IRPA 13

Living with Radiation - Engaging with Society

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Challenges in nuclear medicine radiation dosimetry

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ICRP Committe 3

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Nuclear medicine stands for a small number of investigations compared to diagnostic radiology

Examples:

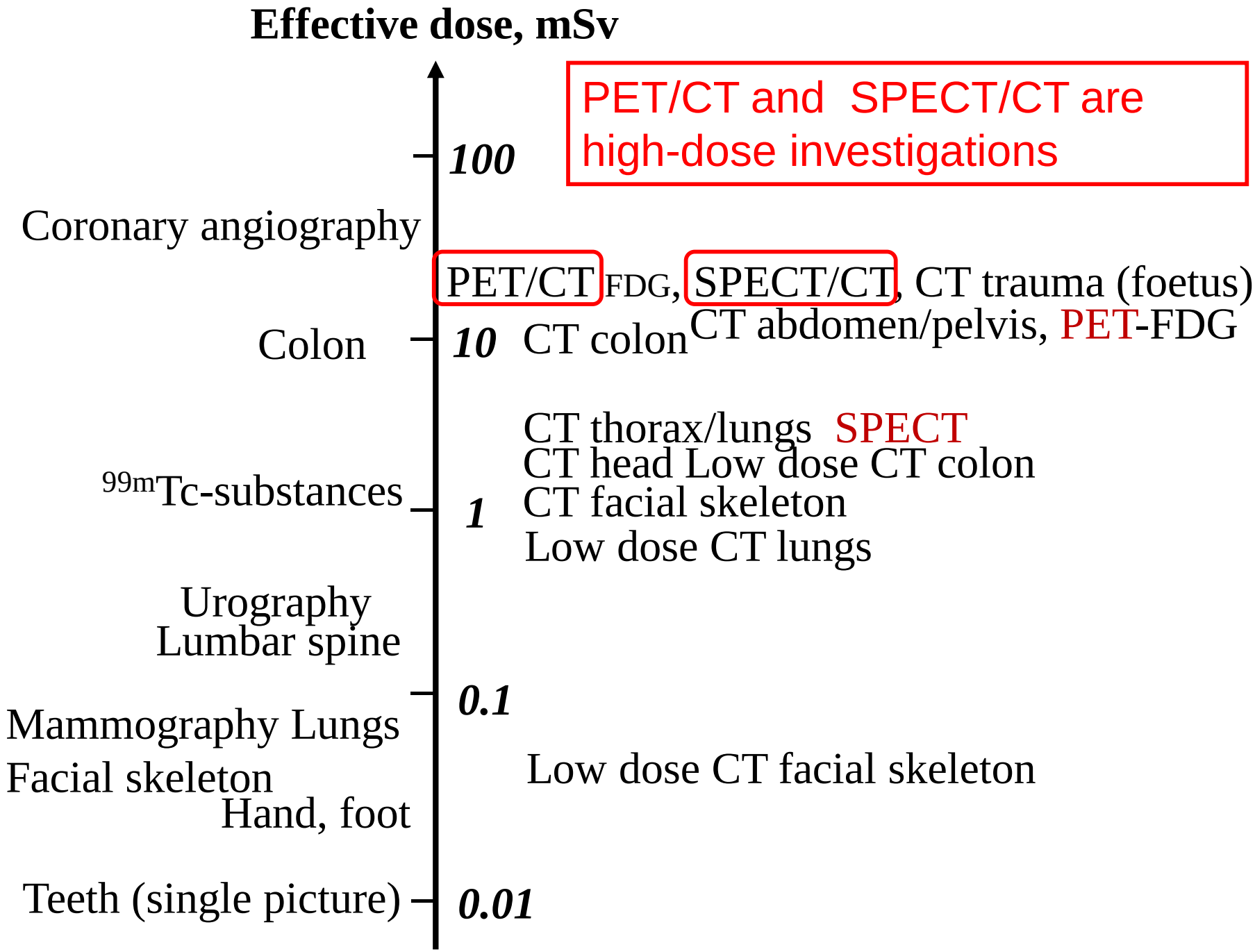
Globally (1997-2007): 1% of diagn radiological exams

Sweden (2005): 2%

USA (2006): 5% of investigations ⇨ 26% of collective dose

Nuclear medicine is expanding

- **Growing use of PET/CT and SPECT/CT (now also PET/MRI)**
- **Oncology and also neurological and cardiac diagnostic procedures**
- **Increasing use of radiotracers in surgical practices**
- **New radiopharmaceuticals (increasing importance of shortlived radionuclides)**


Effective dose, mSv
PET/CT and SPECT/CT are high-dose investigations
100
Coronary angiography
PET/CT FDG, SPECT/CT, CT trauma (foetus)
CT abdomen/pelvis, PET-FDG
10
Colon
CT colon
CT thorax/lungs SPECT
CT head Low dose CT colon
99mTc-substances
1
CT facial skeleton
Low dose CT lungs
Urography
Lumbar spine
0.1
Mammography Lungs
Facial skeleton
Low dose CT facial skeleton
Hand, foot
Teeth (single picture)
0.01

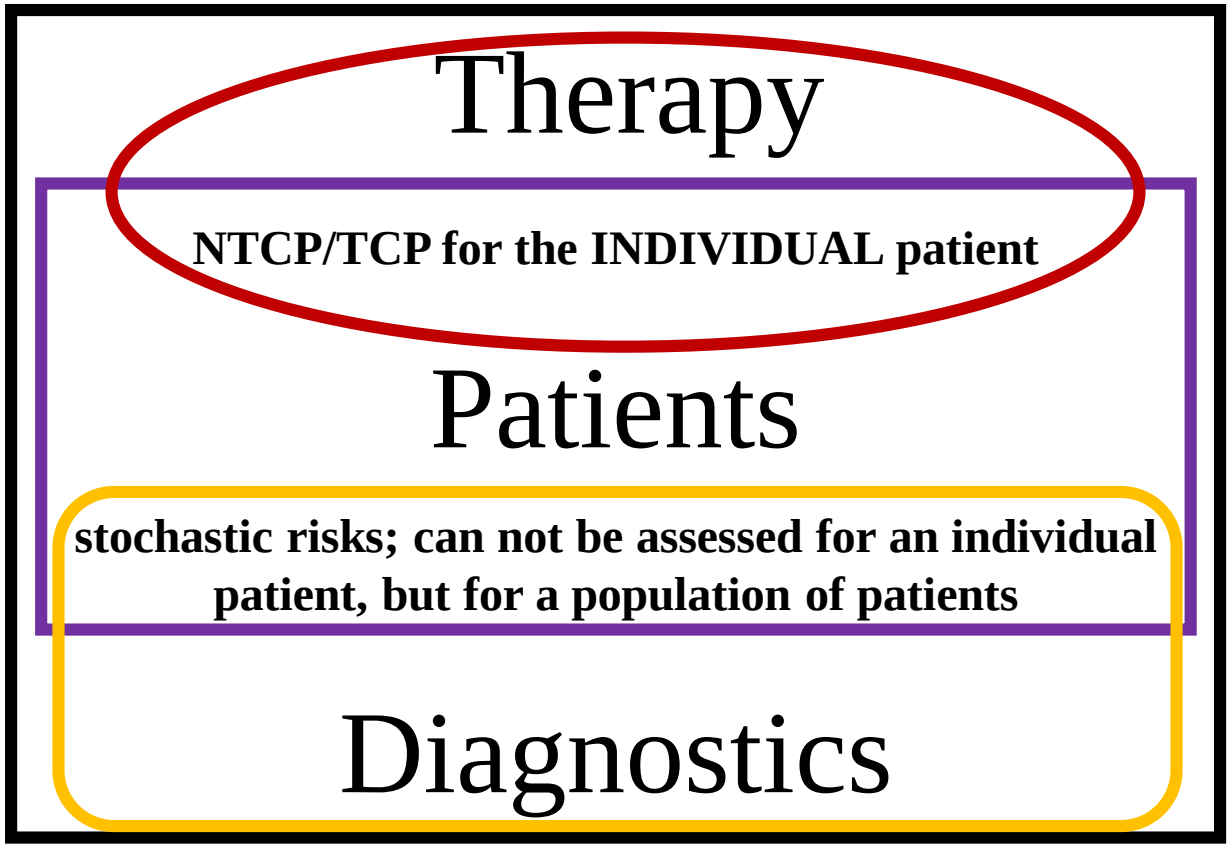
Nuclear medicine also for therapy

Small (Sweden 2010: 2.8%) in relation to nuclear medicine diagnostic procedures

Therapeutic nuclear medicine

• *Hyperthyroidism and thyroid cancer*	*^{131}I-iodide*
• *Polycytemia*	*^{32}P-orthophosphate*
• *Severe pain in metastatic bone disease*	*^{89}Sr-chloride*
	^{153}Sm- or ^{177}Lu-EDTMP
	^{186}Re-EHDP
	^{223}Ra-chloride
• *Tumours (monoclonal antibodies and peptides, receptor specific substances)*	*^{90}Y-Zevalin*
	^{90}Y-,^{131}I-, ^{177}Lu-, ^{211}At-MaB
• *Neuroendocrine tumours*	*^{131}I-mIBG*
	^{90}Y-, ^{177}Lu-octreotate
• *Liver tumours*	*^{90}Y-microspheres (SIRT)*

