EURADOS
European Radiation Dosimetry Group e. V.

EURADOS Report 2021-04

Neuherberg, July 2021

EURADOS Intercomparison on Compartmental Model for ^{18}F-FDG Developed by Hays and Segall

Wei Bo Li, David Broggio, Augusto Giussani, Tomáš Vrba, Kerstin Hürkamp, Alexandra Kamp, Dietmar Noßke, Lara Struelens, Peter Covens

ISSN 2226-8057

ISBN 978-3-943701-28-9

DOI: 10.12768/zz8y-xw93

European Radiation Dosimetry Group e. V.

EURADOS Report 2021-04

Neuherberg, July 2021

EURADOS Intercomparison on Compartmental Model for ^{18}F-FDG Developed by Hays and Segall

Wei Bo Li[1], David Broggio[2], Augusto Giussani[3], Tomáš Vrba[4], Kerstin Hürkamp[1], Alexandra Kamp[3], Dietmar Noßke[3#], Lara Struelens[5], Peter Covens[6]

[1] Helmholtz Zentrum München - German Research Center for Environmental Health (HMGU), Institute of Radiation Medicine, Neuherberg, Germany

[2] Institut de Radioprotection et de Sûreté Nucléaire (IRSN), Fontenay-aux-Roses, France

[3] Federal Office for Radiation Protection (BfS), Oberschleißheim, Germany

[4] Czech Technical University in Prague (CVUT), Prague, Czech Republic

[5] Studiecentrum voor Kernenergie, Centre d'Étude de l'énergie Nucléaire (SCK CEN), Mol, Belgium

[6] Vrije Universiteit Brussel (VUB), Brussel, Belgium

[#] retired

ISSN 2226-8057

ISBN 978-3-943701-28-9

DOI: 10.12768/zz8y-xw93

Imprint

Issued by:
European Radiation Dosimetry Group e. V.
Postfach 1129
85758 Neuherberg
Germany
office@eurados.org
www.eurados.org

The European Radiation Dosimetry Group e.V. is a non-profit organisation promoting research and development and European cooperation in the field of the dosimetry of ionising radiation. It is registered in the Register of Associations (Amtsgericht München, registry number VR 207982) and certified to be of non-profit character (Finanzamt München, notification from 2021-04-23).

Liability Disclaimer

Content

Content i

Abstract iii

1. Compartmental model for ^{18}F-FDG developed by Hays and Segall 1

2. EURADOS implementation of Hays and Segall model for ^{18}F-FDG and transfer rates 3

3. TAC and TIAC for Hays and Segall model for ^{18}F-FDG calculated by EURADOS members 5

3.1 Time activity curve (TAC) in organs/tissues and urinary excretion 5

3.1.1 Intercomparison of TAC calculated by EURADOS members 5

3.2 Time integrated activity coefficients (TIAC) 8

3.2.1 TIAC calculated with arithmetic mean model parameters 8

3.2.2 TIAC calculated with geometric mean model parameters 9

4. Inconsistency of TAC and TIAC between EURADOS and MIRD 11

4.1 Comparison of TAC modelled by EURADOS and MIRD 11

4.2 Comparison of TIAC calculated by EURADOS and MIRD 12

5. Discussion 13

6. Use of Hays and Segall compartmental model for ^{18}F-FDG 15

7. Conclusion 17

8. References 19

9. Annex 21

9.1 TAC in each compartment calculated by IRSN 21

9.2 TAC in each compartment calculated by HMGU 22

9.3 TAC in each compartment calculated by BfS 23

9.4 TAC in each compartment calculated by CVUT 24

Abstract

This report was originated from the analysis of the results of a joint EURADOS-EANM project about the assessment of the external radiation dose rate to comforters and caregivers exposed to patients undergoing nuclear medical diagnostics and therapy. The compartmental model for ^{18}F-FDG developed by Hays and Segall in 1999 was applied by EURADOS members for predicting the time activity curves (TAC) in the source organs and tissues, and the urinary excretion. Inconsistencies have been found between the TAC and the time integrated activity coefficients (TIAC) calculated by EURADOS and those published by Hays and Segall and the Committee on Medical Internal Radiation Dose (MIRD). A quality assurance in form of an intercomparison on the implemented Hays and Segall compartmental model for ^{18}F-FDG was carried out between four institutions of EURADOS voting members to validate the model predictions. The differences in calculated TIAC between EURADOS and MIRD results reach up to a factor of 3.2 by using arithmetic mean model parameters and 3.8 by using geometric mean parameters. The inconsistencies are under investigation in contact with MIRD Committee. A suggestion of updating the compartmental model for ^{18}F-FDG with new available data is made.

1. Compartmental model for ^{18}F-FDG developed by Hays and Segall

The Committee on Medical Internal Radiation Dose (MIRD) develops models for assessing internal radiation doses from administered radiopharmaceuticals in diagnostics and therapy. The MIRD approach is a framework to assess internal dose from incorporated radionuclides, each with its unique radiological characteristics and chemical properties as labelled compounds, in the human body, at organ or tissue level, as well as in fluids, and even in cellular compartments. A compartmental model for ^{18}F-FDG (fluorodeoxyglucose) used for positron emission tomography (PET) scan was developed by Hays and Segall (1999) to meet the need of MIRD Committee of the Society of Nuclear Medicine for the preparation of a dose estimate report for ^{18}F-FDG.

In the study, five adult volunteers (four men, one woman) participated in two complete study sessions one week apart, one session with administration of glucose and one with fasting. The study was performed in a single bed position, with the dynamic data collected with these volunteers over the lower chest area to include the heart and the upper portion of the liver. The kinetics of ^{18}F-FDG in the plasma, erythrocytes, heart, lungs, and liver were measured directly. PET images were obtained for 20 s each during the first 5 min, then for 1 min each during the following 10 min and finally for 5 min each for the next 75 min. Blood samples were collected as close as practical to the mid time point of each PET scan. The actual time of blood collection was recorded and was used in the modelling. In addition, the urinary excretion (representing cumulative bladder uptake of the ^{18}F-FDG) 90 min after the injection was collected. To complete the picture of the most important organs of ^{18}F-FDG distribution, the published parameters describing the kinetics of ^{18}F-FDG in brain (Huang et al. 1980) have been also incorporated to establish the ^{18}F-FDG kinetic model.

The data for organ contents of ^{18}F-FDG for plasma volume, erythrocyte volume, myocardium, lungs, and liver, as well as for total renal excretion, together with the brain kinetic parameters were used by Hays and Segall (1999) to set up a compartmental model as shown in Figure 1. This model is referred to as Hays and Segall compartmental model for ^{18}F-FDG in this report.

The arithmetic mean, standard deviation and geometric mean for the parameters of transfer rates from the donor compartment to the recipient compartment were evaluated by fitting the model to the data. Because there is no significant difference between the parameters for these two glucose and fasting sessions (Hays and Segall, 1999), the data for ten studies were combined. The transfer rates as model parameters for the combined data (n = 10) were tabulated in Hays and Segall (1999: Table 2). As aforementioned, this compartmental model has been used by MIRD Committee for patient dose estimates of ^{18}F-FDG in its Dose Report No. 19 (Hays et al. 2002).

