Paper

INTERNAL DOSE RESEARCH PAPERS

INTDOSKIT: An R-Code for Calculation of Dose Coefficients and Studying Their Uncertainties

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Abstract—**An R-code, which allows the calculation of the time dependent activity distribution based on ICRP reference models, the number of decays in a commitment period, and the dose coefficients for tissues and organs of the human body, has been developed. R Language was chosen due to its powerful mathematical and statistical modeling features, as well as its graphical capabilities. The developed set of functions and constants (called "INTDOSKIT") can be sourced in R-scripts that define or import the models and calculations to be performed. The code has been tested on models of several radionuclides and was successfully validated against reference data taken from ICRP OIR Data Viewer software. Furthermore, the code has been tested and verified on the modeling of the radioactivity of decay chains using data of the ^{233}Ra model presented by Höllriegl and colleagues. The results of calculations with INTDOSKIT demonstrated that the code is able to reproduce the ICRP bioassay data and dose coefficients. Deviations are a few percent only and are due mainly to rounding in the original data. Lastly, the code is able to handle uncertainty and sensitivity studies as demonstrated by the results in a pilot study of injection of ^{241}Am, which estimated geometric standard deviations (GSD) for dose coefficients ranging between 1.25 (bone-surface) and 1.66 (testes); these results are consistent with those obtained from similar studies done by other researchers who reported GSD values ranging from 1.13 to 1.73.**
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Key words: biokinetics; dose assessment; dosimetry, internal; radionuclide

INTRODUCTION

DOSE ASSESSMENTS following intakes of radionuclides require the use of models, as these doses cannot be measured directly; i.e., no operational dose quantities (mSv) are available. Activities (Bq) of the nuclides can be measured in vivo or in vitro. These measurements can be related to the intake (the amount of activity that has entered the body) using biokinetic models describing the behavior of the element in the human body. For a known intake and biokinetic behavior of a radionuclide, the committed dose (i.e., the dose that is accumulated by the decays in the body over a commitment period) can be calculated using dosimetric models. The dosimetric model describes the absorption of radiation quanta emitted following the decay of a radionuclide inside the body. These models are based on computational models of the human body and Monte Carlo Simulations of radiation transport. The International Commission on Radiological Protection (ICRP 2024) describes the concept of internal dose assessment and publishes biokinetic and dosimetric models (ICRP 2015, 2016a and b, 2017, 2019, 2022). Key to the ICRP concept of internal dosimetry is the use of reference models and reference computational phantoms. This allows one to simplify the calculation of doses using dose coefficients, which give a reference dose to the target organ (or the effective dose) for an intake of 1 Bq of the radionuclide. The dose can then be easily calculated by multiplication of intake and dose coefficient.

ICRP provides the dose coefficients for its latest models for workers in electronic form using the program "OIR Data Viewer," which is available as an electronic annex to the documents of the publication of the series "Occupational Intakes of Radionuclides" (OIR) (ICRP 2015, 2016, 2017, 2019, 2022). The solutions of the reference biokinetic models (retention and excretion functions) also are provided by this tool. These data can be applied in the dose assessments. However, the data provided only covers the reference situations, and as reference data, these are given without information on the uncertainties of the values.

In this paper, the authors present the development and the implementation of a code developed using the R programming language (R Core Team 2023), which allows the calculation of dose coefficients based on the methods and models published by ICRP. The code also allows one to calculate doses and dose coefficients for other models

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(e.g., modified models describing the disturbed biokinetic behavior of radionuclides following decorporation therapy) and will be used to study the uncertainty of the models or the sensitivity of the single parameters of the models. In this paper, we present the structure of the code and its validation by reproducing published data. Finally, we show an example of a small uncertainty study that used the code.

MATERIALS AND METHODS

R Language (R Core Team 2023) was chosen for implementing the ICRP system of internal dosimetry, as it is an open-source free software environment, which provides functions for solving the differential equations of the biokinetic models and many statistical functions that will be employed for the uncertainty studies. R-Language has already been used in dosimetry applications (Hernández 2023; Lamart 2017). Another advantage of R-Language is that for accessing elements of arrays and matrices, the code can use names instead of index numbers, which allows one to use names of compartments in the code, thus enhancing its human readability. Mistakes by using wrong indices could be avoided by using the names to access the values, e.g., when biokinetic compartments were assigned to dosimetric source regions in the code. RStudio (Posit 2023) was used as an Integrated Development Environment

INTDOSKIT consists of three files with functions and constants for use in the calculations. The files can be included (sourced) in R-Scripts. Templates of R-Scripts for typical tasks (e.g., calculation of S-Coefficients using ICRP SAF-Data or calculation of a set of dose coefficients) have been developed, and guidance on their use is provided in the documentation of INTDOSKIT. All files containing code are extensively commented to allow users to understand and modify the functions according to their needs. Plain text files in a defined format are used to describe the models and for importing and exporting data. Functions for reading these files and exporting the results of the calculations are provided. The latter allows one to produce files in comma-separated-values (.csv) format that can be imported to spreadsheet software (e.g., Microsoft Excel) for further processing.

Implementation and solving of biokinetic models

Biokinetic models of ICRP are using compartmental formalism (see, e.g., Godfrey 1983; Jacquez 1996, 1999). It is assumed that a nuclide is transported between pools (compartments) of material with kinetically homogeneous behavior. It also is assumed that the material entering the pools is immediately available for transport to another pool. The mass-balance of each pool can be described by a differential equation. The compartmental system is the network of interconnected pools. The system of differential equations for the mass balances of all pools is the mathematical model of the system. For its reference models, ICRP uses a linear first order kinetics approach, which allows one to describe the kinetics of the transfer between pools/compartments using a single number, called a transfer coefficient (ICRP 2015). The transfer between the pools is proportional to the amount of material left in the pool by the material. This allows one to describe the model as matrix $\underline{M}$ of transfer coefficients and a vector $\vec{q}$ of compartment contents. Compartments that are connected by a flow of material have positive values in the matrix element $\underline{M}[\text{from}, \text{to}]$; all other elements are zero. The compartment vector gives the content of the compartments at a given time t. The compartments of the models can be interpreted as different states of the nuclide in the body, which can be either a pool in a part of a given organ, in the whole organ, or be distributed over multiple organs (e.g., soft tissues). For the calculation of doses, each compartment of the biokinetic model must be associated to the corresponding dosimetric source regions, which allocate the decays anatomically in the body.

In its publications, ICRP provides a box model representation of the compartmental system structure (represented as network of connected boxes) and a table of the transfer coefficients of the biokinetic model (ICRP 2015, 2016a, 2017, 2019, 2022). The values of the transfer coefficients are given in units of per day (d^{-1}) for stable isotopes of the elements. The physical decay can be added as additional loss in the compartments, with a transfer coefficient of ln(2)/half-life of the radioisotope in d^{-1}. The loss can be either directed to the environment (loss out of the system) or to a compartment of the biokinetic model of a progeny. The latter allows one to implement decay chains.

