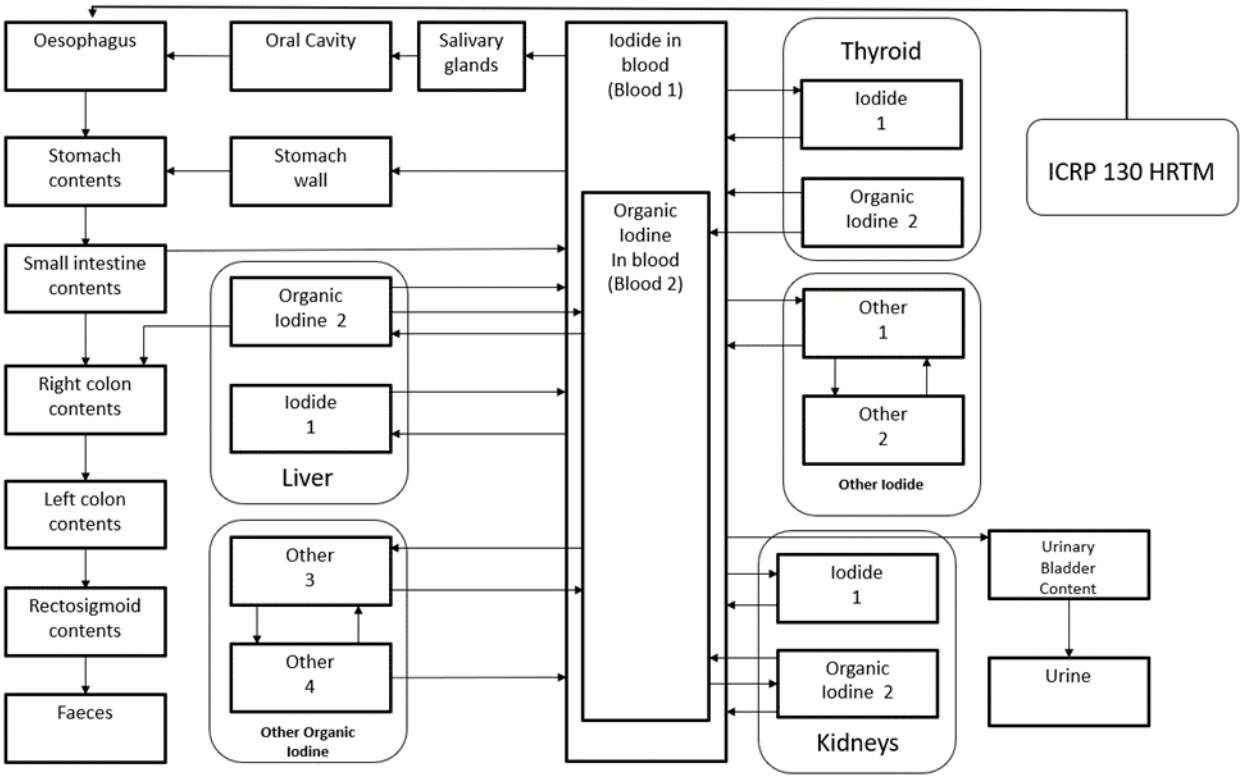

Figure 1: Coupled Inhalation Compartmental Model for iodine (ICRP, 2017).

