

Chapter 18: Internal Dosimetry

**Set of 56 slides based on the chapter authored by
C. Hindorf
of the IAEA publication (ISBN 92-0-107304-6):
*Nuclear Medicine Physics:
A Handbook for Teachers and Students***

Objective: To summarize the formalism of internal dosimetry and present its application in clinical practice.



IAEA

International Atomic Energy Agency

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18.1. The Medical Internal Radiation Dose formalism

18.2. Internal dosimetry in clinical practice

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

Committee Medical Internal Radiation Dose (MIRD)

committee within the Society of Nuclear Medicine, formed in 1965

mission:

to standardize internal dosimetry calculations,
improve published emission data for radionuclide,
enhance data on pharmacokinetics for radiopharmaceuticals

MIRD Pamphlet No. 1 (1968):

unified approach to internal dosimetry, updated several times

MIRD Primer, 1991

most well known version

MIRD Pamphlet 21, 2009

latest publication on the formalism;
meant to bridge the differences in the formalism
used by **MIRD** and International Commission on
Radiological Protection (**ICRP**)



18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

Symbols used in the MIRD formalism

| Symbol | Parameter |
|--------|--------------------|
| R | Type of radiation |
| r_S | Source region |
| r_T | Target region |
| T_D | Integration period |

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

Symbols used to represent quantities and units of the MIRD formalism

| Symbol | Quantity | Unit |
|------------------------------------|---|--|
| $\tilde{A}(r_S, T_D)$ | Time-integrated activity | Bq · s |
| $\tilde{a}(r_S, T_D)$ | Time-integrated activity coefficient | s |
| $D(r_T)$ | Absorbed dose to the target region r_T | Gy |
| \dot{D} | Absorbed dose rate | Gy/s |
| Δ_i | Mean energy of the i th transition per nuclear transformation | J (Bq · s) ⁻¹ or MeV (Bq · s) ⁻¹ |
| E_i | Mean energy of the i th transition | J or MeV |
| $M(r_T, t)$ | Mass of target region | kg |
| $S(r_T \leftarrow r_S, t)$ | Absorbed dose rate per unit activity | mGy (MBq · s) ⁻¹ |
| t | Time | s |
| Y_i | Number of i th transitions per nuclear transformation | (Bq · s) ⁻¹ |
| $\phi(r_T \leftarrow r_S, E_i, t)$ | Absorbed fraction | Dimensionless |
| $\Phi(r_T \leftarrow r_S, E_i, t)$ | Specific absorbed fraction | kg ⁻¹ |

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

The absorbed dose D to a target region from activity in a source region is calculated as the product between the time-integrated activity \tilde{A} and the S value

$$D = \tilde{A} \times S$$

gray (Gy)
(1 J/kg = 1 Gy)

absorbed dose

becquerel · s

cumulated activity:
decays that take place
in a certain source
region

$\text{Gy} \cdot (\text{Bq} \cdot \text{s})^{-1}$
often $\text{mGy} \cdot (\text{MBq} \cdot \text{s})^{-1}$

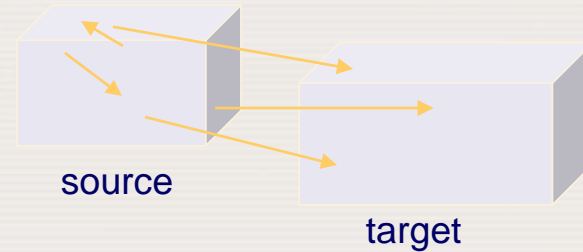
absorbed dose rate per
unit activity, or absorbed
dose per cumulated
activity (or absorbed
dose per decay)