INTDOSKIT uses plain text files to describe a biokinetic model by the names of the compartments, the corresponding source regions, and the values of the transfer coefficients. Functions for reading the model from a file are provided. In the computer's memory, a model is kept as a list of R-variables that can be accessed by the user via model$variable in the user's R-Script. The variables are a list of the names of the compartment "compnames," a list of the names of the dosimetric source regions "bio2dos" and the matrix of the transfer coefficients "tcoeff." In the following text, this list is referred to as "R-Model." The feature of "named objects" in R is used by assigning the names in "compnames" to the variables. This allows one to access a transfer coefficient of the models either by indices (model$tcoefff[i,j]) or by names (model$tcoefff["Blood", "Liver"]); the same holds for the bio2dos-association. The dosimetric source region of a biokinetic compartment "compartment name" can be accessed by calling "bio2dos["compartment name"]." This enhances human readability of the code. After the R-model is set up in R-Script (e.g., by reading it from a file), it can be modified by changing the elements of the tcoeff-matrix. Additional compartments can be added to the model by adding rows and columns to the tcoeff-matrix and adding the names and associations of the new compartments to "compnames" and "bio2dos."

Two R-models of the same radionuclide can be coupled by extending the matrix to contain all compartments. A function "connect_models(…)" is provided to perform this task for two models of the same nuclide. This function merges the tcoeff-matrices into a larger matrix and extends the vectors of compnames and bio2dos. This feature allows the use of one file for the generic model of HATM, HRTM, or wound (ICRP 2006, 2015; NCRP 2006) and to couple this to the systemic model of the radionuclide. A function "delete_compartment(…)" is provided to remove unused compartments from the "R-Model."

For the solution of the "R-Model" of one radionuclide, the matrix of transfer coefficients needs to be converted into a "compartmental matrix" c. This is done by redefining the diagonal elements c_{ii} of the matrix as −1.0 times the sum of the transfer coefficients of all losses from compartment i. (Jaquez 1999). The compartmental system can then be described by eqn (1):

$$\frac{d\vec{q}}{dt} = \vec{T}(t) + \underline{c} \cdot \vec{q}, \qquad (1)$$

where $\vec{q}(t)$ = vector of compartment contents;
$\underline{c}$ = compartmental matrix of transfer coefficients c_{ij};
$c_{ii} = -\left(c_{i0} + \sum_{j \neq i} c_{ij}\right)$; and $\vec{T}(t)$ = vector of input to compartments from outside the system.

Initial conditions of the problem to be solved are defined by preparing a vector q_0, which contains the contents of the compartments at time t = 0. Depending on the route of intake, one or more compartments represented by the elements of q_0 have non-zero elements, while all other elements of q_0 are 0. For the calculation of the initial deposition in the lungs for mono- and polydisperse aerosols, functions have been added in the INTDOSKIT R-code that implement the deposition model of ICRP (1994, 2015).

For solving a model for one radionuclide, two functions "solve_eigen(…)" and "solve_ode(…)" are available in INTDOSKIT. Both functions accept the R-model, a vector of compartmental content at initial time, and a list of times the solution shall be provided. The latter needs to be given in units of days (the same units as used in the R-model). In the first step, these functions set up the compartmental matrix C. The function "solve_eigen(…)" implements an Eigenanalysis of the compartmental matrix for solving the differential equation (Polig 2001). Matrix functions provided by R are used for this. The function "solve_ode(…)" uses the ode-solver provided in the R-library "deSolve" (Soetaert 2010). The deSolve-library provides several algorithms for the numerical solution. The algorithm can be selected as a parameter in the function. Mate-Kole et al. (2023) compared several solvers implemented in the Python language and discussed their performance and the stability and accuracy of the solutions. Using INTDOSKIT, similar observations were made by the developers. Users need to be careful when selecting the algorithm of the solver and should compare solutions obtained with different solvers, especially in the case of decay chains when the matrices representing the systems become extremely sparse, which can be challenging for any solver.

Both INTDOSKIT-functions for solving a biokinetic model return a list of variables referred to as "R-Solution" in this manuscript. All objects returned are named using "compnames," which for convenience is also part of the list. The variable "solution" is a matrix of the dimension "number of compartments in the model" times "number of times" and contains the contents of the compartments at time t. The variable "NDEC" is a vector of length "number of compartments" and contains the number of decays in each biokinetic compartment. This is calculated by numerical integration of the solution of each compartment from t = 0 to the last timepoint of the calculation. The number of decays in the biokinetic compartments is one parameter required in the dose calculation.

Decay chains

For implementing a decay chain, the matrices of the nuclide models (which as R-Models might also include HRTM, HATM, or wound compartments) need to be arranged in a block-diagonal matrix form. The physical decay is then included as a transfer coefficient from the compartment in the parent model to the corresponding compartment(s) in the progeny model. Values of the other elements in the "off-blocks" are zero. A function "decay_chain(…)" is used to set up the decay chain based on the models. For associating the compartments of parent and progeny model, a "connector-file" (plain text) is used. The compartments in the models of the different nuclides might have different names and/or different definitions (e.g., soft-tissues). Each line of the "connector-file" is a list of associated compartment names and a fraction. The function "decay_chain (…)" also requires a list of the names of the nuclides in the chain and a list of the decay constants of the nuclides (in units of per day). It constructs the block diagonal matrix as described above. The names of the compartments are changed to nuclide_name%compartment_name (i.e., Po218%Liver) to allow identification of the nuclide in the solution of the system. The function "decay_chain(…)" returns a list of variables, referred to as "R-Chain." The list contains the "R-Model" of the whole chain, a list "isotopes," which gives the names of the isotopes, and a list "lambdas" that contains the corresponding decay constants (in units of per day). The function "add_decay(…)" allows one to add nuclides to an "R-chain". A decay to an isotope, whose biokinetic behavior is not to be modeled (e.g., a stable nuclide), can be added via the function "add_decay2stable(…)."

A function "solve_chain(…)" was implemented for solving the "R-Chain." It requires the"R-Chain," the vector of initial values in all compartments and the list of times. It solves the system of the whole chain using "solve_ode(…)" and splits the solution into solutions for each radionuclide. These solutions are given in activity units using the lambdas included in the "R-Chain." Like "solve_ode(…)" it returns variables "solution" in units of Bq, "NDEC" and "balance", which now are lists of values named by the nuclides. "Solve_chain(…)" additionally returns a variable called "names," which contains the names of the nuclides in the chain. The single values can be accessed using R syntax; e.g., "solution$Po218$NDEC," gives the values of the NDEC for the nuclide ^{218}Po in the solution of the chain.

