TG 36: dose coefficients for radiopharmaceuticals

Makoto Hosono, MD, PhD
Kindai University, Osaka, Japan

Challenges of Radiological Protection
in Research and Society
referring to Medical Field, Oct 3, 2024, Milan
Sala Napoleonica/Via Sant'Antonio, 12
Università di Milano

ICRP

Federal Office for Radiation Protection

Terms of Reference

Mandate:

Objective: to develop dose coefficients for radiopharmaceuticals administered to patients in diagnostic nuclear medicine.

Main tasks:

- to develop biokinetic models for new substances and to improve current models where needed, aiming towards harmonization with models developed by TG95 (IDC)
- to develop a computer code (IDAC 2.1) implementing the new dosimetric and biokinetic models (QA with BfS code DOSAGE)
- Electronic radiopharmaceutical dose viewer
- to update Publication 128 (2015) using new biokinetic models (if available), new ICRP adult and paediatric reference voxel phantoms, Publication 107 nuclear decay data and Publication 103 dosimetry methodology
- Guidance documents on the collection of data from clinical studies needed for modelling and on the use of the revision of Publication 128

ICRP

TG36 Membership

Chair: Augusto Giussani, Federal Office for Radiation Protection (BfS), Germany
Honourary Co-Chair: Sören Mattsson, Skåne University Hospital Malmö and Lund University, Sweden
Secretary: Martin Andersson, Gothenburg University, Sweden

Members
Makoto Hosono, Kindai University, Japan
Derek Jockish, Francis Marion University, USA
Alexandra Kamp, Federal Office for Radiation Protection (BfS), Germany
Keon Kang, Seoul National University, Korea
Sigrid Leide-Svegborn, Skåne University Hospital Malmö, Sweden
Dietmar Nosske, Germany
Nina Petoussi-Henss, Helmholtz Munich, Germany
Juan Camilo Ocampo Ramos, Memorial Sloan Kettering Cancer Center, USA
Kuangyu Shi, University of Bern, Switzerland
Lars Söderberg, Skåne University Hospital, Sweden
Technical secretary: Franklin Eze, Cyclomedical International, Nigeria

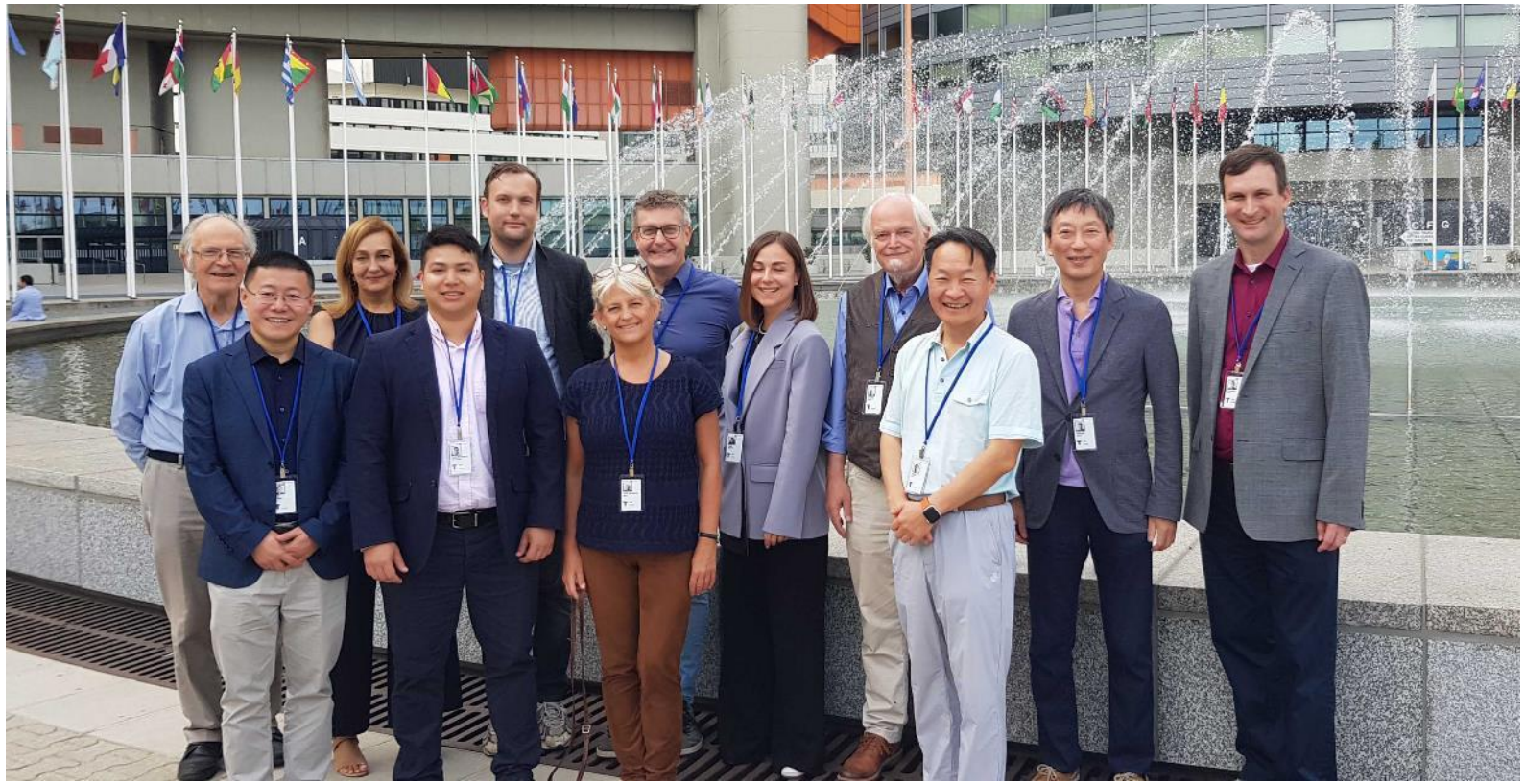
Wesley E. Bolch, University of Florida, USA
Katrine Riklund, Umeå, Sweden
Marie Sydoff, Skåne University Hospital, Lund, Sweden

ICRP

TG36 activities

Monthly webmeetings:
Every 1-3 months

In-person meetings:
Malme
October 2019
Munich
October 2022
Vienna
September 2023



September 2023, IAEA, Vienna

Revision of Publication 128

- Text has been harmonized as far as possible with text of publication on public exposures.
- The work with the update biokinetic models of radiopharmaceuticals (Transition towards fully compartmental models)
- Dynamic bladder model
- Model for the cerebrospinal fluid space
- Brief chapter on dose to embryo and fetus
- Update/Harmonization on breast feeding
- Guidance on extravasation
- About 100 substances

Dissemination of TG-36 results

Submitted manuscript

A.Kamp, M.Andersson, S.Leide-Svegborn, D.Noßke, S.Mattsson, A.Giussani. A revised compartmental model for biokinetics and dosimetry of ^{18}F-FDG. Submitted to EJNMMI Physics

Congress presentations

M.Andersson, A.Giussani, S.Mattsson, L.Johansson: *Age dependent dynamic absorbed dose calculations to the urinary bladder wall for ICRP compartmental models of radiopharmaceuticals*. **ICRP2019**, Adelaide, Australia, 17.-21.11.2019.

