

Uncertainty Quantification in Internal Dose Calculations for Seven Selected Radio-pharmaceuticals

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Concise and informative title

Uncertainty of absorbed Dose

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1 Abstract

2 Dose coefficients of radiopharmaceuticals have been published by the International
3 Commission on Radiological Protection (ICRP) and the Medical Internal Radiation Dose
4 (MIRD) Committee, but without information concerning uncertainties. The uncertainty
5 information of dose coefficients is important, for example, to compare alternative
6 diagnostic methods and choose the method that causes the lowest patient exposure with
7 appropriate and comparable diagnostic quality. For the study presented here, an
8 uncertainty analysis method was developed and used to calculate the uncertainty of the
9 internal doses of seven common radiopharmaceuticals. **Methods:** On the basis of the
10 generalized schema of dose calculation recommended by ICRP and the MIRD Committee,
11 an analysis based on propagation of uncertainty was developed and applied for seven
12 radiopharmaceuticals. The method takes into account the uncertainties contributed from
13 pharmacokinetic models and the so-called S values derived from several voxel
14 computational phantoms previously developed at Helmholtz Zentrum München. Random
15 and Latin hypercube sampling techniques were used to sample parameters of
16 pharmacokinetic models and S values, and the uncertainties of absorbed doses and
17 effective doses were calculated. **Results:** The uncertainty factors (square root of ratio
18 between 97.5th and 2.5th percentiles) for organ absorbed doses are in the range of 1.1 to
19 3.3. Uncertainty values of effective doses are lower in comparison to absorbed doses, the
20 maximum value being approximately 1.4. The ICRP reference values showed a deviation
21 comparable to the effective dose calculated in this study. **Conclusion:** A general statistical
22 method was developed for calculating the uncertainty of absorbed doses and effective
23 doses for seven radiopharmaceuticals. The dose uncertainties can be used to further
24 identify the most important parameters in the dose calculation and provide reliable dose
25 coefficients for risk analysis of the patients in nuclear medicine.

- 26 **Key Words:** uncertainty quantification; internal dosimetry; pharmacokinetic model; voxel
- 27 phantom; nuclear medicine.

28 INTRODUCTION

29 The absorbed and effective dose coefficients (DCs) to the patients from administered
30 radiopharmaceuticals are usually calculated according to the generalized schema
31 recommended by the ICRP and the MIRD of the Society of Nuclear Medicine and
32 Molecular Imaging (SNMMI) (1-3). In these calculations, the mathematical models (4) for
33 the time-dependent activity curves in organs and tissues (pharmacokinetic models), and
34 the mathematical and digital representations of the human body (now voxel phantoms)
35 (5) are initially evaluated. Because of the uncertainties in the image acquisition chains and
36 the variability of the patients, the image-based kinetic models and the reference human
37 phantoms used for the estimation of absorbed doses to patients are subject to large
38 sources of uncertainty (6-8). Hence, for an individual patient, the resulting dose
39 coefficients are uncertain.

40 Generally, the radiation doses to patients are reported without associated uncertainty
41 and this information is important, for example, to compare alternative diagnostic methods
42 and choose the method that causes the lowest patient exposure with appropriate and
43 comparable diagnostic quality. Furthermore, the uncertainty of internal dose is generally
44 greater than that of external dose, for example in external beam radiation therapy. The
45 calculated internal dose is needed for a medical radiation risk analysis for patients.

46 In this study, an uncertainty analysis method, based on the propagation of uncertainty,
47 was set up to analyze the two main sources of uncertainties in internal dose calculation
48 for radiopharmaceuticals, namely, the image-based pharmacokinetic model parameters
49 and the S values derived from different voxel phantoms. This practical method was
50 applied to assess the uncertainty of DCs of seven common used radiopharmaceuticals. The
51 uncertainty factors (UF, defined as the square root of ratio between 97.5th and 2.5th
52 percentiles) for absorbed dose coefficients are in the range between 1.1 and 3.3; for
53 effective dose the UFs are lower in comparison to absorbed dose, the maximum value
54 being about 1.4. The uncertainty of DCs can be used for risk analysis of patients
55 undergoing diagnostic nuclear medicine procedures.

56 **MATERIALS AND METHODS**

57 **Radiopharmaceuticals**

58 In this study, the uncertainty of absorbed dose coefficient and effective dose
59 coefficient are calculated for the following radiopharmaceuticals: ^{18}F -FDG (^{18}F -
60 fluorodeoxyglucose), $^{99\text{m}}\text{Tc}$ -pertechnetate, $^{99\text{m}}\text{Tc}$ -phosphonate, $^{99\text{m}}\text{Tc}$ -sestamibi, $^{99\text{m}}\text{Tc}$ -
61 tetrofosmin, $^{99\text{m}}\text{Tc}$ -MAA (Macroaggregated Albumin) and ^{201}Tl -chloride.