Fig. 1 summarizes the workflow of setting up and solving biokinetic models and shows the corresponding R-functions of INTDOSKIT.

Dosimetric models and dose calculations

Calculation of internal doses in the ICRP methodology (ICRP 2015, 2016) is based on the concept of source regions r_S and target tissues r_T. The latter are the tissues for which the doses are to be calculated. In most cases, the target tissues are defined comprising the whole organ or tissue. For some targets, the location of the cells sensitive to ionizing radiation have been defined as target tissues, e.g., in the walls of bronchiolar airways or in the gastrointestinal tract. Source regions are the parts of the body in which radiation is emitted following the decay of a nucleus. Again, these can be whole organs or parts thereof. ICRP reference models define 43 target tissues and 79 source regions (ICRP 2009, 2016).

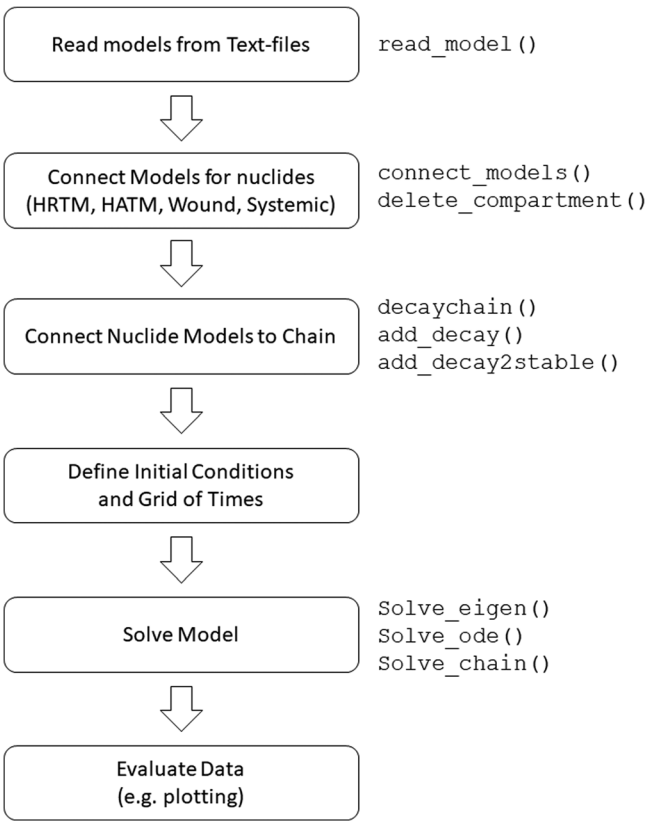

Fig. 1. Basic workflow for the implementation and solution of a biokinetic model using the INTDOSKIT R code. Functions of the code that can be used are given in the right column.

In its Publication 133, ICRP provides specific absorbed fractions (SAF-values), which have been calculated using the adult reference phantoms (ICRP 2009, 2016). These energy-dependent SAF values give the fraction of energy of a radiation quantum emitted in a source region, which is absorbed per mass in a target tissue. The type of radiation quanta emitted and their energies are physical properties of the decaying nuclei. Reference values of these properties to be used in dose calculations have been compiled by ICRP in Publication 107 (ICRP 2008). Both publications have electronic annexes that provide the data in machine readable form. The INTDOSKIT provides functions "read_nuclide(…)" and "read_SAF(…)" to read these formats.

For internal dose calculations, the two kinds of information (radiation emitted in the decay and SAF-value) need to be combined in a (radiation weighted) S-Coefficient $S_w^{M,F}(r_T \leftarrow r_S)$, which provides the dose to a target tissue r_T following one decay of a nucleus in a source region r_S using eqn (2):

$$S_w^{M,F}(r_T \leftarrow r_S) = \sum_R w_R \sum_i E_{R,i} Y_{R,i} \Phi^{M,F}(r_T \leftarrow r_S, E_{R,i}), \quad (2)$$

where

$E_{R,I}$ = Energy of the ith Radiation R, which is emitted following the decay of the nucleus;

$Y_{R,I}$ = Yield of the ith Radiation R per decay of a nucleus (Bq s)$^{-1}$;

w_R = Radiation weighting factor for radiation type R; and

$\Phi^{M,F}(r_T \leftarrow r_S, E_{R,i})$ = specific absorbed fraction (SAF), which gives the fraction of energy $E_{R,i}$ emitted in source region r_S by radiation type R, which is absorbed in the target tissue r_T per mass of target tissue (kg^{-1}) in the male (M) or female (F) anatomic model.

The contribution of the source region to the dose in the target tissue is calculated by multiplying this value with the number of decays in the source region (in the INTDOSKIT R-code: NDEC). The total dose to the target tissue r_T is the sum of the contributions of all source regions r_S. Functions for the calculation of the S-Coefficients for one type of radiation "SCoeff_calcRadtype(…)" (e.g., alpha, electrons, gamma) and for beta spectra "SCoeff_calcBeta(…)" were implemented together with a function "SCoeff_Calc(…)"

combining the use of these to take into account all radiations emitted by a nucleus. These functions require the information on the nucleus from the ICRP 107 compilation (ICRP 2008) and the information on the SAF from the ICRP Publication 133 electronic annex (ICRP 2016). The information on the SAF values is provided on a grid of energies. Cubic spline interpolation is used to calculate values outside of the grid points. The ICRP reference values of the radiation weighting factors w_R are provided in a variable of the code. If these values are unchanged, the unit of the S-Coefficient will be Sv decay^{-1}. If all values are set to 1 (e.g., no radiation weighting applied), the S-Coefficients will be in Gy decay^{-1}, allowing calculation of absorbed dose to organs instead of equivalent doses. The S-Coefficients are stored in a matrix of dimensions r_T x r_S, whose elements are the values of S(r_T, r_S). A function "SCoeff_calcList(…)" has been added to simplify the calculation of the whole matrix, which can be stored in and read from a plain text file for reusing it in other calculations with INTDOSKIT.

In INTDOSKIT, "Other-Tissues" is introduced as source region for the biokinetic compartments "Soft Tissues" in a systemic biokinetic model, which is comprised of several source regions. For calculation of the S-Coefficient S(r_T, Other-Tissues), the S-Coefficients for all source regions r_S included in the definition are calculated and added, weighted by their mass fraction. By doing this, the Other-Tissues source region can be used the same way in dose calculations as in all other source regions; i.e., the number of decays in the biokinetic Soft Tissues compartments is multiplied by the S-Coefficient S(r_T, Other Tissues). The tissues to be included have to be selected from a list of candidate source regions provided in ICRP Publication 133 (ICRP 2016) and the definition of the compartments of the biokinetic model. If a dosimetric source region, which is a candidate for inclusion in Other Tissues, has a biokinetic compartment explicitly assigned to it, it is not included in the Other Tissues source region assigned to the biokinetic soft tissues compartment.