M.Andersson, A.Kamp, D.Noßke, S.Mattsson, A.Giussani: *A revised compartmental model for biokinetics and dosimetry of ^{18}F-FDG*. **EANM21**, Virtual, 20.-23.10.2021.

A.Giussani. *Die Aktualisierung der Dosiskoeffizienten der ICRP für diagnostische Anwendungen in der Nuklearmedizin*. **Nuklearmedizin 2022**, Leipzig, Germany, 27.-30.4.2022.

A.Giussani. Iodine model – an update – **EURADOS Annual Meeting 2022**, Belgrade, Serbia, 21.6.2022

A.Giussani, M.Andersson, M.Hosono, A.Kamp, K.W.Kang, S.Mattsson, D.Nosske, J.C.Ocampo-Ramos, N.Petoussi-Henss. *Quality Assurance of the revised ICRP dose coefficients to patients from diagnostic radiopharmaceuticals*. **European Radiation Protection Week 2022**, Estoril, Portugal, 9.-14.10.2022.

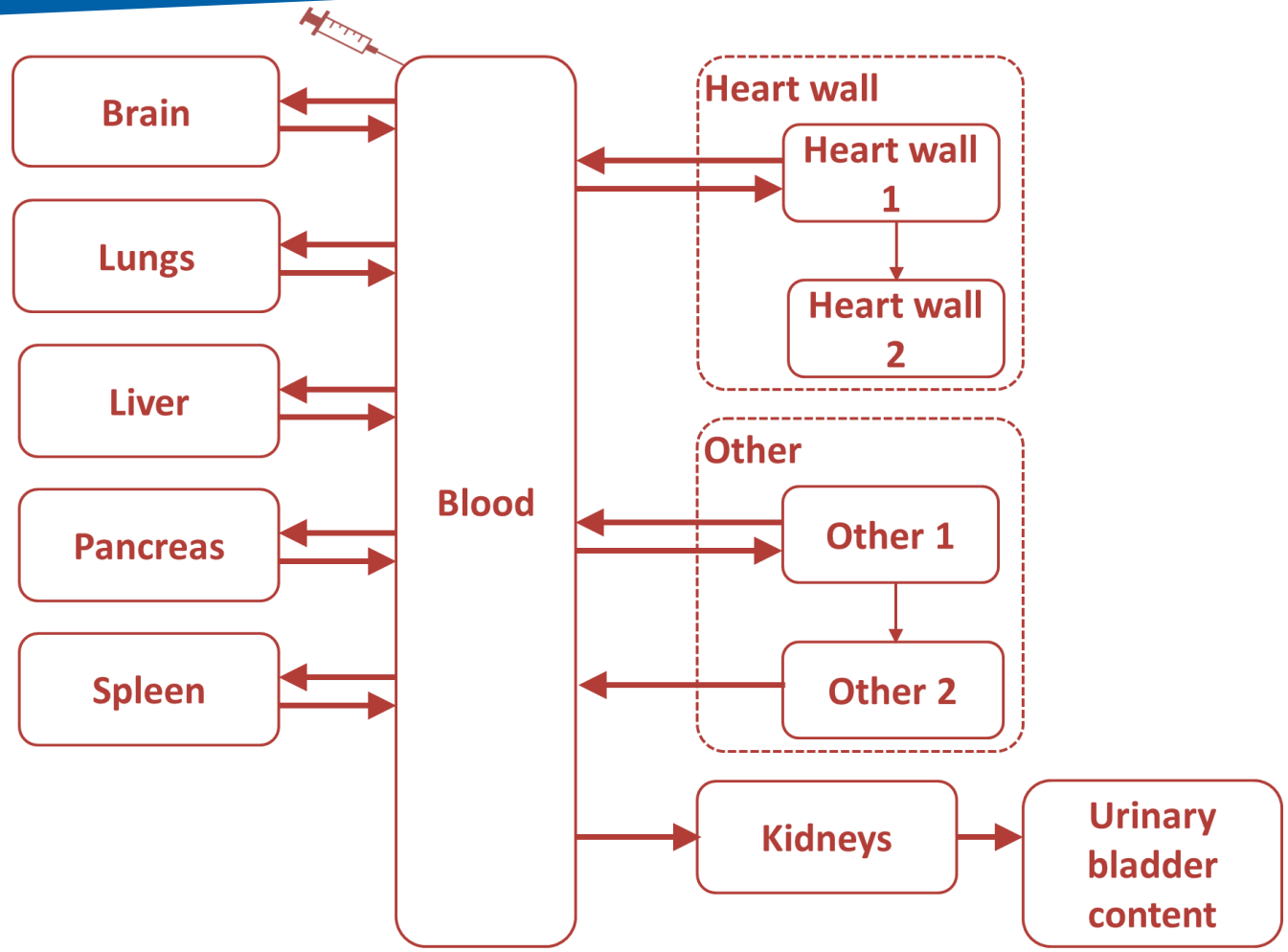
A.Kamp, M.Andersson, A.Giussani, M.Hosono, K.W.Kang, S.Leide-Svegborn, S.Mattsson, D.Nosske, J.C.Ocampo-Ramos, N.Petoussi-Henss, L.Söderberg: *Revision of the reference biokinetic models for dosimetry in diagnostic nuclear medicine*. **EANM22**, Barcelona, Spain, 15.-19.10.2022 (e-Poster).

Biokinetics: New model for FDG

A. Kamp´et al.
A revised compartmental model for biokinetics and dosimetry of ^{18}F-FDG.
Submitted to EJNMMI Physics

Table C.30. Biokinetic data for ^{18}F-fluoro-2-deoxy-D-glucose.