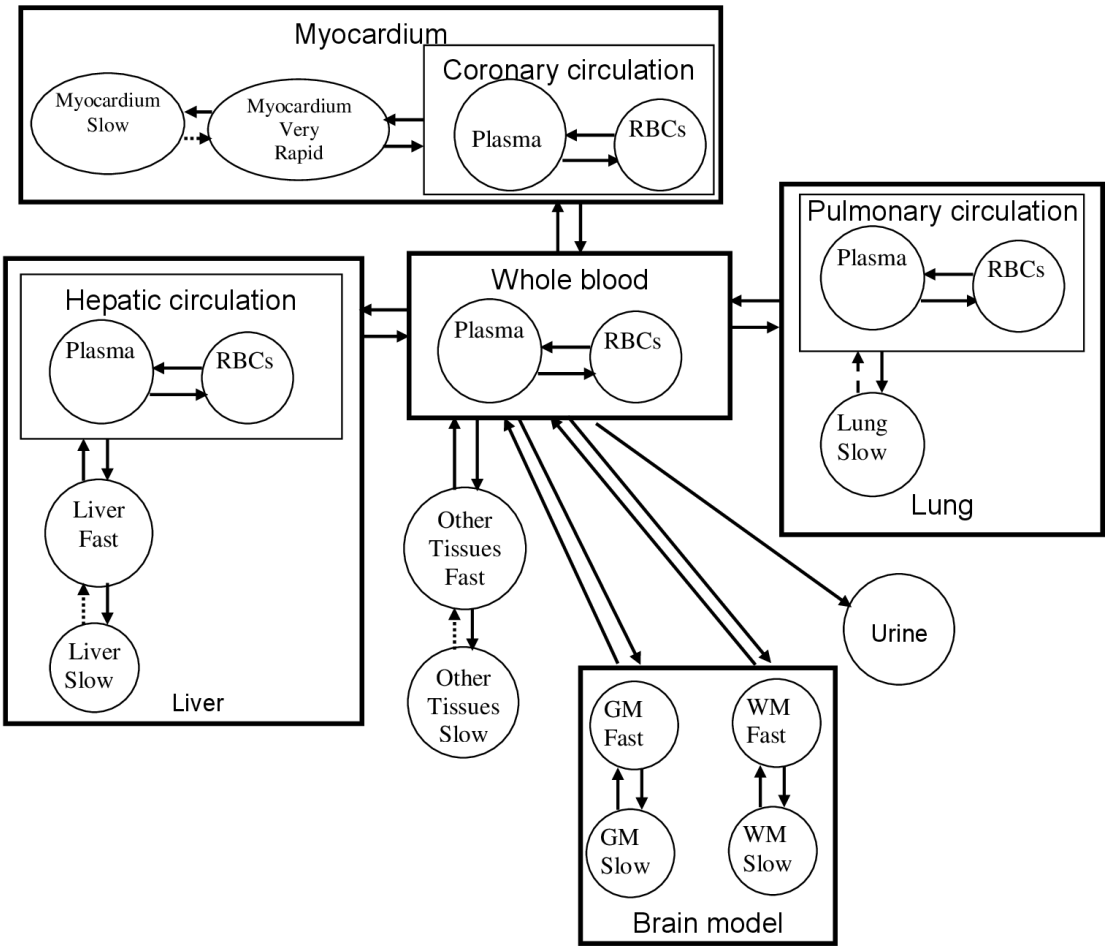

Figure 1: The compartmental model for ^{18}F-FDG developed by Hays and Segall (1999) (Figure was reproduced according to Hays and Segall, 1999). The dotted arrows were set to zero in the final model. GM - gray matter; WM - white matter; RBCs - red blood cells.

2. EURADOS implementation of Hays and Segall model for ^{18}F-FDG and transfer rates

The joint EURADOS-EANM task group implemented the Hays and Segall mathematical model as a compartmental model structure presented in Figure 2. Plasma was set as a central compartment and ^{18}F-FDG was exchanged through it with RBC, liver, lungs, and myocardium directly. The kinetic model of ^{18}F-FDG for brain developed by Huang et al. (1980) was incorporated exchanging with the plasma central compartment. The arithmetic and geometric means of the model transfer rates (*k*) from Hays and Segall (1999) were adopted. The arithmetic and geometric mean transfer rates of brain compartments were taken from Huang et al. (1980) as mentioned in Hays and Segall (1999). These transfer rates are presented in Table 1.

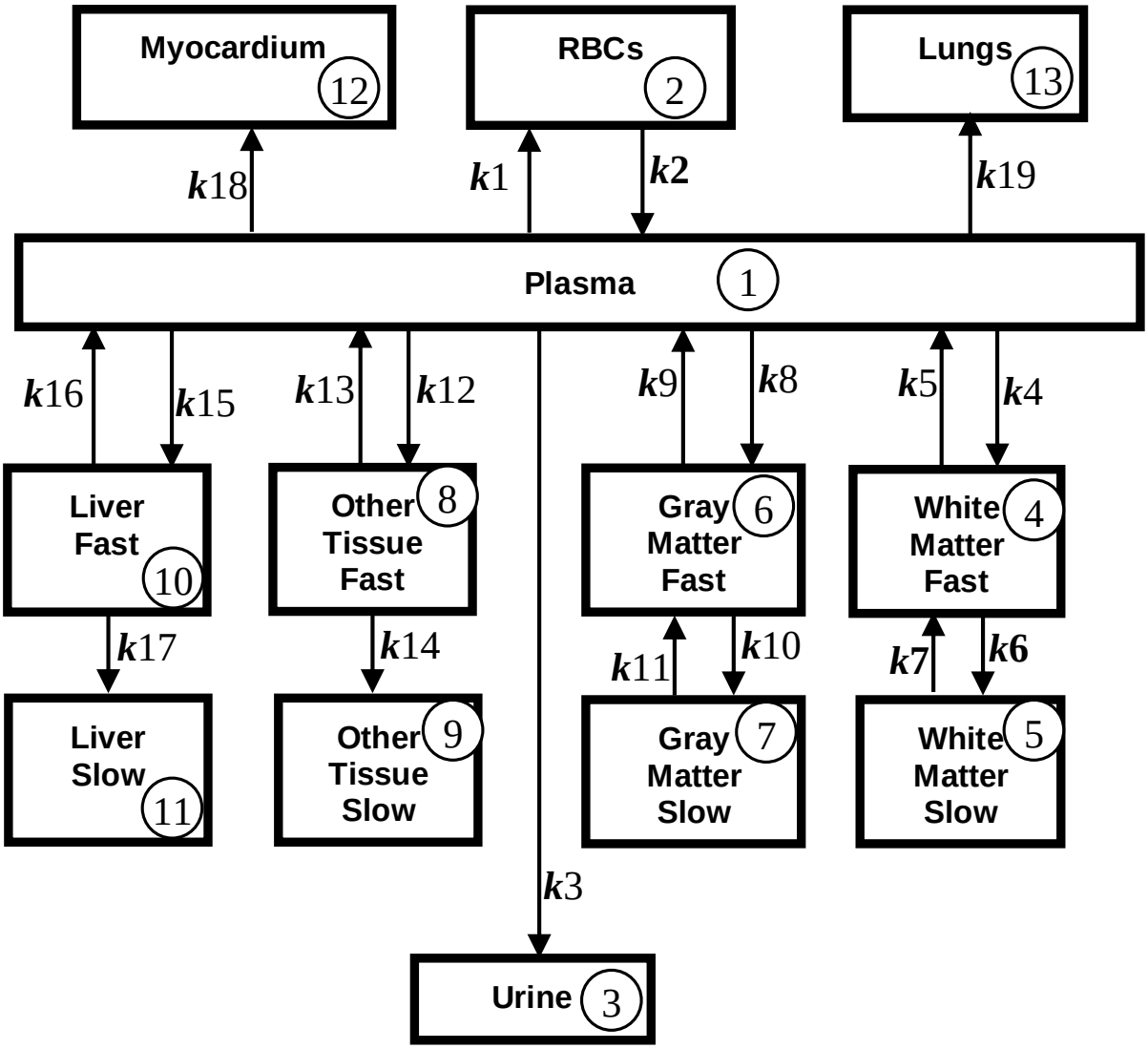

Figure 2: ^{18}F-FDG compartmental model structure implemented by EURADOS (Li and Hoeschen, 2010). RBCs - Red blood cells; *k* – transfer rates

Table 1: Transfer rates* of the compartmental model for ^{18}F-FDG by Hays and Segall.

Organ		Parameter	Transfer rate (min^{-1})	Transfer rate (min^{-1})
From	To		Arithmetic mean	Geometric mean
Plasma	RBCs	*k*1	4.8	4.07
RBCs	plasma	*k*2	8.07	7.35
Plasma	Urine bladder	*k*3	0.0088	0.0085
Plasma	WM Fast	*k*4	0.054	0.052
WM Fast	Plasma	*k*5	0.109	0.10
WM Fast	WM Slow	*k*6	0.045	0.042
WM Slow	WM Fast	*k*7	0.0058	0.0055
Plasma	GM Fast	*k*8	0.102	0.099
GM Fast	Plasma	*k*9	0.13	0.115
GM Fast	GM Slow	*k*10	0.062	0.059
GM Slow	GM Fast	*k*11	0.0068	0.0066
Plasma	Other Fast	*k*12	0.371	0.348
Other Fast	Plasma	*k*13	0.102	0.097
Other Fast	Other Slow	*k*14	0.0167	0.015
Plasma	Liver Fast	*k*15	0.068	0.038
Liver Fast	Plasma	*k*16	0.219	0.186
Liver Fast	Liver Slow	*k*17	0.018	0.006
Plasma	Myocardium	*k*18	0.0053	0.003
Plasma	Lungs	*k*19	0.0017	0.0016

*The transfer rates were taken from the paper of Hays and Segall (1999) and Huang et al. (1980)

RBCs – red blood cells; WM – white matter; GM – gray matter.