62

63 **Calculation of Dose Coefficients**

64 In this work, the generalized schema for radiopharmaceutical dosimetry published by
65 the MIRD Committee and ICRP (3) was used for calculating the internal doses. The
66 absorbed dose $D(r_T, T_D)$ in the target organ r_T is determined by:

67

$$D(r_T, T_D) = \sum_{r_S} \tilde{A}(r_S, T_D) S(r_T \leftarrow r_S) + \tilde{A}(\text{REM}) \quad (\text{Eq. 1})$$

$$\left[\left(M_{\text{TB}} S(r_T \leftarrow \text{TB}) - \sum_{r_S} M_{r_S} S(r_T \leftarrow r_S) \right) / M_{\text{REM}} \right]$$

68 where $\tilde{A}(r_S, T_D)$ is the time-integrated activity in a source organ or region r_S over the
69 integration period T_D , where T_D is commonly taken to be infinity (3); $S(r_T \leftarrow r_S)$ is
70 the radionuclide-specific quantity representing the mean absorbed dose to target tissue
71 r_T per unit activity in source tissue r_S , the so-called S value; M_{TB} and M_{REM} are the organ
72 mass (g) of the total body (TB) without contents of walled organs and the organ mass (g)
73 in the remainder tissues (REM), respectively, with $M_{\text{REM}} = M_{\text{TB}} - \sum M_{r_S}$.

74 The ICRP and the MIRD Committee defined the effective dose E for a reference person
75 by averaging the equivalent doses of female and male (9). However, the objective of this
76 study is to estimate the uncertainty of effective dose, the biokinetic data of the seven
77 radiopharmaceuticals were evaluated from the literature without gender identification
78 and the S values were derived from six male phantoms and one female phantom.
79 Therefore, the uncertainty of effective dose is calculated according to the following
80 formula (10):

$$E = \sum_T w_T H(r_T, T_D) \quad (\text{Eq. 2})$$

81 where w_T is a tissue-weighting factor for the target tissue r_T , and $H(r_T, T_D)$ is the
 82 committed equivalent dose. The tissue-weighting factors w_T published by ICRP (9) were
 83 applied and the uncertainty of factors w_T is not taken into account in this study, which is
 84 related to risk analysis. In addition, the difference between the dose coefficients of female
 85 and male is calculated by using the mathematical and voxel phantoms, respectively (see
 86 Table 2).
 87

88 To quantitatively determine the uncertainties of the dose coefficients (absorbed dose
 89 per administered activity), uncertainties of the S values and the time-integrated activity
 90 $\tilde{A}(r_S, T_D)$ are evaluated first.

91

92 **Determination of the Uncertainty of Time-Integrated Activity**

93 The time-integrated activity of an administered radiopharmaceutical in a source organ
 94 is calculated by solving a system of ordinary linear differential equations with transfer
 95 rates λ_{ij} as described in (4):

$$\frac{dq_i(t)}{dt} = \dot{I}(t) - \sum_{j=0, j \neq i}^n \lambda_{ji} q_j(t) - \lambda_p q_i(t) + \sum_{j=1, j \neq i}^n \lambda_{ij} q_j(t) \quad (\text{Eq. 3})$$

97 where $q_i(t)[Bq]$ is activity of the radioactive substance in compartment i at the time t ;
 98 $\lambda_{ij}[d^{-1}]$ is transfer rate of substance transferred from j to i ; λ_{ji} is the transfer rate from
 99 compartment i to j ; λ_{0i} is loss rate to outside of the system; $\dot{I}(t)[Bq \cdot d^{-1}]$ is the rate of
 100 input from outside of the system; and λ_p is the radioactive decay constant. According to
 101 (3), the time-integrated activity is calculated by $\tilde{A} = \int_0^{T_D} q(t) dt$. The MIRD Committee
 102 has reported such compartmental models and their corresponding model parameters
 103 (transfer rates) for some radiopharmaceuticals.

104 If the transfer rates are expressed by fraction and half-life, the solution for the above
 105 differential equation (Eq. 3) can be obtained. The time-integrated activity can be written
 106 as following (1):

$$\frac{\tilde{A}_s}{A_0} = F_s \sum_{j=n+1}^{n+m} a_j \sum_{i=1}^n [a_i \frac{T_i}{T_i - T_j} (\frac{T_{i,eff}}{\ln(2)} - \frac{T_{j,eff}}{\ln(2)})] \quad (\text{Eq. 4})$$

107
108 where A_0 is the administered activity, F_s is the fractional distribution to organ S , a_i is a
109 fraction of F_s eliminated with a biological half-life T_i , a_j is the fraction of F_s taken up with a
110 biological half-life T_j . Both a_i and a_j follow: $\sum a_i = 1$ and $\sum a_j = 1$. $T_{i,eff}$ and $T_{j,eff}$ are
111 the elimination and uptake effective half-lives, respectively. ICRP applied such
112 mathematical models for many commonly used radiopharmaceuticals and tabulated the
113 corresponding model parameters in its publications (1,11,12). In contrast to the MIRD
114 schema, the time-integrated activity can be calculated here explicitly.