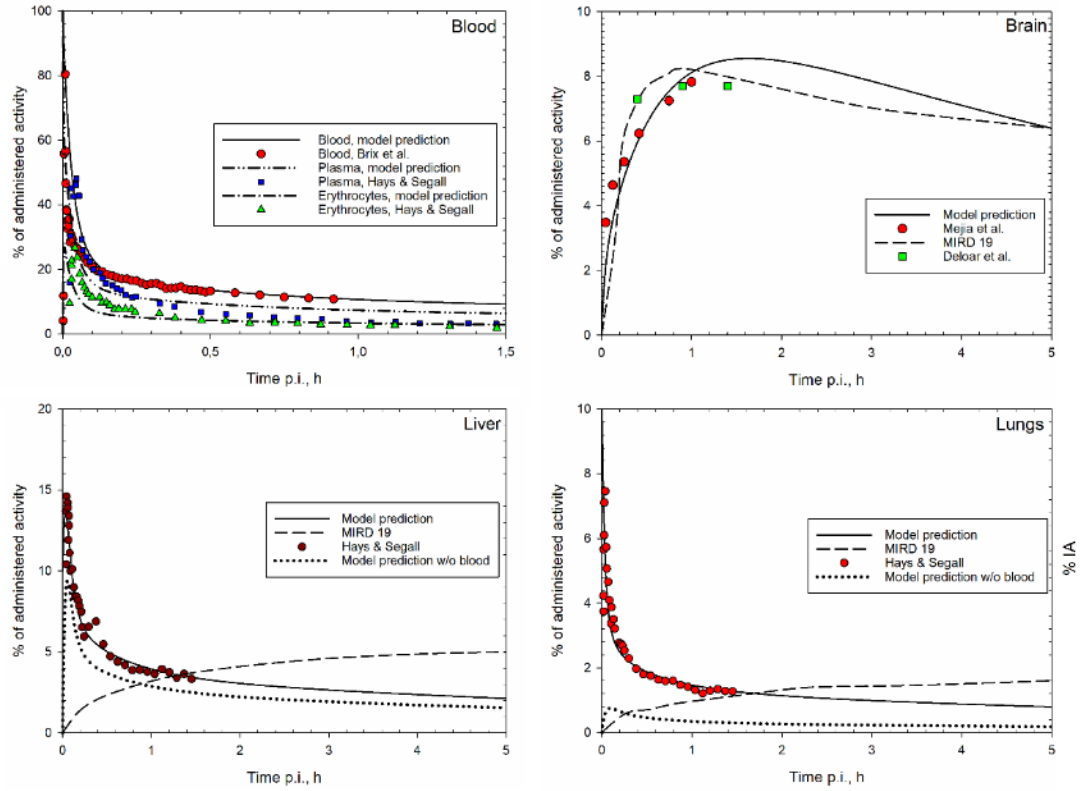
Organ (S)	F_s	T (h)	a
Brain	0.08	∞	1.0
Heart wall	0.04	∞	1.0
Lungs	0.03	∞	1.0
Liver	0.05	∞	1.0
Other organs and tissues	0.80	0.2	0.075
		1.5	0.225
		∞	0.70
Urinary bladder contents	0.24		



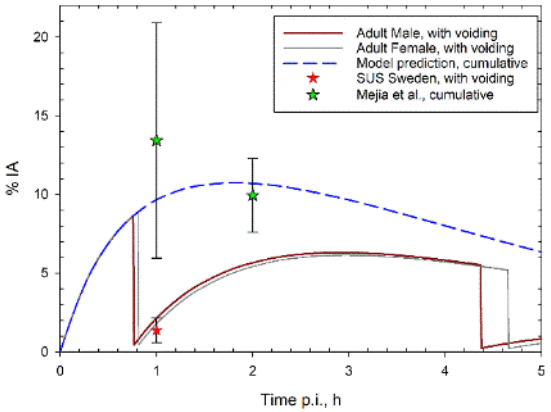
In the revised model, the presence of blood as a central compartment, that is, after an intravenous injection, transfers 2-[^{18}F]FDG to other body organs and tissues, and the inclusion of pancreas and spleen as source regions, which were not considered in Pub 128

The revised model of ^{18}F-FDG

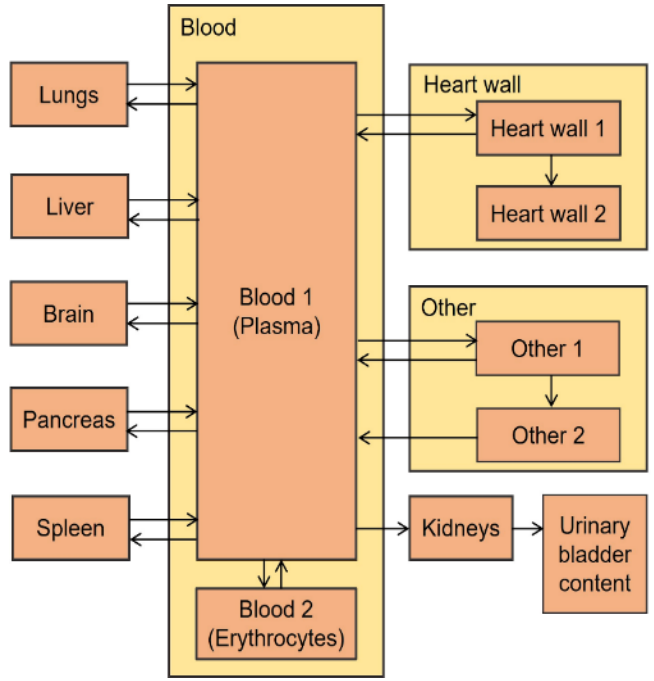
Revised model



Time-activity curves (TAC) in source regions predicted by the proposed biokinetic model along with the experimental data (scattered points).



Dynamic urinary bladder contents.



Structure of the proposed biokinetic model for ^{18}F-FDG

Ref: Andersson et al., EANM Congress 2021

Kamp et., A revised compartmental model for biokinetics and dosimetry of ^{18}F-FDG, submitted EJNMMI Physics

Dynamic bladder model

For the urinary excretion a dynamic urinary bladder model is assumed.

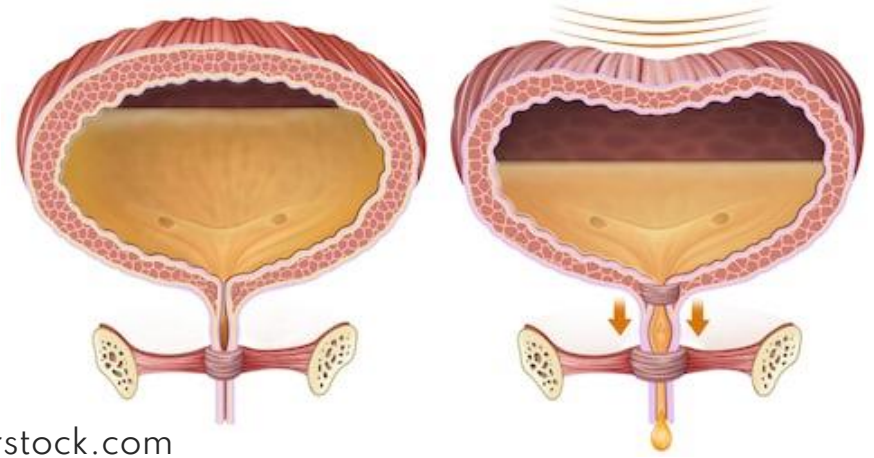
Assumptions for reference individuals:

Bladder is emptied at discrete steps.

Possibility to simulate different emptying schemes

- depending on investigation protocols
- day/night

Flowrate can be increased to account for forced hydration.



