HelmholtzZentrum münchen

German Research Center for Environmental Health

Internal Dosimetry: A Global Perspective

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US NRC RAMP Users Group Virtual Meeting October 28, 2020

Overview

- Concepts of radiation dosimetry
 - Roentgen, r / Absorbed dose, D
- Internal dosimetry
 - A short history
 - Radiation physics, biology and chemistry
 - Human physiology and anatomy
 - Biokinetic models
 - Computational phantoms and Monte Carlo simulations
 - Dosimetric model (ICRP and MIRD)
- Uncertainty and sensitivity
- Internal microdosimetry
- Applications and computer codes
 - Radiation protection / Radon and thoron / Skin dosimetry
 - Radiation epidemiology / Assessment of risk
 - Internal monitoring / Regulation
 - Radiation biology / Radiation medicine
- Future developments

Concepts of Radiation Dosimetry

- 1895 Wilhelm Röntgen discovered X-rays
- 1896 Henri Becquerel discovered radioactivity
- ❖ 1925 Measurement of X-rays by free-air chamber
- 1928 ICRU established a unit "roentgen" for that "quantity" which was measured by free-air chamber
- 1953 ICRU established "absorbed dose"
- 1956 ICRU used the unit "roentgen" for established "exposure dose" and later "exposure" (ICRU 1962), now the SI unit "C kg⁻¹"
- 1538 Paracelsus "Dosis sola facit venenum" the dose makes the poison
- Radiation Dosimetry deals with the measurement of absorbed dose / dose rate resulting from the interaction of ionizing radiation with matters

Absorbed Dose

The absorbed dose, D, is the quotient of $d\bar{\epsilon}$ by dm, where $d\bar{\epsilon}$ is the mean energy imparted by ionizing radiation to matter of mass dm, thus

$$D=\frac{\mathrm{d}\bar{\varepsilon}}{\mathrm{d}m}.$$

Unit: J kg⁻¹ (special name is gray: Gy)

Note: The absorbed dose, D, is considered a point quantity, but it should be recognized that the physical process does not allow dm to approach zero in the mathematical sense.

The <u>energy imparted</u>, ε , to the matter in a given volume is the sum of all energy deposits in the volume, thus

$$oldsymbol{arepsilon} = \sum_i oldsymbol{arepsilon}_i,$$

where the summation is performed over all energy deposits, ε_i , in that volume.

Unit: J

The <u>energy deposit</u>, ε_i , is the energy deposited in a single interaction, i, thus

$$\varepsilon_i = \varepsilon_{\rm in} - \varepsilon_{\rm out} + Q,$$

where $\varepsilon_{\rm in}$ is the energy of the incident ionizing particle (excluding rest energy), $\varepsilon_{\rm out}$ is the sum of the energies of all charged and uncharged ionizing particles leaving the interaction (excluding rest energy), and Q is the change in the rest energies of the nucleus and of all elementary particles involved in the interaction (Q > 0: decrease of rest energy; Q < 0: increase of rest energy).

Unit: J

ICRU 85a, 2011

Internal Dosimetry

...to measure, calculate, estimate, assay, predict and otherwise quantify the radiative energy absorbed by the ionization and excitation of atoms in human tissues as a result of emission of energetic radiation by internally deposited radionuclides...

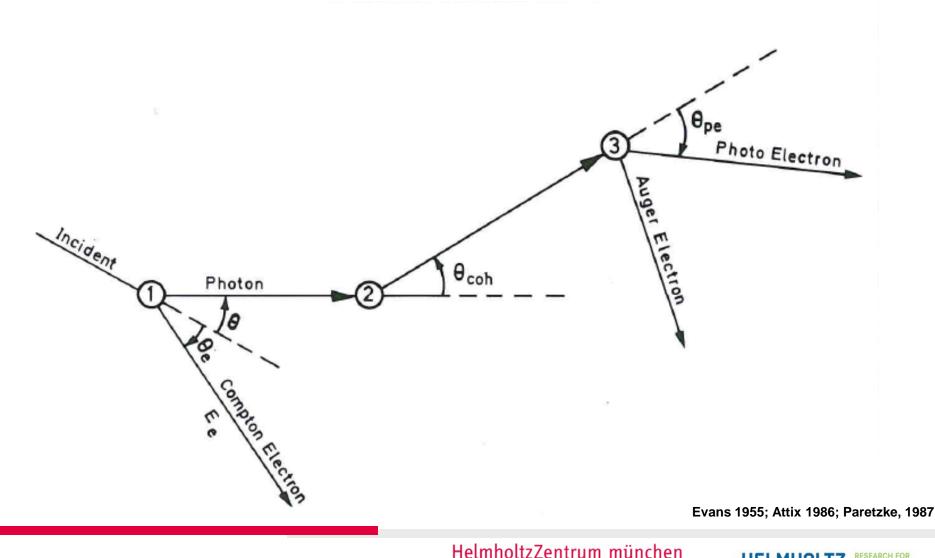
Otto G. Raabe, Internal Radiation Dosimetry, 1994

Internal Dosimetry – A short history

- 1896 Henri Becquerel discovered radioactivity
- 1898 Marie Curie separated polonium and radium
- 1934 Joliot and Curie discovered artificial radioactivity
- 1942 Marinelli calculation of dosage
- 1948 Quimby organs as approx. by sphere, used by ICRP
- 1953 Loevinger outlined a technique for internal dosimetry
- 1966 Loevinger and Berman unified an approach to internal dosimetry
- 1968 Snyder developed math. models of human body and Monte Carlo code for internal dosimetry for MIRD and for ICRP for workers
- 1979 ICRP 30 for workers
- 1989 ICRP (53,80,106,128), (56,67,69,71,72), (68,78,119)
- 2009 MIRD pamphlet No. 21 with ICRP
- 2015 ICRP OIR Part 1,2,3,4,5 for workers
- 202x ICRP EIR for members of the public

