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Review of Uncertain Parameters in ICRP 66 Human Respiratory Tract Model

HPS Annual Meeting

2022

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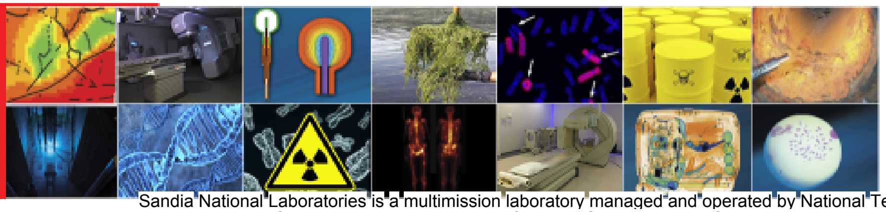

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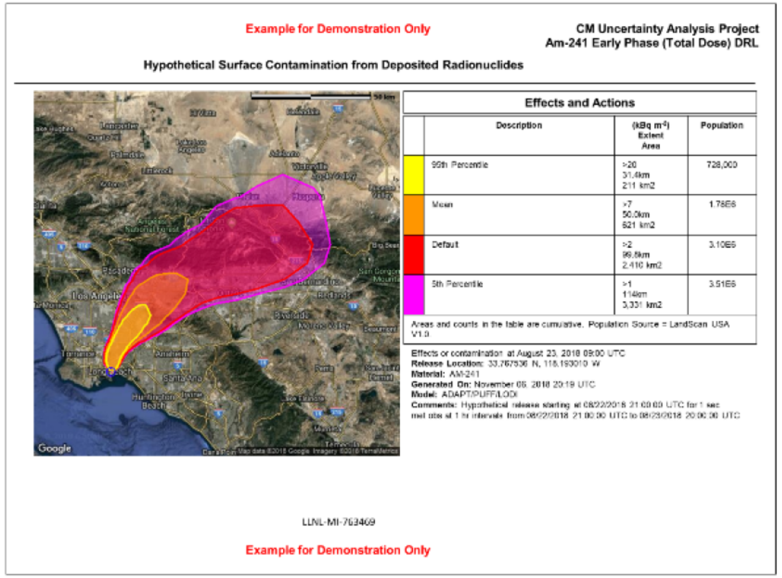
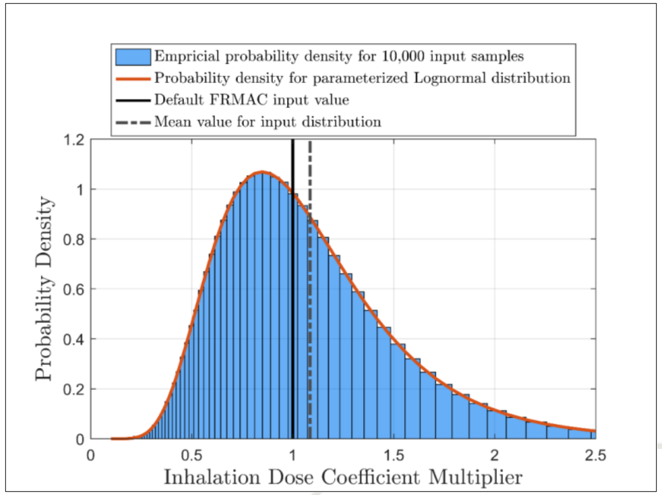
Outline

- Motivation
- The ICRP 66 Human Respiratory Tract Model (HRTM)
- HRTM Implementing Software
- Mathematics basis of HRTM: biokinetics with respiratory clearance and absorption
- Parameter Uncertainty Review
  - Uncertain Parameter Distributions
  - Internal dosimetry and impact of parameters
- Conclusions and Transition to presentation about Ongoing Work

Motivation

- Sandia National Laboratories (SNL) recently developed a methodology to characterize uncertainty in Derived Response Levels (DRLs) used as contours on map products developed by the DOE Consequence Management (CM) program in support of the Federal Radiological Monitoring and Assessment Center (FRMAC)
- Goal is to develop a framework for propagating uncertainty through the HRTM to generate inhalation dose coefficient probability distributions for radionuclides that represent a broader set of incidents to which DOE CM could potentially respond





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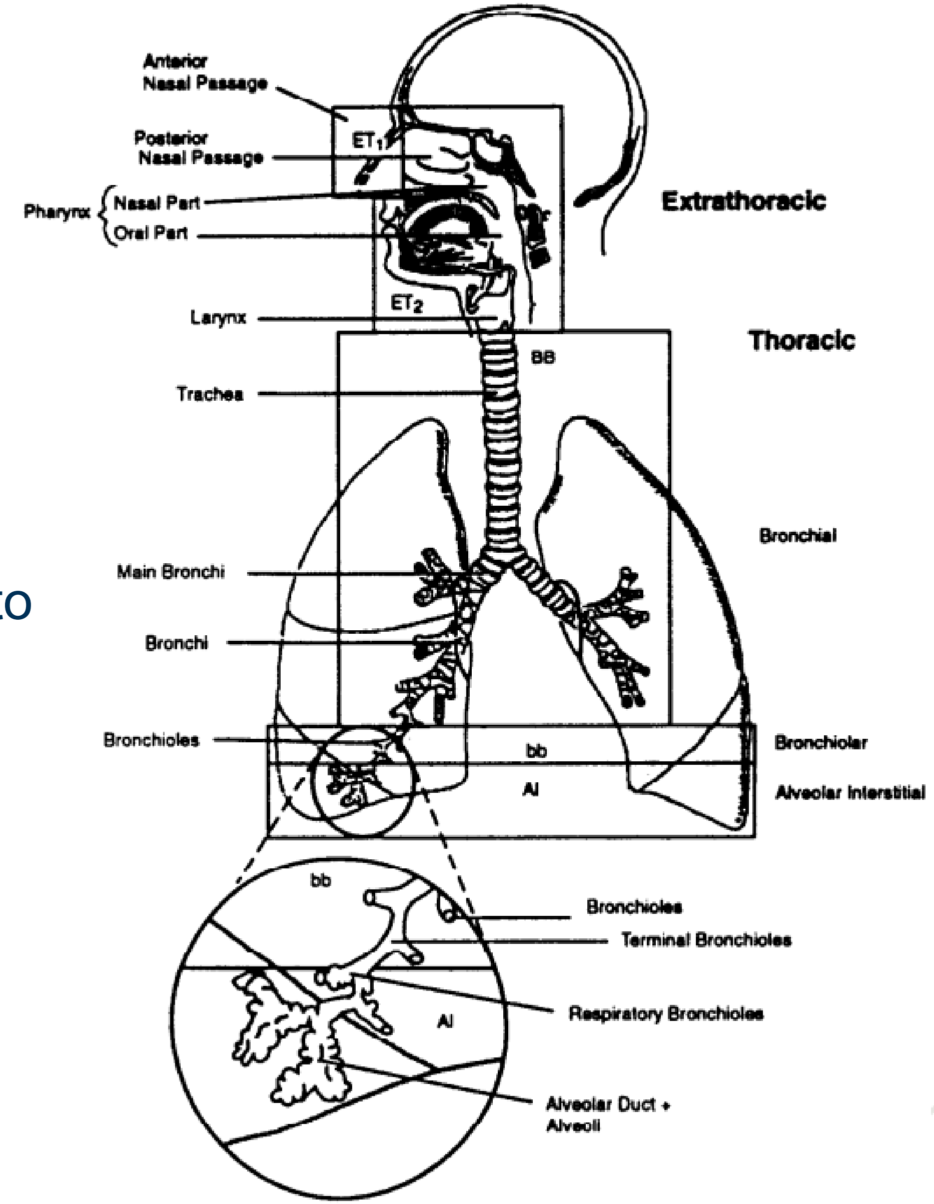
The ICRP 66 Human Respiratory Tract Model (HRTM)

