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# Analytical Derivation of the Overall Uncertainty in Biokinetic and Dosimetric Models of α-, β-, αγ- and βγ- emitters

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The objective of the present study is to assess overall uncertainty in biokinetic and dosimetric models of α , β , αγ , and βγ - emitters. International Standard Organization (ISO) methods on uncertainty assessment have been applied taking into account all biokinetic and dosimetric parameters intervening in the determination of the ingestion dose coefficients of radionuclides. Clear uncertainty budget and well established mathematical formulas were obtained for α -, β -, αγ -, and βγ - emitters from the updated ingestion dose coefficients. This method was applied to $^{238}$U, an αγ - emitter, and can be generalized to other radionuclides. By ranging the relative uncertainty on the Absorbed Fractions, Numbers of transformations, Radiation and Tissue weighting factors and wall parameter from 5% to their nominal values in the literature, an overall relative uncertainty ranging from 126 to 176% was brought out. Thus biokinetic and dosimetric models of radionuclides should be improved to make them more realistic, reducing the above uncertainty. Correlations between Specific Absorbed Fractions of each source and corresponding targets will be taken into account very soon within the framework of a specific study using Monte Carlo calculations.

*Key words:* ingestion dose coefficient, biokinetic model, dosimetric model, uncertainty, FORTRAN 90, SAFs

## 1. Introduction

Because one cannot directly measure the absorbed dose occurring by ingestion and inhalation of radionuclides to a human organ, all internal doses have to be estimated based on individual measurements and on mathematical models that simulate the transfer and bioaccumulation of the radionuclide in the human body that are estimated using biokinetic and dosimetric models[1-3]. Biokinetic models are mathematical representations of the movement of elements and their radioisotopes within the body and their uptake and retention in organs and tissues. They are used to calculate the number of radioactive disintegrations occurring in individual organs and tissues. Dosimetric models represent the geometrical relationships of body structures and are used to calculate dose in target regions (organs and tissues) per disintegration occurring in source regions. Dose coefficients for the ingestion of radionuclides by members

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of the public and workers have been calculated by the International Commission for Radiological Protection (ICRP)[4, 5]. ICRP dose coefficients are calculated using defined biokinetic and dosimetric models, including reference anatomical data for the organs and tissues of human body. They are calculated for reference adults, children of difference ages and fetus at different stages of development[6]. Thus they are not regarded as subject to uncertainty. However, it is recognized that there are uncertainties associated with all aspects of the estimation of doses and risks at low doses[7]. So far the ICRP has not published information on uncertainties in dose coefficients. Uncertainties will arise at each stage of the dose calculation, i.e. in the use of biokinetic and dosimetric models, in the assumptions made to try to equate different types of radiation, in summing contributions from the irradiation of different tissues to give a whole-body dose, and in deriving the total risk. Nevertheless, it is scientifically and ethically necessary to assess the possibility that persons with assigned estimated of internal dose did not in fact receive much large doses. This is the reason to evaluate the uncertainties in assigned dose[3]. Uncertainties in dose estimates will vary substantially between radionuclides, depending on their types and energies of radiation emission, their chemical form, the complexity and knowledge of their behaviour in the body, and the availability of data on which are based model parameters[8, 9]. There are important concerns with respect to the heterogeneity of dose delivery within tissues and cells for short-range charged particle emissions, the extent to which current models adequately represent such interactions with biological targets, and the specification of target cells at risk. Since it is rare that hard data on all sources of uncertainty are available, subjective judgments of experts are usually required in quantifying uncertainties. One might say that the uncertainties themselves are uncertain. Thus, it may be useful to conduct analyses based on alternative assumptions about the nature and magnitude of error[10]. In addition, it is important to distinguish between uncertainty and variability[7]. Uncertainty refers to the level of confidence that can be placed in a given parameter value or prediction of a model or estimate of the central value of dose for a population. As for biological variability, it deals with quantitative differences between different members of that population. However, variability will be an important source of uncertainty in the estimate of a central value when the estimate is based on a few and highly variable observations. Although uncertainty and variability are distinct concepts, the variability in biokinetic characteristics within a population is often an important factor contributing to the uncertainty in a central estimate of a biokinetic quantity[11].

It should be noted that so far no clear uncertainty budget and analytical derivation are established for the ingestion dose coefficients of α-, β-, αγ- and βγ-emitters. That point led us to formulate an approach for the evaluation of uncertainty on biokinetic and dosimetric models of radionuclides described in this work. It takes into account expert judgment and variability in organs and tissue masses, radiation and tissue weighting factors, specific absorbed fractions, organ and tissue retentions, and the localization of stem cells inducing cancer.