Personal

Interactions of Radiation with Matters



Radiation Chemistry

\mathbf{P}	hysic	ochen	aical	stage
	-			

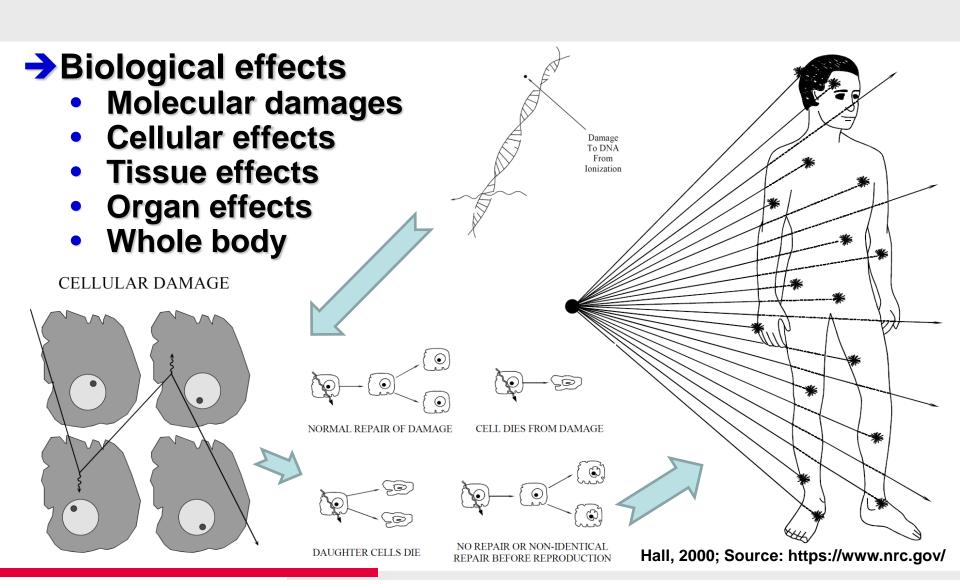
10^{-15}	Electronic excitation: $H_2O \longrightarrow H_2O^*$
10^{-14}	Ion-molecule reactions, e.g. $H_2O^+ + H_2O \longrightarrow {}^{\bullet}OH + H_3O^+$
10^{-13}	Molecular vibration \rightarrow dissociation of excited state:
	$\mathrm{H_2O^*} \longrightarrow \mathrm{H}^{\bullet} + {}^{\bullet}\mathrm{OH}$
10^{-12}	Rotation relation, thermalization of hot electrons,
	hydration of electrons: $e^- \rightarrow e_{\rm aq}^-$

Chemical stage

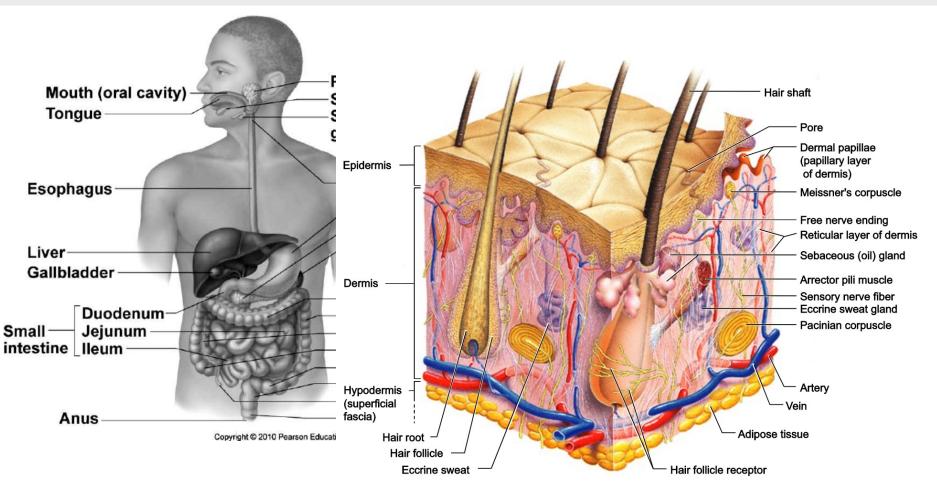
$< 10^{-12}$	Reactions of e^- before hydration with reactive solute
	at high concentrations
10^{-10}	Reactions of e_{aq}^- and other radicals with reactive solute
	$(\text{concentration} \sim 1 \text{ mol} \cdot \text{dm}^{-3})$
$< 10^{-7}$	Reactions in spurs
10^{-7}	Homogeneous distribution of radicals
10^{-3}	Reactions of e_{aq}^- and other radicals with reactive solutes
	(concentration $\sim 10^{-7} \text{ mol} \cdot \text{dm}^{-3}$, i.e. $\sim 0.01 \text{ ppm}$)
1	Free-radical reactions largely completed
10^{3}	Biochemical processes

von Sonntag, 1987; 2006; Magee and Chatterjee, 1987

Biological Effects of Radiation



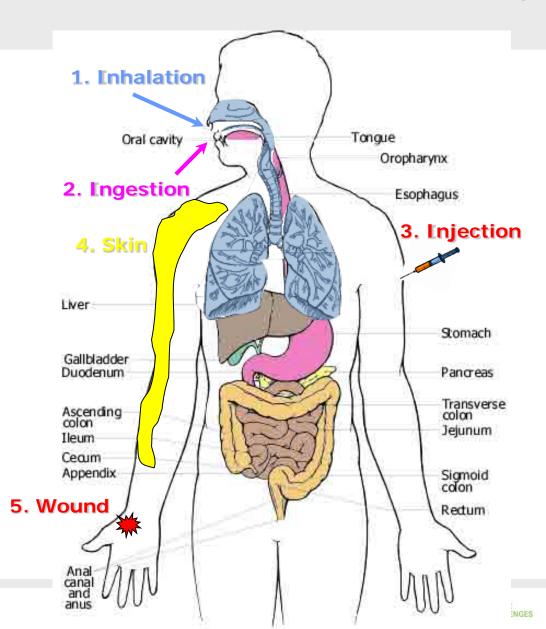
Human Physiological and Anatomical Bases



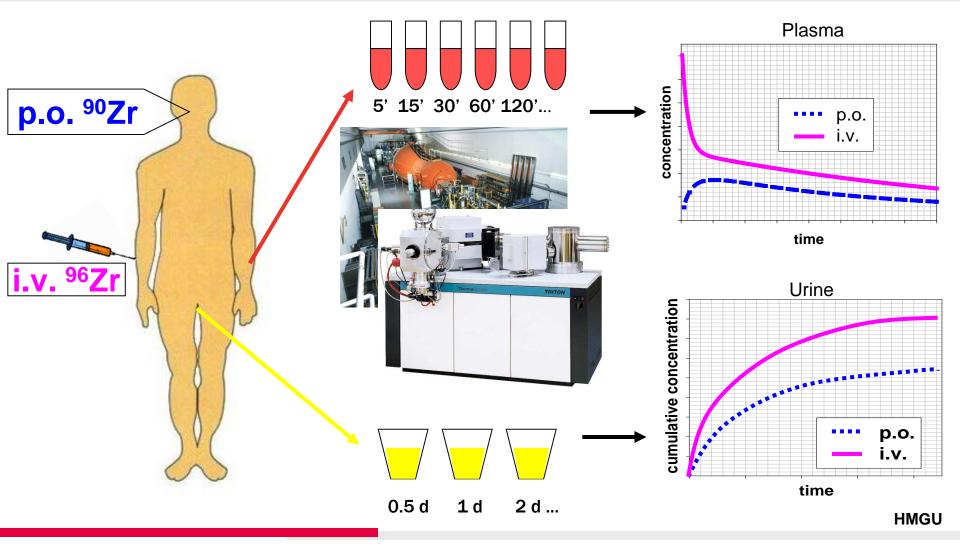
Marieb and Hoehn, Human Anatomy & Physiology, 8th 2010

Incorporation of Radionuclide in Human Body

- 1. Inhalation
- 2. Ingestion
- 3. Injection
- 4. Wound
- 5. Percutaneous resorption
- 6. Instillation
- 7. Other orifice in the body