Source: shutterstock.com

Table 2.41. Reference values for daily urinary excretion (Section 8.3.2)

	Excretion (ml/day)	
Age	Male	Female
Newborn	300	300
1 year	400	400
5 years	500	500
10 years	700	700
15 years	1200	1200
Adult	1600	1200

Voiding periods in ICRP Publication 128

Age (years)	Adult	15 years	10 years	5 years	1 year	Infant
Voiding period (h)	3.5	3.5	3.5	3.0	2.0	2.0

Presentation of data

Name of the radiopharmaceutical (template)

ɪx.1. Biokinetic information

(A.1) Text describing the major biokinetic features of the radiopharmaceutical, including summary of the scientific literature (it will be in most case an adaptation of the current text).,

ɪx.2 Biokinetic model

Table xx.1 – Values of the transfer coefficients

From	To	Value (h^{-1})
Blood 1	Blood 2	1.2E-04
Blood 1	Lungs	5.6E-07
Blood 1	Liver	8.9E-01
Blood 1	Heart Wall 1	2.3E-04
…	…	…
Lung	Blood 1	…
Liver	Blood 1	…
Heart Wall 1	Blood 1	…
Heart Wall 1	Heart Wall 2	…
…	…	…

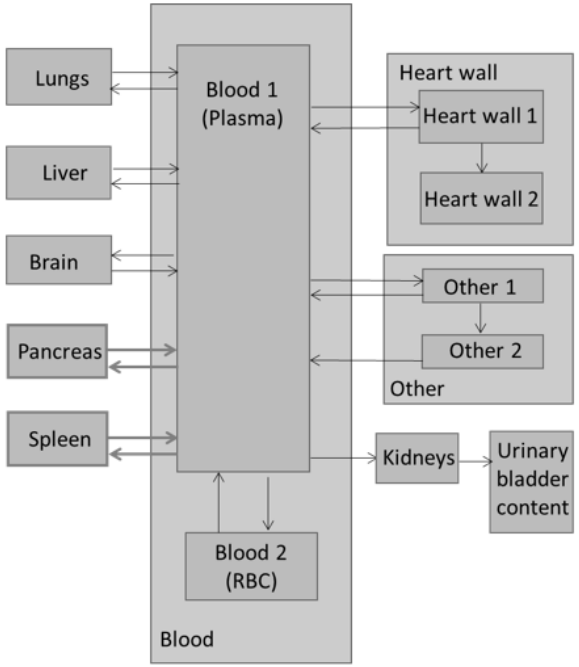


Table xx.2. - Dose coefficients for "Radiopharmaceutical"

I-123 mIBG
(13.27 HOURS)

Absorbed dose in mGy/MBq

	Adults		15 years		10 years		5 years		1 year	
Organs	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Adrenals	6.9E-02	9.6E-02	6.1E-02	7.0E-02	9.5E-02	9.5E-02	1.5E-01	1.5E-01	2.2E-01	2.2E-01
Brain	1.5E-02	1.7E-02	2.8E-02	2.9E-02	4.2E-02	4.2E-02	6.1E-02	6.2E-02	1.0E-01	1.0E-01
Breast	2.1E-02	2.5E-02	2.4E-02	2.6E-02	3.3E-02	3.3E-02	6.0E-02	6.0E-02	9.8E-02	9.8E-02
Colon wall	3.1E-02	3.1E-02	2.9E-02	2.9E-02	4.4E-02	4.3E-02	7.4E-02	7.1E-02	1.5E-01	1.5E-01
Endosteum (bone surface)	2.1E-02	2.5E-02	2.5E-02	2.8E-02	6.5E-02	6.5E-02	8.7E-02	8.6E-02	1.3E-01	1.3E-01
ET region	1.3E-02	1.8E-02	4.2E-02	4.2E-02	5.8E-02	5.8E-02	7.1E-02	7.1E-02	1.1E-01	1.1E-01
Gall bladder wall	1.1E-01	1.2E-01	1.1E-01	1.2E-01	1.5E-01	1.5E-01	2.0E-01	2.0E-01	3.2E-01	3.2E-01
Heart wall	5.7E-02	7.0E-02	6.4E-02	7.8E-02	1.2E-01	1.2E-01	1.8E-01	1.8E-01	3.1E-01	3.1E-01
Kidneys	4.2E-02	5.2E-02	3.1E-02	3.4E-02	5.5E-02	5.6E-02	9.8E-02	9.8E-02	1.8E-01	1.8E-01
Liver	1.7E-01	2.1E-01	2.2E-01	2.4E-01	3.3E-01	3.3E-01	4.7E-01	4.7E-01	8.1E-01	8.1E-01
Lung	5.0E-02	5.9E-02	5.5E-02	6.3E-02	9.2E-02	9.2E-02	1.3E-01	1.4E-01	2.5E-01	2.5E-01
Lymphatic nodes	3.2E-02	3.6E-02	3.0E-02	3.1E-02	4.2E-02	4.2E-02	7.4E-02	7.4E-02	1.3E-01	1.3E-01
Muscle	2.0E-02	2.4E-02	2.2E-02	2.3E-02	3.6E-02	3.6E-02	5.7E-02	5.7E-02	1.1E-01	1.1E-01
Oesophagus	3.7E-02	4.2E-02	3.7E-02	4.5E-02	6.7E-02	6.8E-02	1.1E-01	1.1E-01	1.6E-01	1.6E-01
Oral mucosa	1.5E-02	1.9E-02	4.3E-02	4.2E-02	5.2E-02	5.2E-02	5.9E-02	5.9E-02	8.7E-02	8.7E-02
Ovaries	---	4.5E-02	---	7.6E-02	---	1.0E-01	---	1.5E-01	---	2.6E-01
Pancreas	6.0E-02	5.9E-02	3.4E-02	4.4E-02	6.6E-02	6.6E-02	8.9E-02	8.9E-02	1.4E-01	1.4E-01
Prostate	5.6E-02	---	5.9E-02	---	1.0E-01	---	1.5E-01	---	3.1E-01	---
Salivary glands	4.8E-02	6.0E-02	8.7E-02	8.3E-02	1.1E-01	1.1E-01	1.4E-01	1.4E-01	1.9E-01	1.9E-01
Skin	1.3E-02	1.6E-02	1.6E-02	1.8E-02	2.7E-02	2.7E-02	4.4E-02	4.5E-02	8.4E-02	8.4E-02
Small intestine wall	3.0E-02	3.9E-02	3.0E-02	3.5E-02	4.3E-02	4.5E-02	7.6E-02	8.0E-02	1.5E-01	1.5E-01
Spleen	5.8E-02	7.1E-02	5.8E-02	6.8E-02	9.7E-02	9.7E-02	1.5E-01	1.5E-01	2.8E-01	2.8E-01
Stomach wall	4.4E-02	5.4E-02	4.1E-02	4.8E-02	7.1E-02	7.2E-02	9.6E-02	9.7E-02	2.0E-01	2.0E-01
Testes	1.8E-02	---	3.4E-02	---	4.0E-02	---	7.4E-02	---	1.1E-01	---
Thymus	2.4E-02	2.9E-02	3.2E-02	3.4E-02	5.4E-02	5.4E-02	8.1E-02	8.1E-02	1.5E-01	1.5E-01
Thyroid	1.9E-02	2.3E-02	2.9E-02	2.9E-02	4.2E-02	4.2E-02	7.4E-02	7.4E-02	1.2E-01	1.2E-01
Urinary bladder wall	1.2E-01	1.2E-01	1.4E-01	1.5E-01	1.9E-01	1.9E-01	2.8E-01	2.8E-01	7.2E-01	7.4E-01
Uterus/cervix	---	6.3E-02	---	9.0E-02	---	1.3E-01	---	1.8E-01	---	5.6E-01
Effective dose [mSv/MBq]	**4.7E-02**		**5.2E-02**		**7.7E-02**		**1.1E-01**		**2.1E-01**	