## 2. Materials and methods

### *2.1. Biokinetic models of α-, β-, αγ-, and βγ- emitters*

After intake of injection of radioactive solution, the fraction entering the systemic circulation is distributed in organs and tissues of the body. The number of transformations occurring within specific tissues, organs, or body regions (source regions) over the integration period (50 years for adults and 70 years for children following the intake) by determining the time-integrated activity in each source region[12], is given by the following equation:

$$U_S = I\int_0^{50} r(t)e^{-\lambda t}dt, \quad (1)$$

where $I$ is the incorporated activity, $r$(t) is the retention function depending on time and $\lambda$ is the radioactive decay constant. It is worth mentioning that for our purposes in the present study, the model of uranium based on the generic alkaline earth model given in ICRP Publication 67[4] has been used. The model describes in detail the kinetics of uranium in bone, which is the main site of deposition and retention, and also considers retention in liver, kidneys, and other soft tissues as well as routes of excretion. It takes account of initial uptake onto bone surfaces, transfer from surface to bone volume, and recycling from bone and other tissues to plasma. A fractional uptake from the gastrointestinal tract to blood ($f_1$ value) of 0.02 appearing to be a more realistic value for dietary forms of uranium is adopted here.

In this study retention functions $r$(t) have been computed by means of *Mathematica 5* software applying Eigen values Matrix method[13]. The number of disintegrations $U_S$ in each organ or tissue has been calculated from these functions using *Maple 13* software.

### *2.2. Dosimetric models of α-, β-, αγ-, and βγ- emitters*

The mean energy absorbed in the target region depends on the nature of the radiations emitted in the source regions, the spatial relationships between the source and target regions, and the nature of the tissues between the regions. The details of these considerations are embodied in a radionuclide-specific coefficient called the Specific Effective Energy (*SEE*).

For any radionuclide, source organ *S*, and target organ *T*, *SEE* is defined as:

$$SEE(T \leftarrow S)=\frac{1}{M_T}\sum_i p_i E_i w_{R,i} AF_i(T \leftarrow S) \quad (2)$$

where $p_i$ is the yield of radiations of type $i$ per nuclear transformation, $E_i$ is the average or unique $i$ energy of radiation type $i$, and $w_{R,i}$ is the corresponding radiation weighting factor. $AF_i(T \leftarrow S)$ is the fraction of energy emitted in source region $S$ that is $i$ absorbed within target region $T$, and $M_T$ is the mass of target region $T$.

For contents of walled organs, the dose to the wall is assumed to be the dose at the surface of a half-space, or half the equilibrium dose to the contents. The Specific Absorbed Fraction (*SAF*) is multiplied by a factor, $\upsilon$, to account for the reduced $\alpha$ -dose to radiosensitive cells in the wall. This factor is taken to be unity for $\beta$ -particles and 0.01 for $\alpha$ -particles. Thus the $AF_i(T \leftarrow S)$ is given by:

$$\frac{AF(T \leftarrow S)}{M_T}=\frac{1}{2}\frac{\upsilon}{M_T^c} \quad (3)$$

where $M_T^c$ is the mass of the walled organ. For α- and β -particles, it is generally assumed that $SAF(S \leftarrow S)$ is the inverse of the mass of organ *S*. If source *S* and target *T* are separated, $SAF(T \leftarrow S) = 0$. Exceptions occur for β-radiation when the source and target are in close proximity, for instance in the respiratory tract and in the skeleton[11].

Using equations (2) and (3), *SEE* is given by:

$$SEE(T \leftarrow S)=\sum_i p_i E_i w_{R,i}\left(\frac{AF(T \leftarrow S)}{M_T}+\frac{1}{2}\frac{\upsilon}{M_T^c}\right) \quad (4)$$

The committed equivalent dose is given by the following equation:

$$H_{50,T}=\sum_S H_{50,T}(T \leftarrow S)= k\sum_S U_S SEE(T \leftarrow S)= k(SEE)(U) \quad (5)$$

where $k$=1.6 × 10$^{-10}$ is a conversion factor, *(SEE)* is the matrix of the Specific Effective Energy, and *(U)* is the matrix of the number of disintegrations/ transformations.

$$H_{50,T} = k\sum_i P_i E_i w_{R,i}\sum_S U_S\left(\frac{AF_i(T \leftarrow S)}{M_T}+\frac{1}{2}\frac{\nu}{M_T^C}\right) \quad (6)$$

For reference Female *T* is replaced by *T*'

$$H_{50,T'} = k\sum_i P_i E_i w_{R,i}\sum_s U_S\left(\frac{AF_i(T' \leftarrow S)}{M_{T'}}+\frac{1}{2}\frac{\nu}{M_{T'}^C}\right) \quad (7)$$

The committed effective dose in the body after intake is given by the following equation:

$$E_{50}=\sum_T w_T H_{50,T} = I.e_{ing} \quad (8)$$

where $w_T$ are the tissue weighting factors, $I$ is the incorporated activity, $e_{ing}$ is the ingestion dose coefficient.