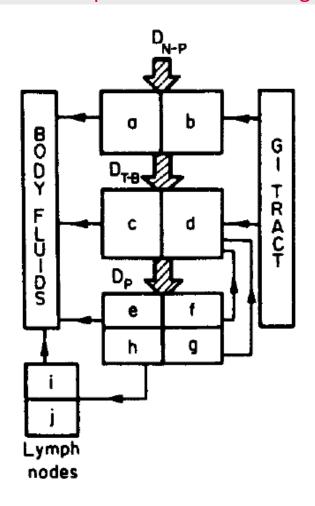


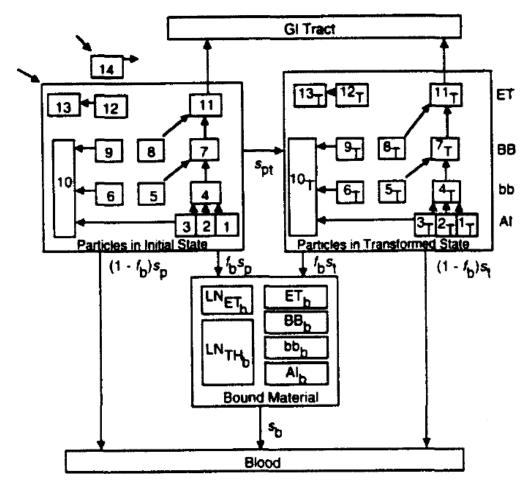
Biokinetic Investigations of Stable Isotopes



Biokinetic Models for Lungs

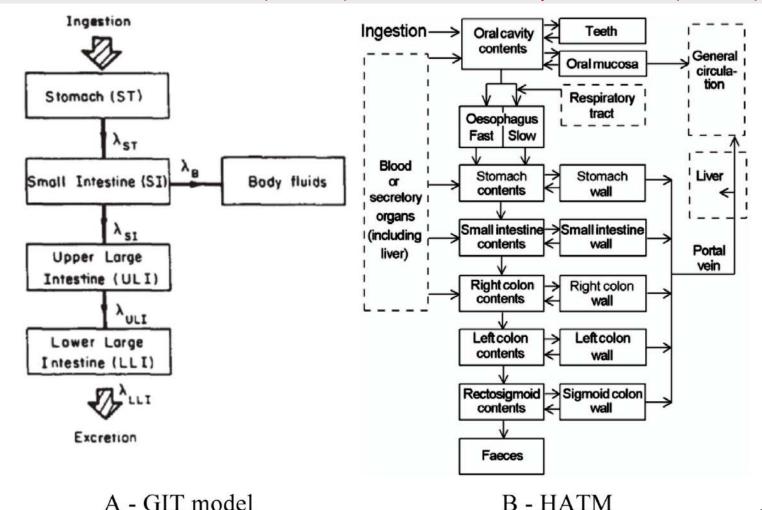
• From simple mathematical lung model (1979) to human respiratory tract model (1994)





Biokinetic Models for Alimentary Tract

From gastrointestinal tract model (A, 1979) to human alimentry tract model (B, 2006)

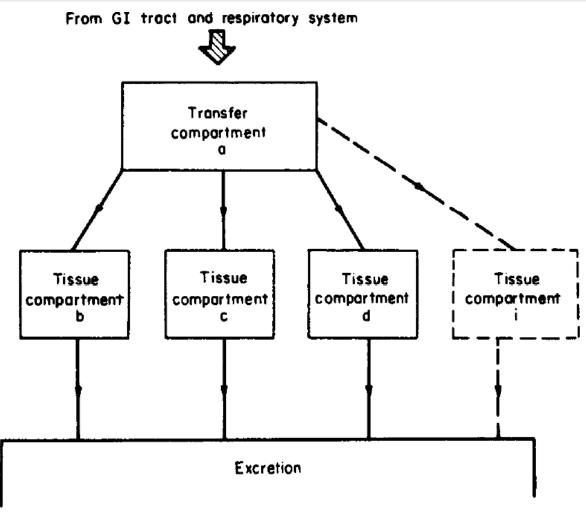


ICRP 30

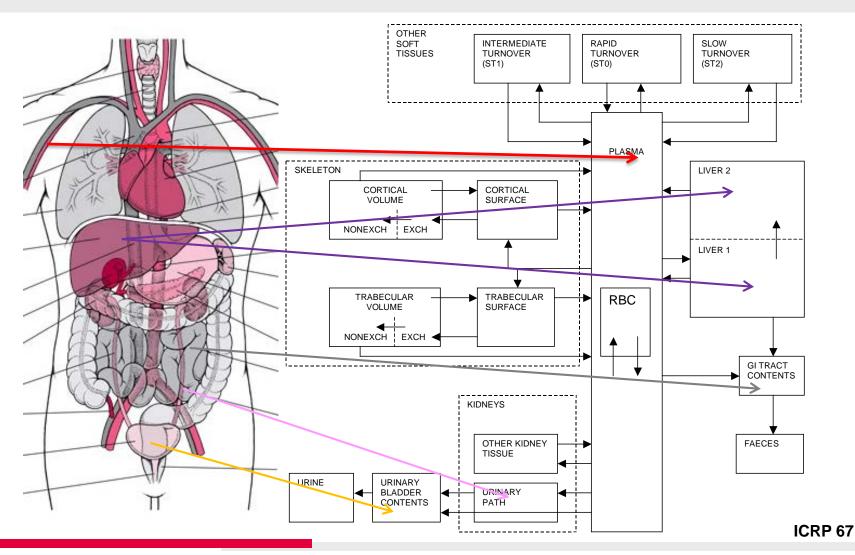
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HELMHOLTZ RESEARCH FOR GRAND CHALLENGES