The half-life of ^{18}F was taken from ICRP 107 (ICRP, 2008): $T_{1/2} = 109.77$ min, i.e. the physical decay constant is $\lambda = 0.0063$ min^{-1}.

3. TAC and TIAC for Hays and Segall model for ^{18}F-FDG calculated by EURADOS members

3.1 Time activity curve (TAC) in organs/tissues and urinary excretion

The Hays and Segall compartmental model (Figure 2) was implemented independently by EURADOS members using different software for compartmental modelling. The calculations were performed using both the arithmetic mean and the geometric mean of the model transfer rates (Table 1). In the following sections, the time activity curves (TAC) and the corresponding time integrated activity coefficients (TIAC) in organs and tissues, and the urinary excretion calculated for 500 min post injection by four participating institutions, namely Institut de Radioprotection et Sûreté Nucléaire (IRSN), Helmholtz Zentrum München (HMGU), the German Federal Office for Radiation Protection (BfS) and the Czech Technical University in Prague (CVUT) are presented.

3.1.1 Intercomparison of TAC calculated by EURADOS members

The complete model predictions of the TAC in each source organ and tissue compartment and the urinary excretion calculated by the EURADOS members are presented in Figure 3 for the arithmetic mean and in Figure 4 for the geometric mean model transfer rates. The results are almost identical for all four institutions. The complete compilation of TAC and urinary excretion data delivered by the four institutions is presented in the annex (chapter 9). Numerical data in table format are available on request.

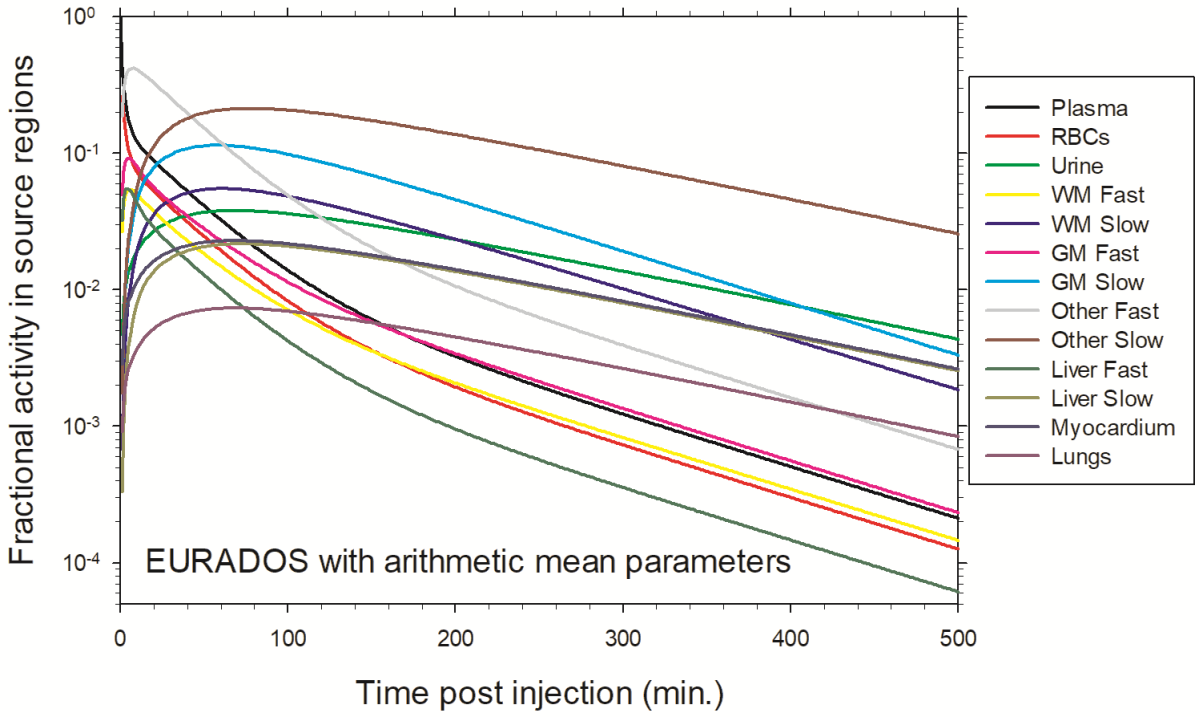

Figure 3: TAC in each compartment modelled by four institutions of EURADOS members using the arithmetic means of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

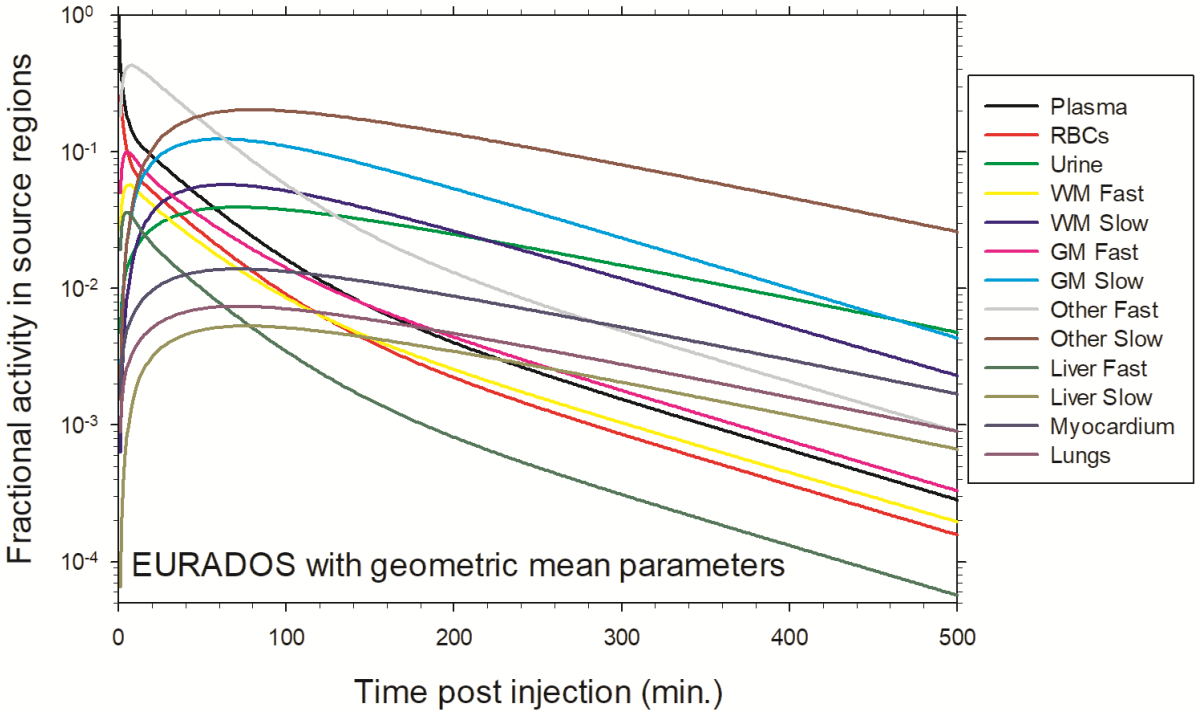

Figure 4: TAC in each compartment modelled by four institutions of EURADOS members using the geometric means of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

A comparison of the TAC in each compartment of the whole source regions (e.g., blood, brain, liver, lungs, myocardium and other) shows a very good agreement for either arithmetic and geometric mean model transfer rates (Figures 5 and 6). It demonstrates a good quality assurance of the calculations by EURADOS members on implementing the model structure and model transfer rates.