Detriment-weighted radiation dose to specific patient groups*: (mSv MBq^{-1})

Patient group 1	DOSE
Patient group 2	DOSE

**additional information which may be given or not, depending on the specific RP*

QA of biokinetic and dosimetric calculations

- For all radiopharmaceuticals the same biokinetic and dosimetric code will be used, and presented in different Dose reports
- The biokinetic solver will be compared mainly with BfS (SAAMII)
- For the QA simplified assumptions will be used to be able to perform comparison with codes use in the OIR/EIR-series

Chapter 4. QA on Time integrated activity coefficients (TIAC)

For Quality Assurance (QA) the time integrated activity coefficients (TIAC) were compared with other biokinetic calulations from CVUT, IRSN and BfS (SAAM). All calulations used the same model perdiction. The results are shown in table below.

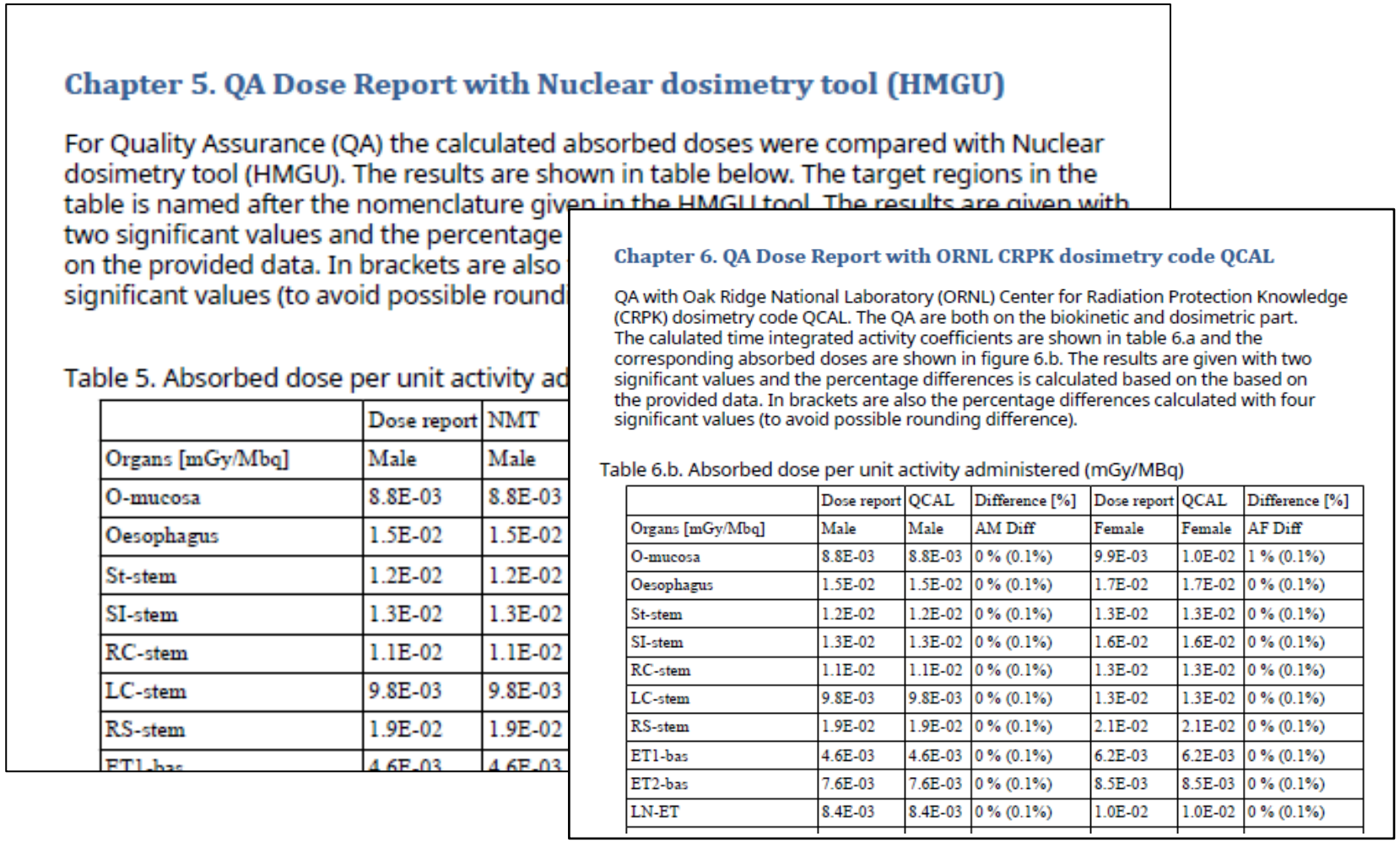
Table 4.1 Organ specific time integrated activity coefficients in MBq-h/MBq.

ORGAN	ICRP (IDAC)	CVUT	IRSN	BfS (SAAM)	% Diff	CVUT/ICRP	IRSN/ICRP	BfS/ICRP
Blood	2.78e-01	2.79e-01	2.79e-01	2.78e-01		0.36 %	0.36 %	0.00 %
Brain	1.82e-01	1.82e-01	1.82e-01	1.82e-01		0.00 %	0.00 %	0.00 %
Lungs	8.25e-03	8.26e-03	8.25e-03	8.25e-03		0.12 %	0.00 %	0.00 %
Liver	7.23e-02	7.24e-02	7.23e-02	7.23e-02		0.14 %	0.00 %	0.00 %
Heart wall	1.32e-01	1.32e-01	1.32e-01	1.32e-01		0.00 %	0.00 %	0.00 %
Kidneys	2.63e-02	2.64e-02	2.64e-02	2.64e-02		0.38 %	0.38 %	0.38 %
Pancreas	6.44e-03	6.45e-03	6.45e-03	6.44e-03		0.16 %	0.16 %	0.00 %
Spleen	6.60e-03	6.61e-03	6.61e-03	6.60e-03		0.15 %	0.15 %	0.00 %
UBC (No voding)	6.40e-01			6.41e-01		N/A	N/A	0.16 %
Other	1.28e+00	1.29e+00	1.29e+00	1.29e+00		0.78 %	0.78 %	0.78 %

Dose report on the validation of biokinetic for ^{18}F-FDG

QA of dosimetric of ^{18}F-FDG

- **Absorbed dose reports were validated against HMGU (Helmholtz Zentrum München) tool and ORNL (Oak Ridge National Laboratory) dosimetry code QCAL**