The doses to the target regions are then calculated by multiplying the Matrix of S-Coefficients with the vector of numbers of decays in the source regions (NDEC). A function "NDECin_ICRPSources(…)" can be used to create this vector from the NDEC-vector of a solved R-Model, and this function uses the bio2dos information of the R-Model to associate the number of decays in the biokinetic compartments to the corresponding source regions. A function "calc_hT(…)" performs these calculations and provides a vector of doses to the target tissues, which can then be

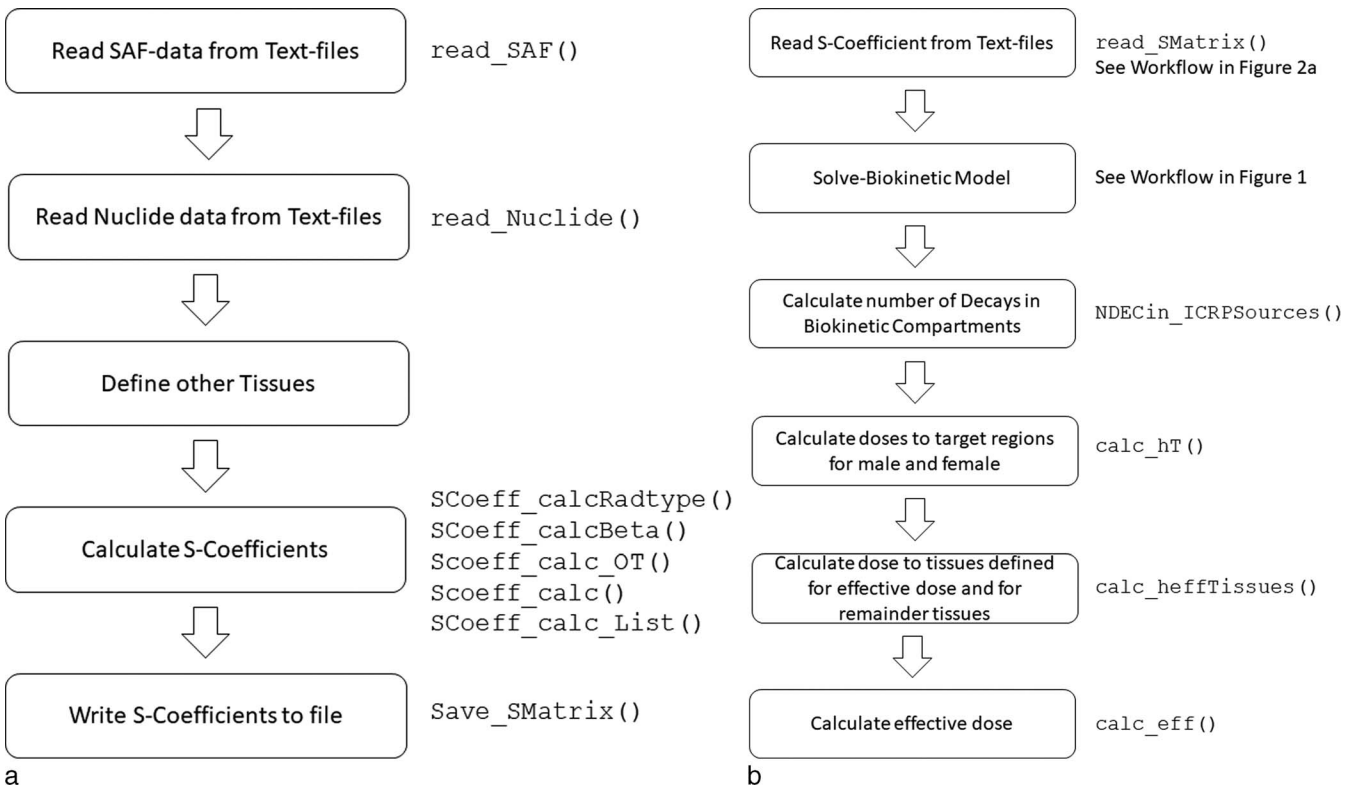

Fig. 2. Sequence of steps in calculation of internal doses using ICRP methodology in INTDOSKIT. (a) Basic workflow for calculation of S-Coefficients using INTDOSKIT. Functions of the code that can be used are given in the right column. The contribution of each Radiation type is calculated separately, which allows evaluating its contribution to the dose. The S-Coefficients can be calculated in Sv decay^{-1} or in Gy decay^{-1} depending on the choice of radiation weighting factors. (b) Basic workflow for calculation of doses using the R code. Functions of the code that can be used are given in the right column. A function calc_doses(), which merges the last three steps, is available for convenient use.

converted to the doses to the organs defined by ICRP for calculation of effective dose. For some of these organs, these are weighted sums of doses to the target regions; e.g., dose to the Tissue "Colon" is the weighted sum of the doses to the target regions RS-stem (0.2), LC-stem (0.4), and RC-stem (0.4), which are the stem cells of the rectosigmoid, the left and the right colon. The function "calc_hEffTissues (…)" has been implemented to perform these calculations, which include calculation of the dose to "Remainder Tissues" (not to be confounded with Other Tissues). The latter is dependent on the biokinetic model, while the remainder tissues comprise all organs/tissues that have no specific tissue weighting factor assigned to them. Calculation of effective dose by sex-averaging male and female equivalent doses to the organs and summing these using tissue weighting factors w_T is implemented in the function "calc_eff(…)." A function "calc_doses(…)", which calculates effective dose and all organ doses and provides them as lists, has been added to INTODSKIT for convenience of the users. Fig. 2 summarizes the steps in the dose calculation and indicates how these are implemented in the code. Templates for calculation of S-coefficients and for the calculation of a list of dose coefficients for a nuclide have been created. These can be adapted to use biokinetic models of other radionuclides.

Validation and application examples

For the validation of INTDOSKIT, the authors implemented biokinetic and dosimetric models of many nuclides and compared the results for different scenarios (injection, ingestion and inhalation) to the data published by ICRP in their OIR Data Viewer (ICRP 2022). Bioassay functions were plotted using graphical capabilities of R, and all data including the dose values calculated were exported to text files for further processing. ICRP Publications 66 and 103 (ICRP 1994, 2015) present tables giving the deposition in different regions of the lungs for different scenarios. These tables as well as the tables given by Klumpp and Bertelli using their KDEP code (Klumpp and Bertelli 2017) could be reproduced by INTDOSKIT with deviations only due to rounding in the published tables.