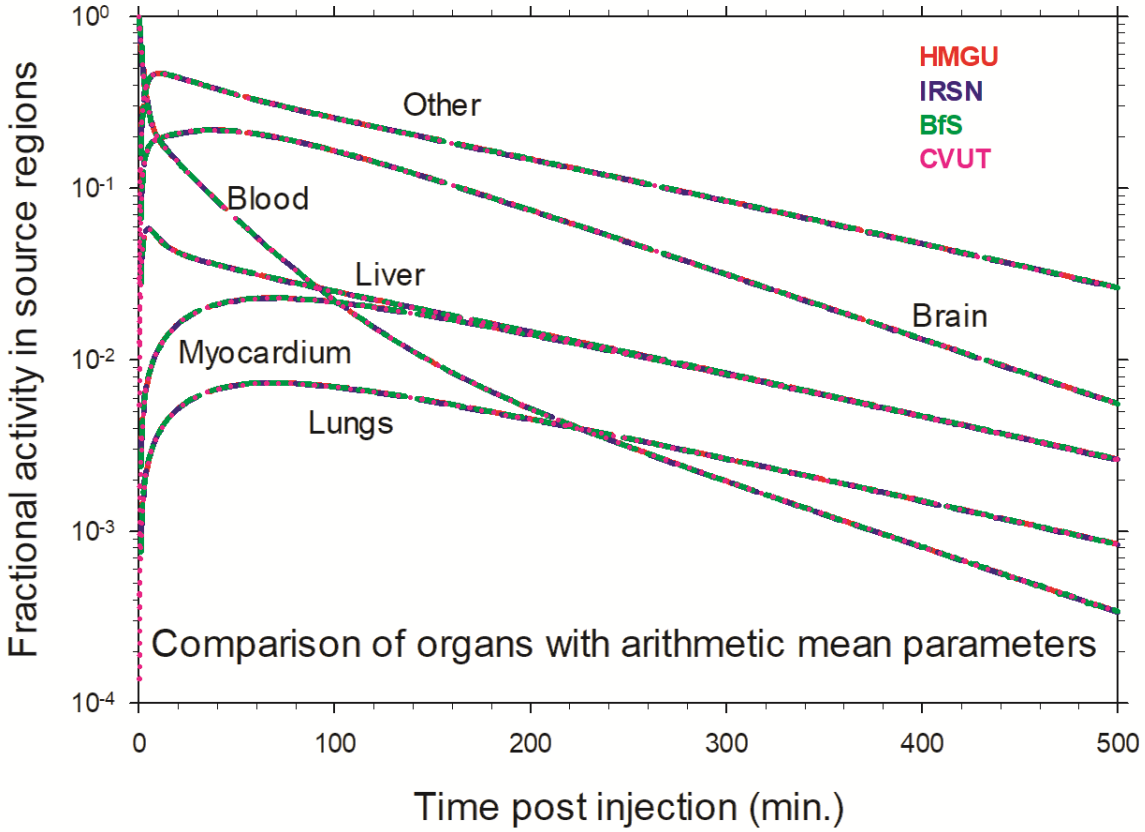

Figure 5: Comparison of TAC in source regions modelled by EURADOS members using the arithmetic mean of model transfer rates.

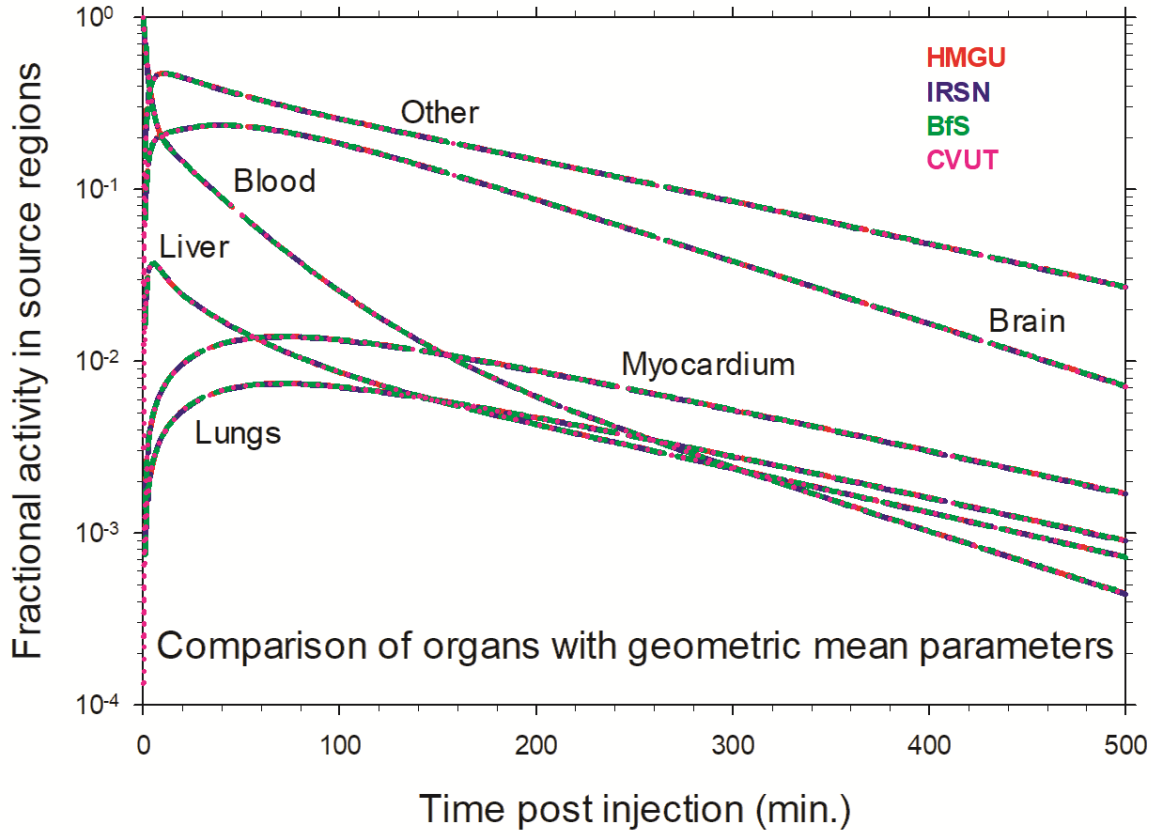

Figure 6: Comparison of TAC in source regions modelled by EURADOS members using the geometric mean of model transfer rates.

3.2 Time integrated activity coefficients (TIAC)

The time-integrated activity is calculated as the area under the curve that describes the activity as a function of time in the source region after the administration of the radiopharmaceutical. The time integrated activity coefficient (TIAC) is defined as the time-integrated activity divided by the administered activity and is given in hours.

3.2.1 TIAC calculated with arithmetic mean model parameters

In Table 2, the TIAC calculated by members of EURADOS using arithmetic mean model transfer rates show a very good agreement among the four institutions.

Table 2: TIAC calculated by using arithmetic mean values of model transfer rates.

Organ	TIAC (h)			
	IRSN	HMGU	BfS	CVUT
Blood	0.197	0.198	0.197	0.197
Plasma	0.124	0.124	0.124	0.124
RBCs	0.073	0.074	0.074	0.073
Urine	0.172	0.172	0.172	0.172
Brain	0.661	0.662	0.662	0.662
WM	0.227	0.227	0.227	0.227
WM Fast	0.048	0.048	0.048	0.048
WM Slow	0.179	0.179	0.179	0.179
GM	0.435	0.435	0.435	0.436
GM Fast	0.076	0.076	0.076	0.076
GM Slow	0.359	0.359	0.359	0.360
Other	1.334	1.334	1.335	1.337
Other Fast	0.367	0.367	0.367	0.367
Other Slow	0.967	0.967	0.968	0.97
Liver	0.133	0.133	0.133	0.133
Liver Fast	0.035	0.035	0.035	0.035
Liver Slow	0.098	0.098	0.098	0.098
Myocardium	0.103	0.103	0.104	0.104
Lungs	0.033	0.033	0.033	0.033

RBCs – red blood cells; WM – white matter; GM – gray matter.

3.2.2 TIAC calculated with geometric mean model parameters

In Table 3, the TIAC calculated by the four participating EURADOS member institutions by using the geometric mean model transfer rates also show a very good agreement.

Table 3: TIAC calculated using geometric mean values of model transfer rates.

Organ	TIAC (h)			
	IRSN	HMGU	BfS	CVUT
Blood	0.211	0.211	0.211	0.211
Plasma	0.136	0.136	0.136	0.136
RBCs	0.075	0.075	0.075	0.075
Urine	0.182	0.183	0.182	0.183
Brain	0.748	0.749	0.748	0.745
WM	0.250	0.250	0.250	0.248
WM Fast	0.055	0.055	0.055	0.055
WM Slow	0.195	0.195	0.195	0.193
GM	0.498	0.499	0.498	0.497
GM Fast	0.089	0.090	0.090	0.089
GM Slow	0.409	0.409	0.409	0.408
Other	1.344	1.348	1.345	1.350
Other Fast	0.399	0.399	0.399	0.400
Other Slow	0.944	0.949	0.945	0.95
Liver	0.051	0.051	0.051	0.051
Liver Fast	0.026	0.026	0.026	0.026
Liver Slow	0.025	0.025	0.025	0.025
Myocardium	0.064	0.065	0.064	0.065
Lungs	0.034	0.034	0.034	0.034

RBCs – red blood cells; WM – white matter; GM – gray matter.