Chapter 5. QA Dose Report with Nuclear dosimetry tool (HMGU)

For Quality Assurance (QA) the calculated absorbed doses were compared with Nuclear dosimetry tool (HMGU). The results are shown in table below. The target regions in the table is named after the nomenclature given in the HMGU tool. The results are given with two significant values and the percentage on the provided data. In brackets are also significant values (to avoid possible round

Table 5. Absorbed dose per unit activity ad

	Dose report	NMT
Organs [mGy/Mbq]	Male	Male
O-mucosa	8.8E-03	8.8E-03
Oesophagus	1.5E-02	1.5E-02
St-stem	1.2E-02	1.2E-02
SI-stem	1.3E-02	1.3E-02
RC-stem	1.1E-02	1.1E-02
LC-stem	9.8E-03	9.8E-03
RS-stem	1.9E-02	1.9E-02
ET1-bas	4.6E-03	4.6E-03

Chapter 6. QA Dose Report with ORNL CRPK dosimetry code QCAL

QA with Oak Ridge National Laboratory (ORNL) Center for Radiation Protection Knowledge (CRPK) dosimetry code QCAL. The QA are both on the biokinetic and dosimetric part. The calulated time integrated activity coefficients are shown in table 6.a and the corresponding absorbed doses are shown in figure 6.b. The results are given with two significant values and the percentage differences is calculated based on the based on the provided data. In brackets are also the percentage differences calculated with four significant values (to avoid possible rounding difference).

Table 6.b. Absorbed dose per unit activity administered (mGy/MBq)

	Dose report	QCAL	Difference [%]	Dose report	QCAL	Difference [%]
Organs [mGy/Mbq]	Male	Male	AM Diff	Female	Female	AF Diff
O-mucosa	8.8E-03	8.8E-03	0 % (0.1%)	9.9E-03	1.0E-02	1 % (0.1%)
Oesophagus	1.5E-02	1.5E-02	0 % (0.1%)	1.7E-02	1.7E-02	0 % (0.1%)
St-stem	1.2E-02	1.2E-02	0 % (0.1%)	1.3E-02	1.3E-02	0 % (0.1%)
SI-stem	1.3E-02	1.3E-02	0 % (0.1%)	1.6E-02	1.6E-02	0 % (0.1%)
RC-stem	1.1E-02	1.1E-02	0 % (0.1%)	1.3E-02	1.3E-02	0 % (0.1%)
LC-stem	9.8E-03	9.8E-03	0 % (0.1%)	1.3E-02	1.3E-02	0 % (0.1%)
RS-stem	1.9E-02	1.9E-02	0 % (0.1%)	2.1E-02	2.1E-02	0 % (0.1%)
ET1-bas	4.6E-03	4.6E-03	0 % (0.1%)	6.2E-03	6.2E-03	0 % (0.1%)
ET2-bas	7.6E-03	7.6E-03	0 % (0.1%)	8.5E-03	8.5E-03	0 % (0.1%)
LN-ET	8.4E-03	8.4E-03	0 % (0.1%)	1.0E-02	1.0E-02	0 % (0.1%)

Dose report on the validation of absorbed dose for ^{18}F-FDG

QA for ^{18}F-FDG (15-, 10- and 5-yrs)

- **TG36 works are dependent on the ICRP SAF Publ. Paediatric Specific Absorbed Fractions (SAFs)**
- **TG36 conducted QA for the preadults, after completed the QA for Adults first**

Table 6.c. 15-yrs. Absorbed dose per unit activity administered (mGy/MBq)

	Dose report	QCAL	Difference [%]	Dose report	QCAL	Difference [%]
Organs [mGy/Mbq]	Male	Male	AM Diff	Female	Female	AF Diff
O-mucosa	2.0E-02	2.0E-02	0 % (0.1%)	2.0E-02	2.0E-02	0 % (0.1%)
Oesophagus	1.6E-02	1.6E-02	0 % (0.1%)	1.6E-02	1.6E-02	0 % (0.1%)
St-stem						
SI-stem						
RC-stem						
LC-stem						
RS-stem						
ET1-bas						
ET2-bas						
LN-ET						
Bronch-bas						
Bronch-sec						
Bchiol-sec						

Table 6.d. 10-yrs . Absorbed dose per unit activity administered (mGy/MBq)

	Dose report	QCAL	Difference [%]	Dose report	QCAL	Difference [%]
Organs [mGy/Mbq]	Male	Male	AM Diff	Female	Female	AF Diff
O-mucosa	2.7E-02	2.7E-02	0 % (0.1%)	2.7E-02	2.7E-02	0 % (0.1%)
Oesophagus	2.5E-02	2.5E-02	0 % (0.1%)	2.5E-02	2.5E-02	0 % (0.1%)
St-stem	1.8E-02	1.8E-02	0 % (0.1%)	1.8E-02	1.8E-02	0 % (0.1%)
SI-stem	1.8E-02	1.8E-02	0 % (0.1%)	1.8E-02	1.8E-02	0 % (0.1%)
RC-stem						
LC-stem						
RS-stem						
ET1-bas						
ET2-bas						
LN-ET						
Bronch-bas						
Bronch-sec						
Bchiol-sec						

Table 6.e. 5-yrs. Absorbed dose per unit activity administered (mGy/MBq)

	Dose report	QCAL	Difference [%]	Dose report	QCAL	Difference [%]
Organs [mGy/Mbq]	Male	Male	AM Diff	Female	Female	AF Diff
O-mucosa	3.3E-02	3.3E-02	0 % (0.1%)	3.3E-02	3.3E-02	0 % (0.1%)
Oesophagus	4.0E-02	4.0E-02	0 % (0.1%)	4.0E-02	4.0E-02	0 % (0.1%)
St-stem	3.1E-02	3.1E-02	0 % (0.1%)	3.1E-02	3.1E-02	0 % (0.1%)
SI-stem	3.3E-02	3.3E-02	0 % (0.1%)	3.4E-02	3.4E-02	0 % (0.1%)
RC-stem	3.7E-02	3.7E-02	0 % (0.1%)	3.8E-02	3.8E-02	0 % (0.1%)
LC-stem	2.8E-02	2.8E-02	0 % (0.1%)	2.9E-02	2.9E-02	0 % (0.1%)
RS-stem	4.8E-02	4.8E-02	0 % (0.1%)	3.9E-02	3.9E-02	0 % (0.1%)
ET1-bas	3.6E-02	3.6E-02	0 % (0.1%)	3.6E-02	3.6E-02	0 % (0.1%)
ET2-bas	2.9E-02	2.9E-02	0 % (0.1%)	2.9E-02	2.9E-02	0 % (0.1%)
LN-ET	3.6E-02	3.6E-02	0 % (0.1%)	3.6E-02	3.6E-02	0 % (0.1%)