In this manuscript, the authors present ^{241}Am (ICRP 2019) as an example of a nuclide that decays into a "stable" (i.e., dosimetrically negligible) progeny. No decay chain was needed to be set up in this case. For testing and validating the implementation of decay chains, the biokinetic model for ^{233}Ra published by Höllriegl et al. (2021) was used as basis for comparison. In the additional materials of their paper, Höllriegl et al. (2021) present the full specification of the models used in their study, which for the work presented here eliminated one source of possible mistakes in implementation. Text-files for the generic models (HATM, HRTM, and wound) and the systemic models of the elements involved were prepared based on the corresponding publications (ICRP 2006, 2015, 2016b, 2019; Höllriegl 2021; NCRP 2006). R-Scripts have been prepared, which read and connect the models, solve them, plot the bioassay functions together with reference data, and finally calculate the dose coefficients.

As an example of a research application of INTDOSKIT, a pilot study of estimation of uncertainties of dose coefficients is presented. This is based on a Monte Carlo algorithm with repeated calculations using model parameters sampled from distributions instead of using the reference values. This type of uncertainty study is also performed by other authors, such as Puncher and colleagues (Puncher 2012a and b; Li 2015). Data produced by these studies is a dataset of multiple estimations of the values of interest. Values of interest could be the bioassay functions, the numbers of decays in biokinetic

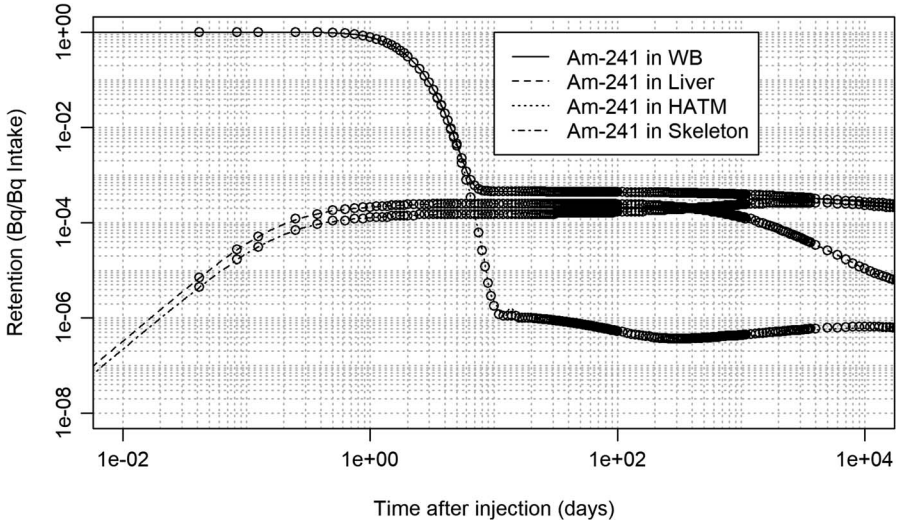

Fig. 3. Retention functions for ingestion of ^{241}Am. Lines are the values calculated using INTDOSKIT, and points are the reference data exported from OIR Data Viewer (ICRP 2022)

compartments, or doses. In the pilot study, retention functions and dose coefficients were calculated. For each dataset, the distribution of the values is analyzed, e.g., by calculation of statistical parameters such as the quantiles of the distribution. A key point for the Monte Carlo type uncertainty studies is the definition of the distribution of the parameters from which actual values will be sampled. In the pilot study presented here, lognormal distributions defined by their mean (=reference value of the parameter) and their width (given as geometric standard deviation GSD) were used for the sampling of parameters. In our pilot study, a value of 1.41 for the GSD, which is comparable to values used by other authors, was chosen. In a study of the plutonium model, Puncher used GSD-values between 1.3 and 1.71 for the parameter distributions (Puncher 2012). We used the same GSD for all parameters, which is a simplifying assumption. However, only limited information about the uncertainty of the transfer-coefficients in biokinetic models is available in the literature. ICRP's reference models are given without any uncertainties, and the transfer-coefficients are seen as reference values (ICRP 2015).

This type of Monte-Carlo study can also be used as sensitivity analysis when only one of the parameters is sampled and all others remain fixed. Here, the influence of this parameter on the distribution of the model's solutions can be evaluated.

The pilot study presented here is for the scenario of injection of ^{241}Am; i.e., only the systemic model has been used. Additional functions have been implemented in INTDOSKIT to perform the sampling and modification of the matrix of transfer coefficients of the model. Information about the distributions to be sampled have been added to the text files describing the models. The statistical capabilities of the R-Language and its libraries (R core team 2023) were used to evaluate the data produced.

RESULTS

The bioassay functions and the dose coefficients calculated using INTDOSKIT are overall in good agreement with reference data. The deviations are less than 4%, which in most cases is due to rounding of reference data. One must keep in mind that the precision of data reported in ICRP OIR Data Viewer is limited to one significant number (ICRP 2019). The S-Coefficients, which are the basis for the dose calculations, could not be validated by direct comparison to reference data, as these values are not available. Indirect validation was possible by comparison of the dose coefficients. Fig. 3 shows the retention functions for the ingestion of ^{241}Am, and Table 1 shows the comparison of the dose coefficients calculated for this scenario.

Results for the implementation of decay chains are also in good agreement, as the tables in the paper of Höllriegel et al. (2021) could be reproduced by INTDOSKIT. As an example, Table 2 shows the deviations in the number of decays for the different nuclides in the organs. Most values differ by less than 1%, while some values are showing deviations in the order of magnitude of 10%. These rather large deviations can be explained by rounding of values in the publication. For example, the deviation of 11% for ^{207}Tl in Compartment UB-Cont are due to the values 0.04 (Höllriegl

Table 1. Comparison of organ dose coefficients calculated with INTDOSKIT with reference values from ICRP OIR Data Viewer (ICRP 2019) for ingestion of ^{241}Am. Three digits are given for the calculations using INTDOSKIT, while only two digits are provided in the reference data from ICRP OIR Data Viewer. Thus, deviations are expected due to rounding off. Dose coefficients for effective Dose for other scenarios are also provided.