### *2.3. Ingestion dose coefficient update and uncertainty assessment*

The ingestion dose coefficient is defined as the effective dose corresponding to the *1 Bq* intake of the radionuclide. A new computational method evaluating ingestion dose coefficients for members of the public and for workers is proposed in ICRP publication 103[14] to replace the method used in ICRP publication 67[4]. The effective dose is computed from the equivalent dose assessed for organ or tissue *T* of the Reference male $H_T$, and Reference female $H_{T'}$, including the remainder tissues as in the following equations:

$$E_{50}=\sum_T w_T\left[\frac{H_{50,T}+H_{50,T'}}{2}\right] \quad (9)$$

The committed effective dose for protection purposes is based on the mean doses in organs or tissues of the human body. It is defined and estimated in a Reference Person. This quantity provides a value which takes account of the given exposure conditions but not of the characteristics of a specific individual. In particular, the tissue weighting factors are mean values representing an average over many individuals of both sexes.

Using equations (1)- (9), the committed effective dose after intake of of αγ- or βγ- emitters is given by the following equation:

$$\begin{aligned}E_{50} &= \sum_T w_T \frac{H_{50,T}+H_{50,T'}}{2}\\ &= \sum_T \frac{w_T}{2}\left(k\sum_i P_i E_i w_{R,i}\sum_s U_S\left(\frac{AF_i(T' \leftarrow S)}{M_{T'}}+\frac{1}{2}\frac{\nu}{M_{T'}^C}\right)\right.\\ &\quad \left. + k\sum_i P_i E_i w_{R,i}\sum_s U_S\left(\frac{AF_i(T \leftarrow S)}{M_T}+\frac{1}{2}\frac{\nu}{M_T^C}\right)\right)\\ &= \frac{1}{2}k\sum_i P_i E_i w_{R,i}\sum_{T,S} w_T U_S\left[\left(\frac{1}{2}\frac{\nu}{M_T^C}+\frac{1}{2}\frac{\nu}{M_{T'}^C}\right)\right.\\ &\quad \left.+\left(\frac{AF_i(T \leftarrow S)}{M_T}+\frac{AF_i(T' \leftarrow S)}{M_{T'}}\right)\right]\end{aligned} \quad (10)$$

where $w_{R,i}$ is the radiation weighting factor equal to 20 for α- particles, 1 for β- particles and γ- radiation. The term

$\upsilon\left(\frac{1}{M_T^c}+\frac{1}{M_{T'}^c}\right)$ is not considered for non-walled organs.

The updated values of $w_T$[14] and SAF calculated by Cristy and Eckerman[15] have been used in the present work to calculate the ingestion dose coefficients. For intake of 1 Bq, the committed effective dose gives the ingestion dose coefficient of αγ- and βγ- emitters:

$$E_{50}=\frac{1}{4}k\sum_{R,i}w_{R,i}\,p_i E_i\sum_{T,S}w_T U_S\left[\upsilon\left(\frac{1}{M_T^c}+\frac{1}{M_{T'}^c}\right)+2\left(\frac{AF(T\leftarrow S)}{M_T}+\frac{AF(T'\leftarrow S)}{M_{T'}}\right)\right]=e_{ing} \quad (11)$$

This formula can be generalized to pure α-, β- emitters. In this case, the Absorbed Fractions AF=1.