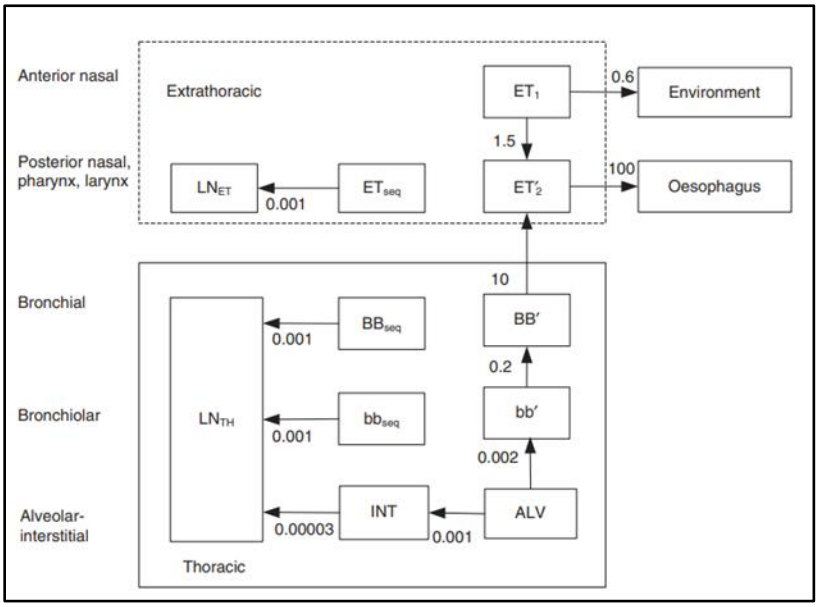

Figure 2: The ICRP revised Human Respiratory Tract compartment model representing time-dependent particle transport of material (ICRP Publication 130 HRTM) (ICRP, 2015). Arrows illustrate the mechanical clearance from one compartment to the other alongside values depicting reference transfer coefficients in unit of d^{-1}

The complexities of the ICRP particle deposition model were deciphered and reconstructed into a standalone computational module and integrated into the in-house dose coefficient toolkit. This was a necessary step to allow maximum flexibility to perform sensitivity analysis. With the well-established deterministic toolkit, a systematic review of particle deposition components within the ICRP Publication 130 HRTM was conducted, assigning probability distribution density functions to parameters that may be uncertain. These distributions were incorporated into the in-house dose calculator, utilizing Latin Hypercube Sampling to generate 10,000 sample sets of input vectors. Using Occupational Intake of Radionuclide (OIR) as a scenario, the biodistribution and committed effective dose coefficients were computed for ^{131}I type F, considering a lognormally distributed particle size of 5 µm. Additionally, a Random Forest regression model, an AI algorithm, coupled with SHapley Additive exPlanations (SHAP) was employed for sensitivity analysis to predict feature importance.

Results: The results obtained from the reconstructed deposition computational module were benchmarked against the particle deposition fractions published by the ICRP for the human respiratory tract. The calculations demonstrated a 1.05% relative difference and a 0.7% absolute difference, indicating a strong agreement with historical published data. Additionally, the deterministic dose coefficient derived from the in-house toolkit was compared to the ICRP published dose coefficient based on the OIR methodology, depicting a relative difference of 0.4%. Statistical analysis indicated that the ICRP published dose coefficient (1.1E-08 Sv/Bq) marginally exceeded the 75th percentile of observed sample sets, with a log-gamma distribution identified as the best-fit probability distribution (Figure 3). Furthermore, sensitivity analysis, incorporating Random Forest coupled with SHAP, revealed that altering the alveolar interstitial regional value of the respiratory tract significantly affected the overall dose coefficient value (Figure 4), keeping all other systemic clearance rates constant.

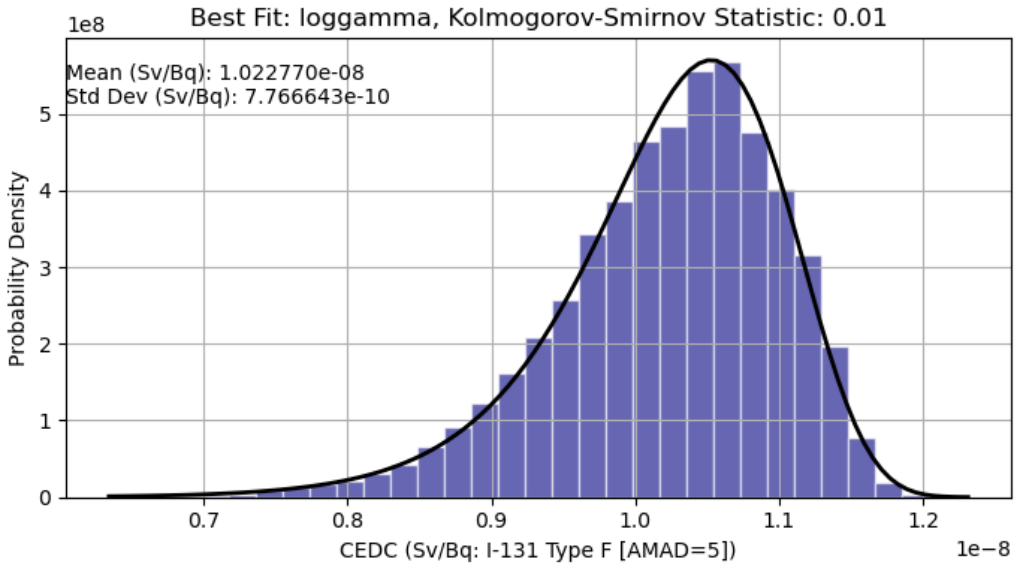

Figure 3: Best fit distribution predicted for ^{131}I of type F assuming OIR methodology with a lognormal particle size of 5 µm.