Organ	Dose coefficients (Sv Bq^{-1}) INTDOSKIT	ICRP OIR Data Viewer	Deviation (%)
Dose coefficients for equivalent dose (Sv Bq^{-1}) – Ingestion (male)			
Bone marrow	9.10×10^{-08}	9.10×10^{-08}	± 0%
Colon	1.11×10^{-08}	1.10×10^{-08}	+ 1%
Lung	8.64×10^{-09}	8.60×10^{-09}	+ 1%
Stomach	1.14×10^{-08}	1.10×10^{-08}	+ 3%
Testes	7.55×10^{-08}	7.50×10^{-08}	+ 1%
Urinary bladder	1.44×10^{-08}	1.40×10^{-08}	+ 3%
Oesophagus	1.13×10^{-08}	1.10×10^{-08}	+ 3%
Liver	3.69×10^{-07}	3.70×10^{-07}	± 0%
Thyroid	1.25×10^{-08}	1.30×10^{-08}	- 3%
Bone Surface	1.16×10^{-06}	1.20×10^{-06}	- 3%
Brain	1.40×10^{-08}	1.40×10^{-08}	± 0%
Breast	1.40×10^{-08}	1.40×10^{-08}	± 0%
Salivary glands	1.40×10^{-08}	1.40×10^{-08}	± 0%
Skin	1.39×10^{-08}	1.40×10^{-08}	- 1%
Adrenals	1.18×10^{-08}	1.20×10^{-08}	- 1%
ET of HRTM[a]	1.27×10^{-08}	1.30×10^{-08}	- 2%
Gall bladder	1.40×10^{-08}	1.40×10^{-08}	± 0%
Heart	1.25×10^{-08}	1.30×10^{-08}	- 4%
Kidneys	2.82×10^{-08}	2.80×10^{-08}	+ 1%
Lymphatic nodes	1.38×10^{-08}	1.40×10^{-08}	- 2%
Muscle	1.43×10^{-08}	1.40×10^{-08}	+ 2%
Oral mucosa	1.46×10^{-08}	1.50×10^{-08}	- 2%
Pancreas	1.19×10^{-08}	1.20×10^{-08}	- 1%
Prostate	1.40×10^{-08}	1.40×10^{-08}	± 0%
Small intestine	1.11×10^{-08}	1.10×10^{-08}	+ 1%
Spleen	9.65×10^{-09}	9.60×10^{-09}	+ 1%
Thymus	1.40×10^{-08}	1.40×10^{-08}	± 0%
Dose Coefficients for effective dose (Sv/Bq)			
Ingestion ($f_A = 5 \times 10^{-4}$)[b]	5.91×10^{-08}	5.90×10^{-08}	± 0%
Injection	1.18×10^{-04}	1.20×10^{-04}	-1 %
Inhalation (Type M, AMAD = 5 mu)[c]	7.90×10^{-06}	8.00×10^{-06}	-1 %

[a] ET of HRTM: Part of the respiratory tract, consisting of the anterior nasal passage (the ET_1 region) and the posterior nasal passage, pharynx, and larynx (the ET_2 region) (ICRP 2015).

[b] f_A: Fraction of Activity ingested that enters the bloodstream (ICRP 2006).

[c] AMAD: Activity Median Aerodynamic Diameter (Measure of size of inhaled aerosols) (ICRP 2015).

Table 2. Deviations in the calculation of numbers of decays for INTDOSKIT and the publication of Höllriegel (2021).[a]

Source Region	^{223}Ra	^{219}Rn	^{215}Po	^{211}Pb	^{211}Bi	^{207}Tl
Blood	0.7%	0.2%	0.2%	0.3%	0.2%	0.2%
Other-Tissues	0.1%	0.1%	0.1%	0.0%	-0.2%	0.1%
C-bone-S	-0.1%	0.0%	0.0%	0.0%	-0.3%	0.0%
C-bone-V	-0.1%	-0.1%	-0.1%	-0.1%	-0.4%	-0.1%
T-bone-S	0.0%	0.0%	0.0%	-0.1%	-0.3%	0.0%
T-bone-V	-0.1%	-0.1%	-0.1%	-0.1%	-0.4%	-0.1%
C-marrow	-9.9%	-10.1%	-10.1%	-3.1%	-3.1%	1.1%
T-marrow	0.7%	0.5%	0.5%	0.1%	-0.2%	0.1%
Kidneys	-0.1%	-0.3%	-0.3%	0.7%	-0.5%	-0.1%
UB-cont	11.9%	11.8%	11.8%	-3.5%	-4.3%	-5.6%
Liver	-0.1%	-0.1%	-0.1%	0.0%	-0.3%	-0.1%
Skin	0.9%	0.7%	0.7%	-1.0%	-1.2%	0.0%
Spleen	-0.9%	-1.2%	-1.2%	0.9%	0.7%	3.8%
Testes	-7.2%	-7.4%	-7.4%	-6.0%	-6.2%	-1.4%
SI-cont	NA	NA	NA	-10.8%	-5.7%	-14.7%
RC-cont	0.0%	0.0%	0.0%	-0.1%	-0.3%	0.0%
LC-cont	0.0%	0.0%	0.0%	0.0%	-0.3%	-0.1%
RS-cont	0.0%	0.0%	0.0%	0.0%	-0.3%	-0.1%

[a] Values given are the percent deviation of INTDOSKIT to the data presented by Höllriegel. Most deviations are due to rounding in the values.

et al. 2021) vs. 0.0448 in this study, which round to the same value of 0.04.

As example for the results of the pilot study on uncertainty analysis, Fig. 4 shows the retention of injected ^{241}Am in liver. In Fig. 4a, besides the retention over time, the quartiles and the 5%-/95%-quantiles of the distribution of the retention are shown. The development of the GSD of the distributions of the retentions over time is shown in Fig. 4b. After 1 d, the GSD of the retention reaches a value of approximately 1.2, and after 500 d, this value slowly increases to a value of 1.95, which is reached around 10,000 d when a decrease starts again. The interpretation of this observation is beyond the scope of this manuscript and will be given when the final study is published. Fig. 5 shows a histogram of the distribution of the dose coefficients for effective dose together with fits of gamma, beta, and lognormal-distribution densities to the data. Fig. 6 shows boxplots of the distributions for the dose coefficients. Table 3 compiles some of the statistical parameters of the distributions. The GSD values of the distributions of the dose coefficients calculated in the pilot study are between 1.25 (Bone-Surfaces) and 1.66 (Testes), with most values being around 1.45. These values are consistent with the values reported by other authors. In his study of uncertainty of dose coefficients for ingestion of plutonium, Puncher reports GSD values between 1.13 and 1.73 when only the systemic parameters are sampled (Puncher 2012). The means of the distributions are higher than the reference values, which is an effect also observed by other authors (Puncher 2012; Li 2015). Medians are better estimators of the reference values. This effect will be investigated in further studies.

DISCUSSION

A good agreement of the calculated dose coefficients with the reference values could be achieved in the calculations with INTDOSKIT. The results on the numbers of decay (see Table 2) demonstrate that the biokinetic models are correctly implemented in INTDOSKIT. The same holds for the dosimetric models, as the agreement in the dose coefficients, which are based on these numbers of decays, is of the same level as well. Thus, the authors conclude that the calculation of S-Coefficients is also implemented correctly.

It was observed that the selection of time steps has a rather large influence on the results of the calculation, which is an expected issue, given that differential equations are solved numerically by the code. Fast kinetic processes could be underestimated by a grid with time steps too large for the problem.