115 The time-integrated activity \tilde{A}_s is a function of parameters F_s, a_i, a_j, T_i, T_j (ICRP
116 analytical method) or parameter λ (MIRD compartmental method). To calculate the
117 uncertainty of the \tilde{A}_s , the Latin hypercube sampling (LHS) technique (13) was used for
118 sampling the parameters in the function. The range between the minimum and maximum
119 values of each parameter is divided into 500 intervals on the basis of equal probability.
120 One value from each interval is selected at random with respect to the probability density
121 in the interval. The 500 values thus obtained for the first parameter are paired in a
122 random manner (equally likely combinations) with the 500 values of the second
123 parameter. These 500 pairs are combined in a random manner with the 500 values of the
124 third parameter to form 500 triples and so forth until 500 k-tuples are formed. In this
125 manner one get an $n \times k$ matrix of input where the i^{th} row contains values of each of the k
126 input variables to be used on the i^{th} run ($n=500$ runs) of the computer model.

127 To illustrate the MIRD compartmental-model approach, the model structure, the mean
128 values and the standard deviations of the model parameters for ^{18}F -FDG were taken from
129 Hays et al. (14). The minimum and maximum values and the type of the distribution of the
130 model parameters for the LHS sampling were taken from Li et al. (15). The FDG
131 compartmental model is depicted in figure 1. For the other six radiopharmaceuticals,
132 based on a normal distribution and a confidence interval of 95%, the minimum and
133 maximum values were calculated as following:

$$134 \quad \text{Min} = \mu - 1.96\sigma$$

135
$$Max = \mu + 1.96\sigma \quad (Eq. 5)$$

136 For the negative values, which occurred in some parameters, a lognormal distribution was
 137 assumed. The minimum and maximum values were then recalculated based on the
 138 lognormal distribution.

$$\mu^* = \frac{\mu}{\sqrt{1 + \left(\frac{\sigma}{\mu}\right)^2}}$$

139
$$\sigma^* = \exp\left(\sqrt{\log\left(1 + \left(\frac{\sigma}{\mu}\right)^2\right)}\right) \quad (Eq. 6)$$

140 After the geometric mean μ^* and the geometric standard deviation σ^* (16) were
 141 determined, the minimum and maximum values (97.5th and 2.5th percentiles of the
 142 lognormal distribution) were calculated with a confidence interval of 95%:

143
$$Min = \mu^* / (\sigma^*)^{1.96}$$

144
$$Max = \mu^* \times (\sigma^*)^{1.96} \quad (Eq. 7)$$

145 The mean values of the model parameters for ¹⁸F-FDG and ²⁰¹Tl-chloride, in accordance
 146 with the ICRP analytical method, were taken from ICRP Publication 106 (12), for ^{99m}Tc-
 147 pertechnetate, ^{99m}Tc-phosphonate and ^{99m}Tc-MAA from ICRP Publication 53 (1), and for
 148 ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin from ICRP Publication 80 (11). To calculate the
 149 uncertainty of the model parameter, a normal distribution with a coefficient of variation
 150 (CV) of 0.2 was assumed. Some parameters for the source organs, marked with a dagger
 151 (Supplemental Tables 2-8), were not specified; however, the time-integrated activity was
 152 indicated.

153 For ¹⁸F-FDG, the uncertainties of the time-integrated activity were calculated by both
 154 MIRD and ICRP models. For the remaining six radiopharmaceuticals, the calculations were
 155 performed solely by the ICRP method because there is no proposed compartmental model
 156 published by the MIRD Committee.

157

158 **Determination of Uncertainty of S Values**

159 The S values were calculated by the specific absorbed fraction values (SAF values), the
 160 energy and yield of emitting radiation. The SAF values are the fraction of radiation *R* of

161 energy E emitted within the source region that is absorbed per unit mass in the target
 162 region. In our laboratory, the SAF values for seven different phantoms (Table 1) were
 163 calculated by applying the Monte Carlo radiation transport simulation technique (17). The
 164 decay energies and yields, which were taken from the ICRP Publication 107 (18), are
 165 assumed to be constant in the present uncertainty analysis. Therefore, the uncertainty of
 166 the S values is the fractional uncertainty of the SAF values. The standard deviation and
 167 mean values were determined from the SAF values of the seven phantoms. For lognormal
 168 distributions, the geometric mean and the geometric standard deviation were calculated
 169 from which the minimum and maximum values for the SAFs were determined.

170 The SAF values of electrons for some walled organs were not simulated. For SAF values
 171 of electrons with energies less than 100 keV, the following approximations have been
 172 made (19):

$$173 \quad \Phi(r_T \leftarrow r_S) = \begin{cases} 1/M_T & \text{for } r_T = r_S \\ 0 & \text{for } r_T \neq r_S \\ 0.5/M_c & \text{for } r_T = \text{wall}, r_S = \text{contents} \\ & \text{of walled organ} \\ 1/M_{TB} & \text{for } r_S = \text{Total body} \end{cases} \quad (\text{Eq. 8})$$

174 where r_T is target region, r_S source region, TB total body, M_T and M_{TB} masses of the
 175 target regions and of the total body, respectively, and $\Phi(r_T \leftarrow r_S)$ is the specific absorbed
 176 fraction. The minimum and maximum values required for the LHS method were calculated
 177 according to the same principle as in the determination of the uncertainties of the model
 178 parameters.