- Components of the HRTM
  - Morphometry
  - Respiratory physiology
  - Radiation biology
  - Particle deposition
  - Particle clearance
  - Dosimetry
- All components of the HRTM carry with them uncertainty that must be considered in order to propagate uncertainty through the model
- Regions of the HRTM
  - Extrathoracic
  - Thoracic
  - Bronchial
  - Bronchiolar
  - Alveolar



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HRTM Implementing Software

- Several codes have been developed to implement and solve the HRTM
  - Lung Dose Uncertainty Code (LUDUC) – T.E. Huston (2003)
    - Utilizes Latin Hypercube Monte Carlo sampling with uncertainty distributions based on work by Bailey and Roy (1994)
  - Activity and Internal Dose Estimates (AIDE) – Luiz Bertelli (2008)
  - Klumpp Dose Evaluation Program (KDEP) – Implementation of ICRP HRTM by John Klumpp and Luiz Bertelli (2017)
  - Integrated Modules for Bioassay Analysis (IMBA) – UK Health Security Agency (2003)
    - Built on Lung Dose Evaluation Program (LUDEP) – A. Birchall et al. (1991)
    - Maximum likelihood method; Monte Carlo sampling with superimposed random data on geometric standard deviation
  - Dose and Risk Calculation (DCAL) – Oak Ridge National Laboratory (2006)
  - Multi-Path Particle Dosimetry Model (MPPD) – Applied Research Associates (ARA) (rev. 2017)
  - Radiological Exposure Dosimetry Calculator (REDCAL) - Georgia Tech (2022+)

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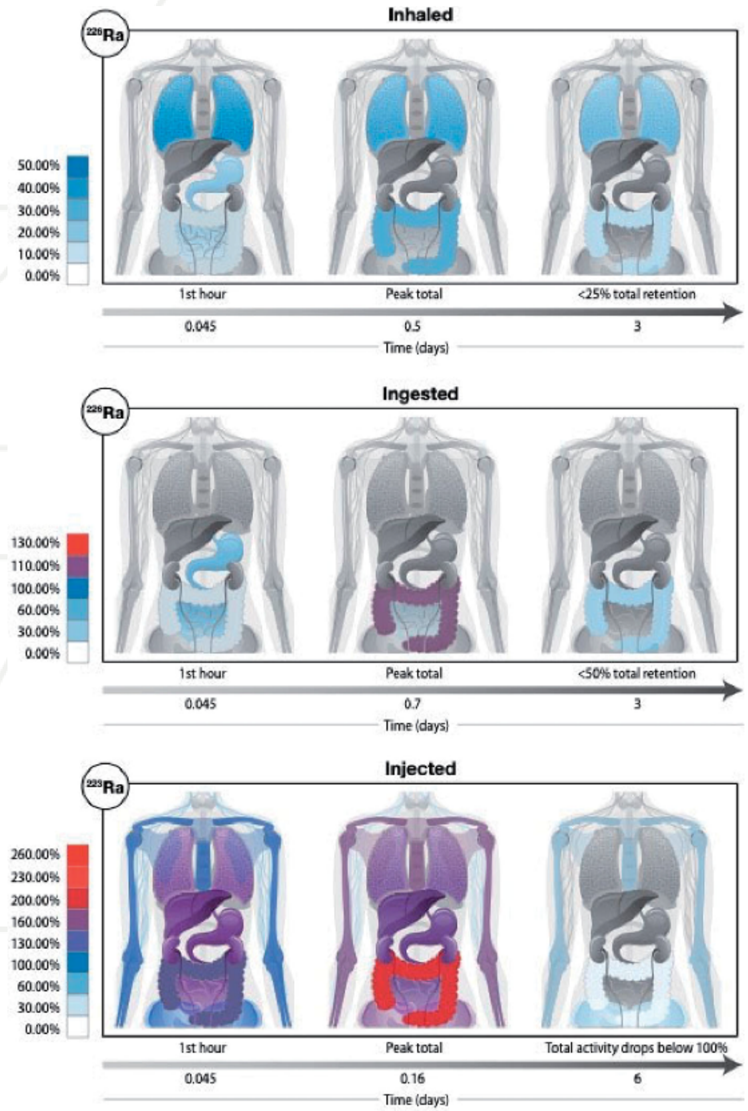
Solving System of ODEs for Organ Activity: Biokinetics

- $$\frac{d}{dt}\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} L(Y_1) & \cdots & G(TR_1) & 0 \\ 0 & \ldots & G(TR_2) & 0 \\ 0 & \ldots & L(Y_{21}) & 0 \\ \vdots & \ldots & 0 & L(Y_n) \end{bmatrix}\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix}$$
- Terms| L: Loss, G: Gain, TR: transfer rate
- Equation for blood activity as a function of time for Iodine-131
- $$\frac{d(Blood\ [Bq])}{dt} = -(TR_{21} + TR_{32} + DR)Y_{21} + TR_2Y_1 + TR_4Y_2 + TR_7Y_3 + TR_9Y_4 + TR_{11}Y_5 + TR_{13}Y_6 + TR_{15}Y_7 + TR_{17}Y_8 + TR_{19}Y_9 + TR_{22}Y_{10} + TR_{24}Y_{11} + TR_{25}Y_{12} + TR_{20}Y_{13}$$
- Blood: losses to thyroid and bladder; gains AI (1,2,3), bbi(gel, sol, seq), BBi(gel, sol, seq), Lymph Nodes (ET, Th), ET2(sur, seq)



The anatomical location and the total magnitude of radioactivity of radium and its various progeny is depicted following three intake scenarios: (top) inhalation of the radioisotope ^{226}Ra, (middle) ingestion of the radioisotope ^{226}Ra, and (bottom) injection of the radioisotope ^{223}Ra.