In setting up the biokinetic models for the calculations, it was seen that the interpretation of the ICRP reference models and especially the treatment of soft tissue compartments was

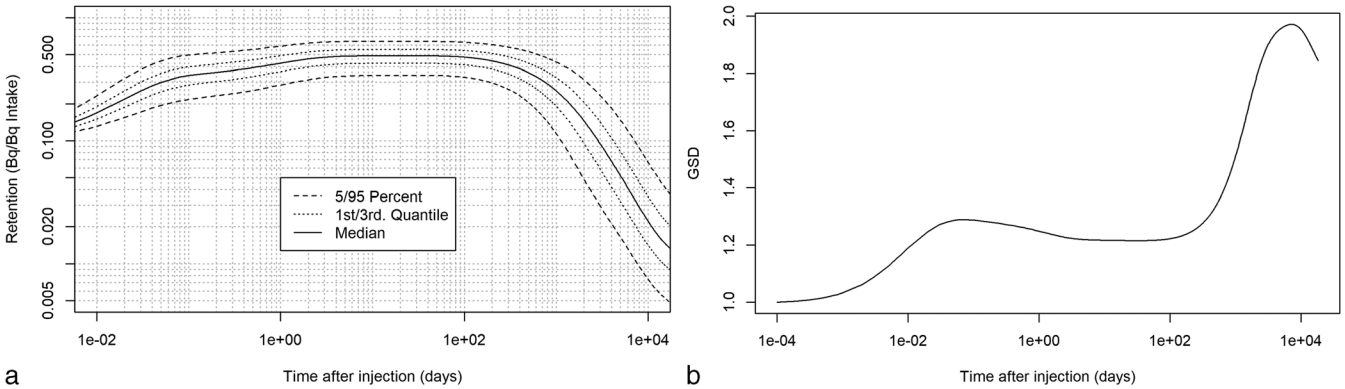

Fig. 4. Uncertainty analysis for injection of ^{241}Am. (a) Retention of ^{241}Am in the liver vs. time. The line gives the median of the distributions of the retention calculated at each time point using 5,000 repetitions. The dotted lines show the 1st and 3rd quantile, amd the dashed lines show the 5% and the 95% quantile of the distributions of the retention calculated at each timepoint. (b) Geometric standard deviations GSD of Retention in Liver vs. time.

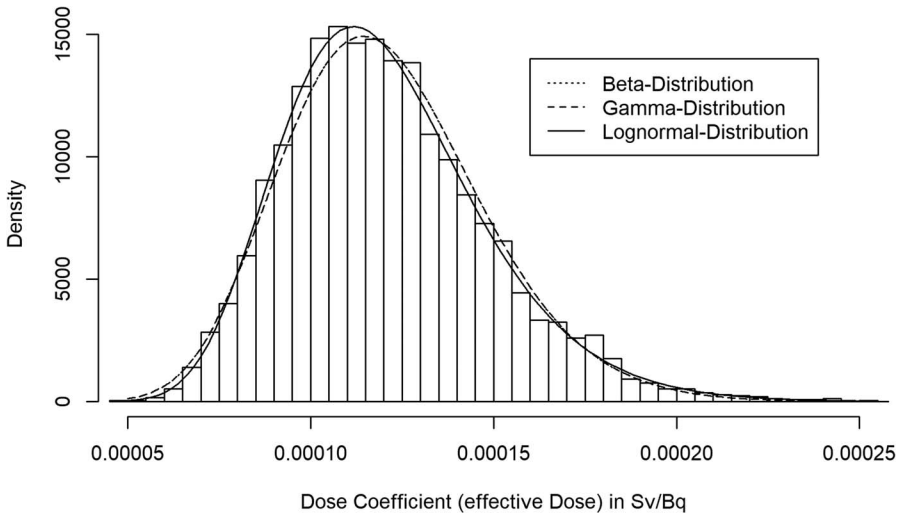

Fig. 5. Distribution of dose coefficients for effective dose for injection of ^{241}Am. The histogram shows the data for 5,000 repetitions in our Monte-Carlo Study. Lines show fits of beta-, gamma- and lognormal distributions to the data. The fits of beta- and gamma-distributions are barely distinguishable.

one source of errors. Implementing a model requires a careful check of all values entered. The coupling of the models is another source of possible mistakes, as the compartments in the systemic models might have different interpretations, and the models of progeny might need modification to implement an independent kinetics of parent and progeny as foreseen by ICRP (2015). Some information about the necessary changes to the models is given in the description of the models by ICRP. However, this information differs in level of detail and type of information provided. For some elements (e.g., thorium), the values of the changed parameters are given. In other cases (e.g., uranium), biological half-lives, which need to be converted to parameter values, are given. The assignment of dosimetric source regions to the biokinetic compartments ("bio2dos" in INTDOSKIT) is another source of erroneous results. In the approach for this work, the source region Other-Tissues for which S-coefficients are calculated needs to be defined, which is not straightforward for all cases, especially in decay chains. In general, more guidance on the application of ICRP models would be appreciated by the authors. A common format for providing the model parameters electronically could be considered by ICRP.

The results of the uncertainty study example demonstrate the applicability of INTDOSKIT for this kind of Monte-Carlo study. A higher number of repetitions of the calculations will improve the accuracy of these studies. Detailed analysis and interpretation of the results (e.g., the time-dependence of GSD; Fig. 5) is necessary. A study with a higher number of repetitions will be presented in a separate publication.

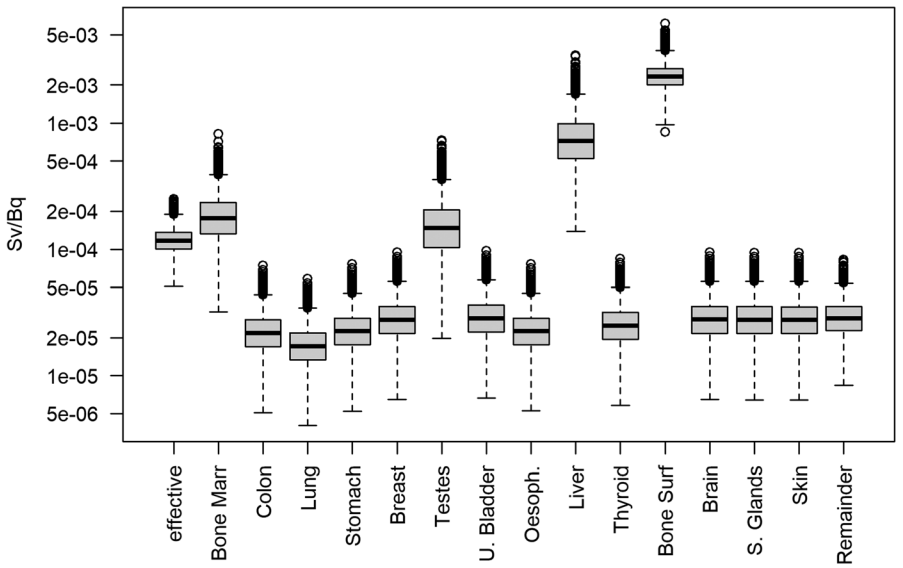

Fig. 6. Example of an uncertainty analysis for injection of ^{241}Am, in which 5,000 samples were taken. Boxplots of the distributions of the dose coefficients for effective dose and equivalent doses to the organs. The box gives the range of 25%- to 75%-quantile, the bar is the median, and the antenna the 5%-/95%-quantile of the distribution. Points show the datapoints, which are outside of the antennae.