Mathematical Model for Kinetic Description of Radionuclides in Body - Systemic

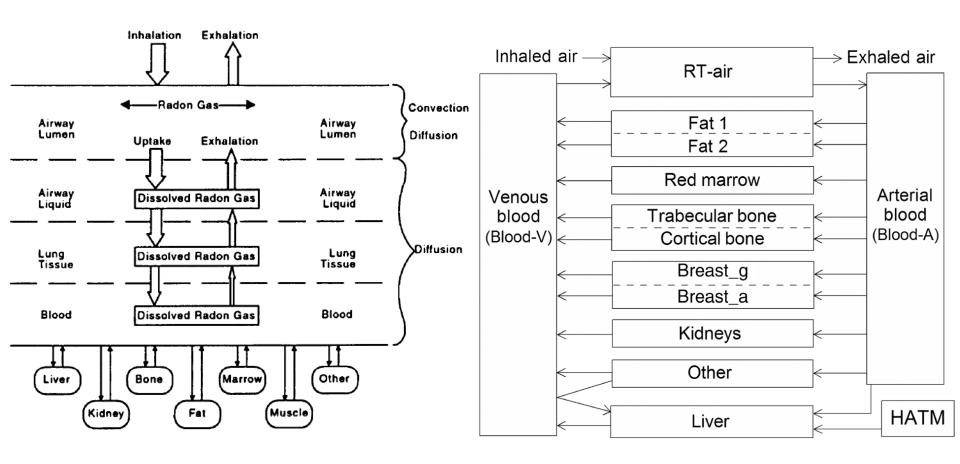


Systemic Biokinetic Model for U, Pb and Ra

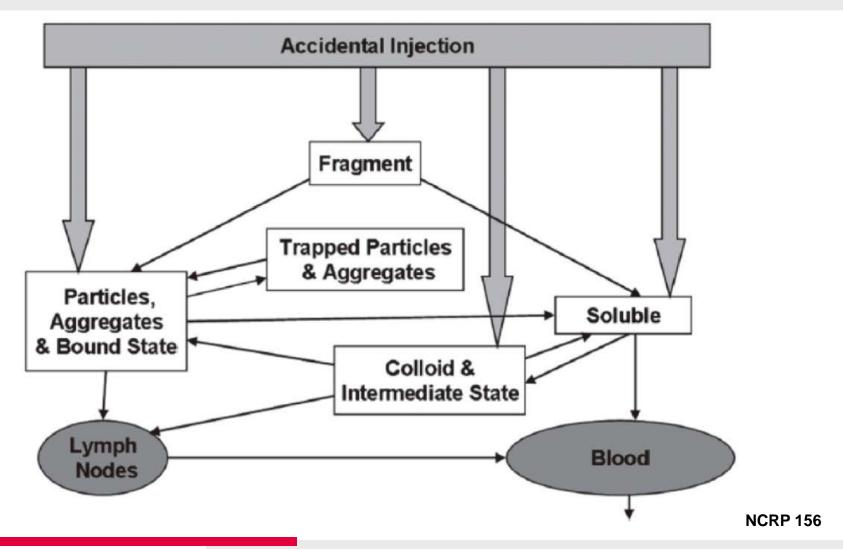


Biokinetic Model for Radon Gas

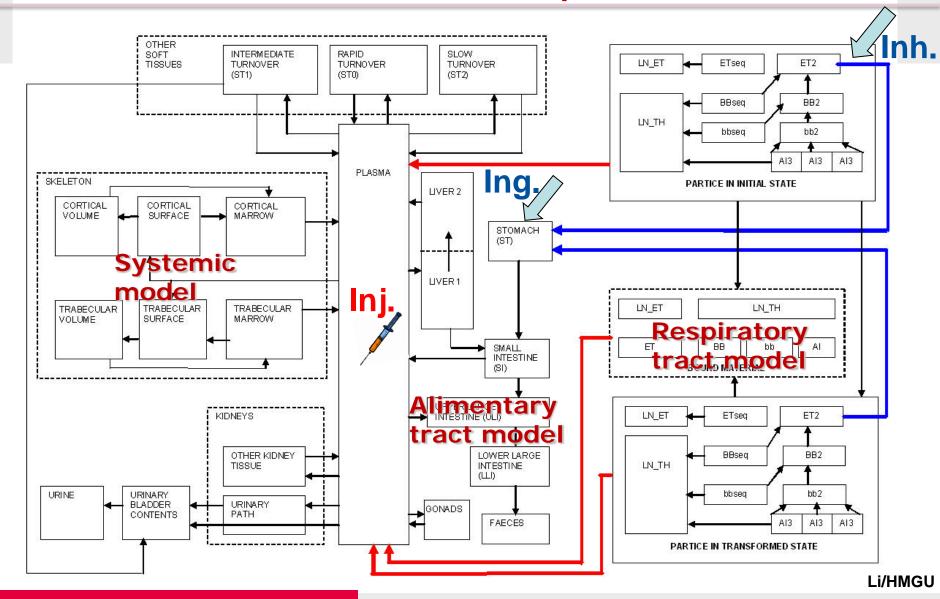
From ICRP 66 (1994) to ICRP OIR Part 3 (2017)



Biokinetic Model for Radionuclide-Contaminated Wounds



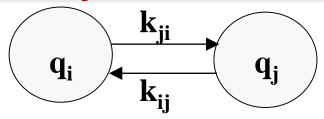
Generic Biokinetic Models for Incorporated Radionuclides



German Research Center for Environmental Health



Mathematical Formulation – System of First-Ordor Ordinary Differential Equations



The ordinary differential equations describe the time-dependent behaviour of the materials in each compartment:

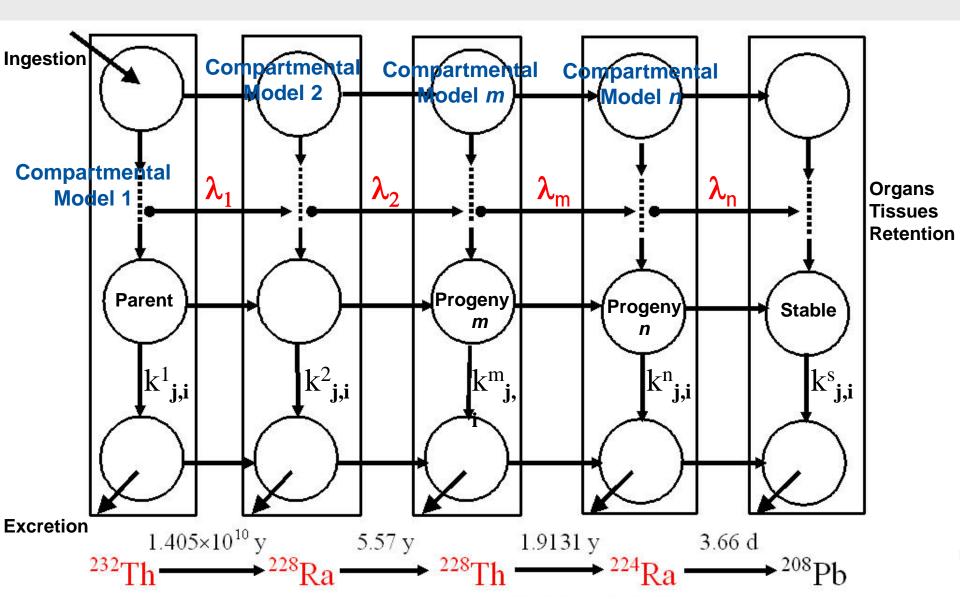
$$\frac{dq_i}{dt} = \sum_{j=1}^{n} k_{ij} q_j - q_i \sum_{j=1}^{n} k_{ji} \qquad j \neq i$$

The exchange processes are assumed linear processes of first order

- ► The retention in the compartments can be expressed by biological half lives
- ► The solution of the ordinary differential equation system is a linear combination of exponential functions:

$$q_i(t) = \sum_{j=1}^{n} a_{lj} e^{-\lambda_j t}$$
 $l = 1, 2, ... n$

Treatment of Decay Products of Radionuclides



Skin Model – in between external and internal exposure

SPECIAL SYMPOSIUMS

FALL 2020

RAMP USERS GROUP

VIRTUAL MEETING







October 27, 2020

VARSKIN TECHNICAL MEETING

9:30-9:35 | VARSKIN Introduction

Vered Shaffer | Office of Nuclear Regulatory Research, U.S. NRC

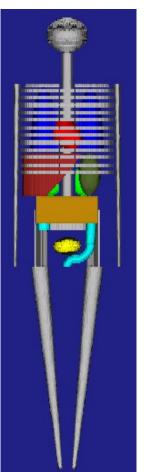
11:05-11:30 | VARSKIN's New Wound Dosimetry Model