Reproduced from Abergel et al. The enduring legacy of Marie Curie: impacts of radium in 21st century radiological and medical sciences (2022).

Tissue weights ICRP 60/61 remainder formulation

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Parameter Uncertainty Review: Parameter Distributions

- Review of the literature yielded a comprehensive list of parameters that contribute to uncertainty within the HRTM
  - Total Parameters: 69
    - Deposition: 26
      - Regional deposition, sub-region breakdown (compartment fractions), Breathing parameters
    - Clearance: 23
      - Mechanical clearance, Clearance type (F,M,S, V), Blood absorption rates, Macrophage uptake rate
    - Dosimetry: 20
      - Phantom series used with radiation transport modeling, Decay data (ICRP 107), Tissue Weights, Remainder formulation

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Summary of Evaluated Inputs

Parameter	Consideration	Basis & Impact
Particle size	Uncertain (lognormal)	Aerosol generation results in range of particle sizes
Breathing rate	Uncertain (public versus worker parameter range)	Regional deposition based on activity-dependent ventilation rate
Deposition fractions (Regional and compartmental)	Uncertain (function of aerosol parameters)	Method of transport determines method of deposition (sedimentation/impaction)
Lung model rates (Absorption/Clearance values, dissolution rates)	Uncertain (distribution around type: F/M/S)	Dissolution rates greatly impact the dose values to the lungs
Anatomical differences in lung geometry and volume (scaling factors)	Static values (reference values ICRP 66)	Volume scaling impacts flow through airways and thus deposition. Would like CFD modeling to determine the impact
Dosimetry values (Tissue Weighting factors, Specific Absorbed Fractions (SAF))	Static values (tissue weights from ICRP 60)	Changes in SAF value require radiation transport runs with new organ geometry and organ volumes

Regional Deposition Efficiency

Table 12. Recommended parameters for substitution in the model of regional deposition for the fraction of intake inhaled and exhaled through the nose, I_{n_E}, for any subject, as functions of respiratory variables and anatomical size

Phase	Filter j	Region	Regional Deposition Efficiency, η_i — Aerodynamic $\eta_{ae} = 1-\exp(-aR^p)$: a	Aerodynamic: R	Aerodynamic: p	Thermodynamic $\eta_{th} = 1-\exp(-aR^p)$: a	Thermodynamic: R	Thermodynamic: p	Volumetric Fraction $\phi_j^{a,b}$
Inhalation	1	ET_1^c	3.0×10^{-4}	$d_{ae}^2 \dot{V}_a SF_t^3$	1	18	$D(\dot{V}_a SF_t)^{-1/4}$	1/2	1
	2	ET_2^d	5.5×10^{-5}	$d_{ae}^2 \dot{V}_a SF_t^3$	1.17	15.1	$D(\dot{V}_a SF_t)^{-1/4}$	0.538	1
	3	BB	4.08×10^{-6}	$d_{ae}^2 \dot{V} SF_t^{2.3}$	1.152	$22.02\ SF_t^{1.24}\ \psi_{th}^e$	Dt_B	0.6391	$1-\frac{V_D(ET)}{V_T}$
	4	bb	0.1147	$(0.056 + t_b^{1.5}) \times d_{ae} t_b^{-0.25}$	1.173	$-76.8 + 167\ SF_b^{0.65}$	Dt_b	0.5676	$1-\frac{[V_D(ET)+V_D(BB)]}{V_T}$
	5	AI	$0.146\ SF_A^{0.98}$	$d_{ae}^2 t_A$	0.6495	$170 + 103\ SF_A^{2.13}$	Dt_A	0.6101	$1-\frac{[V_D(ET)+V_D(BB)+V_D(bb)]}{V_T}$
Exhalation	6	bb	0.1147	$(0.056 + t_b^{1.5}) \times d_{ae} t_b^{-0.25}$	1.173	$-76.8 + 167\ SF_b^{0.65}$	Dt_b	0.5676	$1-\frac{[V_D(ET)+V_D(BB)]}{V_T}$
	7	BB	2.04×10^{-6}	$d_{ae}^2 \dot{V} SF_t^{2.3}$	1.152	$22.02\ SF_t^{1.24}\ \psi_{th}$	Dt_B	0.6391	$1-\frac{V_D(ET)}{V_T}$
	8	ET_2^d	5.5×10^{-5}	$d_{ae}^2 \dot{V}_a SF_t^3$	1.17	15.1	$D(\dot{V}_a SF_t)^{-1/4}$	0.538	1
	9	ET_1^c	3.0×10^{-4}	$d_{ae}^2 \dot{V}_a SF_t^3$	1	18	$D(\dot{V}_a SF_t)^{-1/4}$	1/2	1

- Deposition efficiency is the fraction of particles that enter a region that is deposited in that region
- ICRP 66 recommends addressing uncertainty via a scaling factor *c* on fitting parameter *a* that represents a 95% confidence bound on experimental data
- ICRP 66 has tabulated default deposition fractions as a function of breathing rate (Table F.1-6)
- Table 12 (above) shows formulae to calculate deposition efficiency as a function of breathing parameters including a scaling factor for anatomical size

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Compartmental Deposition Fraction

- After deposition into the 5 primary regions of the respiratory tract model, the deposition is further partitioned into compartments for use in the clearance model
- ICRP 66 recommends an uncertainty factor of 2-3 to define the 95% confidence interval for compartmental deposition fractions
- The slow-clearing fraction of particles deposited in the BB and bb regions are dependent on particle size. Bolch et al (2003) recommends adding a random error term to introduce uncertainty to the slow-clearing fraction

Table 17. Reference values of parameters for the compartment model to represent time-dependent particle transport from human respiratory tract

B. Partition of deposit in each region between compartments[b]

Region or deposition site	Compartment	Fraction of deposit in region assigned to compartment[c]
ET_2	ET_2	0.9995
	ET_{seq}	0.0005
BB	BB_1	$0.993-f_s$
	BB_2	f_s
	BB_{seq}	0.007
bb	bb_1	$0.993-f_s$
	bb_2	f_s
	bb_{seq}	0.007
AI	AI_1	0.3
	AI_2	0.6
	AI_3	0.1

[a] The half-times are approximate since the reference values are specified for the particle transport rates and are rounded in units of d^{-1}. A half-time is not given for the transport rate from AI_3 to LN_{TH}, since this rate was chosen to direct the required amount of material to the lymph nodes. The clearance half-time of compartment AI_3 is determined by the sum of the clearance rates from it.