179 A computer program called "DoseU", written in C#, was developed at the Helmholtz
 180 Zentrum München for calculating the uncertainty of the absorbed dose and effective dose
 181 coefficients according to Eq. 1 and Eq. 2. As input, 500 sample values of the k parameters
 182 of time-integrated activity and S values were generated, and were entered in the
 183 computer code "DoseU". As output, 500 values of absorbed and effective dose
 184 coefficients were calculated that were further used for calculating the statistics, for
 185 example, 2.5th, 25th, 75th and 97.5th percentiles, the mean values and standard deviation of
 186 the dose coefficients.

187 To demonstrate the deviations in the calculation of dose coefficients with the same
188 time-integrated activities and different phantoms, dose coefficients calculated using voxel
189 phantoms (17) and mathematical phantoms (20) were compared.

190 **RESULTS**

191 The uncertainty of the model parameter for ^{18}F -FDG, expressed in maximum and
192 minimum values, and the distribution type required for sampling are summarized in the
193 Supplemental Tables 1 and 2. The data for the rest of the radiopharmaceuticals, according
194 to the ICRP analytical method, can be found in the Supplemental Tables 3-8.

195 For a quantitative description of uncertainty, the uncertainty factor (UF) (21) was used.
196 The uncertainty-associated quantity can be expressed in terms of lower and upper
197 bounds, A and B, respectively. The UF for a confidence interval of 95 % is defined as the
198 square root of ratio between 97.5th (B) and 2.5th (A) percentiles. The uncertainty factors
199 for the time-integrated activity varied generally from 1.0 to 2.0. The calculated minimum
200 and maximum values and the type of distribution for the S values are not listed here for
201 reasons of space.

202 The uncertainties of the dose coefficients are presented in figures 2-5 (logarithmic
203 representation) in the form of boxplots. The boundary line between the two colors of the
204 box reflects the median value. The lower and the upper edge of the box represent,
205 respectively, the 25th and 75th percentile; within the box are the 50th percentiles of all
206 values. The upper and lower end of the whiskers shows the 2.5th and 97.5th percentile,
207 respectively.

208 For ^{18}F -FDG, the uncertainty of the dose coefficients, according to the MIRD
209 calculation, varies from 1.2 to 1.7; the large coefficient of variation of the S value (liver-to-
210 UB wall, 29%) leads to the larger UF in UB wall of 1.9. According to the ICRP calculation,
211 the UF ranges from 1.1 to 1.9, especially for brain with a greater UF of 1.5 and UB wall a
212 UF of 1.9. For $^{99\text{m}}\text{Tc}$ -pertechnetate, the UF varies from 1.1 to 1.5, for $^{99\text{m}}\text{Tc}$ -phosphonate
213 from 1.2 to 2.4; the large UF of 2.4 in the brain with $^{99\text{m}}\text{Tc}$ -phosphonate is due to the large
214 geometric standard deviations of the S values of bone-to-brain (2.92) and UB cont-to-brain
215 (2.4). The UFs for $^{99\text{m}}\text{Tc}$ -sestamibi are from 1.1 to 1.6, and for $^{99\text{m}}\text{Tc}$ -tetrofosmin from 1.1
216 to 1.7. For $^{99\text{m}}\text{Tc}$ -MAA, the UF varies from 1.2 to 2.4, particularly for thymus with a greater
217 UF of 2.4; the large UF of 2.4 in the thymus with $^{99\text{m}}\text{Tc}$ -MAA is due to the large coefficient
218 of variation of the S values of liver-to-thymus (25%) and kidney-to-thymus (28%). Finally,

219 the UF of ^{201}Tl -chloride varies from 1.3 to 3.3, with greater uncertainties for lungs (UF =
220 2.8) and kidneys (UF = 3.3); the very large UF of 3.3 in the kidneys with ^{201}Tl -chloride is due
221 to the large geometric standard deviations of the S values of bone-to-kidney (2.9) and
222 kidney-to-kidney (3.2), respectively.

223 The uncertainties of effective dose coefficients are presented in figure 6. The
224 uncertainty factor varies from 1.1 ($^{99\text{m}}\text{Tc}$ -sestamibi) to 1.4 (^{201}Tl -chloride). For comparison,
225 the dose coefficients and deviations of ^{18}F -FDG between the two different types of
226 phantoms are shown in table 2.

227 **DISCUSSION**

228 The uncertainties in the absorbed dose can mainly be attributed to the uncertainties in
229 the time-integrated activity which is associated with the pharmacokinetic model
230 parameters and the uncertainties of the S values which were derived from the voxel
231 phantoms. For model parameters for there was insufficient information upon which to
232 base an estimate of the uncertainty, we assumed a coefficient of variation of 20%. The
233 mean energy of electrons was used in the calculation of the S values from the SAF values.

234 The mean values of the dose coefficients calculated in the present work were
235 compared with the values reported by other investigators to show the development of the
236 internal dose calculation and the advanced imaging technology in nuclear medicine.