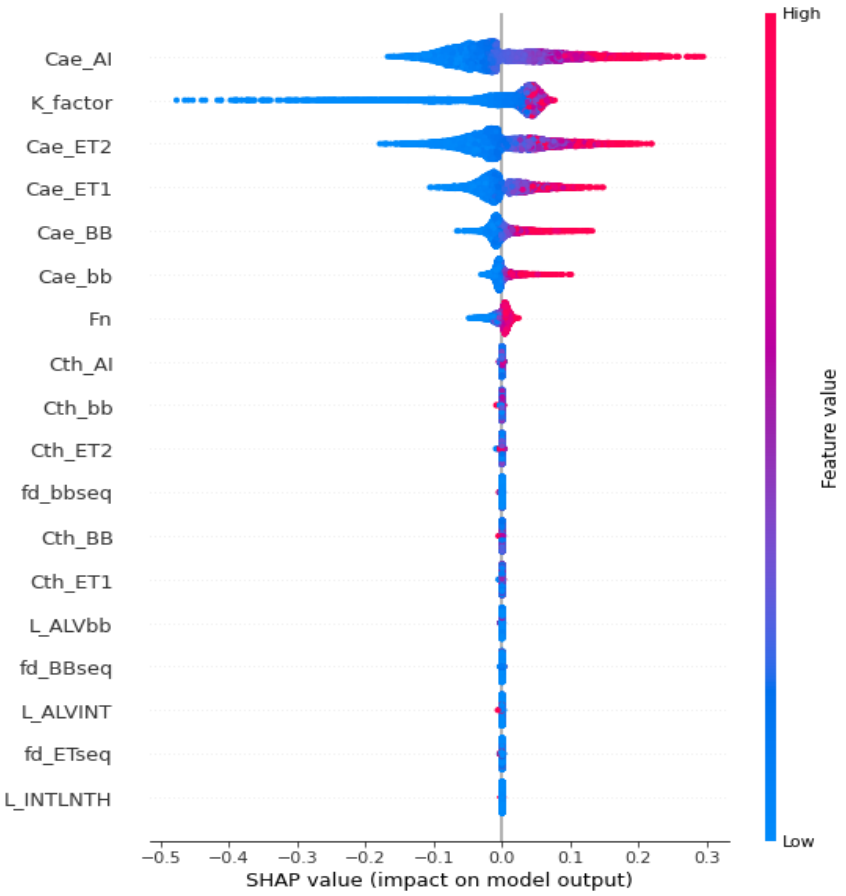

Figure 4: Parameter importance predicted utilizing Random Forest coupled with SHAP for ^{131}I of type F with a lognormal particle size of 5 μm.

Conclusion: This study offers a unique stochastic perspective on radionuclide metabolism, providing insights for realistic radiological or nuclear inhalation scenarios, thus enhancing consequence management and medical countermeasures applications.

Relevance to CIRMS: Enhancing dosimetric estimation by incorporating uncertainties and variabilities in biokinetic and dosimetry model parameters is vital for improving medical countermeasure delivery and formulating effective radiation protection guidelines in decision-making and consequence management applications, which are of particular interest to the CIRMS community. These efforts complement the community's focus on measurement standardization, rendering a synergistic role in updating existing dosimetry standards and practices. The primary author's endeavors are characterized by a commitment to advancing Physiologically Enhanced Biokinetic Models, which align seamlessly with pharmacokinetic modeling principles used in pharmaceuticals and nuclear medicine applications. He is currently being train as a nuclear and radiological engineer and working with a vibrant team in the Radiological Engineering, Detection, and Dosimetry Laboratory at Georgia Tech.

References:

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