Dosimetry in nuclear medicine



We want to know the absorbed dose in all irradiated tissues/organs of interest

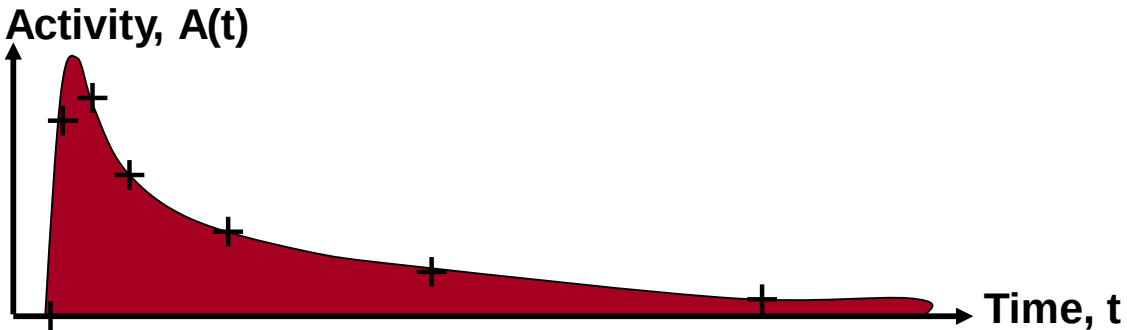
- **Biokinetics**
- **Dose calculations (radionuclide decay, body geometry, organ volume, etc…)**

Varying needs for accuracy in therapy and diagnostics

Therapy: better than +/- 5% (like external radiation therapy)
Diagnostics: +/- say 20%

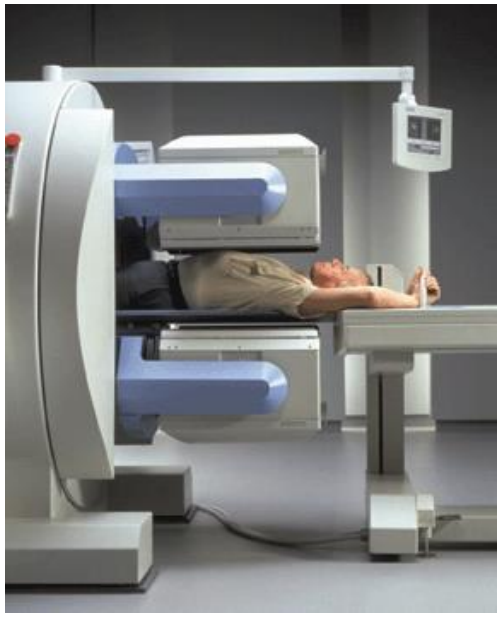
Can we meet these needs for accuracy?

The major contributor to uncertainty in absorbed dose estimations is ***the activity quantification and how frequently the measurements can be done***



Biokinetics, A(t)

- **Quantification of activity in organs and tissues**
- **Blood and excreta sampling**



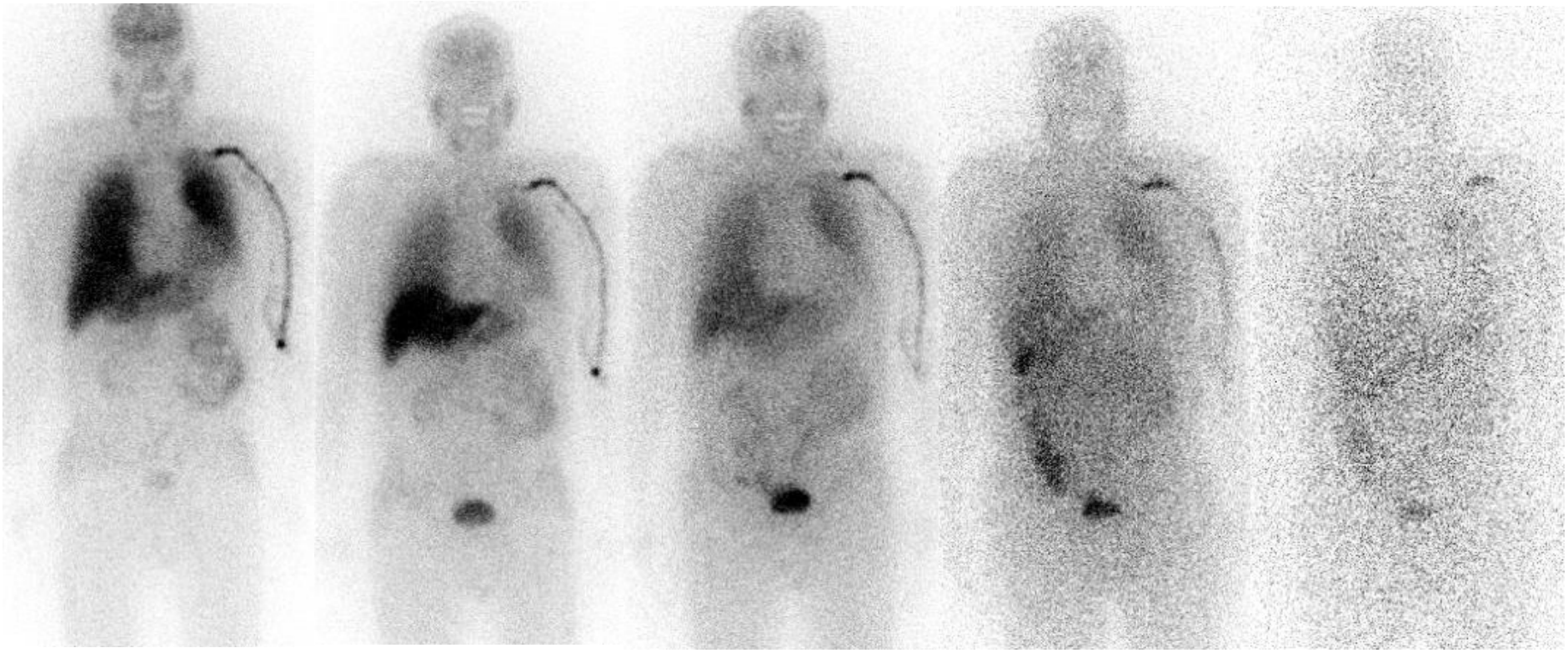
Methods:

1) **Serial planar gamma camera imaging, conjugate view method** (geometric mean to anterior-posterior projections), attenuation and scatter correction
2) **SPECT(/CT)** with attenuation and scatter corrections