237 For ^{18}F -FDG, dose coefficients were reported by ICRP (1,11,12), MIRDC Committee (22),
238 and many other groups (23-29). A strong variation of absorbed doses in some target
239 organs was shown. For example, for lungs our calculated value of $0.0208 \text{ mGy MBq}^{-1}$ is
240 compared to $0.0046 \text{ mGy MBq}^{-1}$ reported by Khamwan et al. (29) and $0.094 \text{ mGy MBq}^{-1}$ by
241 Mejia et al. (23); for spleen, our value of $0.0122 \text{ mGy MBq}^{-1}$ is compared to the value of
242 $0.05 \text{ mGy MBq}^{-1}$ by Reivich et al. (25) and $0.04 \text{ mGy MBq}^{-1}$ by Jones et al. (26). A greater
243 variation was also found in the comparison of skin between our calculated mean value of
244 $0.00813 \text{ mGy MBq}^{-1}$ and the reported value of $0.0011 \text{ mGy MBq}^{-1}$, and between our
245 calculated mean value of $0.01 \text{ mGy MBq}^{-1}$ for breast and the reported value of 0.0733
246 mGy MBq^{-1} (29). For the remaining target organs all reference values are within or close to
247 our calculated uncertainty range.

248 The dose coefficient uncertainties of $^{99\text{m}}\text{Tc}$ -pertechnetate and $^{99\text{m}}\text{Tc}$ -MAA were also
249 compared to the values reported by ICRP (1,11). For $^{99\text{m}}\text{Tc}$ -pertechnetate the reported
250 values for breast, liver, lungs, kidneys, spleen and thymus are within our calculated
251 uncertainty range. For all other target organs, there is a greater deviation of the reported
252 values from our calculated dose coefficient values.

253 For $^{99\text{m}}\text{Tc}$ -phosphonates, except for red bone marrow, testes and kidneys, other organ
254 dose coefficients reported by ICRP (1,11) and Subramanian (30) are within our calculated
255 uncertainty range. For $^{99\text{m}}\text{Tc}$ -sestamibi, only the values of gallbladder wall reported by

256 ICRP (11), Higley et al. (31) and Wackers et al. (32), are in our calculated uncertainty range.
257 Dose coefficients for breast, liver, red bone marrow, stomach wall and thymus are in good
258 agreement with values reported in (32). For the remaining target organs, there are greater
259 deviations between the reported values and our calculated uncertainty ranges.

260 For ^{99m}Tc -tetrofosmin, absorbed dose coefficients reported by ICRP (11) and Higley et
261 al. (31) are comparable to our calculated values; however, there is greater deviation for
262 brain and breast. The absorbed dose coefficients reported for liver, spleen, thymus and R-
263 marrow are in the range of the present calculated uncertainty.

264 For ^{201}Tl -chloride, absorbed dose coefficients reported by ICRP (1,11,12) and by other
265 groups like Thomas et al. (33), Castronovo et al. (34), Krahwinkel et al. (35) and Higley et
266 al. (31), are compared to our calculated values. The coefficients for organs of red marrow,
267 kidneys, SI wall and spleen in reference (35) are consistent with our calculated values. For
268 other organs, values reported in (35) are lower compared to the range of calculated
269 uncertainty and the values reported by other investigators (1,11,12,33-35) are greater.

270 The absorbed dose coefficients reported by ICRP are often not in the calculated
271 uncertainty range. This is because the ICRP used the S values which were derived from the
272 mathematical phantom. These S values often differ greatly from those used in the present
273 calculation. The influence of the S values on the absorbed dose of ^{18}F -FDG was shown in
274 table 2. The significant difference was found in UB cont. In the mathematical phantom,
275 the SAFs for electrons were not explicitly simulated, but approximated according to the
276 formula (Eq. 8). Zankl et al. (17) showed that, by using different mathematical and voxel
277 phantoms, the difference in the dose calculation can be greater than 150 %.

278 The reference effective dose coefficients reported by ICRP (1,11,12) were compared to
279 our calculated values. With the exception of ^{18}F -FDG, all ICRP reference values are higher
280 than the calculated values and lay outside of the uncertainty range. The uncertainty of
281 tissue-weighting factor was not taken into account as calculating the uncertainty of
282 effective dose coefficients. However, an example of calculation using tissue-weighting
283 factors with a coefficient of variation of 20% showed no significant effect of uncertainty of

284 tissue-weighting factor on uncertainty of effective dose coefficient. The coefficient of
285 variation varies less than 1%.

286 In addition to the theoretical analysis, the patient count rate in SPECT and PET are, in
287 clinical practice, subject to a large uncertainty, and this uncertainty of count rate
288 propagates to the time-integrated activities and will thus affect the overall uncertainties
289 of the dose estimates.

290 CONCLUSION

291 In the present work, a general method was developed for calculating the uncertainty
292 of absorbed dose and effective dose coefficients of seven radiopharmaceuticals commonly
293 used in nuclear medicine. The uncertainties for organ absorbed doses are in the range of
294 1.1 to 3.3 and for effective dose in the range of 1.1 to 1.4. The urinary bladder wall is the
295 tissue which most commonly shows the highest degree of uncertainty. Furthermore, the
296 uncertainty information can be used to identify the most influential model parameter so
297 that scientific efforts can be invested for updating the pharmacokinetic models and
298 consequently reducing the uncertainty of absorbed dose.