The related standard uncertainty to the above ingestion dose coefficient is computed using the following equation given in the Guide of the Uncertainty Measurements (GUM)[16] :

$$u_C^2(y)=\sum_{i=1}^{N}(\frac{\partial f}{\partial x_i})^2u^2\ (x_i)+2\sum_{i=1}^{N-1}\sum_{j=i+1}^{N}(\frac{\partial f}{\partial x_i})(\frac{\partial f}{\partial x_j})u(x_i,x_j) \quad (12)$$

where the ingestion dose coefficient is identified by the following equation:

$$y=f(w_R,\ w_T,\ p_R,\ E_R,\ v,\ U_S,\ M_T^c,\ M_{T'}^c,\ M_T,\ M_{T'},\ AF_T) \quad (13)$$

The second term in the right hand of Eq. (12) known as correlation term is neglected in the present study. This term will be considered within the framework of a forthcoming study using Monte Carlo calculations. The term of correlation is justified by the following equation:

$$\sum_T\left[M_T\left(\frac{AF(T\leftarrow S)}{M_T}\right)\right]=1 \quad (14)$$

showing correlations between SAFs of each source and the corresponding targets. $u_i$ represents the standard uncertainty of the variable $i$. For a given source, these correlations are neglected due to the total absorption of α-particles within the source. Exceptions are within skeletal structures and within regions of the respiratory tract (ICRP 66, Table H.1)[17].

The following equation shows that the precision to determine the Absorbed Fractions (AF) is independent of the gender:

$$\left(\frac{u_{AF(T\leftarrow S)}}{AF(T\leftarrow S)}\right)=\left(\frac{u_{AF(T'\leftarrow S)}}{AF(T'\leftarrow S)}\right) \quad (15)$$

## 3. Results and Discussion

### *3.1. Uncertainty on the ingestion dose coefficient*

The following equation is obtained using the general formula given in the GUM [16]:

$$\left(\frac{u_{e_{ing}}}{e_{ing}}\right)^2=\sum_{i=1}^{2}f_{w_{r_i}}^2\left(\frac{u(w_{r_i})}{w_{r_i}}\right)^2+\sum_{j=1}^{5}f_{E_{r_j}}^2\left(\frac{u(E_{r_j})}{E_{r_j}}\right)^2+\sum_{j=1}^{5}f_{p_{r_j}}^2\left(\frac{u(p_{r_j})}{p_{r_j}}\right)^2$$
$$+\sum_{k=1}^{20}f_{w_{T_k}}^2\left(\frac{u(w_{T_k})}{w_{T_k}}\right)^2+\sum_{k=1}^{20}f_{U_{S_k}}^2\left(\frac{u(U_{S_k})}{U_{S_k}}\right)^2+f_{\nu}^2\left(\frac{u(\nu)}{\nu}\right)^2$$
$$+\sum_{l=1}^{7}f_{M_{T_l}^c}^2\left(\frac{u(M_{T_l}^c)}{M_{T_l}^c}\right)^2+\sum_{l=1}^{7}f_{M_{T_l}^c}^2\left(\frac{u(M_{T_l}^c)}{M_{T_l}^c}\right)^2+\sum_{k=1}^{20}f_{M_{T_k}}^2\left(\frac{u(M_{T_k})}{M_{T_k}}\right)^2$$
$$+\sum_{k=1}^{20}f_{M_{T_k'}}^2\left(\frac{u(M_{T_k'})}{M_{T_k'}}\right)^2+\sum_{k=1}^{20}f_{AF_k}^2\left(\frac{u(AF_k)}{AF_k}\right)^2+\sum_{k=1}^{20}f_{AF_k'}^2\left(\frac{u(AF_k')}{AF_k'}\right)^2 \quad (16)$$

where $f_{xi}$ are given in the Appendix from equations (A.1) to (A.12). i refers to number of radiations. j refers to number of energy of photons or particles stemming from the disintegrations of $^{238}$U. l refers to number of walled organs. k refers to number of organs/ tissues whose tissue weighting factor is known. It also corresponds to the number of numbers of transformations, masses of target organs/tissues, and Absorbed Fractions. One should keep in mind that the formula (16) is derived for $^{238}$U, an αγ- emitter. It can be applied to other αγ- or βγ- emitters. In this case, numbers i, j, k, l should be known.

A subroutine was written using FORTRAN 90 to determine the relative uncertainty of the ingestion dose coefficient applied to the case of $^{238}$U.

Figure 1 shows variation of the overall relative uncertainty of the ingestion dose coefficient depending on the weighted relative uncertainty on radiation and tissue weighting factors $(f_{w_{r,i}}\frac{u_{w_{r,i}}}{w_{r,i}})$ and $(f_{w_{T,i}}\frac{u_{w_{T,i}}}{w_{T,i}})$, on the number of transformations $(f_{U_{S,i}}\frac{u_{U_{S,i}}}{U_{S,i}})$, on the wall parameter $(f_\nu\frac{u_\nu}{\nu})$ and on the absorbed fractions $(f_{AF_i}\frac{u_{AF_i}}{AF_i});(f_{AF_i'}\frac{u_{AF_i'}}{AF_i'})$. Plotting in Figure 1 has been obtained by ranging each of the relative uncertainty on $w_R$, $w_T$, $v$, $U_S$, $AF_T$ except uncertainties on masses given in ICRP Publication 89[18] and in Grandmaison *et al* [19]. Relative uncertainties on the remaining variables were kept at 5% for each variable. For instance when uncertainty on $w_R$ is ranging, relative uncertainties on