4. Inconsistency of TAC and TIAC between EURADOS and MIRD

4.1 Comparison of TAC modelled by EURADOS and MIRD

To compare the TAC in the source regions between EURADOS members and MIRD Committee, the decay-corrected ^{18}F-FDG time activity curves in the organs and tissues, i.e. brain, heart, liver, lungs and in urine were calculated and presented in Figure 7 for the EURADOS results and in Figure 8, taken from MIRD dose estimation report No. 19 (Hays et al. 2002). Note that the scale of the y-axis in Figure 7 is larger than that in Figure 8. Especially for TAC in brain, the difference between EURADOS and MIRD is obvious. Furthermore, the TAC for liver and heart in Figure 8 were seemingly swapped.

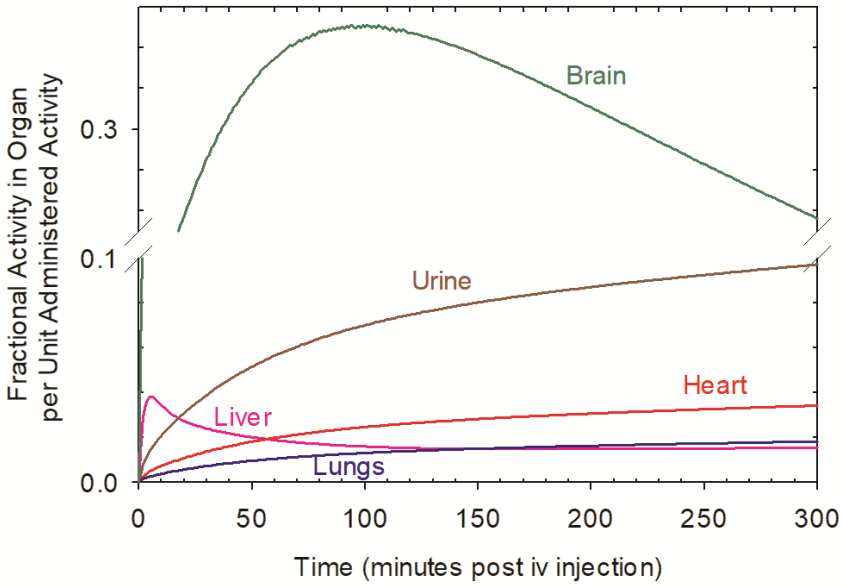

Figure 7: TAC for decay-corrected ^{18}F-FDG activity in normal human brain, heart, lungs, liver, and in urine modelled by EURADOS members using the geometric means of model transfer rates.

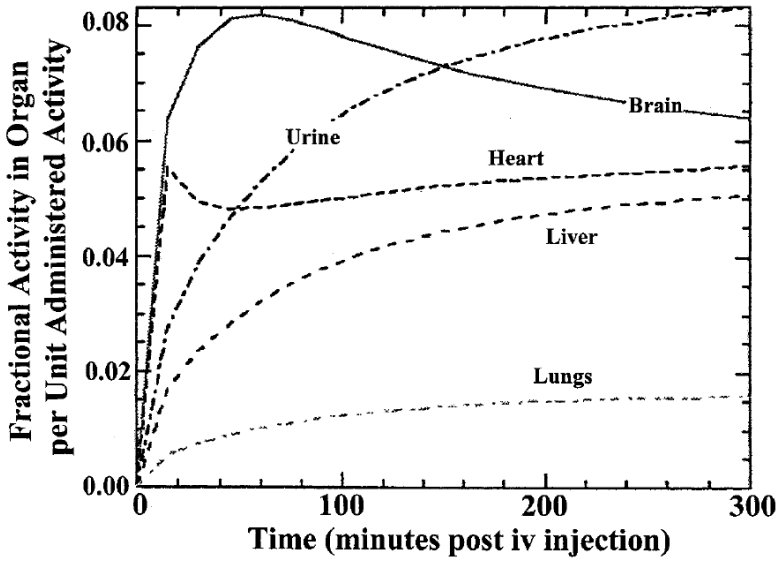

Figure 8: TAC for decay-corrected ^{18}F-FDG activity in normal human brain, heart, lungs, liver, and in urine. These curves are based on the model presented in Hays and Segall (1999), using geometric means of model parameters derived from fits of data from 13 individual studies (Figure taken from Hays et al. 2002).

4.2 Comparison of TIAC calculated by EURADOS and MIRD

The TIAC in source regions calculated by the EURADOS members were compared to the "tau" values published by Hays and Segall (1999) and in the MIRD dose report (Hays et al. 2002) in Table 4. The differences between the EURADOS estimates and the corresponding MIRD "tau" values are substantial, the ratio of EURADOS/MIRD calculated values ranges from 0.3 to 3.8.

Table 4: Comparison of TIAC (Tau values in Hays et al. (2002)) between EURADOS (mean values of four institutions) and MIRD Committee.

Organ	TIAC/Tau (h)					
	EURADOS	MIRD	EURADOS/ MIRD	EURADOS	MIRD	EURADOS/ MIRD
	Arithmetic mean transfer rates			Geometric mean transfer rates		
Blood	0.198	0.276	0.7	0.211	0.250	0.8
Plasma	0.124	0.171	0.7	0.136	0.161	0.8
RBCs	0.074	0.095	0.8	0.075	0.089	0.8
Urine	0.172	0.227	0.8	0.183	0.216	0.8
Brain	0.662	0.245	2.7	0.748	0.230	3.3
WM	0.227	0.070	3.2	0.249	0.066	3.8
WM Fast	0.048			0.055		
WM Slow	0.179			0.194		
GM	0.435	0.174	2.5	0.499	0.164	3.0
GM Fast	0.076			0.090		
GM Slow	0.359			0.409		
Other	1.334	1.790	0.7	1.348	1.785	0.8
Other Fast	0.367			0.399		
Other Slow	0.967			0.949		
Liver	0.133	0.161	0.8	0.051	0.150	0.3
Liver Fast	0.035			0.026		
Liver Slow	0.098			0.025		
Myocardium	0.103	0.133	0.8	0.065	0.115	0.6
Lungs	0.033	0.084	0.4	0.034	0.079	0.4

RBCs – red blood cells; WM – white matter; GM – gray matter.

5. Discussion

The present report was originated in the framework of the joint EURADOS-EANM project for external dose rate estimation for the comforters and caregivers exposed to patients undergoing nuclear medical diagnostics and treatment, in which the ^{18}F-FDG compartmental model, developed by Hays and Segall (1999), was applied. The TAC of organ regions and the urine in bladder for ^{18}F-FDG were needed to estimate the absorbed doses received by the comforters in close vicinity to the patients. During the quality assurance of the model implementation, the TIAC in source organs were also computed and the inconsistency in the TAC and TIAC between EURADOS results and the values reported by Hays and Segall (1999) and the MIRD Committee (Hays et al. 2002) described in chapter 4 was observed.

To explore the reasons of the inconsistency between the values of TAC and TIAC calculated by EURADOS members and those published by MIRD, a letter written by the authors has been sent to the Chairperson and members of the MIRD Committee (Li et al. 2020). The MIRD Committee acknowledged the receipt of the letter, but at present no feedback has been given on the differences in the modelling approaches and results.

6. Use of Hays and Segall compartmental model for ^{18}F-FDG

The compartmental model for ^{18}F-FDG reported by Hays and Segall (1999) was adopted in the MIRD Committee FDG dose report (Hays et al. 2002). The TIAC values used for the dose calculation therein were, however, the averaged values of the TIAC calculated by Hays and Segall (1999) and other TIAC values available in the literature. Moreover, TIAC values of additional source organs, such as pancreas and spleen retrieved from literature, were as well used in the MIRD dose report No. 19 (Hays et al. 2002).

The goal of developing pharmacokinetic models is to predict the TAC for patients administered with radiopharmaceuticals and to estimate the absorbed doses for organs and tissues of the patients themselves, as well as for caregivers, comforters and medical staff. ^{18}F-FDG is one of the most widely used radiopharmaceuticals in nuclear medicine. It has been applied not only in diagnostics, but also for outcome prediction in patients undergoing prostate-specific membrane antigen (PSMA)-targeted radioligand treatment (Michalski et al. 2021). EURADOS suggests that the present ^{18}F-FDG model by Hays and Segall (1999) might be updated using available data, such as for pancreas and spleen before being further applied to various studies. In addition, the inconsistencies observed during this intercomparison should be discussed and eliminated, if possible.

7. Conclusion

In this report, EURADOS members of four voting member institutions implemented the compartmental model for ^{18}F-FDG developed by Hays and Segall (1999) for external dose calculation purposes within a joint EURADOS-EANM project on the estimate of external dose rates of caregivers and medical staffs exposed to patients who undergo nuclear imaging and treatment. However, an inconsistency of the model predicted TAC and TIAC between the EURADOS members and the MIRD results (Hays et al. 2002) has been found. The inconsistency is still under investigation in contact with MIRD Committee.