3) **PET(/CT)** attenuation and scatter correction

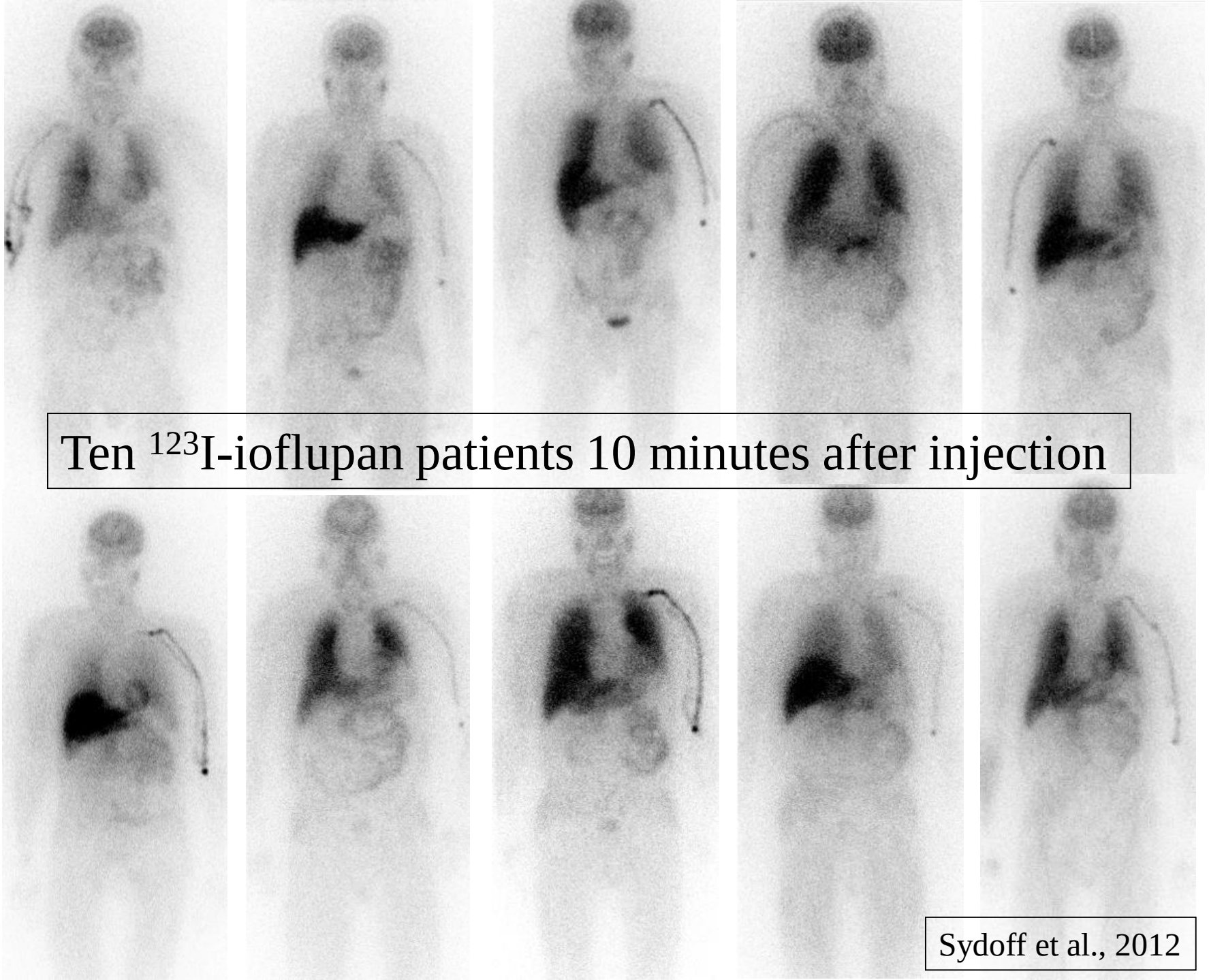
Most quantification methods based on iterative methods

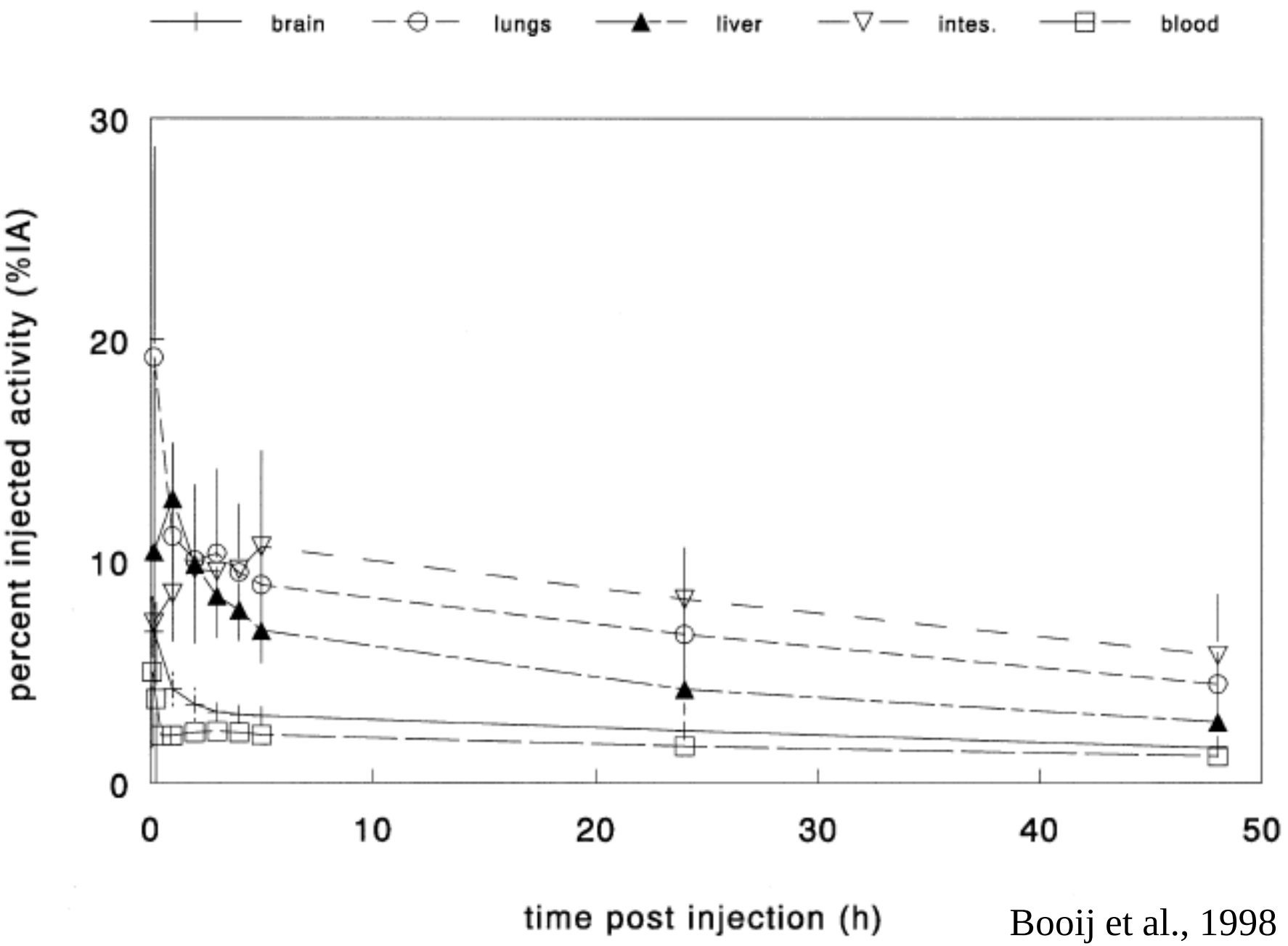
A patient measured at 5 times after injection of ^{123}I-ioflupan