David Hamby | Renaissance Code Development

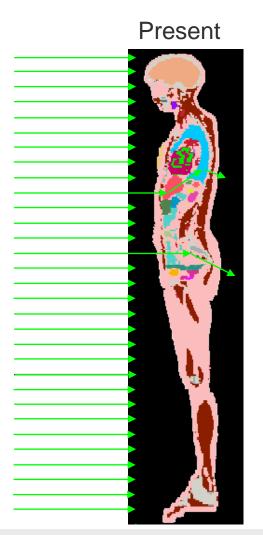


Computational Phantoms

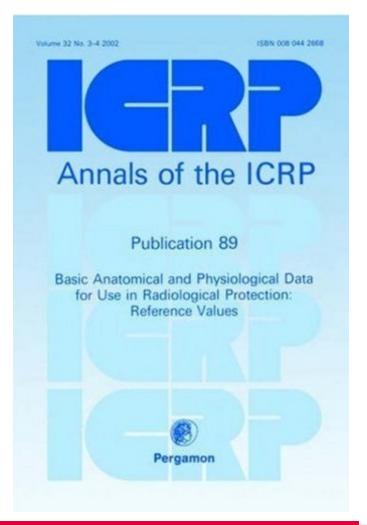
Past



- Model of the radiation source
- Model of the body
- Physical models of
 - radiation interactions
 - energy depositions



Developing Phantoms according to ICRP Reference Persons



Main characteristics specified in ICRP Publication 89:

Table 2.9. Reference values for height, mass, and surface area of the total body

	Heig	ht (cm)	Mass (kg)				
Age	Male	Female	Male	Female			
Newborn	51	51	3.5	3.5			
1 year	76	76	10	10			
5 years	109	109	19	19			
10 years	138	138	32	32			
15 years	167	161	56	53			
Adult	176	163	73	60			

Reference masses for 56 organs, organ groups, and tissues

Reference Computational Phantoms (ICRP)



Select segmented voxel models of male and female individual whose body height and mass closely resemble the ICRP 89 reference values

"Golem": 176 cm, 69 kg (176 cm, 73 kg) "Laura": 167 cm, 59 kg (163 cm, 60 kg)

Modify these segmented voxel models in several steps



Laura

Computational Voxel Phantoms at HMGU

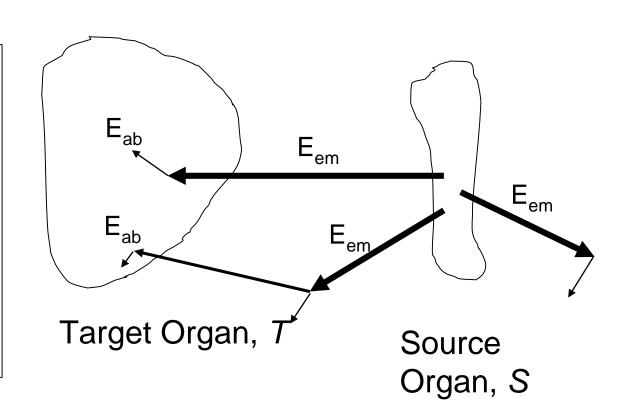


Calculation of AFs using Monte Carlo Radiation Transport Codes with Phantoms

$AF(T \leftarrow S)$

absorbed fraction, i.e. fraction of the energy absorbed by target organ T in relation to the energy emitted by source organ S

$$AF(T \leftarrow S) = \frac{\sum E_{abs}}{\sum E_{em}}$$



Generalized Formalism for Internal Dosimetry

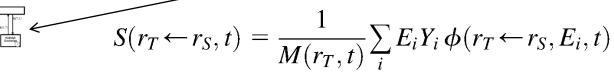
Mean organ absorbed dose

(MIRD/ICRP)



$$d(r_T, T_D) = \sum_{r_S} \int_0^{T_D} a(r_S, t) S(r_T \leftarrow r_S, t) dt$$





Organ equivalent dose
$$=\frac{1}{M(r_T,t)}\sum_i \Delta_i \phi(r_T \leftarrow r_S, E_i, t)$$

$$h(r_T, T_D) = \sum_{r_s} \widetilde{a}(r_s, T_D) S_w(r_T \leftarrow r_S)$$

Effective dose

$$e(\tau) = \sum_{T} w_{T} \left[\frac{h_{T}^{M}(\tau) + h_{T}^{F}(\tau)}{2} \right]$$

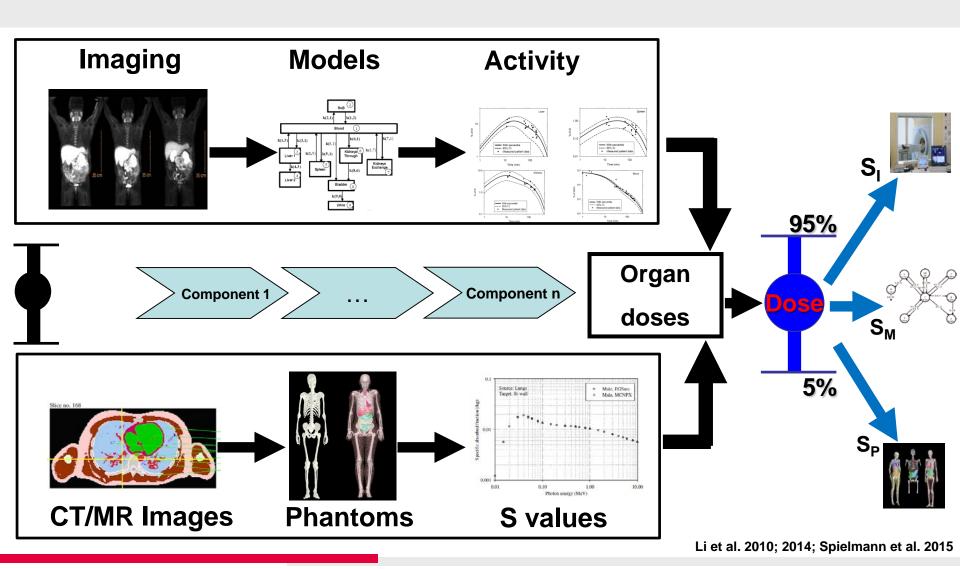
$$S_{w}\left(r_{T}\leftarrow r_{S}\right) = \sum_{R} w_{R} \sum_{i} \frac{E_{R,i} Y_{R,i} \phi\left(r_{T}\leftarrow r_{S}, E_{R,i}\right)}{M\left(r_{T}\right)}.$$