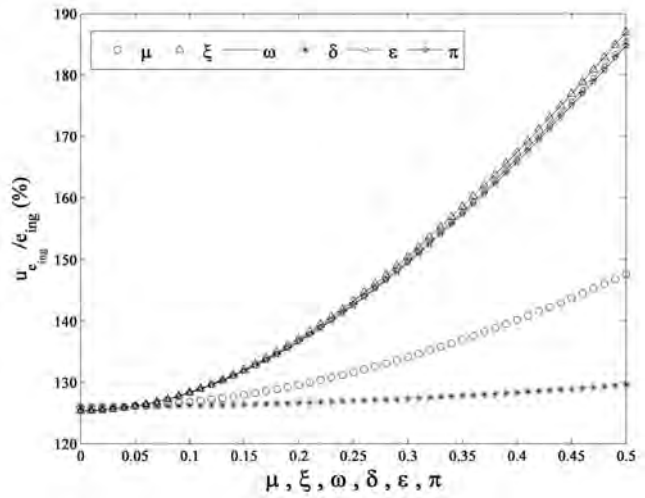


**Fig. 1.** Variation of the overall relative uncertainty of the ingestion dose coefficient depending on the weighted relative uncertainty on the number of transformations, on the radiation and tissue weighting factors, on the absorbed fractions, and on the wall parameter.
$\mu = f_{w_{T_i}} \frac{u_{w_{T_i}}}{w_{T_i}}$ ; $\xi = f_{w_{R_i}} \frac{u_{w_{R_i}}}{w_{R_i}}$ ; $\omega = f_{U_{S_i}} \frac{u_{U_{S_i}}}{U_{S_i}}$ ; $\delta = f_{\upsilon} \frac{u_{\upsilon}}{\upsilon}$ ; $\varepsilon = f_{AF_i} \frac{u_{AF_i}}{AF_i}$ ; $\pi = f_{AF_i} \frac{u_{AF_i}}{AF_i}$.

$w_T$, $v$, $U_S$, $AF$ are fixed. The behavior of $f_{w_{T,i}} \frac{u_{w_{T,i}}}{w_{T,i}}$ and $f_{U_{S,i}} \frac{u_{U_{S,i}}}{U_{S,i}}$ is similar as shown in Table 1. The variation of the above weighted relative uncertainty is parabolic except the linear variation of the weighted relative uncertainty on the wall parameter concerning walled organs. An overall relative uncertainty of 126% is obtained when 5% is considered for each of the relative uncertainty on the variables as said above. The overall relative uncertainty of 153% is found out by considering the nominal relative uncertainty on the absorbed fractions at 5%, on the wall parameter at 50%, on the number of transformations and on the radiation and tissue weighting factors at 20% each of them.

Based on the optimal values commonly reported in the literature, relative uncertainty on the number of transformations, on the radiation and tissue weighting factors at 30% each of them, relative uncertainty on the absorbed fractions at 5%, and on the wall parameter at 50%, an overall relative uncertainty of 176% is obtained.

The overall relative uncertainty attributable to the ingestion dose coefficient ranges from 126% to 176%. As already said, this value is high but considering various variables of the uncertainty budget discussed above, this level of uncertainty was expected. Thus the biokinetic and dosimetric models of radionuclides should be improved to reduce these uncertainties making these models more realistic. Although these calculations are made for $^{238}$U, it can be applied to other radionuclides.

**Table 1.** Contribution of each variable of the ingestion dose coefficient to the overall relative uncertainty

| Variable | Weighted relative uncertainty (%) $f_{xi}$ $(u_{xi}/x_i)$ |
|---|---|
| Radiation weighting factor, $w_R$ | 0.37 |
| Emission probability, $p_R$ | 0.038 |
| Energy, $E_R$ | 0.0017 |
| Tissue weighting factor, $w_T$ | 1.21 |
| Number of transformations, $U_T$ | 1.21 |
| Wall parameter, $\upsilon$ | 0.057 |
| Mass of contents (man), $M_T^c$ | 12.4 |
| Mass of contents (woman), $M_T^c$ | 11.6 |
| Mass of organ/tissue (man), $M_T$ | 34 |
| Mass of organ/tissue (woman), $M_T$ | 36.6 |
| Absorbed Fraction (man), $AF_T$ | 1.17 |
| Absorbed Fraction (woman), $AF_T$ | 1.16 |