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

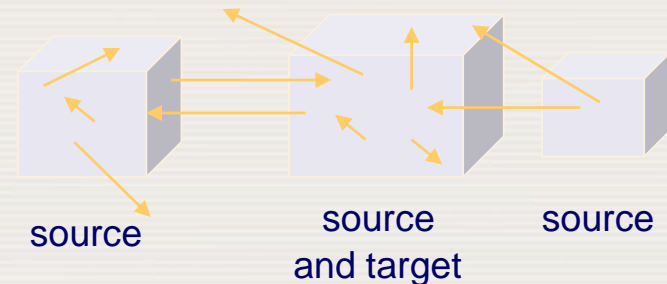
The source region is denoted r_S and the target region r_T :

$$D(r_T) = \tilde{A}(r_S) \cdot S(r_T \leftarrow r_S)$$



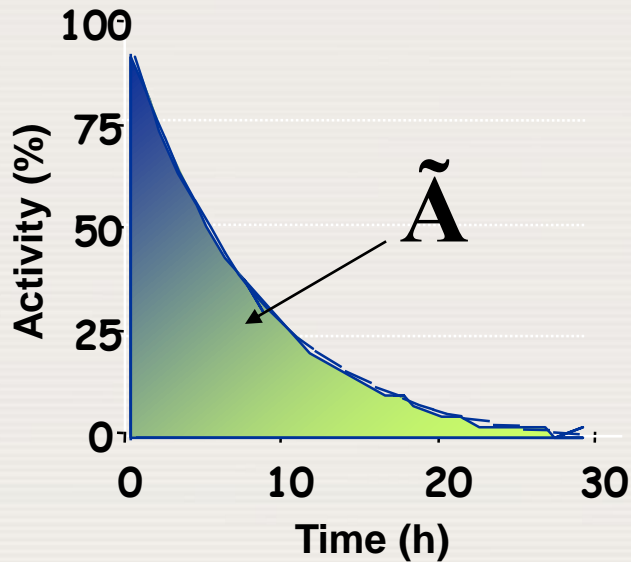
or, in case of several source regions:

$$D(r_T) = \sum_S \tilde{A}(r_S) \cdot S(r_T \leftarrow r_S)$$



18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts



The **number of decays** in the source region, denoted 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 ($A(r_s, t)$).

commonly determined by

- ➡ consecutive **quantitative imaging** sessions;
- ➡ direct measurements of the **activity on a tissue** biopsy or a blood sample
- ➡ single **probe measurements** of the activity in the whole body.
- ➡ **compartmental modelling** (theoretical method)

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18.1.1. Basic concepts

The time-integration period is commonly chosen from the time of administration of the radiopharmaceutical until infinite time. However, the integration period should be matched to the **biological endpoint** studied in combination with the time period in which the **relevant absorbed dose is delivered** (T_D).

$$\tilde{A}(r_S) = \int A(r_S, t) dt = \int_0^{T_D} A(r_S, t) dt = \tilde{a}(r_S) \cdot A_0$$

$$\tilde{a}(r_S) = \frac{\tilde{A}(r_S)}{A_0}$$

Is defined as the **time-integrated activity coefficient**, being A_0 the administered activity; it has the unit of time (e.g. s, or h). In the MIRD Primer it was named '**residence time**'