[b] See Paragraph 181, Chapter 5 for default values used for relating f_s to d_{ae}.

[c] It is assumed that the slow-cleared fraction f_s is size-dependent. For modelling purposes f_s is taken to be:

$$f_s = 0.5 \text{ for } d_{ae} \leq 2.5\sqrt{\rho/\chi}\ \mu\text{m and}$$

$$f_s = 0.5\, e^{-0.63(d_{ae}\sqrt{\chi/\rho}-2.5)} \text{ for } d_{ae} > 2.5\sqrt{\rho/\chi}\ \mu\text{m.}$$

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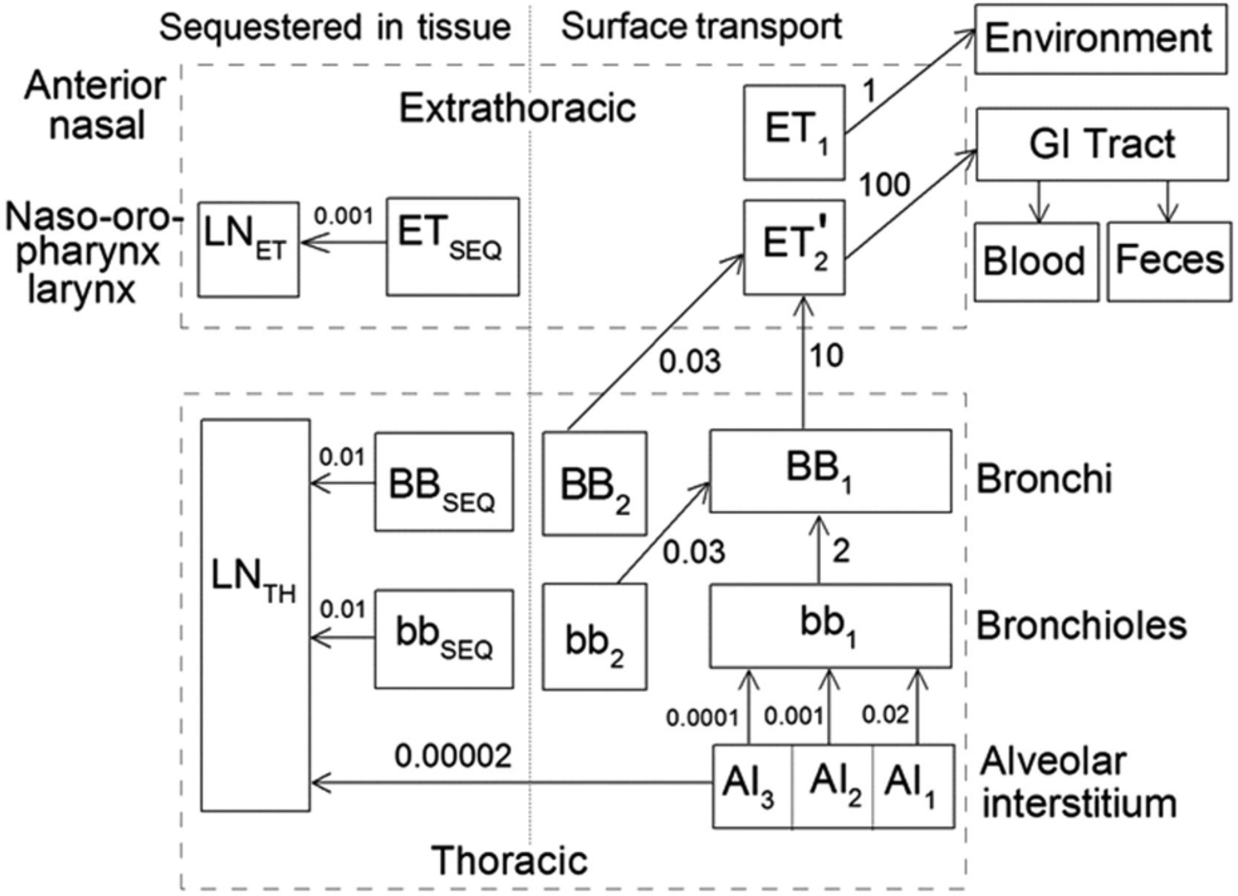
Fractional Clearance Rate

- Type F clearance rates (without blood absorption), intercompartmental relationships
  - Clearance up the respiratory tract
  - Clearance into lymph nodes
- Blood absorption
  - Main lungs regions that feed into blood
  - Chemical form affects dissolution rates



Current Challenges: Survey Methods for ODE Solving

- Initial value problem
- Python functions
  - Solve_IVP
    - Radau, LSODA, BDF, RK45, …
  - ODEINT
    - FORTRAN ODEPACK LSODA
- Eigenvalue problem
  - Python
    - Linear algebra package
- Stiffness of system, I-131
  - 2157.414
  - Magnitude ratio of transfer coefficients for ET2-seq

- Required Inputs
  - Defined transfer rates $[days^{-1}]$
  - Deposition fractions: initial activity at time = 0.00, normalized to inhaled activity
    - Subcategory fractions
      - BBi as a region of lung gets a DF
        - -gel, -sol, and –seq compartments get a fraction of the DF
  - Method function
    - Derivatives as a function of Y_n & t