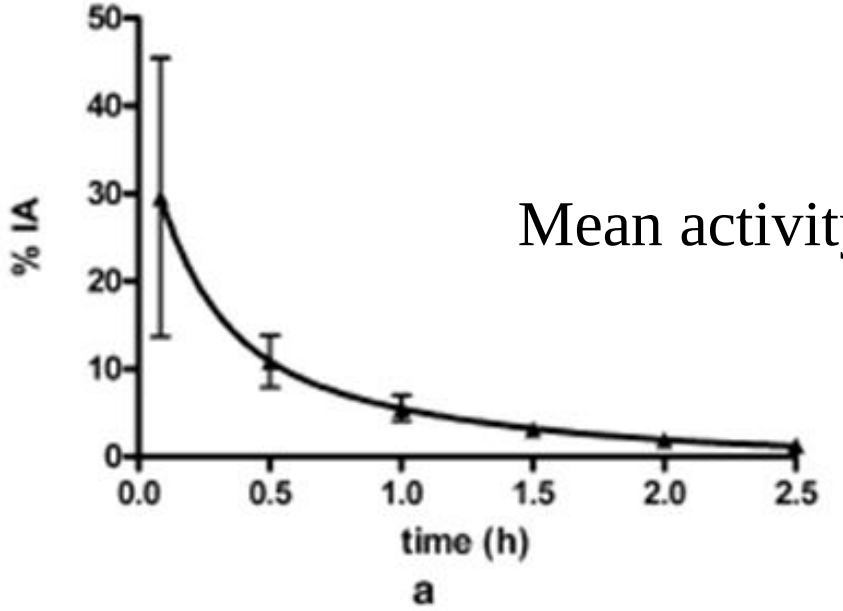
10 min 1 h 4 h 24 h 48 h

Sydoff et al., 2012

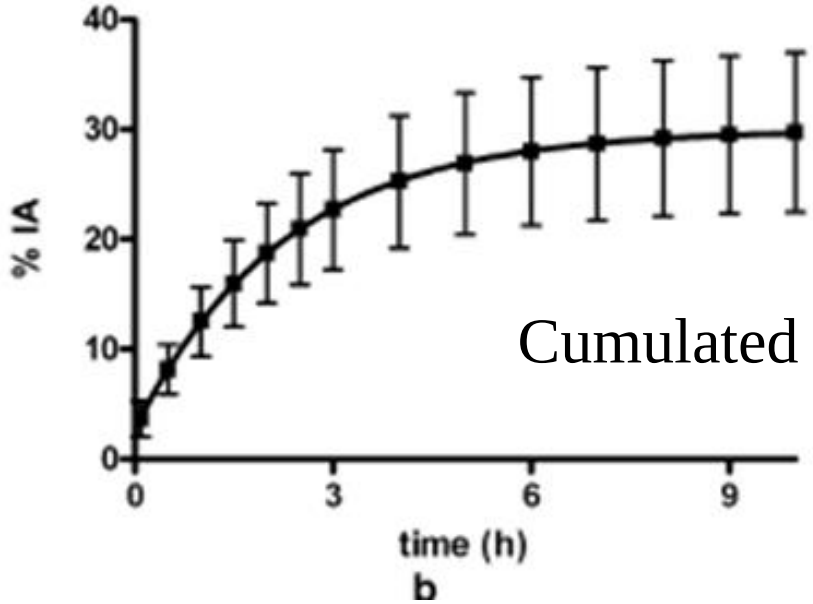

Ten ^{123}I-ioflupan patients 10 minutes after injection
Sydoff et al., 2012



Booij et al., 1998



Mean activity in blood

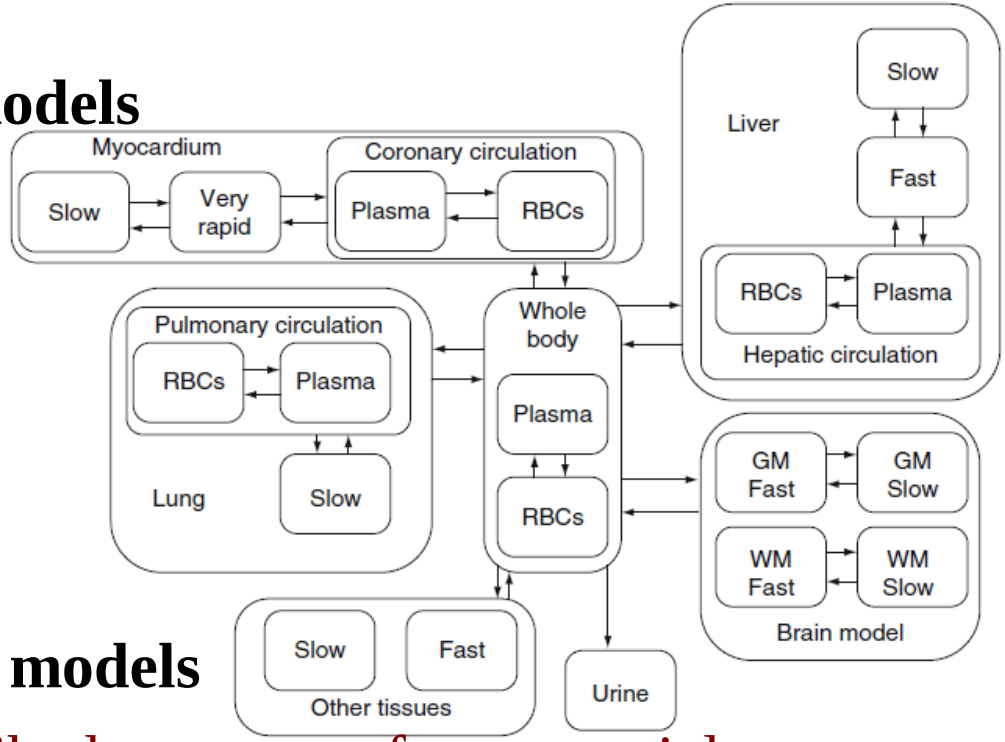


(decay corrected)

Cumulated urinary excretion

Biokinetics

Aim: Detailed compartment models



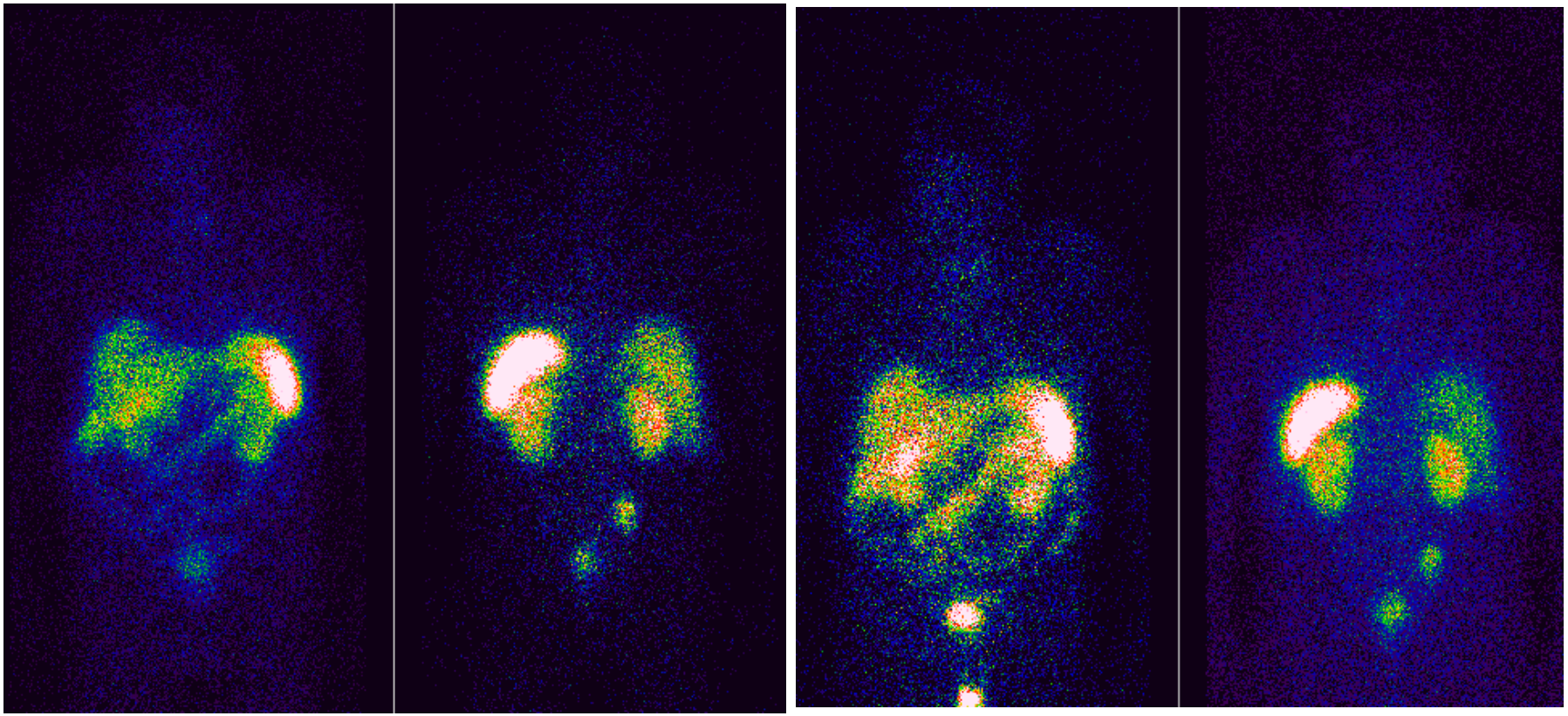
Reality: Descriptive biokinetic models

- The biokinetics is often described as a sum of exponentials

$$A_S(t) = \sum_{i=1}^{n} k_i \, e^{-(\lambda_i + \lambda_p)t} \qquad \frac{\tilde{A}_S}{A_0} = F_S \sum_{j=n+1}^{n+m} a_j \sum_{i=1}^{n} \left\{ a_i \frac{T_i}{T_i - T_j} \left[\exp\left(\frac{-\ln(2)}{T_{i,eff}} t \right) - \exp\left(\frac{-\ln(2)}{T_{j,eff}} t \right) \right] \right\}$$