299 **ACKNOWLEDGEMENT**

300 This work was financially supported by the German Federal Ministry for the
301 Environment, Nature Conservation, Building and Nuclear Safety (BMUB) under the
302 Contract No. 3612S20013. The authors thank Mr. Randolph Caldwell for the English
303 improvement of the manuscript.

304 **CONFLICT OF INTEREST**

305 The authors declare that they have no conflict of interest.

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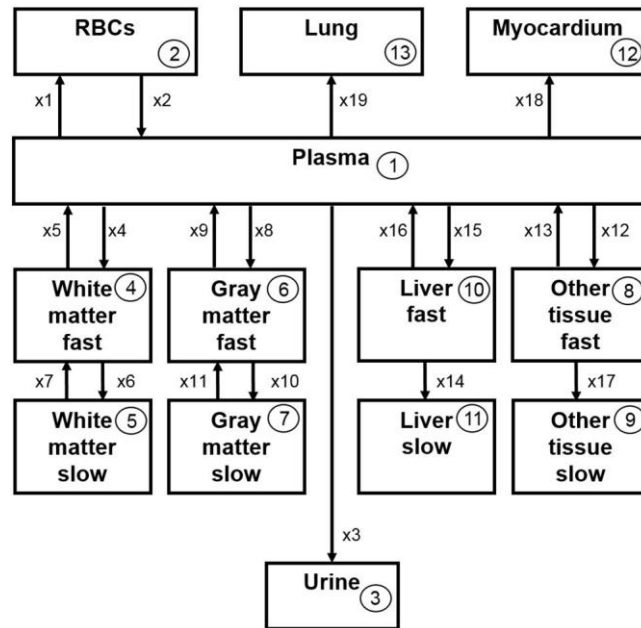
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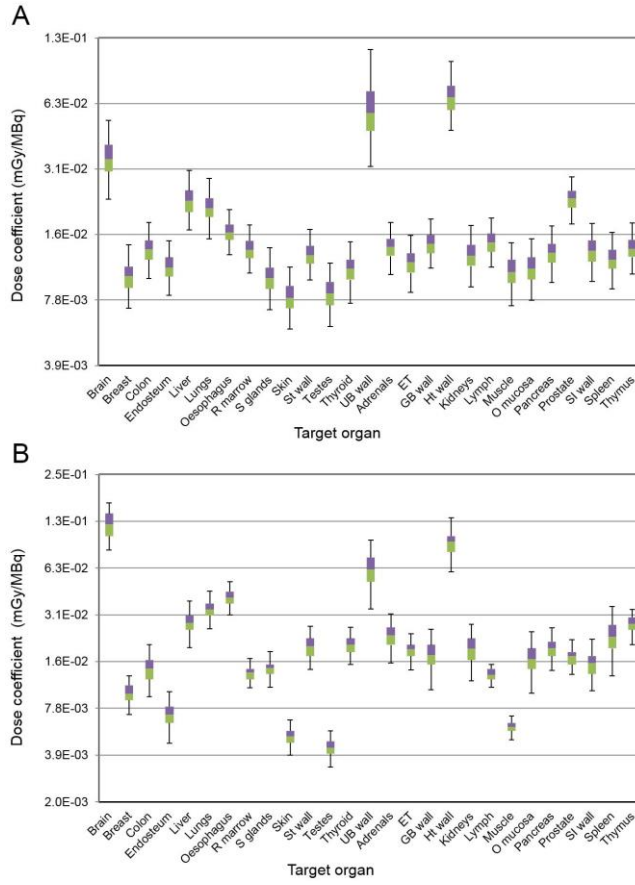


430

431 FIGURE 1. Compartmental model for ^{18}F -FDG developed by MIRDC Committee

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(14). RBCs are red blood cells.