Bolch et al. 2009

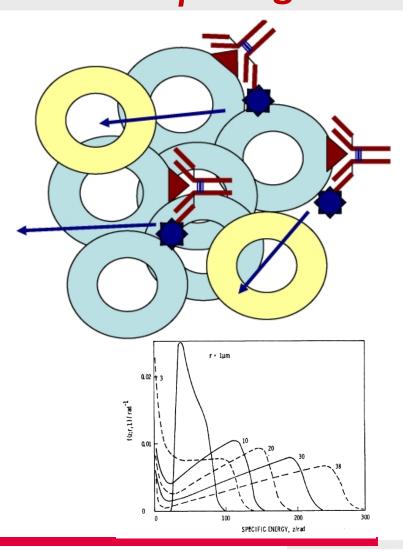
Computer Codes for Internal Dosimetry

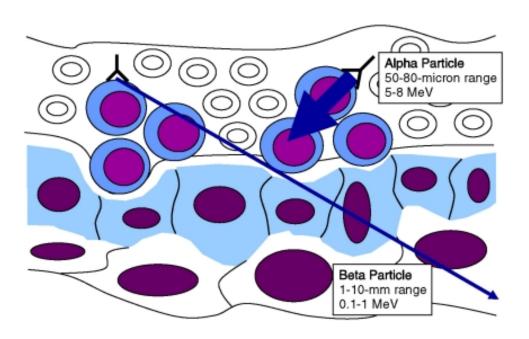
- Not complete
- SAAM II biokinetic modeling
- MATLAB biokinetic modeling and dosimetry
- MATHEMATICA biokinetic modeling and dosimetry
- SEECAL / DCAL dose coefficients
- IMBA -> TAURUS
- TAURUS dose coefficients and internal monitoring
- IDEA System dose coefficients and internal monitoring
- IDSS dose coefficients and internal monitoring
- AIDE dose coefficients and internal monitoring
- MONDAL dose coefficients
- DOSAGE dose coefficients
- PLEIADES dose coefficients
- OLINDA/EXM nuclear medicine dosimetry
- IDAC-Dose dose for radiopharmaceuticals

Uncertainty and Sensitivity Analysis



Internal Microdosimetry α - and β - targeted Radiopharmaceuticals in Cells





$$f_{\nu}(z) = \int_{0}^{z} f_{1}(x) f_{\nu-1}(z-x) dx \qquad (\nu = 2, 3, ...)$$

$$f(z; D) = \sum_{\nu=0}^{\infty} e^{-n} \frac{n^{\nu}}{\nu!} f_{\nu}(z), \quad \text{with} \quad n = \frac{D}{\overline{z}_{F}}$$

NAP 2007; Li et al. 2018

Applications of Internal Dosimetry

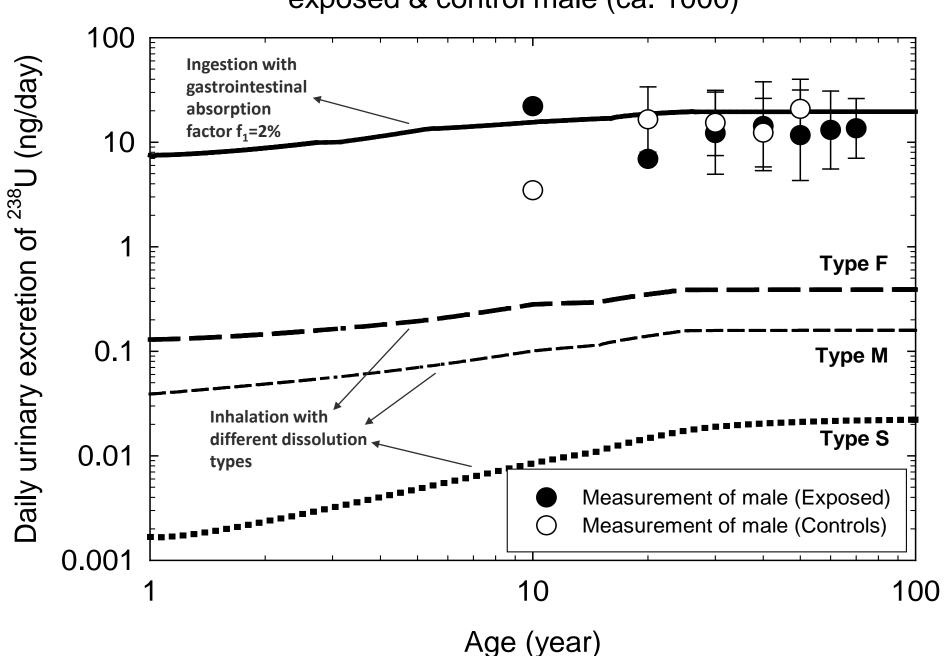
Modeling of ²³⁸U in human body from ingestion and inhalation

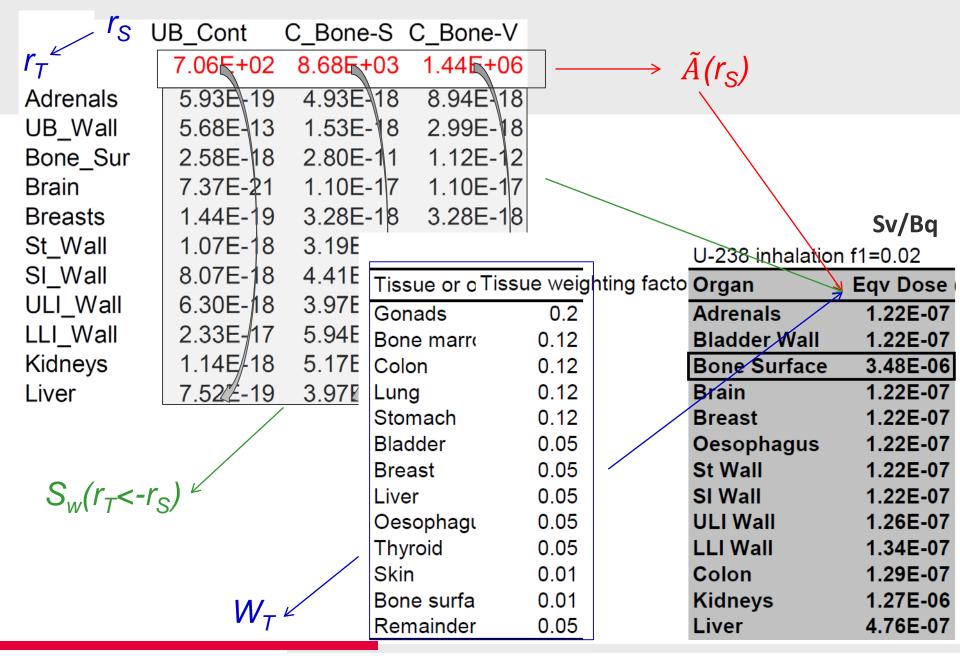
Input for biokinetic modeling and dose calculation

- ²³⁸U is a naturally occurring element, can be found in soil and rock and in water
- ²³⁸U can be found in the air and in the foodstuffs
- We are inhaling ²³⁸U everyday (20 mBq/day)
- We are taking ²³⁸U everyday by eating and drinking (16 mBq/day)
- Modeling the content and calculating the dose of ²³⁸U
- We are taking 1.3 mg ²³⁸U everyday totally
- There is about 10 60 mg ²³⁸U in our body
- Urinary excretion of ²³⁸U per day ~ 20 ng