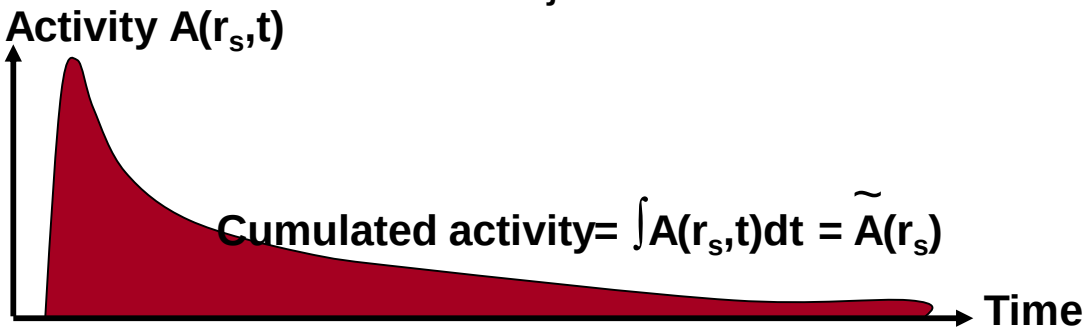
- These are “net models” which describes what we can measure
- There is usually no unique transformation of a net model to a compartment model. (This is possible only if the structure of the compartment model is known).

^{111}In octreotide



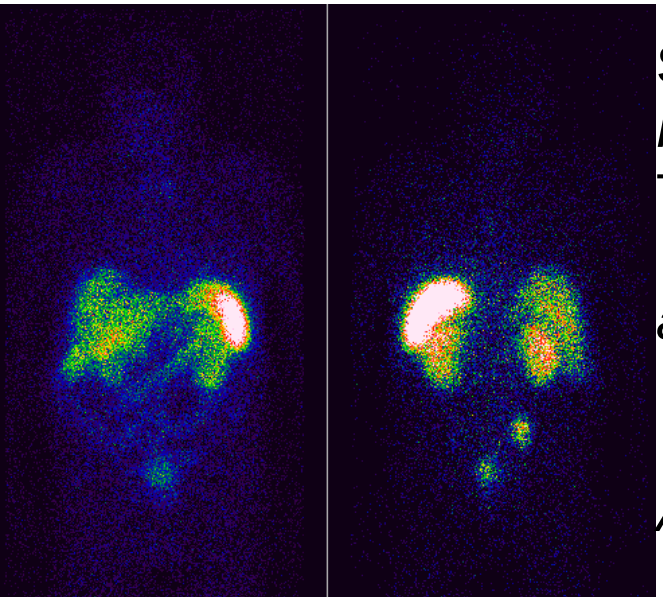
front back front back

4 hours after inj. 24 hours after inj.



Biokinetic data – Indium-labelled octreotide

Organ (S)	F_s	T (h)	a	$\tilde{A}_s/A_0$(h)
Thyroid	0.001	60	1.0	0.046
Kidneys	0.06	60	1.0	2.8
Liver	0.06	2.0	0.40	2.6
		60	0.30	
		1680	0.30	
Spleen	0.05	60	1.0	2.3
Other organs and tissues	0.829	3.0	0.90	6.9
		60	0.10	
Urinary bladder contents	1.0			
Adult, 15 years, 10 years				1.7
5 years				1.4
1 year				0.91



S - Source organ or tissue

F_s - Fractional distribution to S

T - Biological half-time for an uptake or elimination component

a - Fraction of F_s taken up or eliminated with the corresponding half-time. A negative value indicates an uptake phase.

$\tilde{A}_s/A_o$- Cumulated activity in S per unit of adm activity

From cumulated activities to organ/tissue absorbed dose
Computational models = ”Phantoms”

Diagnostics: ICRP Reference phantoms

Why?

To be able to compare information between hospitals

To be able to compare different investigation methods

Therapy:

Realistic phantoms tailored to the individual patient

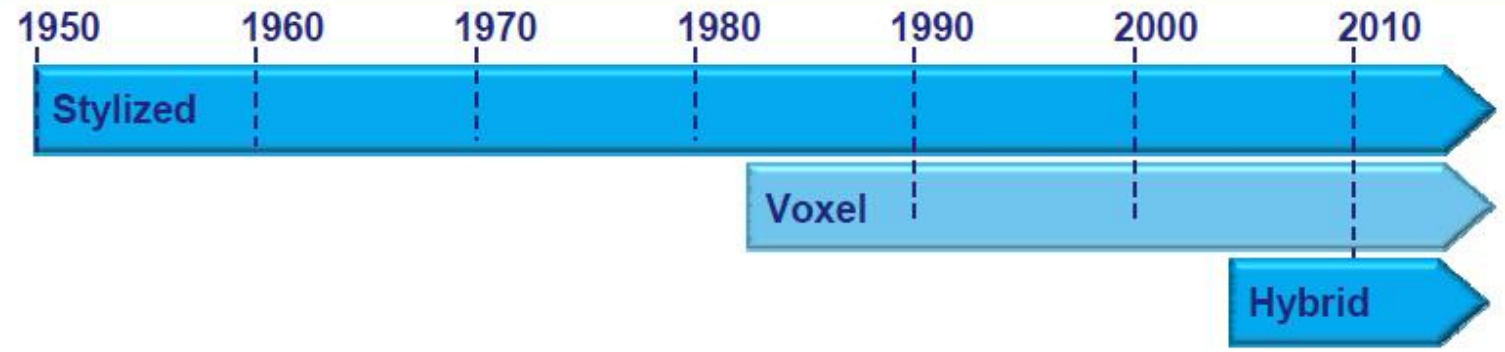
Why?

Weight and lenght differ

Organ masses differ

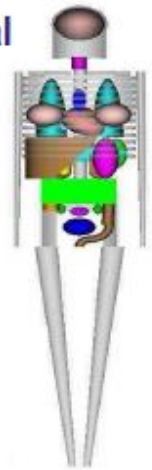
Distances between organs differ

Calculation of absorbed dose: Evolution of computational models

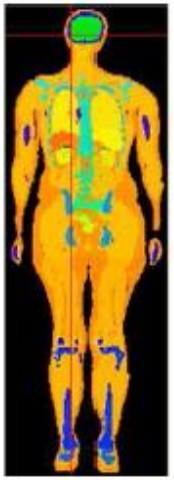


ICRU sphere 1950's

Mathematical 1980's

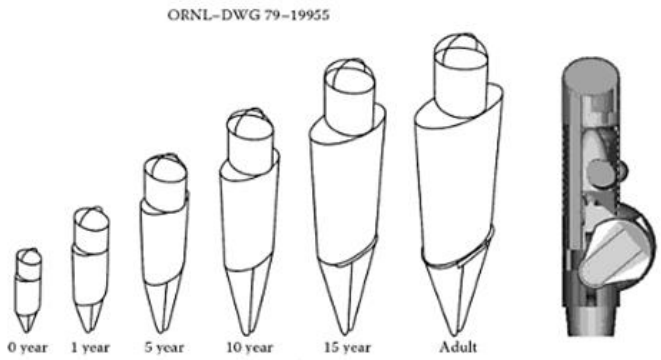


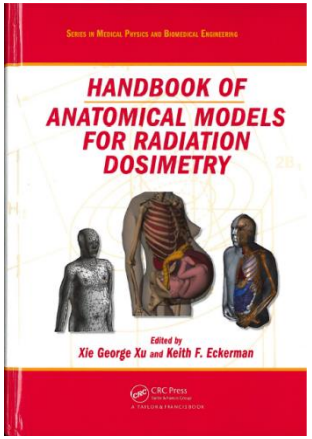
Voxel or tomographic model



Hybrid polygon mesh NURBS-surfaces

www.peddose.net





http://www.virtualphantoms.org/index.html

MIRD/ORNL Cristy and Eckermann Hermaphrodites

Dose calculations

$$\overline{D}_{(Target \leftarrow Source)} = \tilde{A}_{Source} \cdot S_{(Target \leftarrow Source)}$$