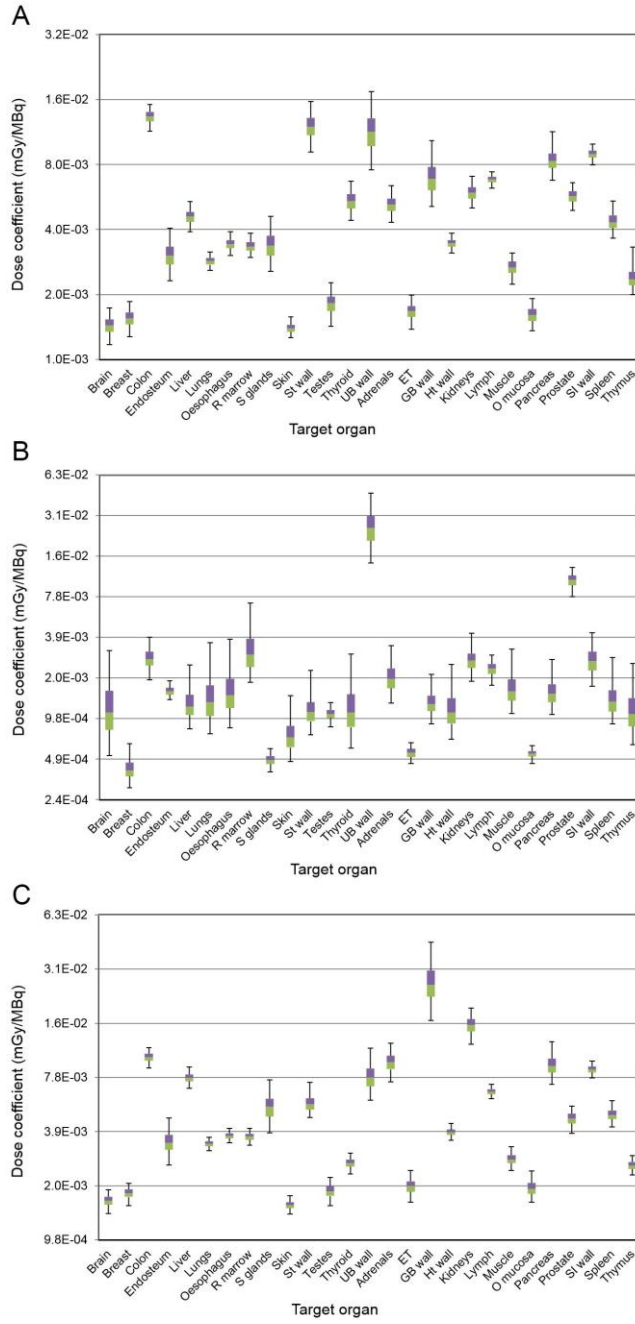


433

434 FIGURE 2. Dose coefficient for ¹⁸F-FDG. According to (A) the ICRP schema and to

435

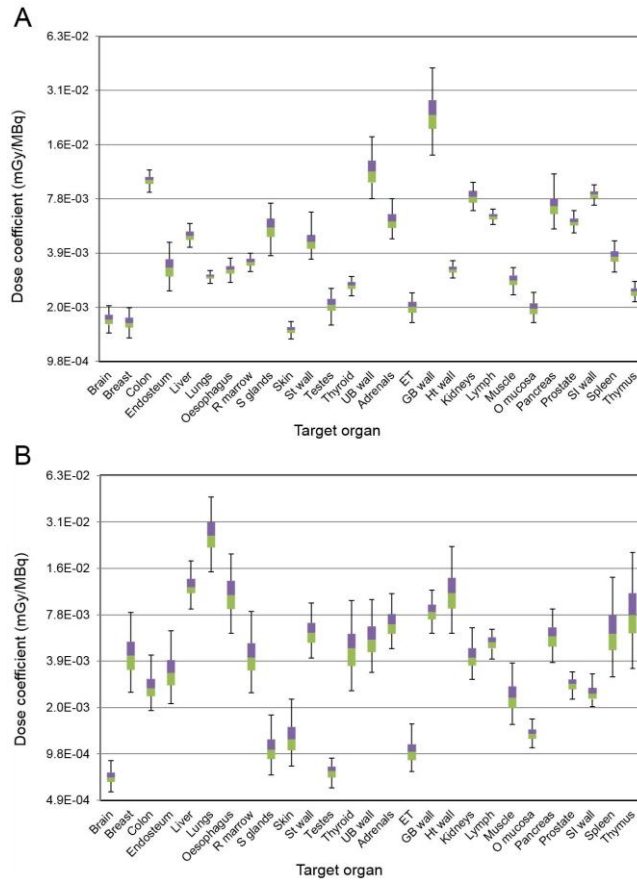
(B) the MIRD schema.



436

437 FIGURE 3. Dose coefficient for (A) ^{99m}Tc -pertechnetate, (B) ^{99m}Tc -phosphonate

438 and (C) ^{99m}Tc -sestamibi. According to the ICRP schema.