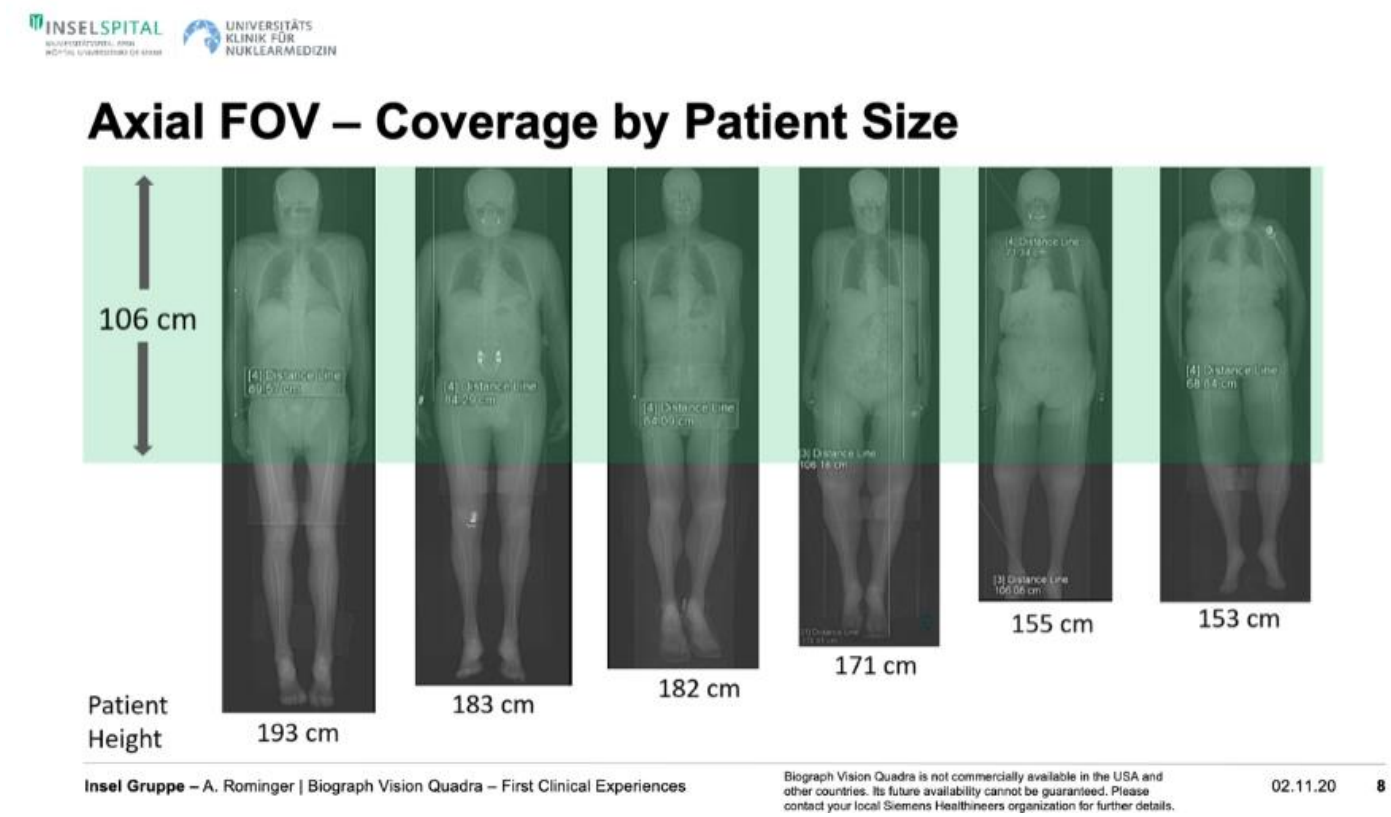
Dose report on the validation of absorbed dose for ^{18}F-FDG

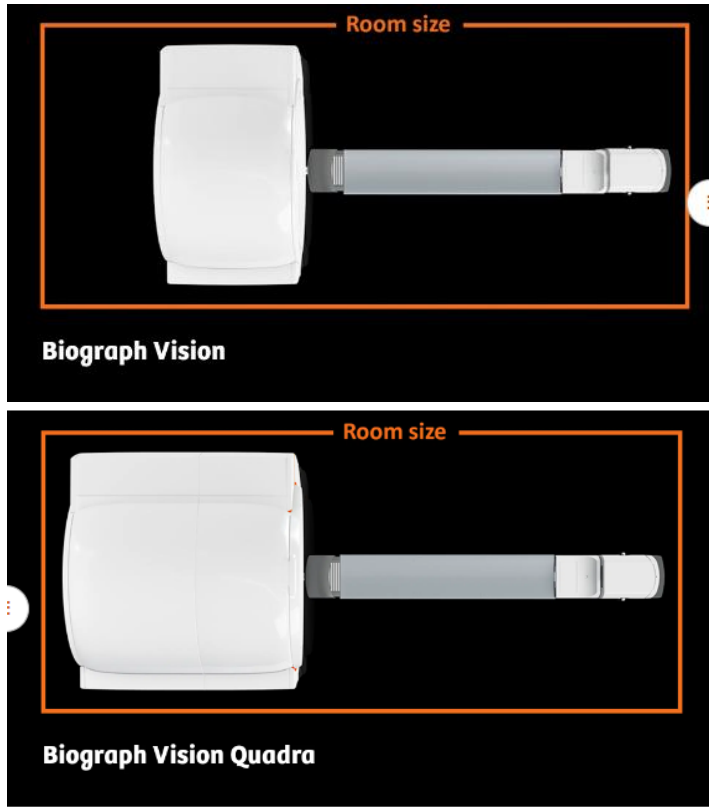
Special cases

- Dose coefficients were not necessarily calculated for all radiopharmaceuticals for all age groups/sexes, depending on the foreseen application. E.g. Substances administered for Parkinson's or Alzheimer's diagnostics, or PSMA (Prostata specific membrane antigen) ➔ **BE AWARE FOR NEW APPLICATIONS!**

- Detriment-weighted effective dose be calculated if patients of one sex only are involved, or for pathological situations with anatomical changes with respect to reference:
  - thyroid after ablation;
  - liver/spleen for diffuse parenchymal disease;
  - unilateral kidney blockage.