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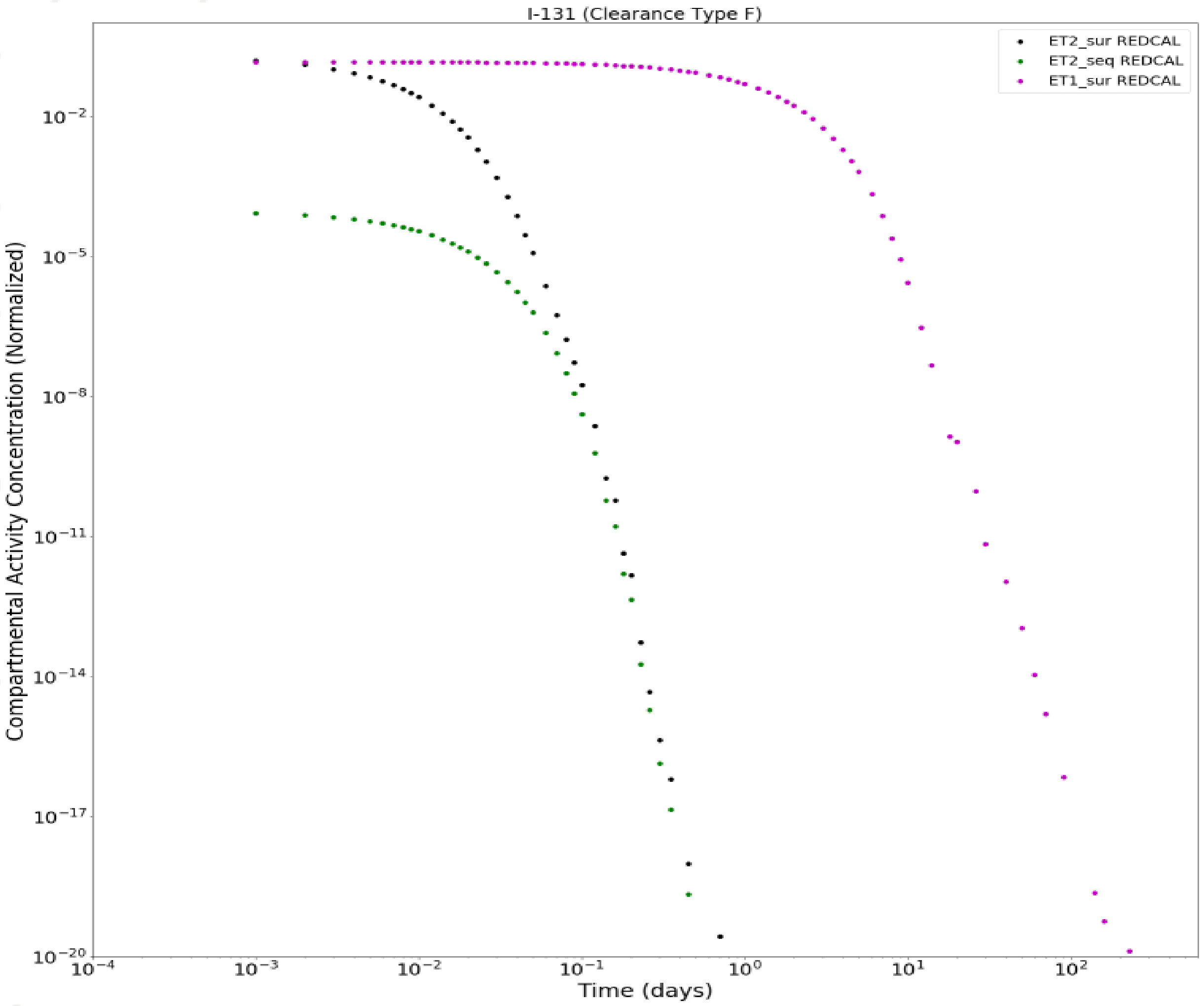
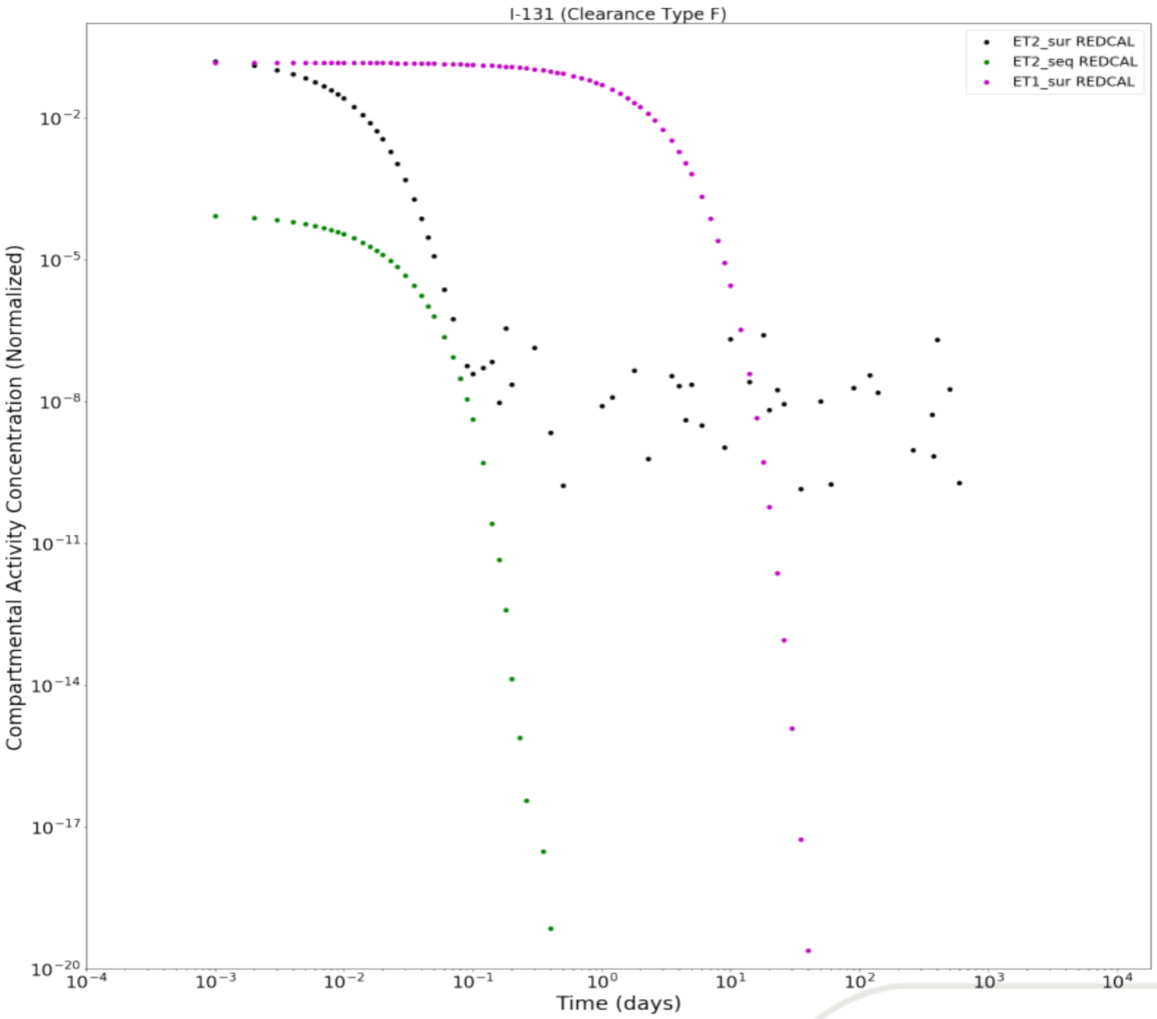
Current Challenges: Mathematical Kinetic Solving