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

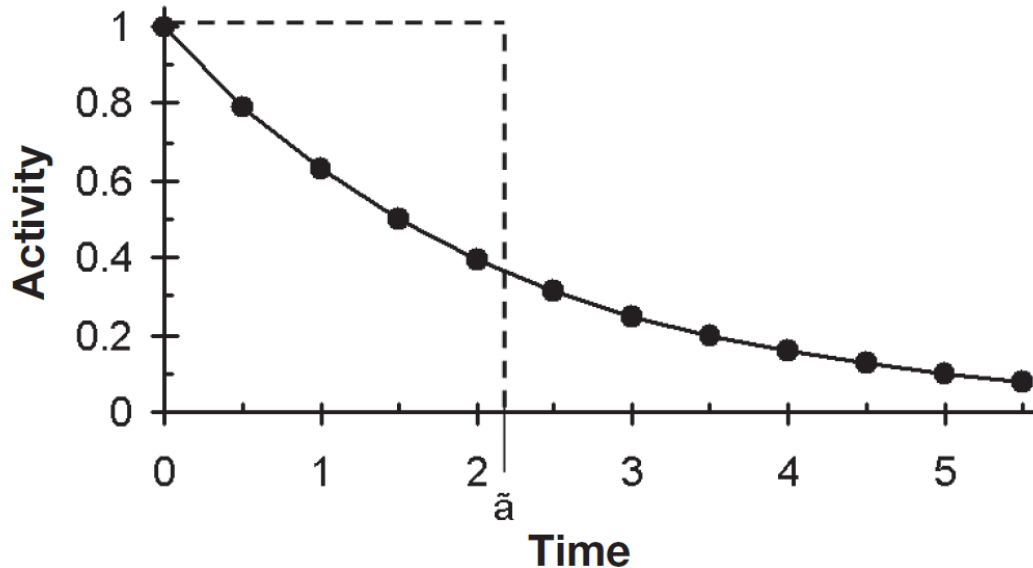


FIG. 18.1. The time-integrated activity coefficient (the residence time in the MIRD Primer [18.3]) is calculated as the time-integrated activity divided by the injected activity, which gives an average time the activity spends in the source region.

The **area under the curve** $A(t)$ equals the area for the **rectangle** and \bar{a} , the number of decays per unit activity, can be described also as an average **time that the activity spends in a source region**.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

$$S = \frac{E Y \phi}{M(r_T)}$$

Energy emitted

probability Y for radiation with energy E to be emitted

absorbed fraction of the energy emitted from the source region that is absorbed in the target region.

$EY: \Delta$

mean energy emitted per decay of the radionuclide

mass of target region



depends on the **shape, size and mass** of the source and target regions, the **distance** and **type** of material between the source and the target regions, the **type of radiation** emitted from the source and the **energy** of the radiation

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

The full formalism also includes a summation over **all of the transitions i per decay**

$$S(r_T \leftarrow r_S) = \sum_i \frac{\Delta_i \phi(r_T \leftarrow r_S, i)}{M(r_T)}$$

ϕ divided by the mass of the target region is named the **specific absorbed fraction Φ** :

$$\Phi(r_T \leftarrow r_S, E_i) = \frac{\phi(r_T \leftarrow r_S, E_i)}{M(r_T)}$$

The mass of both the source and target regions can vary in time: ϕ will change as a function of time after the administration (e.g. tumours, thyroid, lymph nodes)

$$\Phi(r_T \leftarrow r_S, E_i, t) = \frac{\phi(r_T \leftarrow r_S, E_i, t)}{M(r_T, t)}$$

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

The **total mean absorbed dose** to the target region $D(r_T)$ is given by summing the separate **contributions from each source** region r_S

$$D(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S)$$

The **self-absorbed dose**

- commonly gives the largest fractional contribution to the total absorbed dose in a target region
- refers to when the source and target regions are identical,

The **cross-absorbed dose**

- when source and the target regions are different

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.1. Basic concepts

The full time dependent version of the MIRD formalism includes the the absorbed dose rate (\dot{D}):

$$D(r_T, T_D) = \sum_{r_S} \int_0^{T_D} \dot{D}(r_T, t) dt = \sum_{r_S} \int_0^{T_D} A(r_S, t) S(r_T \leftarrow r_S, t) dt$$

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.2. The time-integrated activity in the source region

\tilde{A}
time-integrated activity
in a source region

- physical meaning: number of decays in the source region during the relevant time period.
- named the cumulated activity in - the MIRD Primer

$A(t)$
activity vs. time-integrated activity
in a source region

often described by a sum of exponential functions

(j = number of exponentials, A_j = initial activity for the j th exponential, λ = decay constant for the radionuclide, λ_j = biological decay constant, t the time after administration.