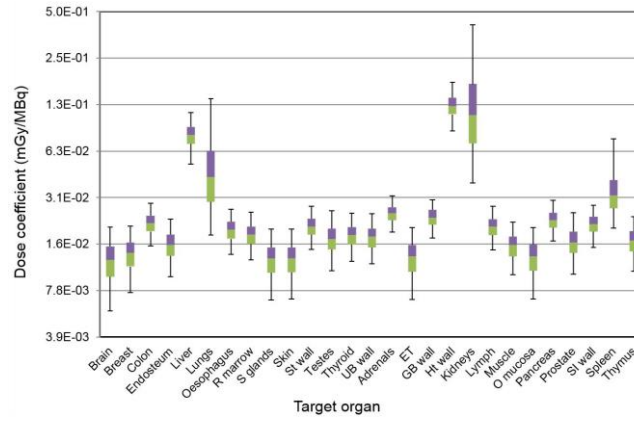


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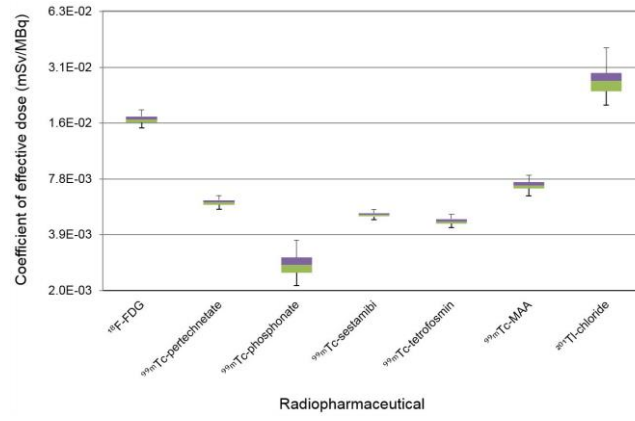
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FIGURE 4. Dose coefficient for (A) ^{99m}Tc -tetrofosmin and (B) ^{99m}Tc -MAA. According to the ICRP schema.



442

443 FIGURE 5. Dose coefficient for ^{201}Tl -chloride. According to the ICRP schema.



444

445

FIGURE 6. Effective dose coefficients. According to the ICRP schema.

446 **Tables**

447

TABLE 1

448

Phantom Data

| Phantom Name | RCP-AM | RCP-AF | Frank | Golem | MadPat | VisHum | Voxelman |
|--------------------------|------------|------------|----------------|------------|---------------|---------------|---------------|
| Gender | m | f | m | m | m | m | m |
| Age | 38 | 43 | 48 | 38 | 69 | 38 | |
| Height (cm) | 176 | 167 | 174 | 176 | 172 | 180 | 178 |
| Weight (kg) | 73 | 60 | 95 | 69 | 70 | 103 | 70 |
| Number of voxels (mill.) | 1,9 | 3,9 | 23,7 | 1,9 | 6,9 | 20,1 | |
| Coverage | Whole body | Whole body | Head and trunk | Whole body | Head to thigh | Head to thigh | Head to thigh |

449

450

TABLE 2

451

Deviations in absorbed dose calculation for the reference voxel phantoms

452

and mathematical phantoms for ^{18}F -FDG.

| Target | Voxel Phantom | Math. Phantom | Voxel Phantom | Math. Phantom | Male Phantom | Female Phantom |
|----------|---------------|---------------|---------------|---------------|-----------------|-----------------|
| | Male | Male | Female | Female | Voxel/ Math. | Voxel/ Math. |
| Brain | 3.5E-02 | 3.8E-02 | 3.9E-02 | 4.4E-02 | 8.5% | 13.0% |
| Breast | 9.1E-03 | 9.2E-03 | 1.2E-02 | 1.1E-02 | 1.6% | 5.4% |
| Colon | 1.2E-02 | 1.3E-02 | 1.5E-02 | 1.5E-02 | 6.7% | 2.4% |
| Liver | 2.2E-02 | 2.2E-02 | 2.7E-02 | 2.8E-02 | 0.1% | 3.8% |
| Lungs | 2.0E-02 | 2.0E-02 | 2.4E-02 | 2.5E-02 | 0.4% | 3.6% |
| R-marrow | 1.2E-02 | 1.2E-02 | 1.4E-02 | 1.4E-02 | 6.4% | 4.2% |
| Skin | 7.3E-03 | 8.3E-03 | 8.7E-03 | 9.7E-03 | 13.8% | 11.6% |
| St wall | 1.2E-02 | 1.1E-02 | 1.4E-02 | 1.3E-02 | 10.7% | 3.1% |
| Thyroid | 1.0E-02 | 1.1E-02 | 1.2E-02 | 1.3E-02 | 8.6% | 7.7% |
| UB wall | 6.9E-02 | 2.2E-01 | 1.0E-01 | 2.8E-01 | 212.8% | 184.8% |
| Adrenals | 1.3E-02 | 1.3E-02 | 1.6E-02 | 1.5E-02 | 0.4% | 2.0% |
| ET | 1.0E-02 | 1.1E-02 | 1.2E-02 | 1.3E-02 | 3.9% | 3.7% |
| GB wall | 1.4E-02 | 1.3E-02 | 1.6E-02 | 1.5E-02 | 7.9% | 7.6% |
| Ht wall | 6.2E-02 | 6.7E-02 | 7.9E-02 | 8.9E-02 | 7.2% | 12.2% |
| Kidneys | 1.2E-02 | 1.1E-02 | 1.4E-02 | 1.4E-02 | 3.1% | 0.9% |
| Muscle | 9.5E-03 | 1.1E-02 | 1.1E-02 | 1.3E-02 | 14.4% | 12.1% |
| Pancreas | 1.3E-02 | 1.3E-02 | 1.4E-02 | 1.6E-02 | 2.6% | 14.2% |
| SI wall | 1.3E-02 | 1.2E-02 | 1.6E-02 | 1.5E-02 | 5.2% | 6.9% |
| Spleen | 1.2E-02 | 1.1E-02 | 1.3E-02 | 1.4E-02 | 4.0% | 1.8% |
| Thymus | 1.2E-02 | 1.2E-02 | 1.6E-02 | 1.4E-02 | 3.2% | 7.5% |

453