### *3.2. Contribution of various variables to the relative overall uncertainty*

#### *3.2.1. Mass ($M_T$)*

The variability in organ and tissue masses is taken into account as uncertainty in mass knowing that the central value corresponds to the reference person. For all organs and tissues, there is a distribution of values statistically representative coming from different persons, and depending on sex, age, state of health, and another genetic factor, or just due to natural variability. In most concrete cases, the mass of given organ is not measured for the subjects of dose assessment. Exceptions are patients for whom advanced imaging techniques provide information about the volume, and size, thus, mass of some organ. One should note that the amount of energy deposited in an organ can be correlated with the mass of that organ. A large organ will receive a large amount of energy from the activity that it is carrying because the escape of penetrating radiation is reduced compared to a smaller organ. A larger organ also represents a bigger target and will receive a larger amount of energy due to the radiation originating from radionuclides accumulated in other organs[3]. Data used in this work to evaluate ingestion dose coefficients and related uncertainty stem from the ICRP publication 89[18] and the study reported by Grandmaison *et al.*[19] As shown in Table 1, the contribution of the weighted relative uncertainty of the organ/ tissue masses to the relative uncertainty of the ingestion dose coefficient is about 95%, making them the main contributors to the overall uncertainty. It should be noted that this contribution takes into account the weight of the relative uncertainty on each mass in the overall uncertainty of the ingestion dose coefficient.

#### *3.2.2. Number of transformations ($U_T$)*

The number of transformations, $U_T$ comes from the

radionuclide retention in human body. The reliability of biokinetic models depends on the quality of data on which they are based, including the availability of human data[7]. And the biokinetic model of uranium was much more experienced in laboratory animals, and extrapolated data in humans to overcome the lack of knowledge, and replace some human questionable data[3]. Interspecies extrapolation of biokinetic data is based on the concept of a general biological regularity across the different species with regard to cellular structure, and organ structure. However, despite the broad structural, functional, and biochemical similarities among mammalian species, interspecies extrapolation of biokinetic data has proven to be an uncertain process[12]. For a number of elements and their radioisotopes, there are few and even no human data for use in model development or validation, and reliance is placed on the results of animal experiments and chemical analogues. Moreover the uncertainty in fractional uptake from the gastrointestinal tract to blood ($f_1$ value) varies considerably from one element to another[11]. Apart from the limitations imposed by the extrapolation of animal data to humans, there is a potentially important deficit in knowledge of biological variability in population groups, occurring between normal healthy adults and children, between different racial and ethnic groups, and resulting from differences in health status between similar individual members of a population groups.

As displayed in Table 1, the contribution of the weighted relative uncertainty of the number of transformations to the relative uncertainty of the ingestion dose coefficient is about 1.2%. This value takes into account the weight of the relative uncertainty on the number of transformations in the overall uncertainty of the ingestion dose coefficient.

*3.2.3. Specific Absorbed Fraction (SAF)*

The Monte Carlo simulation of radiation transport is frequently used to estimate the *SAF*s for photon emissions. This approach can produce significant statistical errors in situations where few interactions are expected to occur, such as the cases involving low initial energies or target organs that are relatively small or remote from important sources of activity[11].

Moreover simplifying assumptions made in the calculation of dose are not always realistic. It is for instance the case of the homogeneous distribution of both radionuclides and deposited energy within source regions and target cells within target regions. Uncertainties are also introduced by assumptions made in the formulation of mathematical phantoms. Data of Cristy and Eckerman[15] indicate that the *SAF*s for photons vary substantially with age for some energies, source organs, and target organs. As a rule, uncertainties in *SAF*s are greater for children than adults due to greater uncertainties concerning typical sizes and shapes of organs of children. As shown in Table 1, the contribution of the weighted relative uncertainty of the absorbed fractions to the relative uncertainty of the ingestion dose coefficient is about 2.3%.