Our implementation and application showed a large difference of TAC and TIAC in brain and liver in comparison to the MIRD published data with differences between a factor of 3.8 for the calculated TIAC for white matter in brain and a factor of 0.3 for liver with geometric mean model parameters. MIRD Committee was asked to review their model. An action to update the Hays and Segall compartmental model for ^{18}F-FDG is suggested.

Currently, ICRP is developing a compartmental model for ^{18}F-FDG in the framework of updating the ICRP Publication 128 (2015). It would be of interest to compare the ICRP model and Hays and Segall compartmental model (1999) as soon as the ICRP model is published. The results will be of interest to apply the most reliable model for ^{18}F-FDG in the ongoing and further planned EURADOS-EANM activities.

8. References

Hays MT and Segall GM 1999. A mathematical model for the distribution of fluorodeoxyglucose in humans. *J Nucl Med.* **40** 1358-1366.

Hays MT, Watson EE, Thomas SR, Stabin MG 2002. MIRD dose estimate report No. 19: Radiation absorbed dose estimates from ^{18}F-FDG. *J Nucl Med.* **43** 210-214.

Huang SC, Phelps ME, Hoffman EJ, Sideris K. Selin CJ, Kuhl DE 1980. Noninvasive determination of local cerebral metabolic rate of glucose in man. *Am J Physiol: Endocrinol Metab* **238(1)** 69-82.

ICRP 2008. Nuclear decay data for dosimetric calculations. ICRP Publication 107. *Ann. ICRP* **38 (3).**

ICRP 2015. Radiation dose to patients from radiopharmaceuticals: A compendium of current information related to frequently used substances. ICRP Publication 128. *Ann. ICRP* **44(2S)**.

Li WB and Hoeschen C 2010. Uncertainty and sensitivity analysis of biokinetic models for radiopharmaceuticals used in nuclear medicine. *Radiat Prot Dosim.* **139(1-3)** 228–231.

Li WB, Vanhavere F, Broggio D, Giussani A, Noßke D, Vrba T 2020. Compartmental model of ^{18}F-FDG. EURADOS Letter to MIRD Committee on 4.5.2020.

Michalski K, Ruf J, Goetz C, Seitz AK, Buck AK, Lapa C, Hartrampf PE 2021. Prognostic implications of dual tracer PET/CT: PSMA ligand and ^{18}F-FDG PET/CT in patients undergoing ^{177}Lu-PSMA radioligand therapy. *Eur J Nucl Med Mol Imaging.* **48(6)**: 2024–2030.

9. Annex

The TAC calculated by the four institutions are identical, proven through performing a cross comparison in pairs by plotting the TAC of one institution against another institution. In this Annex, the TACs in each compartment are plotted in Figures A1-A8 for reference.

9.1 TAC in each compartment calculated by IRSN

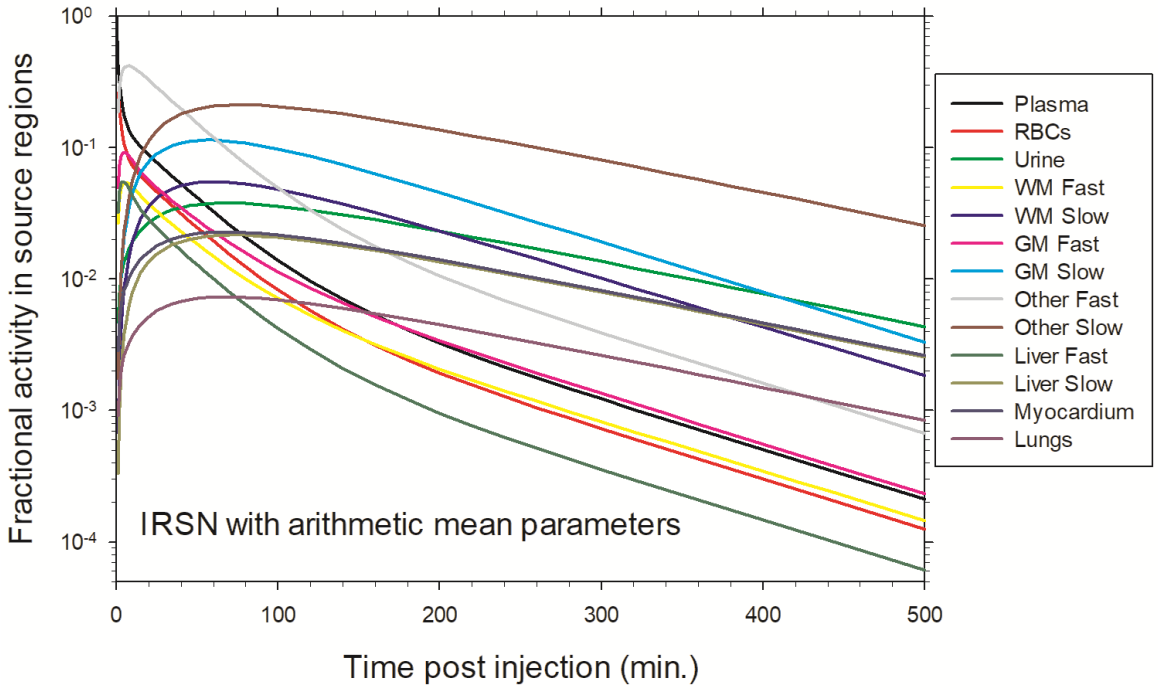

Figure A1: TAC modelled by IRSN using the arithmetic mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

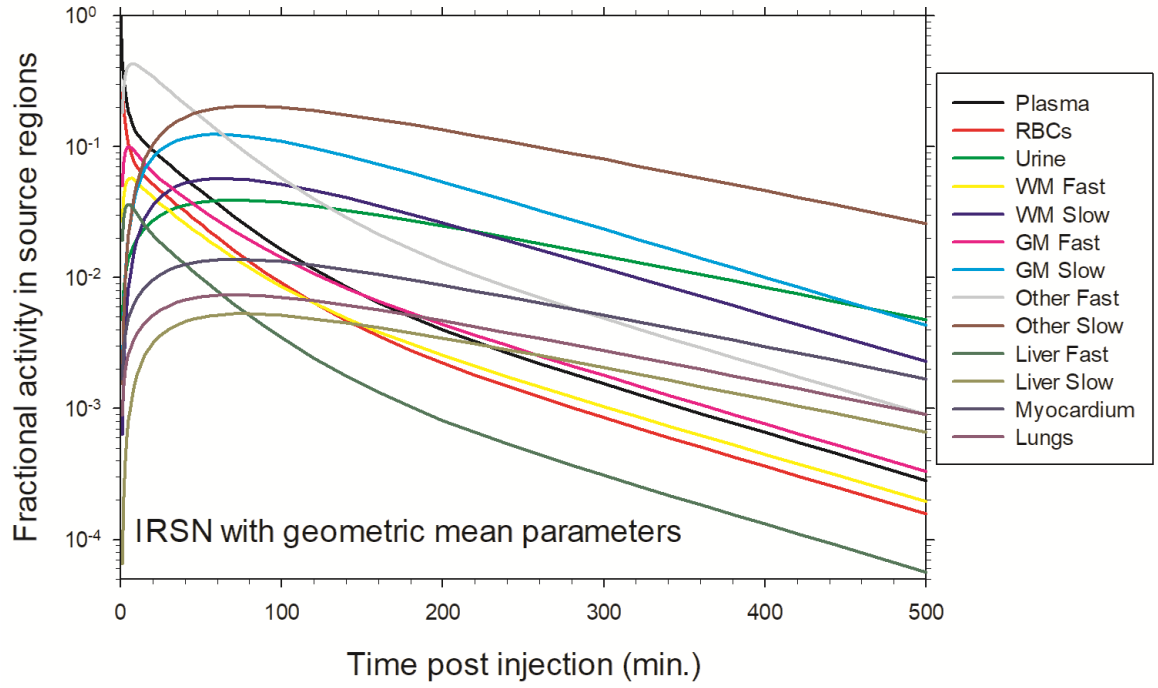

Figure A2: TAC modelled by IRSN using the geometric mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