Table 3. Statistical information on the distributions of dose coefficients in the pilot study for injection of ^{241}Am.[a]

	undisturbed	Min.	1st Quartile	Median	Mean	3rd Quartile	Max.	GM	GSD
effective Dose	1.16×10^{-04}	4.82×10^{-05}	1.01×10^{-04}	1.18×10^{-04}	1.21×10^{-04}	1.37×10^{-04}	2.71×10^{-05}	1.18×10^{-04}	1.26
Bone-Marrow	1.86×10^{-04}	3.70×10^{-05}	1.32×10^{-04}	1.78×10^{-04}	1.92×10^{-04}	2.35×10^{-04}	7.71×10^{-04}	1.76×10^{-04}	1.53
Colon	2.29×10^{-05}	4.58×10^{-06}	1.71×10^{-05}	2.21×10^{-04}	2.34×10^{-05}	2.83×10^{-05}	9.04×10^{-05}	2.19×10^{-05}	1.45
Lung	1.80×10^{-05}	3.62×10^{-06}	1.34×10^{-05}	1.73×10^{-05}	1.84×10^{-05}	2.22×10^{-05}	7.10×10^{-05}	1.72×10^{-05}	1.45
Stomach	2.36×10^{-05}	4.72×10^{-06}	1.76×10^{-05}	2.27×10^{-05}	2.41×10^{-05}	2.91×10^{-05}	9.32×10^{-05}	2.26×10^{-05}	1.45
Breast	2.92×10^{-05}	5.82×10^{-06}	2.17×10^{-05}	2.81×10^{-05}	2.98×10^{-05}	3.60×10^{-05}	1.15×10^{-04}	2.79×10^{-05}	1.45
Testes	1.55×10^{-04}	1.31×10^{-05}	1.04×10^{-04}	1.46×10^{-04}	1.66×10^{-04}	2.07×10^{-04}	7.17×10^{-04}	1.46×10^{-04}	1.66
Urinary Bladder	3.00×10^{-05}	5.99×10^{-06}	2.23×10^{-05}	2.88×10^{-05}	3.06×10^{-05}	3.70×10^{-05}	1.18×10^{-04}	2.86×10^{-05}	1.45
Oesophagus	2.36×10^{-05}	4.74×10^{-06}	1.76×10^{-05}	2.27×10^{-05}	2.41×10^{-05}	2.91×10^{-05}	9.31×10^{-05}	2.26×10^{-05}	1.45
Liver	7.50×10^{-04}	1.28×10^{-04}	5.27×10^{-04}	7.31×10^{-04}	8.15×10^{-04}	1.01×10^{-03}	3.19×10^{-03}	7.29×10^{-04}	1.61
Thyroid	2.62×10^{-05}	5.24×10^{-06}	1.95×10^{-05}	2.52×10^{-05}	2.67×10^{-05}	3.23×10^{-05}	1.03×10^{-04}	2.50×10^{-05}	1.45
Bone-Surface	2.40×10^{-03}	9.45×10^{-04}	2.01×10^{-03}	2.32×10^{-03}	2.38×10^{-03}	2.69×10^{-03}	6.21×10^{-03}	2.32×10^{-03}	1.25
Brain	2.92×10^{-05}	5.85×10^{-06}	2.17×10^{-05}	2.81×10^{-05}	2.99×10^{-05}	3.60×10^{-05}	1.15×10^{-04}	2.79×10^{-05}	1.45
Salivary-Glands	2.91×10^{-05}	5.82×10^{-06}	2.17×10^{-05}	2.80×10^{-05}	2.97×10^{-05}	3.59×10^{-05}	1.15×10^{-04}	2.78×10^{-05}	1.45
Skin	2.90×10^{-05}	5.79×10^{-06}	2.16×10^{-05}	2.79×10^{-05}	2.97×10^{-05}	3.58×10^{-05}	1.15×10^{-04}	2.77×10^{-05}	1.45
Remainder	2.92×10^{-05}	6.66×10^{-06}	2.28×10^{-05}	2.86×10^{-05}	3.02×10^{-05}	3.58×10^{-05}	1.03×10^{-04}	2.85×10^{-05}	1.39

[a] Values are in Sv Bq − 1 (GM = geometric mean, GSD = geometric standard deviation).

The templates for the R-Scripts have proven to be useful for "quickly" setting up new calculations. The use of plain text files for setting up models also proved to be a good choice as this enhanced readability and editing is not dependent on special software.

The dosimetric calculations presented in this manuscript are based on the SAF-values presented in the electronic annex of ICRP Publication 133 (ICRP 2016). These are calculated using the ICRP reference voxel phantoms (ICRP 2009). If the SAF-values for the pediatric phantoms (ICRP 2020a) or the mesh phantoms (ICRP 2020b) are available, these could be used by INTDOSKIT as well.

The INTDOSKIT R-code now is ready for application in future studies. However, some issues and open points listed below remain:

- In the current version, the use of neutron SAF-values (ICRP 2016) is not foreseen. This is a very special case, which is not required in the current studies by the authors. It is planned to implement these functions to be able to use them as well; and
- Time-dependent biokinetic models are foreseen for members of the public (e.g., considering changes in metabolism during childhood and adolescence or maturity). Here, the transfer coefficients will become time-dependent. This needs to be implemented in INTDOSKIT, which in the current version can only handle constant values of the transfer coefficients.

CONCLUSION AND OUTLOOK

The R code presented in this text was developed with the aim of calculation of dose coefficients using ICRP methodology and ICRP reference models. This goal could be achieved as shown in the examples. The pilot study showed the applicability of the R code for evaluation of uncertainties of dose coefficients. The arguments for the authors' selection of R-Language were confirmed because the feature of "named objects" and the statistical capabilities of this language could be well employed and significantly simplified the coding itself, as well as the studies including the evaluation of the produced datasets. For example, a simple R-command could be used for the calculation of statistical parameters of the distributions or generating the boxplots.

At the moment, the files containing the code of INTDOSKIT, documentation, templates, and examples are available at the gitlab of KIT (https://gitlab.kit.edu/bastian.breustedt/intdoskit) or directly from the authors upon request. It is planned to be made publicly available as an R-Library, which requires some changes to adapt the code and transform it and its documentation into the proper R-Library format.

The authors consider the INTDOSKIT R-code presented in this manuscript as validated and will apply it in their future studies. Based on the needs of these studies, it will be extended with new functionality, which is rather easy using the modular structure of the code.

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