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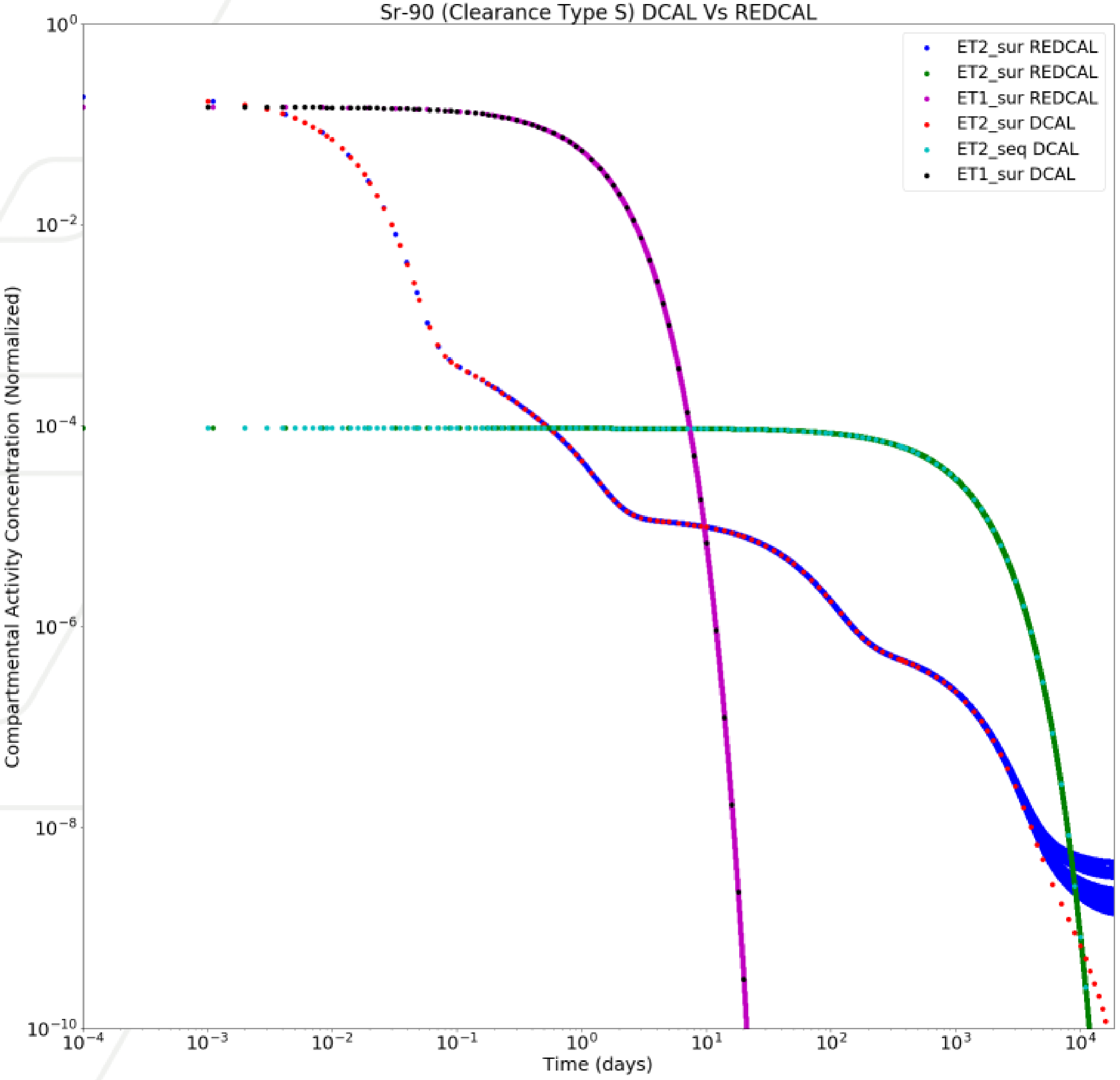