The sum of the j coefficients A_j gives the total activity in the source region at the time of administration ($t = 0$):

$$A(r_T, t) = \sum_j A_j \cdot e^{-t(\lambda + \lambda_j)}$$

$$\lambda = \frac{\ln 2}{T_{1/2}}$$



$$\frac{1}{T_{1/2, \text{eff}}} = \frac{1}{T_{1/2, j}} + \frac{1}{T_{1/2}}$$

The physical half-life $T_{1/2}$ and the biological half-life $T_{1/2, j}$ can be combined into an effective half-life $T_{1/2, \text{eff}}$

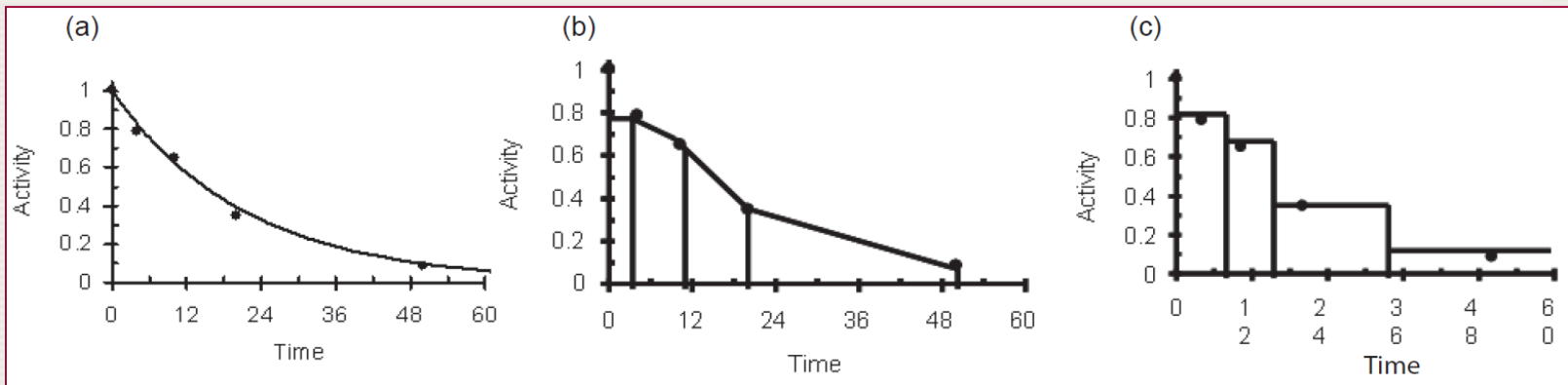
18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.2. The time-integrated activity in the source region



$$\tilde{A} = \int_0^{\infty} A(r_S, 0) e^{-t(\lambda + \lambda_j)} dt = \frac{A(r_S, 0)}{\lambda + \lambda_j} \quad \text{a}$$

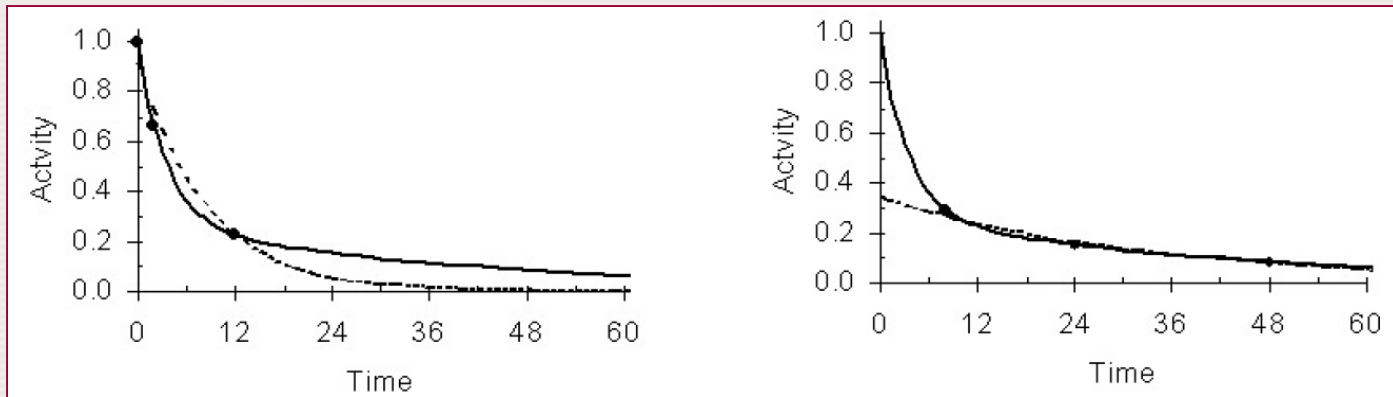
Besides the time integral of multiexponential functions (a), other functions could be used, such as trapezoidal (b) or Riemann integration (c)