Li et al. 2005; 2006; 2009

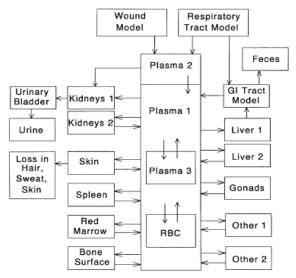
Model prediction (diet/air age-dependent) vs. exposed & control male (ca. 1000)





The Case of Mr. Alexander Litvinenko





Leggett and Eckerman, 2001

SPIEGEL ONLINE

30. November 2006, 11:02 Uhr

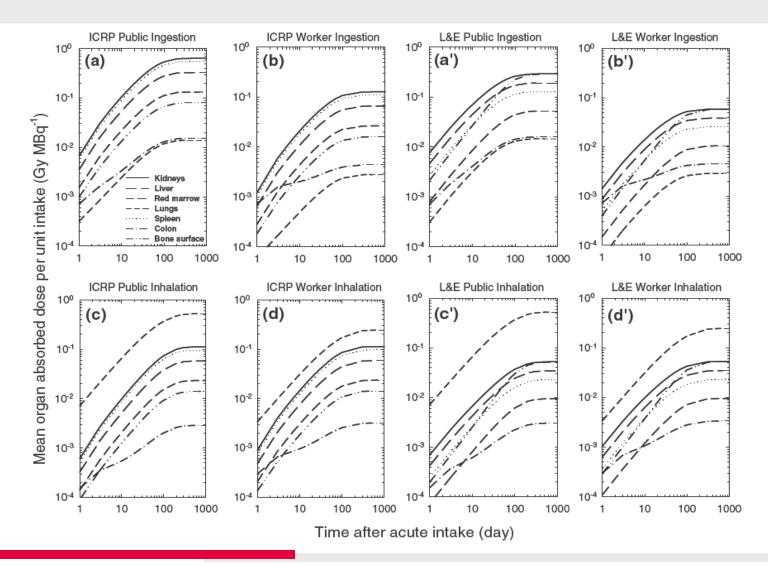
CHRONIK

Der Fall Litwinenko

Der mysteriöse Tod des Alexander Litwinenko: Wer vergiftete den Kreml-Kritiker? Eine Chronik der Affäre.

- November: Litwinenko trifft in einem Londoner Hotel mit dem ehemaligen KGB-Spion Andrej Lugowoi und zwei v einem Sushi-Restaurant den italienischen Sicherheitsexperten Mario Scaramella, um diesen zur Ermordung der krit Später wird ihm schlecht.
- 3. November: Litwinenko wird in das Barnet General Hospital in London gebracht.
- 11. November: Litwinenko teilt dem Radiosender BBC mit, dass er vergiftet worden sei und sich in sehr schlechter
- 17. November: Litwinenko wird ins University College Hospital verlegt und unter bewaffneten Schutz gestellt.
- 20. November: Litwinenko wird auf die Intensivstation verlegt. Die Polizei nimmt Ermittlungen auf. Ein Kreml-Spreverwickelt sei.
- 22. November: Die Klinik teilt mit, dass sich Litwinenkos Zustand erheblich verschlechtert hat.
- November: Litwinenko stirbt um 21.21 Uhr (22.21 Uhr MEZ).
- **24. November:** Eine von Litwinenko auf dem Sterbebett diktierte Erklärung wird veröffentlicht. Darin macht er den Der Kreml weist die Vorwürfe zurück. Die britische Gesundheitsbehörde HPA teilt mit, dass in Litwinenkos Urin die r Spuren werden auch in Litwinenkos Haus im Norden von London, in dem am 1.11. besuchten Sushi-Restaurant un
- 27. November: Die britische Regierung leitet eine offizielle Untersuchung zum Tod Litwinenkos ein.
- 29. November: Die Gesundheitsbehörde HPA kündigt Untersuchungen der Krankenschwestern, Pfleger und Ärzte einer radioaktiven Substanz an Bord von Flugzeugen der British Airways.
- 30. November: In weiteren Maschinen werden radioaktive Spuren gefunden.

Organ Absorbed Dose



The Amount of Po-210 Mr. A. Litvinenko Might **Have Ingested or Drunk**

Table 3 Possible incorporation of ²¹⁰Po estimated for Mr. Alexander Litvinenko using the biokinetic the assumption of different damaged organ and the lethal absorbed dose

and L&E [15] with

	Red box (5 Gy ^b)	ne marrow ^a			Kidneys ⁶ (6 Gy ^b)			ers	(8 Gy ^b)			
Biokinetic model	ICRP	L&E	ICRP	L&E	ICRP	_	e_ 0.5	L&E	ICRP	L&E	ICRP	L&E
f ₁ Value Estimated intake	0.1	0.1	0.5	0.5	- ki	110	0.5	0.5	0.1	0.1	0.5	0.5
(MBq)	546	1,408	109		M	230	27	46	351	473	70	94
(μg)	3.3	8.5		UC	υ.8	1.4	0.2	0.3	2.1	2.9	0.4	0.6
f ₁ Value Estimated intake (MBq) (μg) a Critical organ b Lethal absorbed of	dose VE	of P	0-2,									