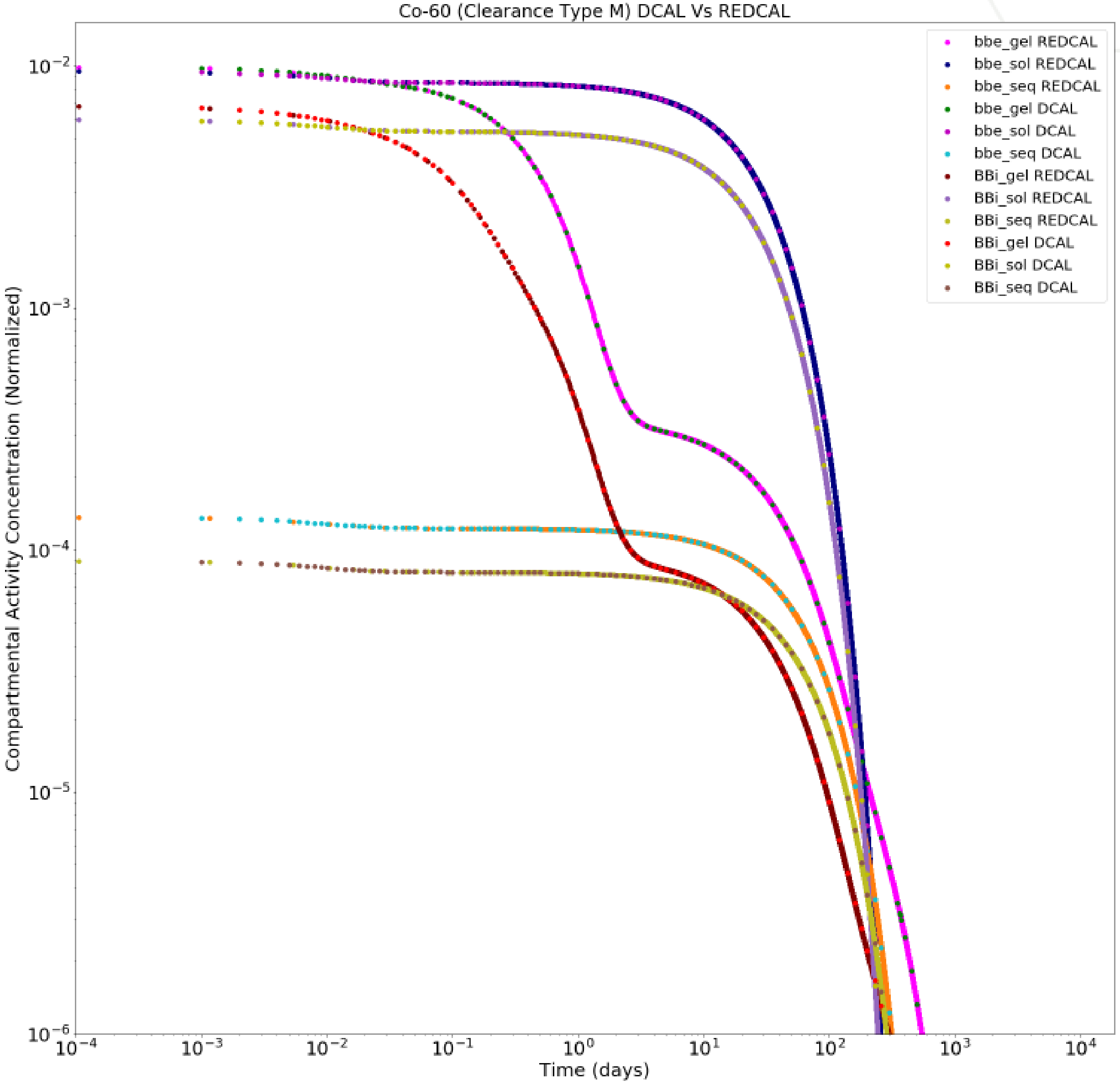

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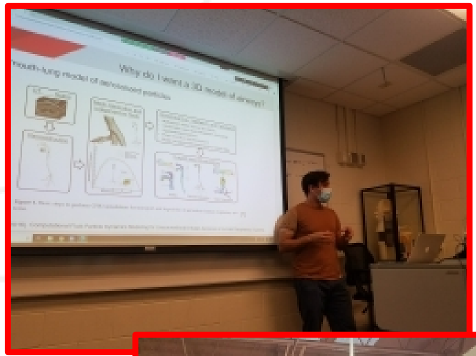
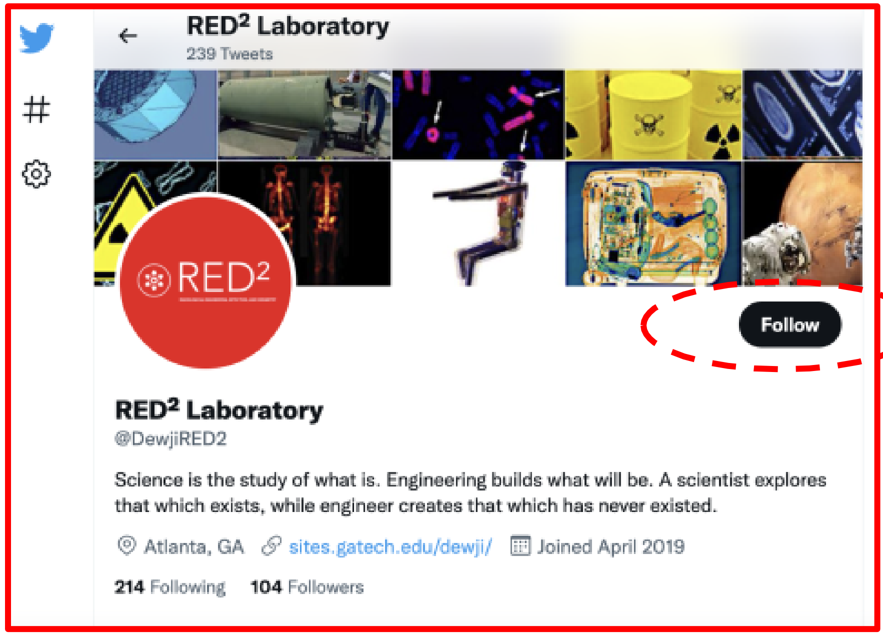
Conclusion

- A framework for propagating uncertainty through the HRTM to generate inhalation dose coefficient probability distributions is being developed
- Several codes have been developed to solve the HRTM and attempt to address the uncertainty
- ICRP 66 HRTM is comprised of 69 uncertain parameters, of which this project is handling 27
- Next presentation covering the impact of the project in more detail from a consequence management perspective

Questions!





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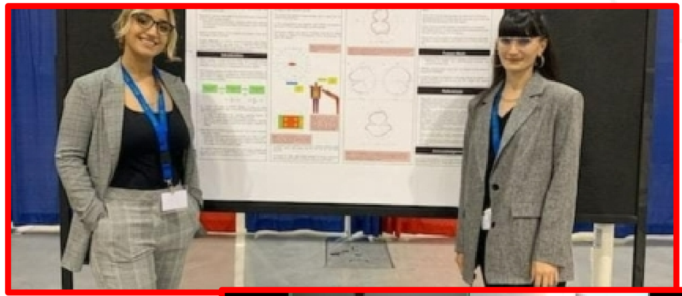