9.2 TAC in each compartment calculated by HMGU

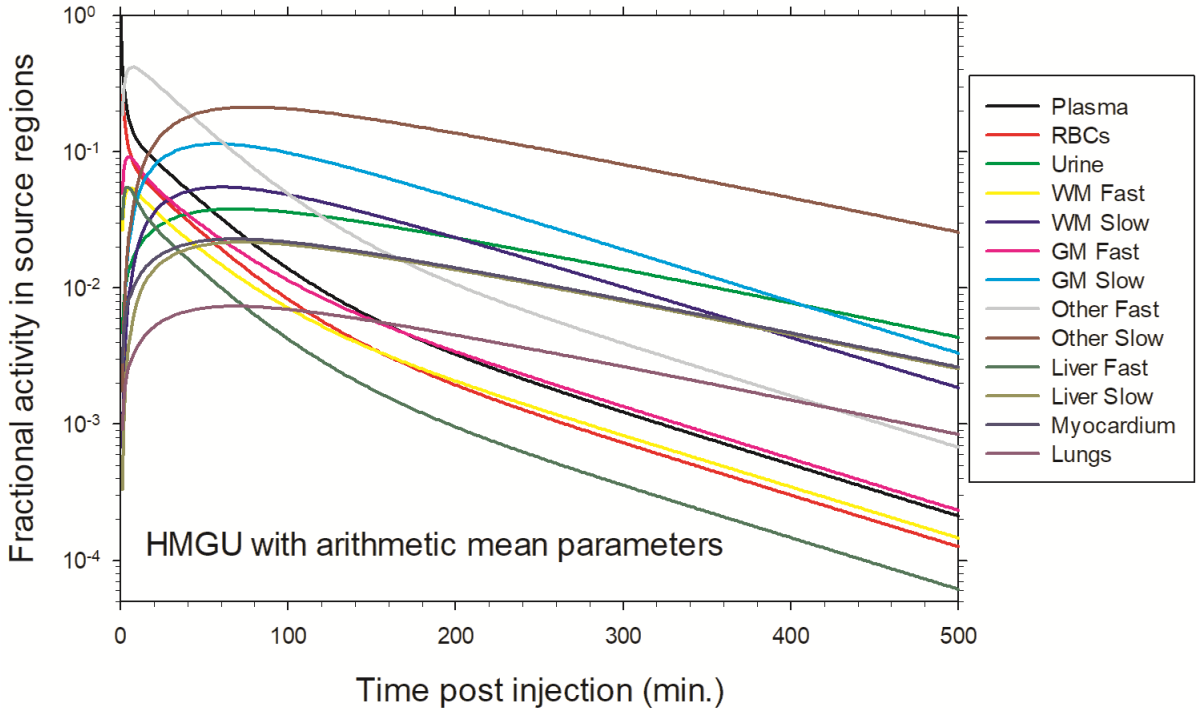

Figure A3: TAC modelled by HMGU using the arithmetic mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

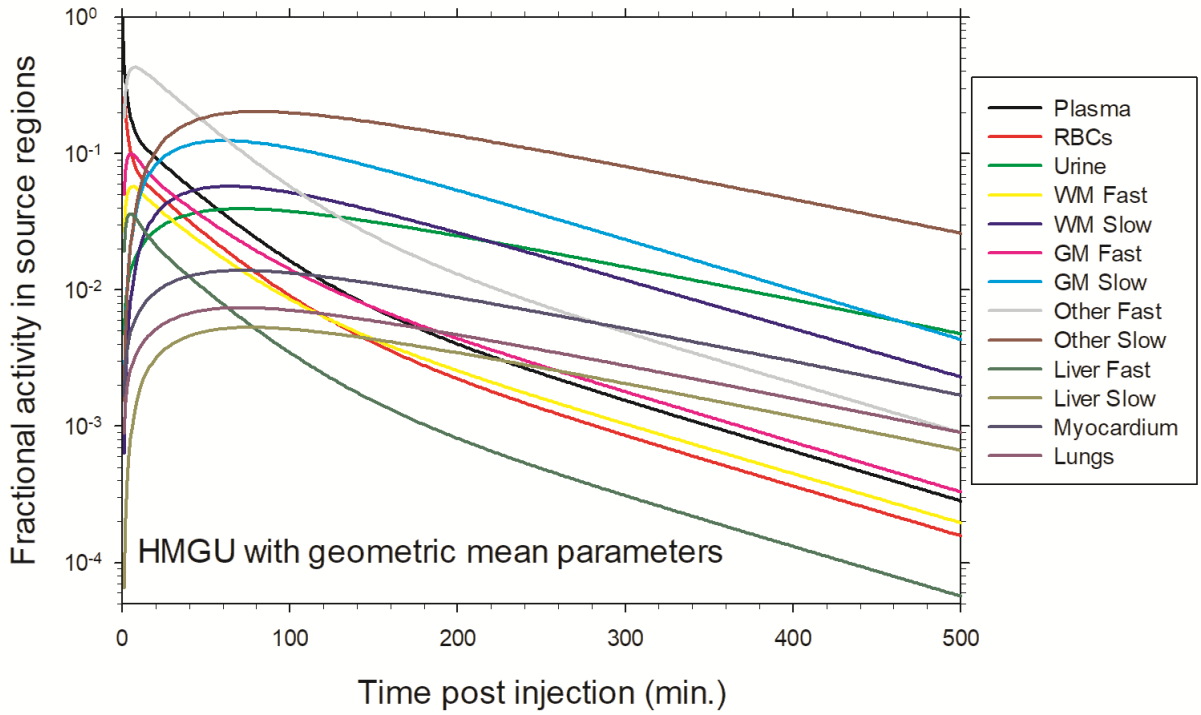

Figure A4. TAC modelled by HMGU using the geometric mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

9.3 TAC in each compartment calculated by BfS

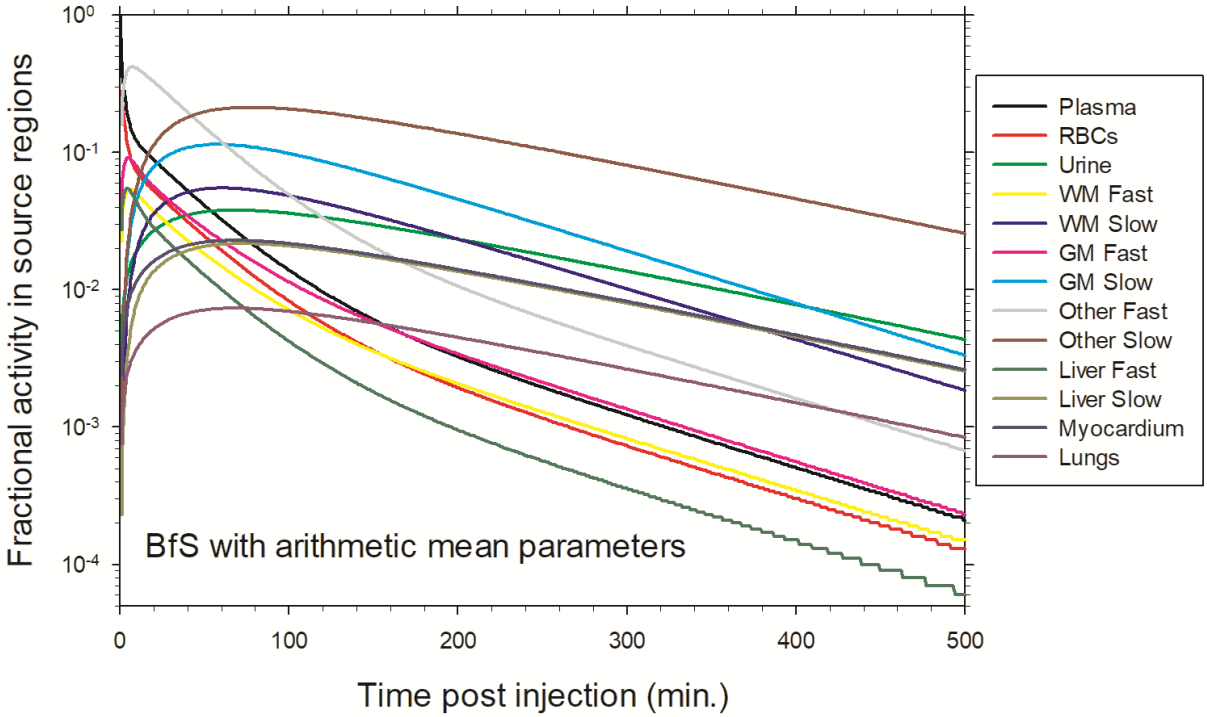

Figure A5: TAC modelled by BfS using the arithmetic mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