C.20.4. Absorbed doses for ^{111}In-octreotide

^{111}In 67.9 h

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	5.8E-02	7.5E-02	1.1E-01	1.7E-01	2.9E-01
Bladder	2.0E-01	2.5E-01	3.7E-01	4.6E-01	5.6E-01
Bone surfaces	2.7E-02	3.3E-02	5.0E-02	7.5E-02	1.4E-01
Brain	9.6E-03	1.2E-02	2.0E-02	3.2E-02	5.7E-02
Breasts	1.2E-02	1.5E-02	2.3E-02	3.7E-02	6.7E-02
Gallbladder	5.2E-02	6.3E-02	9.2E-02	1.4E-01	2.2E-01
Gastrointestinal tract					
Stomach	4.3E-02	5.0E-02	7.7E-02	1.1E-01	1.8E-01
Small intestine	2.9E-02	3.7E-02	5.9E-02	9.0E-02	1.5E-01
Colon	2.9E-02	3.5E-02	5.5E-02	8.6E-02	1.4E-01
(Upper large intestine	3.0E-02	3.7E-02	5.8E-02	9.4E-02	1.5E-01)
(Lower large intestine	2.7E-02	3.3E-02	5.2E-02	7.5E-02	1.2E-01)
Heart	2.5E-02	3.2E-02	4.8E-02	7.0E-02	1.2E-01
Kidneys	4.1E-01	4.9E-01	6.7E-01	9.6E-01	1.6E+00
Liver	1.0E-01	1.3E-01	2.0E-01	2.7E-01	4.8E-01
Lungs	2.3E-02	3.0E-02	4.4E-02	6.7E-02	1.2E-01
Muscles	2.0E-02	2.6E-02	3.8E-02	5.6E-02	1.0E-01
Oesophagus	1.4E-02	1.8E-02	2.7E-02	4.3E-02	7.7E-02
Ovaries	2.7E-02	3.5E-02	5.3E-02	8.0E-02	1.3E-01
Pancreas	7.2E-02	8.8E-02	1.3E-01	2.0E-01	3.2E-01
Red marrow	2.2E-02	2.6E-02	3.9E-02	5.3E-02	8.5E-02
Skin	1.1E-02	1.3E-02	2.1E-02	3.2E-02	5.9E-02
Spleen	5.7E-01	7.9E-01	1.2E+00	1.8E+00	3.1E+00
Testes	1.7E-02	2.2E-02	3.7E-02	5.4E-02	8.7E-02
Thymus	1.4E-02	1.8E-02	2.7E-02	4.3E-02	7.7E-02
Thyroid	7.5E-02	1.2E-01	1.8E-01	3.7E-01	6.8E-01
Uterus	3.9E-02	4.9E-02	7.7E-02	1.1E-01	1.6E-01
Remaining organs	2.4E-02	3.2E-02	4.9E-02	8.0E-02	1.3E-01
Effective dose (mSv/MBq)	5.4E-02	7.1E-02	1.1E-01	1.6E-01	2.6E-01

Protocols

Type of equipment/measurements

Image quantification (corrections performed; attenuation, scatter, dead time, reconstruction parameters for SPECT or PET, background subtraction)

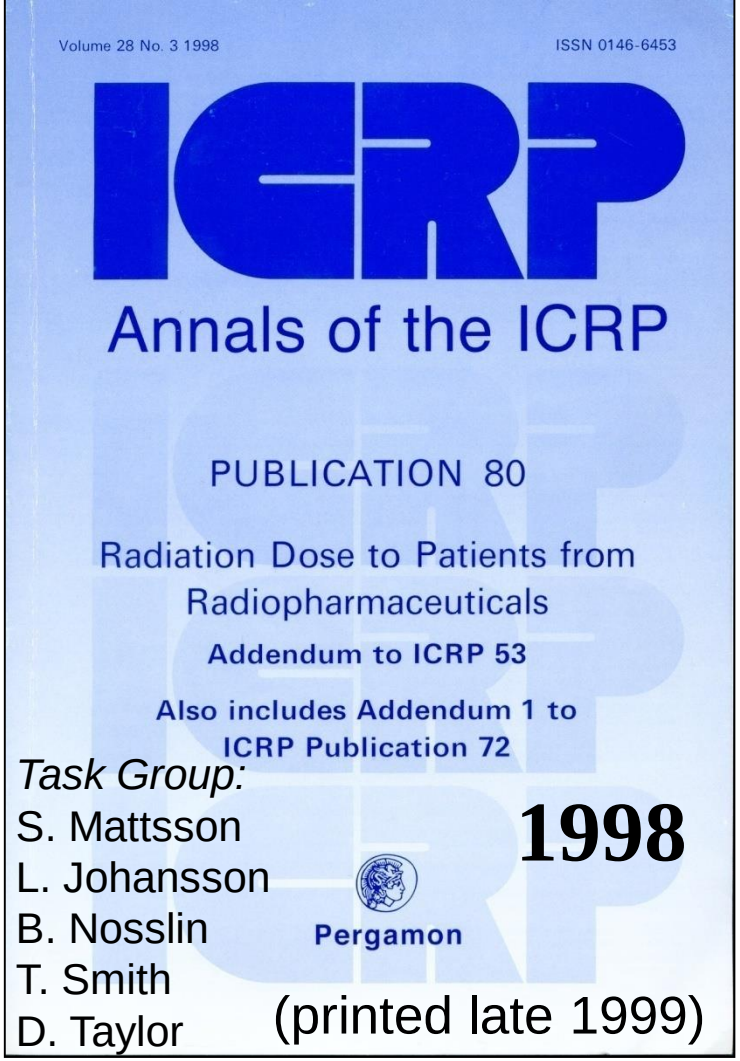
Time points on time-activity curves. Integration

Bladder voiding interval

Dose computation model

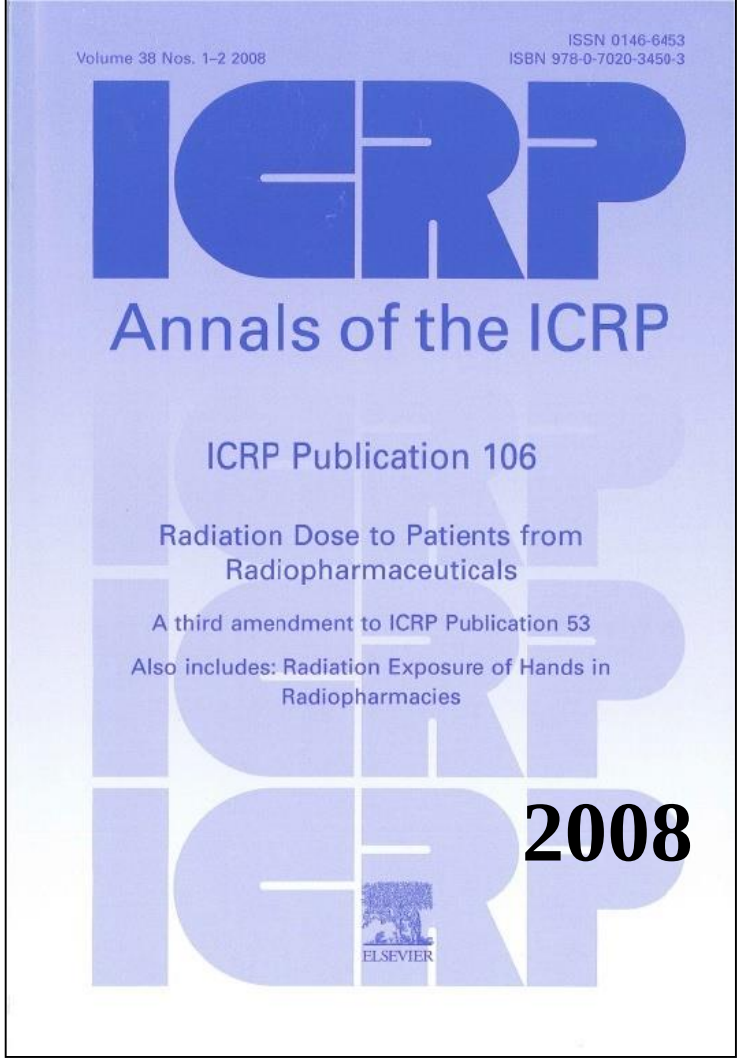
For the effective dose calculation; Set of tissue-weighting factors

Number of participant in the study



ICRP Publication 80 (Addendum 2)