18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.2. The time-integrated activity in the source region

Biological data collection impacts on absorbed dose accuracy.



The **shape of the fitted curve** can be strongly influenced by the **number and timing** of the individual activity measurements

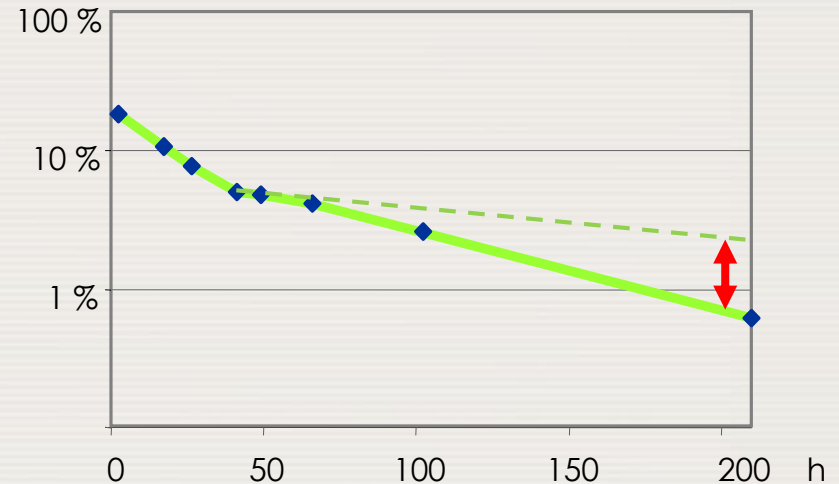
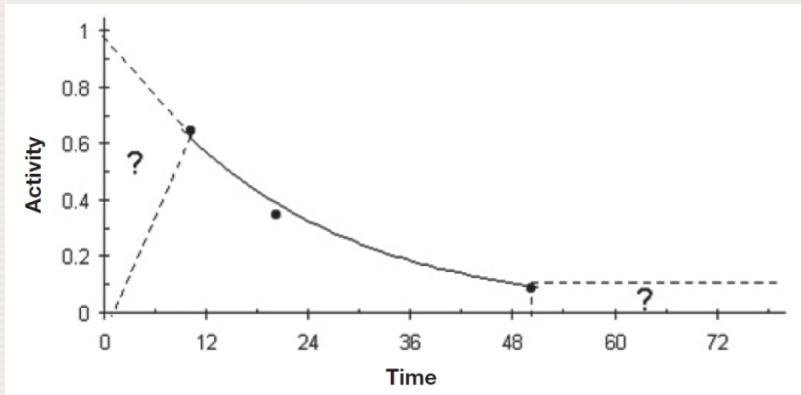
Three data points per exponential phase should be considered the minimum data required to determine the pharmacokinetics

Data points should be followed for at least two to three effective half-lives.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.2. The time-integrated activity in the source region

Extrapolation **from time zero** to the first measurement of the activity, and extrapolation from the last measurement **to infinity**, can also strongly influence the accuracy in the time-integrated activity.



18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

S value for a certain radionuclide and source–target combination: generated from **Monte Carlo simulations** in a computer model of the anatomy.

First models

Analytical phantoms, anatomy described by analytical equations, with spheres or cylinders placed in the coordinate system to represent structures of the anatomy. Several **analytical phantoms** exist: adult **man**, non-pregnant **female**, **pregnant** woman for each trimester of pregnancy, **children** (from the newborn and up to 15 years of age) as well as models of the **brain**, **kidneys** and unit density **spheres**.