Dynamic data from University of Bern





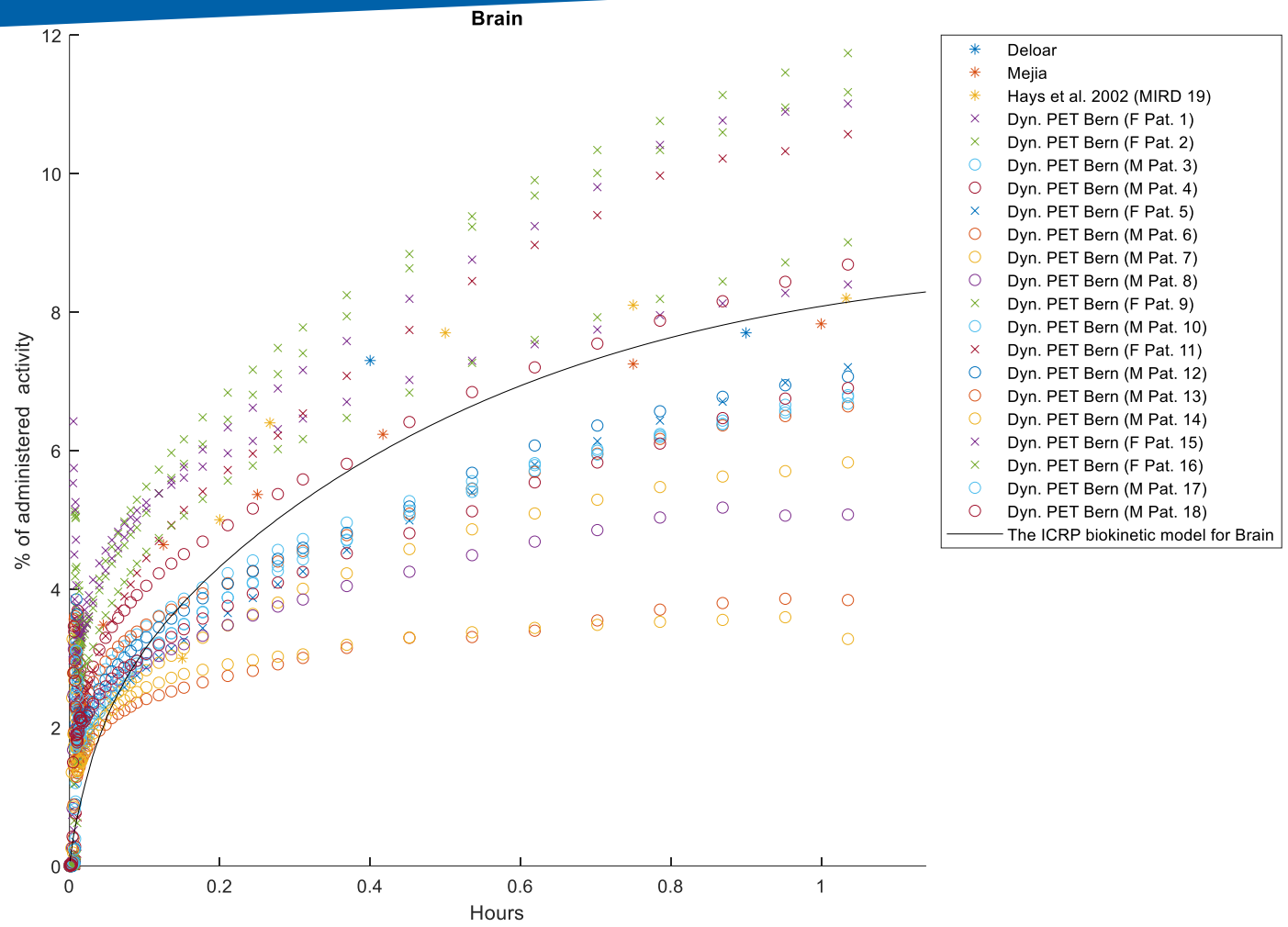
FOV with 106 cm

New TG-36's member Kuangyu Shi, University of Bern, Switzerland has a PET camera with a FOV with 106 cm

Images from www.siemens-healthineers.com - A quantum leap in PET/CT imaging, Clinicians and researcher at Inselspital Bern University hospital share experience with Biograph Vision Quadra

Dynamic collection of data

- Dynamic collection of data and automatic segmentation of organs
- Data transfer agreement between Univ. of Bern and ICRP
- Good agreement between data and new model proposed by ICRP TG (Here: brain as an example)



Model prediction for brain for ^{18}F-FDG with new dynamic patient data

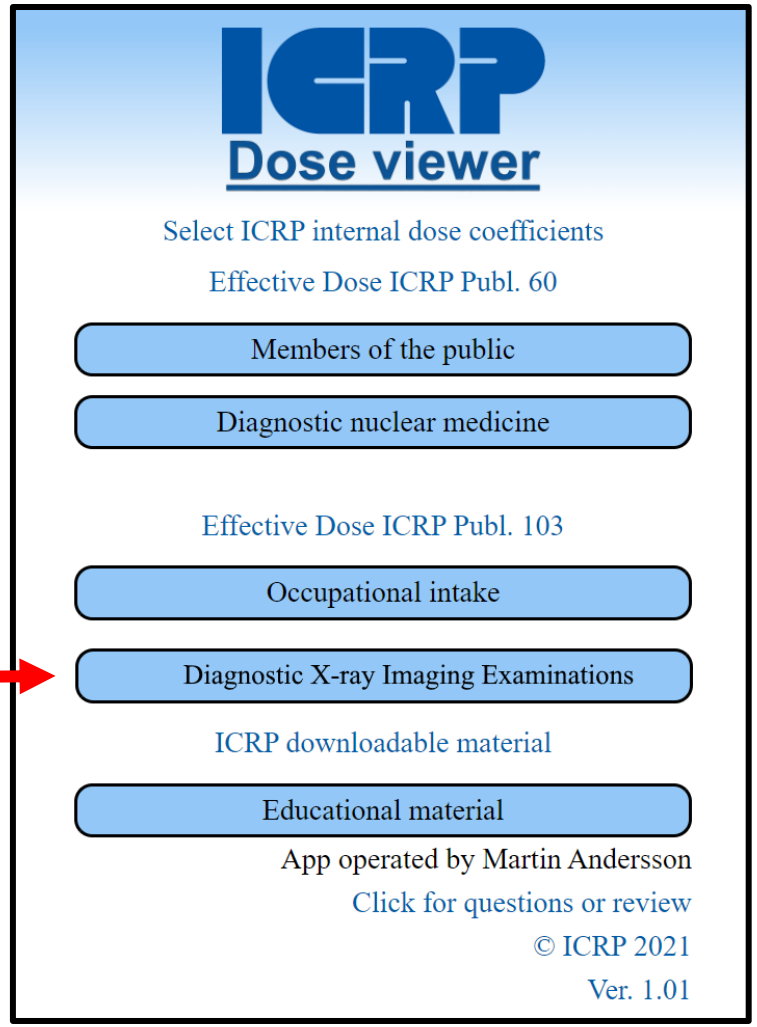
CONTENTS

ICRP Dose viewer app

The app has been released and is available on:

- Google Play (Android)
- App Store (IPhone)

- Currently working on including data from TG113



Possible view on updated main page for Dose viewer with data of TG113

Summary

- TG36 is finalizing the new report, revision of Publication 128.
- This report gives age-dependent dose coefficients for patients undergoing diagnostic investigations in nuclear medicine. This document replaces Publication 128 and all related documents.
- As in the previous Publications, dose coefficients are presented in this report for 3-mo-old infants, 1-, 5-, 10-, and 15-y-old children, and adults.
- The data provided in the report are tables of organ absorbed doses per activity administered (mGy MBq–1) , given separately for male and female, and effective dose per activity administered (mSv MBq–1) for each age group.

ICRP

www.icrp.org