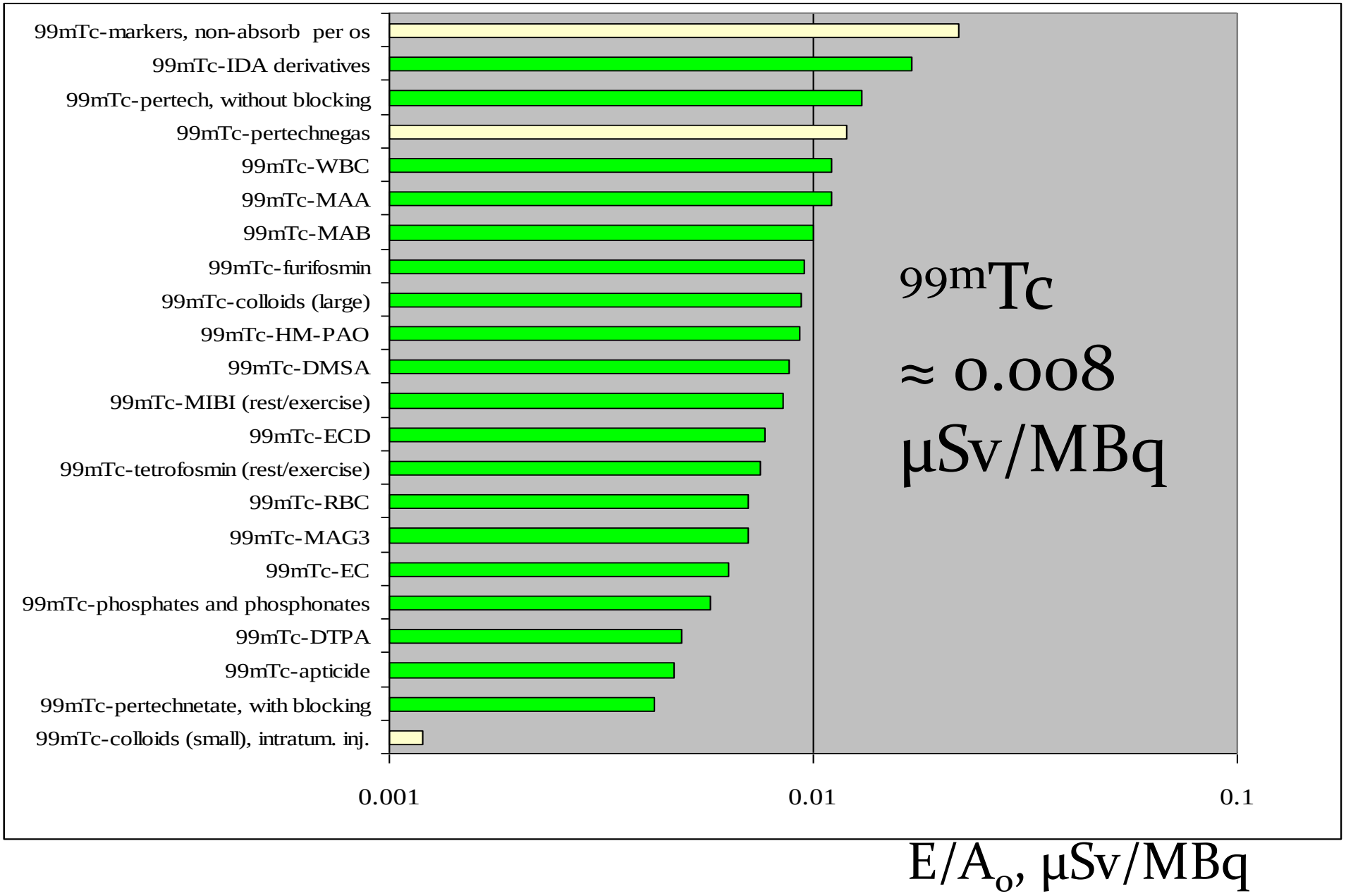
10 new radiopharmaceuticals + recalculations of 19 frequently used ones in Publ 53.



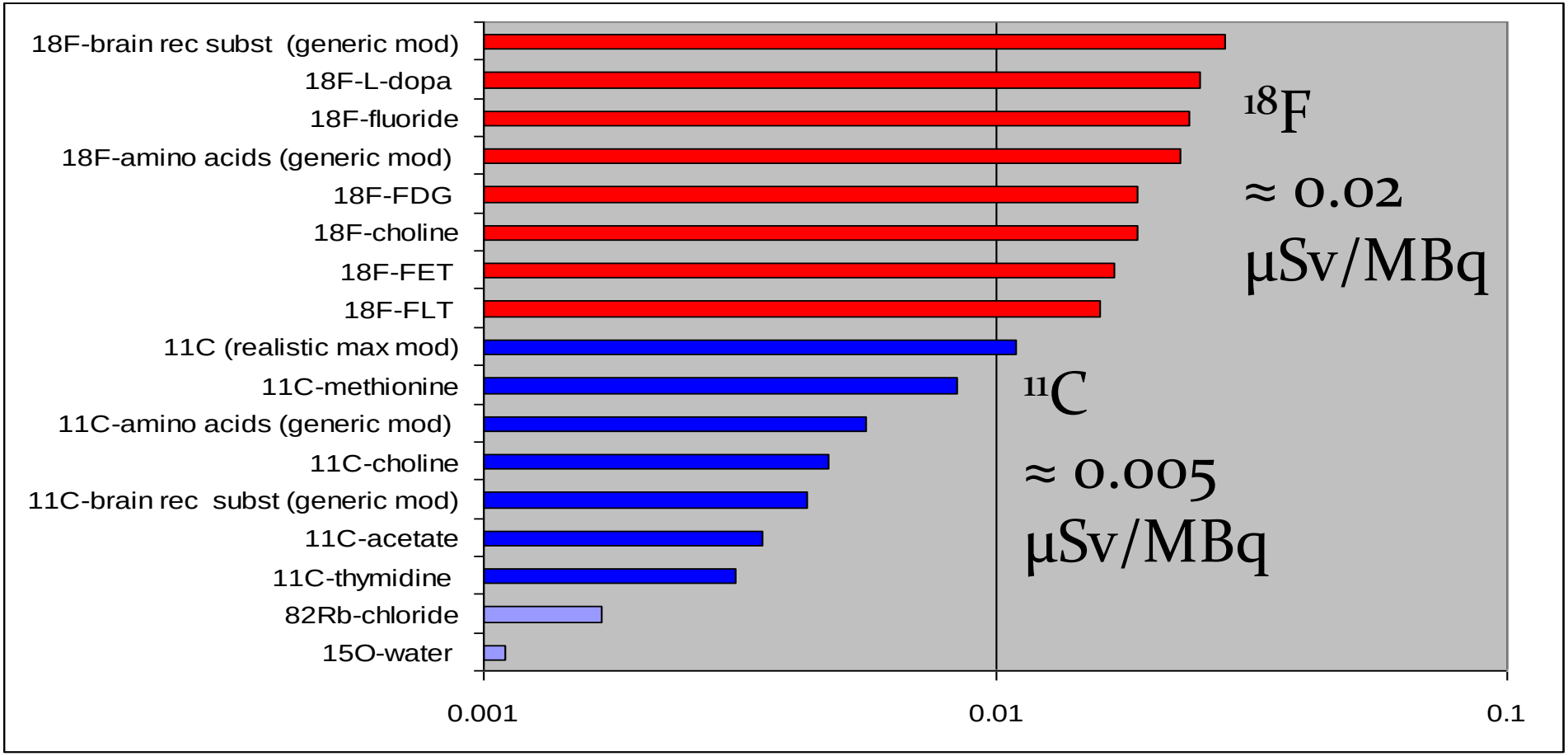
ICRP Publication 106 (A third amendment)

33 radiopharmaceuticals in current use. Recommendations on breast feeding interruptions.