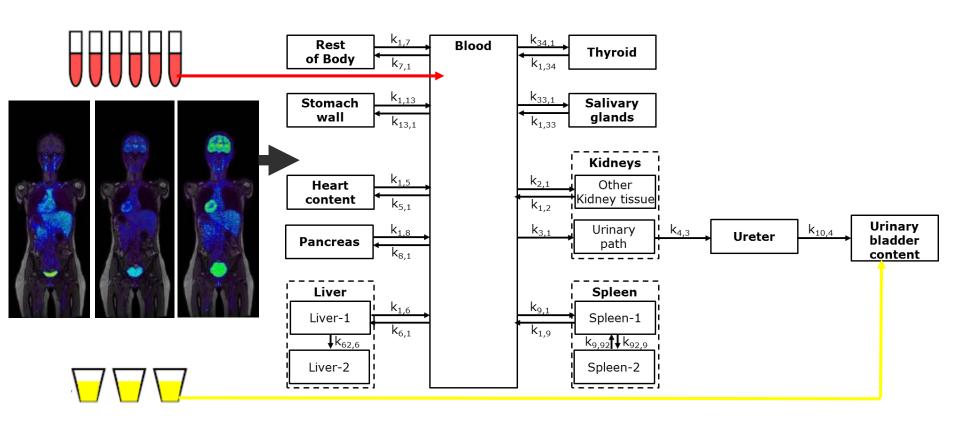
Critical organ

Li, et al. 2008

Lethal absorbed dose

Applications of Internal Dosimetry

Image-based biokinetic model and dosimetry for new radiopharmaceuticals

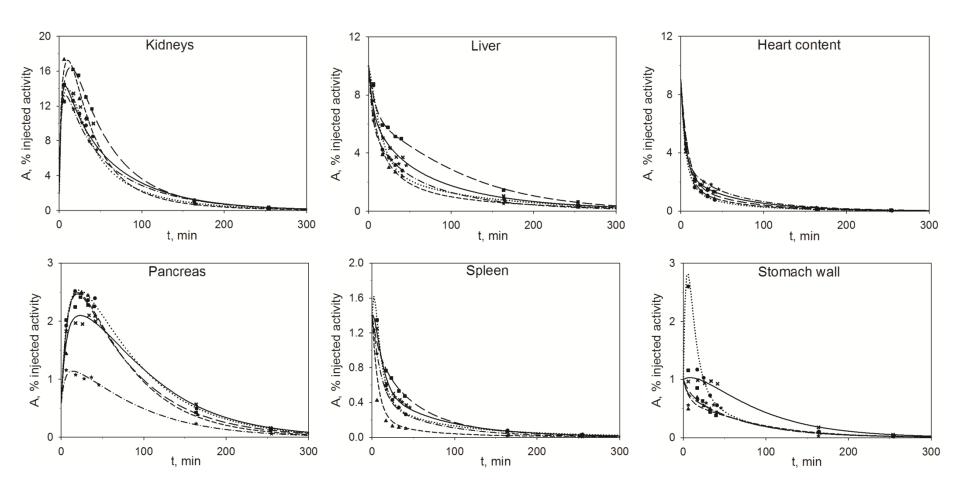


Radiopharmaceutical: BAY94-9392 for five patients

Zvereva et al., 2016

Organ Activity Kinetics for Patients

BAY94-9392:



Organ Doses and Effective Doses for Patients

The doses can be used to estimate the patient health risk

Table 2. Organ absorbed-dose coefficients, [mGy/MBq] and effective-dose coefficients, [mSv/MBq]

				1102/04 51-						1104/04 6 1			1105/04 1		
	1101/94-female			1102/94-female			1103/94-male			1104/94-female			1105/94-male		
Target organ	Concept-1	Concept-2	%Diff	Concept-1	Concept-2	%Diff	Concept-1	Concept-2	%Diff	Concept-1	Concept-2	%Diff	Concept-1	Concept-2	%Diff
Red marrow	8.30E-03	8.26E-03	0.6%	7.79E-03	7.78E-03	0.2%	7.76E-03	7.78E-03	-0.3%	7.73E-03	7.66E-03	1.0%	6.55E-03	6.18E-03	6.0%
Colon	1.19E-02	1.06E-02	12.0%	1.06E-02	9.67E-03	9.9%	1.03E-02	9.30E-03	10.4%	1.13E-02	1.01E-02	12.4%	1.01E-02	7.93E-03	27.0%
Lungs	9.57E-03	6.36E-03	50.4%	8.62E-03	6.18E-03	39.6%	7.82E-03	5.85E-03	33.7%	8.73E-03	5.63E-03	54.9%	8.27E-03	4.31E-03	91.9%
Stomach wall	2.87E-02	2.87E-02	0.0%	1.89E-02	1.89E-02	0.0%	1.37E-02	1.38E - 02	-0.3%	2.58E-02	2.57E-02	0.2%	1.51E-02	1.48E-02	1.9%
Bladder wall	6.29E - 02	6.32E-02	-0.5%	5.27E-02	5.29E-02	-0.5%	6.83E-02	6.87E-02	-0.6%	6.17E-02	6.19E - 02	-0.4%	6.16E-02	6.20E-02	-0.6%
Oesophagus	9.10E-03	7.21E-03	26.2%	8.36E-03	6.92E-03	20.7%	7.94E-03	6.74E-03	17.9%	8.09E-03	6.26E-03	29.4%	7.52E-03	4.93E-03	52.6%
Liver	2.13E-02	2.08E-02	2.3%	2.68E-02	2.65E-02	1.3%	1.38E-02	1.36E-02	1.9%	1.85E-02	1.80E-02	2.8%	1.39E-02	1.31E-02	6.6%
Thyroid	1.89E-02	1.87E-02	1.1%	1.21E-02	1.20E-02	1.2%	1.36E-02	1.36E-02	0.2%	1.49E-02	1.47E-02	1.6%	9.45E-03	9.03E-03	4.6%
Salivary glands	7.93E - 03	7.98E - 03	-0.6%	5.78E-03	5.84E-03	-1.1%	6.20E-03	6.35E-03	-2.4%	6.35E-03	6.38E - 03	-0.4%	4.85E-03	4.80E-03	1.1%
Heart wall	1.62E-02	1.53E-02	5.8%	1.69E-02	1.63E-02	4.1%	1.57E-02	1.53E-02	2.9%	9.28E-03	8.41E-03	10.5%	7.51E-03	6.33E-03	18.5%
Kidneys	1.16E-01	1.16E-01	0.2%	1.41E-01	1.41E-01	0.1%	9.22E-02	9.19E-02	0.3%	1.02E-01	1.01E-01	0.3%	9.64E-02	9.58E-02	0.7%
Adrenals	1.98E-02	1.87E-02	5.9%	2.20E-02	2.12E-02	3.9%	1.77E-02	1.70E-02	4.1%	1.78E-02	1.67E-02	6.5%	1.81E-02	1.64E-02	10.1%
Pancreas	7.29E-02	7.27E-02	0.3%	7.17E-02	7.12E-02	0.7%	3.27E-02	3.25E-02	0.8%	7.66E-02	7.61E-02	0.7%	5.88E-02	5.77E-02	1.9%
Small intestine	1.57E-02	1.43E-02	10.1%	1.44E-02	1.33E-02	8.2%	1.17E-02	1.07E-02	9.1%	1.49E-02	1.35E-02	10.4%	1.15E-02	9.32E-03	23.3%
Spleen	2.10E-02	2.04E-02	3.0%	2.27E-02	2.22E-02	2.0%	1.39E-02	1.35E-02	3.0%	1.97E-02	1.91E-02	3.2%	1.11E-02	9.95E-03	11.3%
Extrathoracic airways (ET)	4.54E-03	4.24E-03	7.1%	3.91E-03	3.70E-03	5.4%	3.88E-03	3.72E-03	4.2%	4.22E-03	3.91E-03	8.0%	3.09E-03	2.48E-03	24.6%
Thymus	6.62E-03	5.45E-03	21.3%	5.86E-03	4.99E-03	17.5%	5.67E-03	5.04E-03	12.6%	5.94E-03	4.80E-03	23.8%	4.94E-03	3.43E-03	44.2%
Effective dose coefficient	1.68E-02	1.61E-02	4.4%	1.47E-02	1.42E-02	3.7%	1.24E-02	1.20E-02	3.2%	1.55E-02	1.48E-02	4.8%	1.18E-02	1.07E-02	10.0%

Zvereva et al., 2016



Future Developments

- Biokinetic data and models including radiopharmaceuticals
- Next generation mesh-type computational phantoms
- Next generation age-dependent dose coefficients (DCs) for members of the public
- → Implementation of new biokinetic models and DCs in monitoring and in regulation
- Special topic hot particles
- → Patient specific internal dosimetry in medicine
- Microdosimetry in molecular radiotherapy
- → Machine learning & Deep learning applications

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