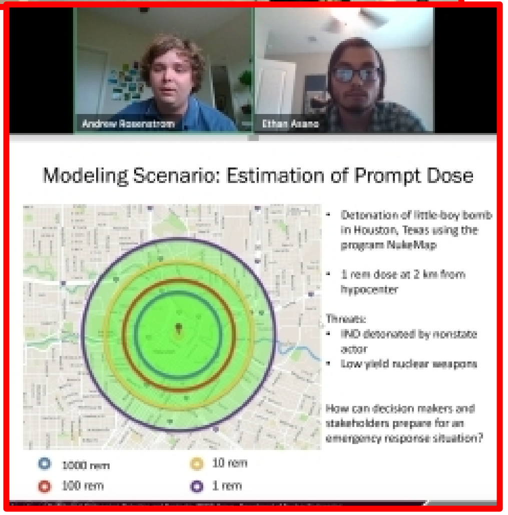

Day	Paper#	Room	Author(s)	Title
2022-07-18	**MPM-D.1**	Centennial Ballroom 300D	H Lee, GA Agasthya et al.	Machine Learning Methods and Multivariate Epidemiology in Radiation Risk Assessment Models
2022-07-18	**MPM-B.8**	Centennial Ballroom 300B	A Rosenstrom, M Santana et al.	High Power Beam Dump Shielding Design for the LCLS-II-HE Low Emittance Injector
2022-07-19	**TPM-D.10**	Centennial Ballroom 300D	DE Margot, AE Kalinowski et al.	Review of Uncertain Parameters in ICRP 66 Human Respiratory Tract Model (HRTM)
2022-07-19	**TPM-D.9**	Centennial Ballroom 300D	LD Cochran, CM Jelsema et al.	Uncertainty Propagation in ICRP 66 Human Respiratory Tract Model (HRTM)
2022-07-20	**WAM-D.1**	Centennial Ballroom 300D	EA Asano, SA Dewji	Efficiency Comparison of Hybrid Radiation Transport Variance Reduction Methods for Wide Area Environmental Contamination Assay Applications

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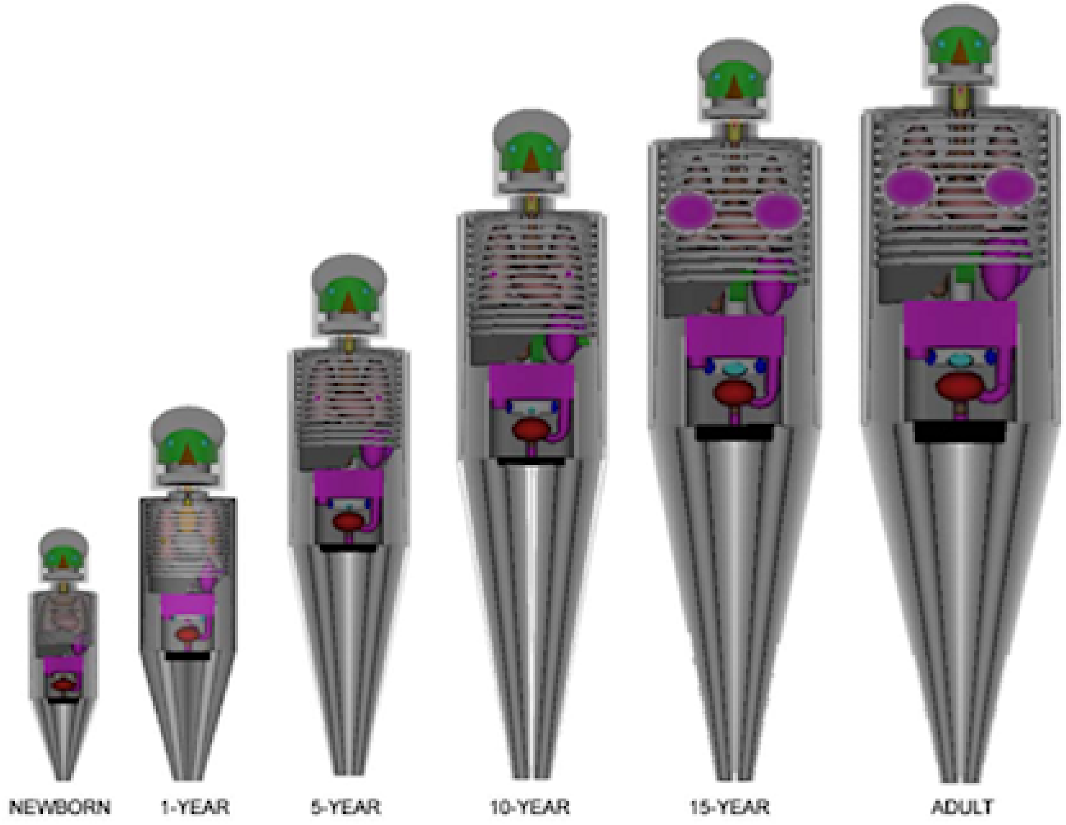
Ra-223 Decay Chain: Half-lives and Branching Fractions

	Nuclide	Halflife	f1		Nuclide	f2		Nuclide	f3		Nuclide
1	Ra-223	11.43d	1.0+00->	2	Rn-219						
2	Rn-219	3.96s	1.0+00->	3	Po-215						
3	Po-215	1.781E-3s	1.0+00->	4	Pb-211						
4	Pb-211	36.1m	1.0+00->	5	Bi-211						
5	Bi-211	2.14m	1.0+00->	6	Tl-207	2.8-03->	7	Po-211			
6	Tl-207	4.77m									
7	Po-211	0.516s									

Ra-226 Decay Chain: Half-lives and Branching Fractions

	Nuclide	Halflife	f1		Nuclide	f2		Nuclide	f3		Nuclide
1	Ra-226	1600y	1.0+00->	2	Rn-222						
2	Rn-222	3.8235d	1.0+00->	3	Po-218						
3	Po-218	3.10m	1.0+00->	4	Pb-214	2.0-04->	5	At-218			
4	Pb-214	26.8m	1.0+00->	6	Bi-214						
5	At-218	1.5s	1.0+00->	6	Bi-214	1.0-03->	7	Rn-218			
6	Bi-214	19.9m	1.0+00->	8	Po-214	2.1-04->	9	Tl-210			
7	Rn-218	3.5E-2s	1.0+00->	8	Po-214						
8	Po-214	1.643E-4s	1.0+00->	10	Pb-210						
9	Tl-210	1.30m	1.0+00->	10	Pb-210						
10	Pb-210	22.20y	1.0+00->	11	Bi-210	1.9-08->	12	Hg-206			
11	Bi-210	5.013d	1.0+00->	13	Po-210	1.3-06->	14	Tl-206			
12	Hg-206	8.15m	1.0+00->	14	Tl-206						
13	Po-210	138.376d									
14	Tl-206	4.200m									

Dosimetric Models



- To create a dose coefficient, biokinetic models integrated with physical dosimetry models
  - Biokinetics defines source strength as a function of time
  - Phantom defines geometry for radiation transport modeling
    - Organ masses & volumes
- Decay type & data (ICRP 107)
- Quantities
  - $U(T) = \int_0^T A(t)dt$
  - $AF(T,S) = \frac{T\ energy\ absorption}{S\ energy\ emission}$
  - $SEE\left(T \underset{t}{\leftarrow} S\right) = \frac{1}{M_T} \sum_R^{Rn} W_R E_R Y_R AF_R(T \underset{t}{\leftarrow} S, E_R)$

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