*3.2.4. Wall parameter (υ)*

Furthermore the value of $U$ for walled organs is not based on calculations of energy deposition but is a cautiously high value based on an acute toxicity study on rats[20]. Cancers are generally considered to originate from stem cells; cells that possess unlimited reproductive capacity[21]. The localization of stem cells inducing cancer is not well established for some walled organs. *SAF*s for $\alpha$ -particles are zero for all of the contents regions of the Human Alimentary Tract Model due to the depth of the target cells in relation to the range of the α-particles in tissue. Thus, when target cells are situated at a depth of greater than around 40 or 50 μm in the wall, α-particles emitted cannot penetrate the wall to the depth of the target region[21]. As illustrated in Table 1, the contribution of the weighted relative uncertainty of the wall parameter to the relative uncertainty of the ingestion dose coefficient is about 0.06% showing the low impact of the wall parameter in the overall uncertainty of the ingestion dose coefficient.

*3.2.5. Radiation weighting factor ($w_R$)*

Radiation weighting factors ($w_R$) are used as a simple representation of the different effectiveness of different radiations in causing stochastic effects at low doses[6]. Relative biological effectiveness (*RBE*) is an empirical quantity depending on the biological system and the conditions of the experiment. *RBE* is usually found to vary with dose, frequently increasing for high *LET* radiation to a maximum value at low doses. There are limitations to the determination of generally applicable *RBE* values because of the non-homogeneity of the energy deposition. The range of the $\alpha$ -particles in tissues is small and the precise nature and location of the target cells in some of the most relevant tissues is not known. Hence the calculated doses are associated with substantial uncertainties and result in a broad range of *RBE* values from epidemiological and experimental studies[22]. The $w_R$ for $\alpha$ -particles has been set equal to 20, but this is merely a rough representation of estimated values of *RBE* that show considerable variations[7, 22]. As shown in Table 1, the contribution of the weighted relative uncertainty of the radiation weighting factors to the relative uncertainty of the ingestion dose coefficient is about 0.37%.

*3.2.6. Tissue weighting factor ($w_T$)*

Tissue weighting factors ($w_T$) express the contribution of individual organs and tissues to overall detriment from cancer and hereditary effects, relating to whole body

radiation exposure, tissue weighting factors are based on values of relative detriment, calculated separately for males and females and applying to populations of all ages[6]. There are uncertainties in radiation risk estimates which stem from several sources. The most familiar is statistical uncertainty, represented by confidence limits. When an estimate based on a particular exposed population is applied to other populations or to other radiation sources, further uncertainty is introduced. Differences between radiation sources can produce uncertainty owing to random or systematic error in dose estimates in either the original or the secondary population[10].

The major sources of uncertainty on tissue weighting factors come from uncertainties on the validity of the methods by which they were derived (e.g. animal models, extrapolation from large acute doses such as A-bomb survivors, radiotherapy patients, and professional judgment) and the subjective nature of the quantity they are meant to represent. In addition, the use of tissue weighting factors for $^{238}$U intake implicitly assumes that organ sensitivities are independent of dose rate.

Risk-based radiological protection depends strongly on the assumption that estimates based on studies of informative exposed populations can be applied to other exposed populations. Combined analyses of dose-response data from different populations provide valuable information relevant to that assumption. Unfortunately, such information is available for very few site-specific cancers. Transfers of risk estimates between populations pose a particularly difficult problem for cancer sites for which baseline rates differ widely between the two populations.

Other major sources of uncertainty include possible interaction of radiation exposure with other cancer risk factors. This problem is similar to that of transfer of risk estimates between populations. Despite the relatively large number of data on radiation risk, the question of how to transfer risk estimates derived from one population to a different population remains unanswered[23].

Some radiation-related cancers are sex-specific and, for many others, sex is a major modifier of radiation-related risk. In accordance with current ICRP procedures, intermediate and final numerical risk estimates presented here are sex-averaged. Radiation risks have been also calculated by retaining sex specificity of intermediate results and sex-averaging only at the final stage[14]. As shown in Table 1, the contribution of the weighted relative uncertainty of the tissue weighting factors to the relative uncertainty of the ingestion dose coefficient is about 1.2%.

## 4. Conclusion and future prospects

New published data and ICRP publications brought new data and computational methods that require the update of the ingestion dose coefficients of radionuclides. The overall relative uncertainty attributed to these updated ingestion dose coefficients ranges from 126 to 176% for the specific case of $^{238}$U. This method applied to $^{238}$U, an αγ- emitter can easily be extended to α-, β-, and βγ-emitters. The large uncertainty observed is in agreement with what is expected because of the substantial uncertainties in biokinetic and dosimetric data. Whence biokinetic and dosimetric models of radionuclides should be improved to make them more realistic, reducing the uncertainties. Correlations between Specific Absorbed Fractions of each source and corresponding targets will be taken into account within the framework of a specific study using Monte Carlo calculations.