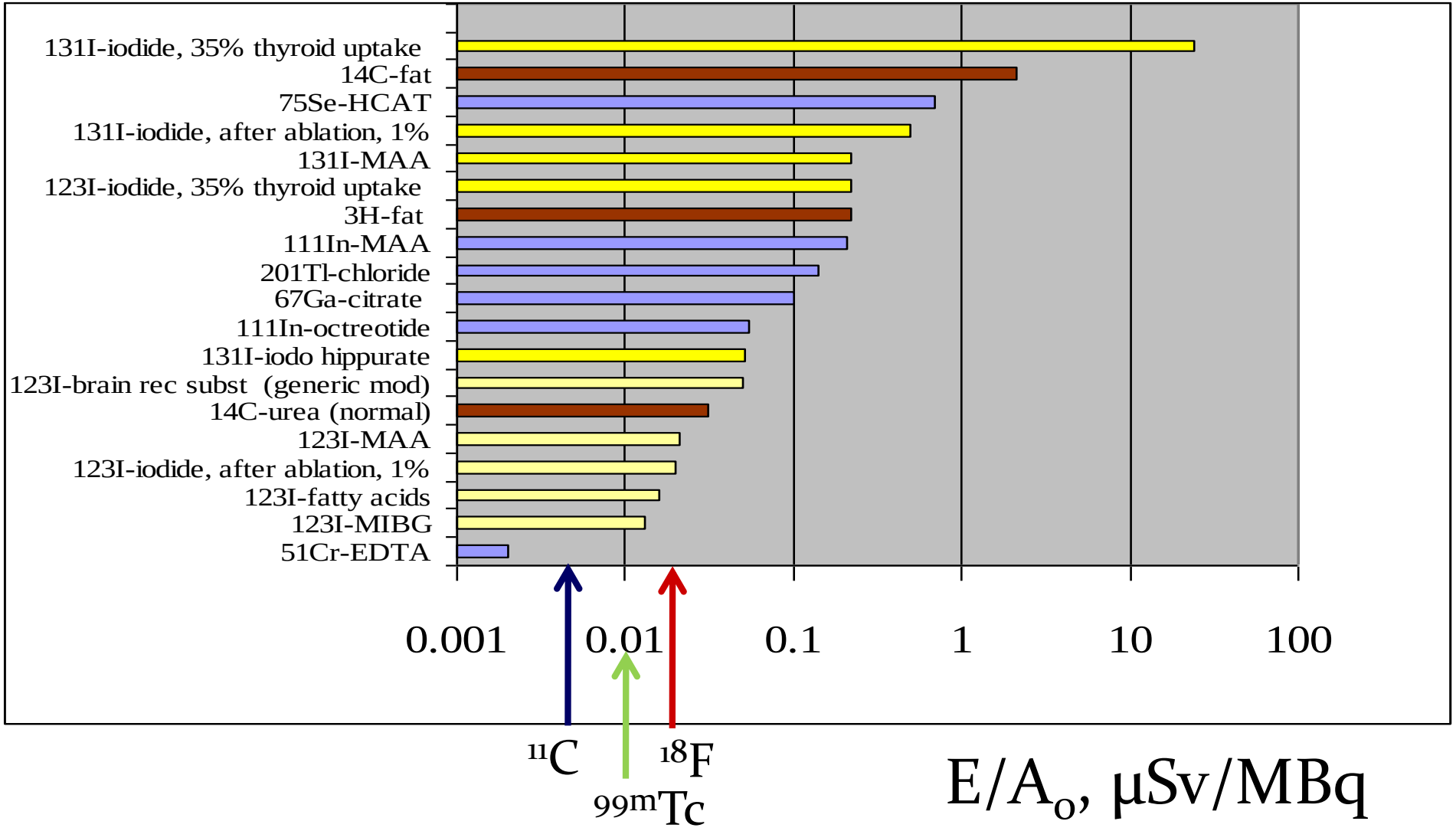
^{99m}Tc-substances

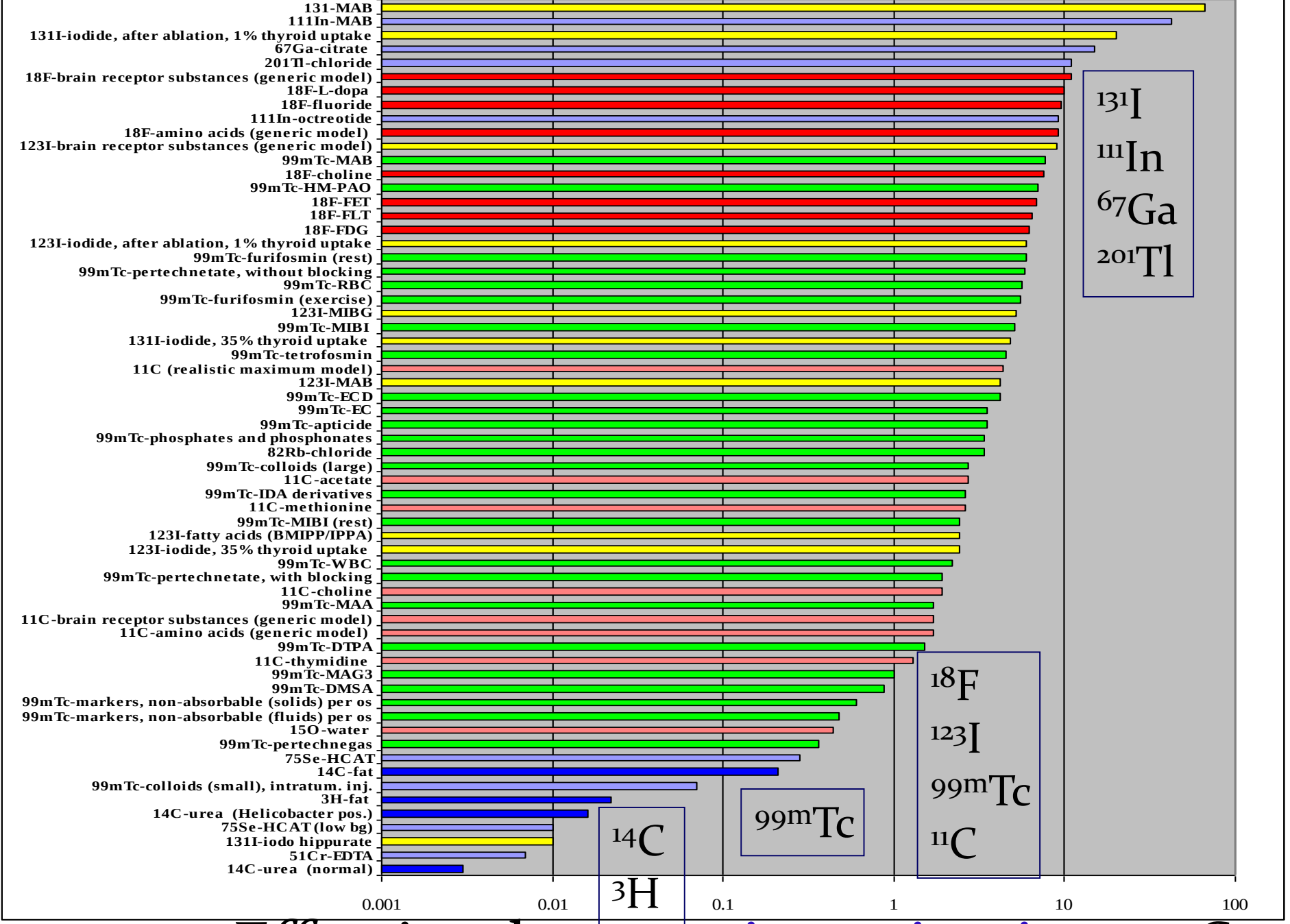


PET-substances



^{201}Tl- ^{131,125,123}I-, ^{111}In-, ^{75}Se-, ^{67}Ga-, ^{51}Cr-, ^{14}C-, ^{3}H-substances





Effective dose per investigation, mSv

Can we meet the accuracy requirements?

Therapy: No and Yes?

Diagnostics: Yes and No

Serial planar imaging scans + SPECT in combination +/- 10-20%
PET +/- 10% if very accurate attenuation, scatter and random corrections

"…the accuracy of quantifying the concentration of a radionuclide in regions within the body can be < 5% with SPECT or PET imaging, and provided there are no overlapping structures containing radioactivity, similar accuracy can also be obtained with planar gamma camera imaging" (Frey et al., 2012)

Challenges (Diagnostics):

- For some substances biokinetic data are old (more than 20 years). Need to generate new data on biokinetics and dosimetry using state-of-the-art equipment
- Few subjects per study. More volunteers are needed.
- Biokinetic data for children
- Biokinetic data for various ages
- Gender specific data
- Biokinetic data for ill
- More uniform dosimetry protocols
- Dose distributions within organs and tissues
- Review of CT protocols for SPECT/CT and PET/CT imaging. DRLs
- Epidemiological studies

Challenges (Therapy):

- Dose planning before therapy, No therapy without dose planning!
- Individual patient biokinetics
- Individual dose calculations
- Dose distributions within organs and tissues
- Same protocol for different hospitals and clinics for measurements of biokinetic data and for dosimetry
- A formalism for the addition of doses from nuclear medicine therapy and external radiation therapy for patients receiving both treatments (BED)

Thank you for listening!

… and don´t forget to collect biokinetic data from your patients!

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INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

Task Group on Radiation Dose to Patients from Radiopharmaceuticals