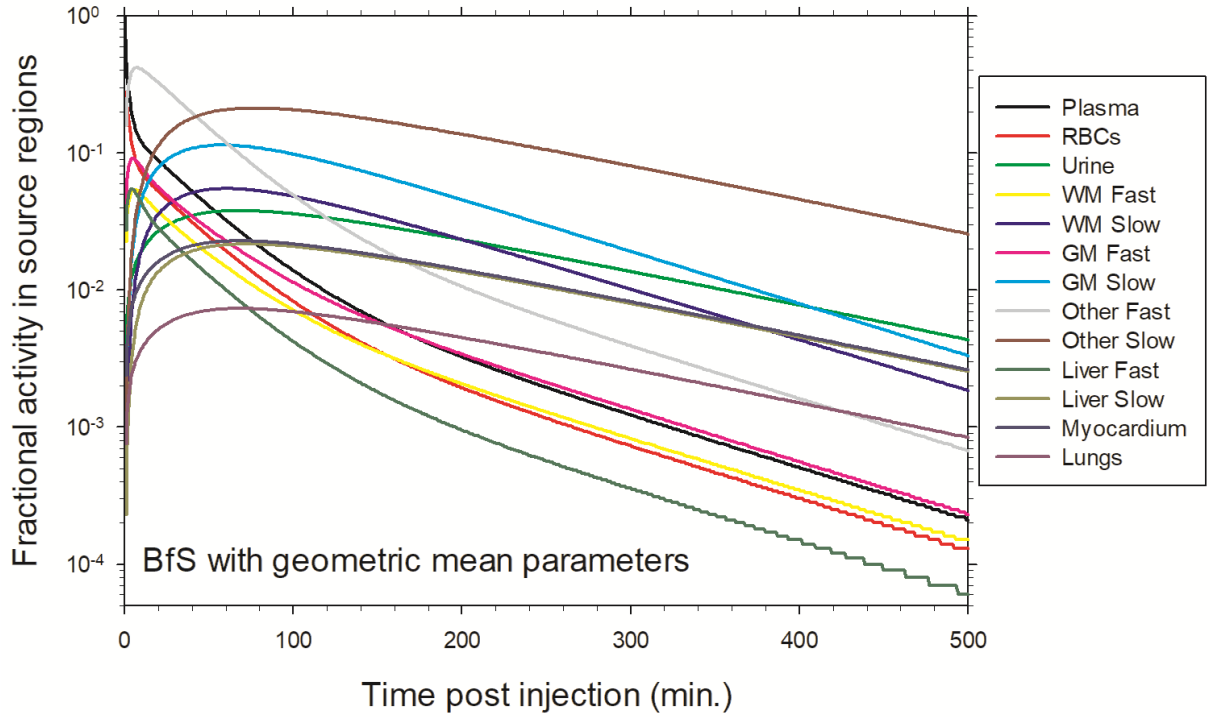

Figure A6: TAC modelled by BfS using the geometric mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

9.4 TAC in each compartment calculated by CVUT

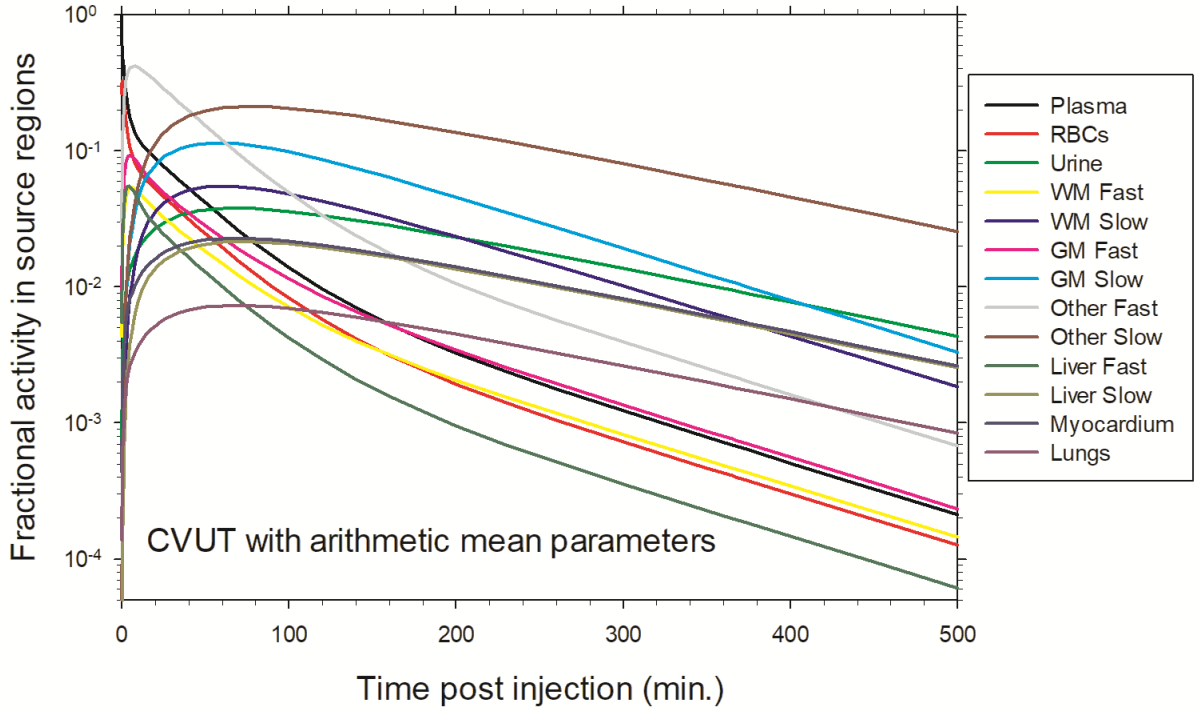

Figure A7: TAC modelled by CVUT using the arithmetic mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.

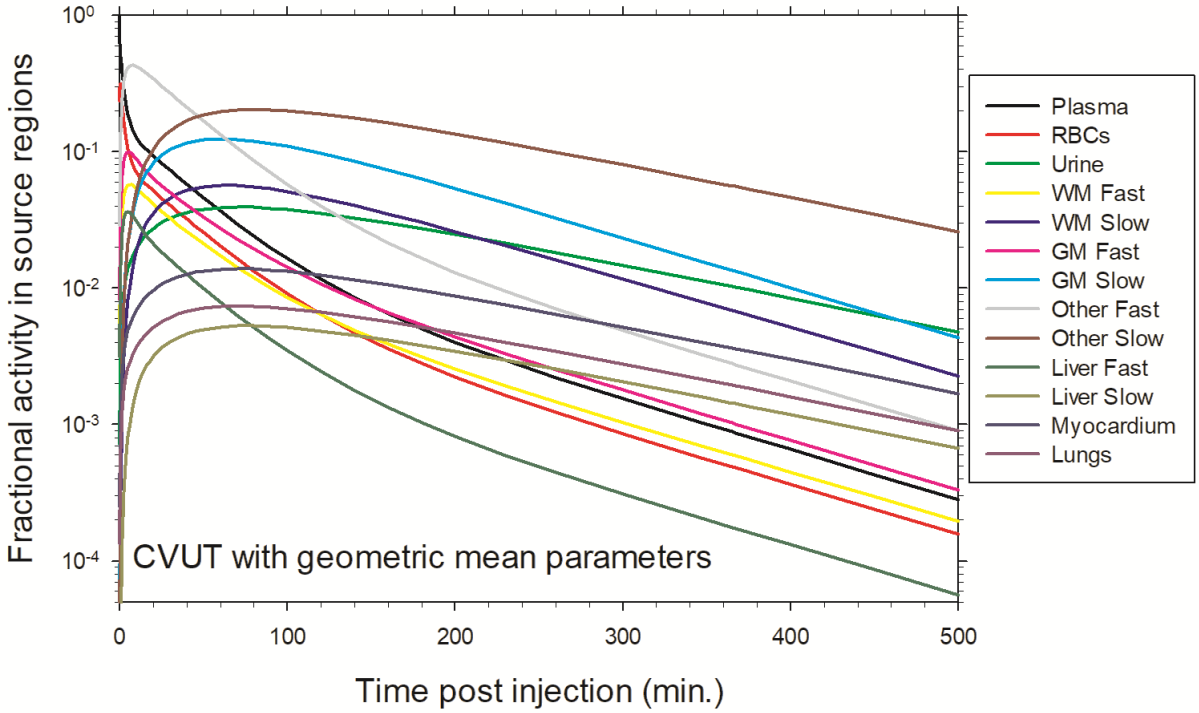

Figure A8: TAC modelled by CVUT using the geometric mean of model transfer rates. RBCs – red blood cells; WM – white matter; GM – gray matter.