## Appendix

The following equations, from A.1 to A.12, are calculated using general formula given by the International Standard Organization in the Guide of the Uncertainty Measurements[16]:

$$f_{w_{r_i}} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_{j\neq i} w_{r_j} p_{r_j} E_{r_j} \sum_{T,S} w_T U_S \left[\nu\left(\frac{1}{M_T^c}+\frac{1}{M_{T'}^c}\right)+2\left(\frac{AF}{M_T}+\frac{AF'}{M_{T'}}\right)\right]\right] \quad \text{(A.1)}$$

$$f_{E_{r_i}} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_{j\neq i} w_{r_j} p_{r_j} E_{r_j} \sum_{T,S} w_T U_S \left[\nu\left(\frac{1}{M_T^c}+\frac{1}{M_{T'}^c}\right)+2\left(\frac{AF}{M_T}+\frac{AF'}{M_{T'}}\right)\right]\right] \quad \text{(A.2)}$$

$$f_{P_{r_i}} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_{j\neq i} w_{r_j} p_{r_j} E_{r_j} \sum_{T,S} w_T U_S \left[\nu\left(\frac{1}{M_T^c}+\frac{1}{M_{T'}^c}\right)+2\left(\frac{AF}{M_T}+\frac{AF'}{M_{T'}}\right)\right]\right] \quad \text{(A.3)}$$

$$f_{w_{T_i}} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_{j} w_{r_j} p_{r_j} E_{r_j} \sum_{\substack{T_V,\,S_V \\ V\neq i}} w_{T_V} U_{S_V} \left[\nu\left(\frac{1}{M_{T_V}^c}+\frac{1}{M_{T_V'}^c}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF_V'}{M_{T_V'}}\right)\right]\right] \quad \text{(A.4)}$$

$$f_{U_{S_i}} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right] \quad \text{(A.5)}$$

$$f_{\nu} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\sum_{T,S} w_T U_S\left[2\left(\frac{AF}{M_T}+\frac{AF'}{M_{T'}}\right)\right]\right] \quad \text{(A.6)}$$

$$f_{M^c_{T_i}} = -\left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\left[w_{T_i}U_{S_i}\left[\nu\left(\frac{1}{M^c_{T_i}}\right)+2\left(\frac{AF_i}{M_T}+\frac{AF'_i}{M_{T'_i}}\right)\right]+\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right]\right] \quad \text{(A.7)}$$

$$f_{M^c_{T'_i}} = -\left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\left[w_{T_i}U_{S_i}\left[\nu\left(\frac{1}{M^c_{T_i}}\right)+2\left(\frac{AF_i}{M_T}+\frac{AF'_i}{M_{T'_i}}\right)\right]+\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right]\right] \quad \text{(A.8)}$$

$$f_{M_{T_i}} = -\left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\left[w_{T_i}U_{S_i}\left[\nu\left(\frac{1}{M^c_{T_i}}+\frac{1}{M^c_{T'_i}}\right)+2\left(\frac{AF_i}{M_T}\right)\right]+\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right]\right] \quad \text{(A.9)}$$

$$f_{M_{T'_i}} = -\left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\left[w_{T_i}U_{S_i}\left[\nu\left(\frac{1}{M^c_{T_i}}+\frac{1}{M^c_{T'_i}}\right)+2\left(\frac{AF'_i}{M_{T'_i}}\right)\right]+\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right]\right] \quad \text{(A.10)}$$

$$f_{AF_i} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\left[w_{T_i}U_{S_i}\left[\nu\left(\frac{1}{M^c_{T_i}}+\frac{1}{M^c_{T'_i}}\right)+2\left(\frac{AF'_i}{M_{T'_i}}\right)\right]+\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right]\right] \quad \text{(A.11)}$$

$$f_{AF'_i} = \left[1-\frac{1}{4}k\times e_{ing}^{-1}\sum_j w_{r_j}p_{r_j}E_{r_j}\left[w_{T_i}U_{S_i}\left[\nu\left(\frac{1}{M^c_{T_i}}+\frac{1}{M^c_{T'_i}}\right)+2\left(\frac{AF_i}{M_T}\right)\right]+\sum_{\substack{T_V,S_V\\V\neq i}} w_{T_V}U_{S_V}\left[\nu\left(\frac{1}{M^c_{T_V}}+\frac{1}{M^c_{T'_V}}\right)+2\left(\frac{AF_V}{M_{T_V}}+\frac{AF'_V}{M_{T'_V}}\right)\right]\right]\right] \quad \text{(A.12)}$$

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## Conflict of Interest Disclosure

The authors declare that they have no conflict of interest.

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