Second generation of phantoms

Voxel based phantoms, offering the possibility of more detailed models of the anatomy. They can be based on the **segmentation of organs** from tomographic image data, such as CT images.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

Third generation phantoms

Created using Non-Uniform Rational Spline (**NURBS**).

NURBS: mathematical model used in **computer graphics to represent surfaces**, that represents both geometrical shapes and free forms with the same mathematical representation, and **the surfaces are flexible** and can easily be rotated and translated.

Movements in time (breathing, cardiac cycle), can be included, allowing for **4-D representations** of the phantoms.

Anatomical phantoms for the calculation of S values for use in **pre-clinical studies** on **dogs, rats** and **mice** have also been developed.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

**radiation
emissions**

penetrating (p): $\phi_p \approx 0$. \longrightarrow electrons
e.g.
non-penetrating (np): $\phi_{np} \approx 1$ \longrightarrow photons

common assumption, but **oversimplification**

Validity: dependent on the **energy** of the radiation, the **size of the source** region \rightarrow to be assessed on a case by case basis

Electrons: $\phi > 0.9$ if the mass of the unit density sphere is **> 10 g** and the electron energy **< 1 MeV**. Electrons as non-penetrating radiation at an **organ** level (humans). As the mass decreases, the approximation ceases to be valid

Photons: $\phi < 0.1$ if the mass of the sphere **< 100 g** and photon **energy > 50 keV**. Photons as penetrating radiation is valid in **most pre-clinical situations**
As the mass increases, the approximation becomes inappropriate

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

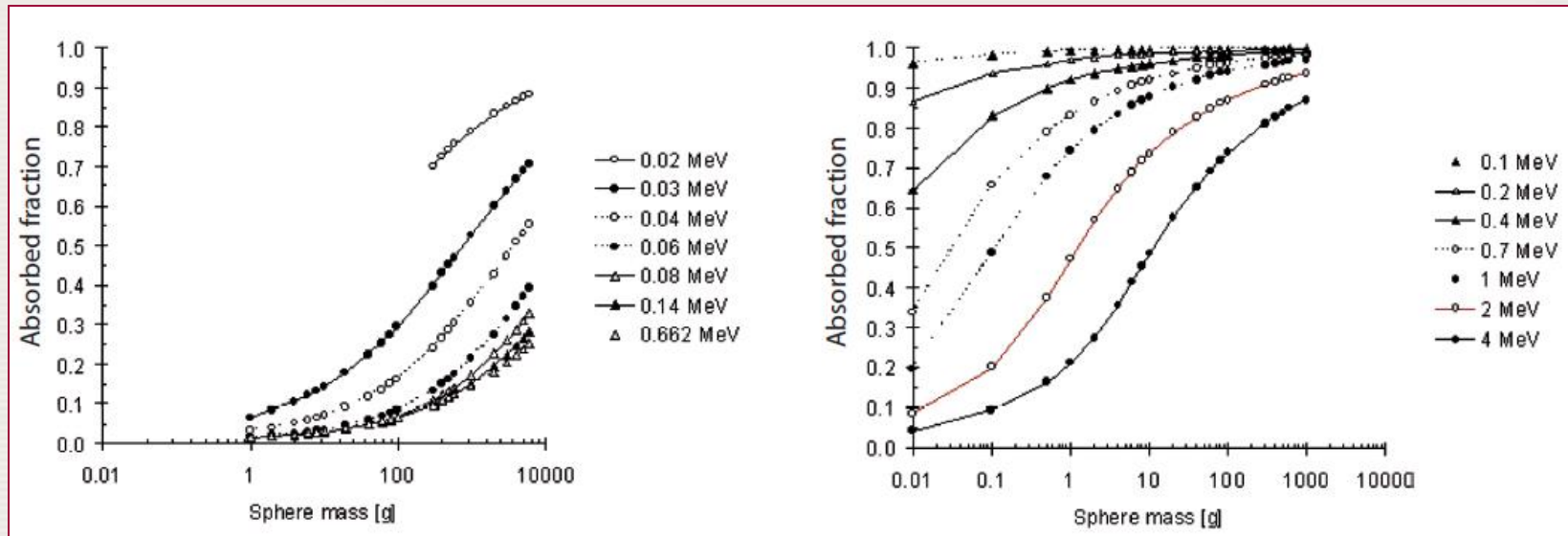
In order to adjust the S value tabulated to the true mass of the target region, the **self absorbed S values** can be scaled by mass according to:

$$S(r_T \leftarrow r_T, \text{scaled}) \approx S(r_T \leftarrow r_T, \text{tabulated}) \cdot \frac{M(r_T, \text{tabulated})}{M(r_T, \text{scaled})}$$

ϕ is considered to be **constant** in the interval of scaling, so the **change in S** is set equal to the **change in mass**

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

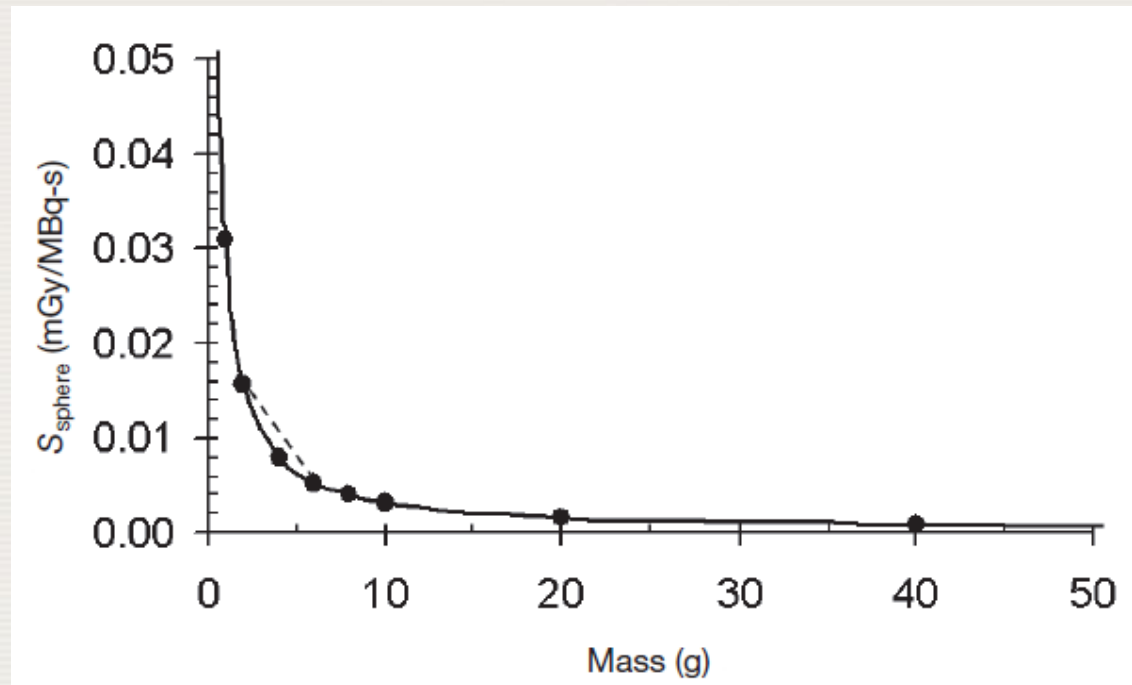


Absorbed fraction for unit density spheres as a function of the **mass** of the spheres for mono-energetic **photons** (left) and **electrons** (right)

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

A linear interpolation should never be performed in S value tables, giving S values that are too large.



18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

The recalculation of the S value can be more accurate by separating the total **S value for penetrating** and one for **non-penetrating radiation (S_p , S_{np})**.

If it is assumed $\phi_{np} = 1$, **S_p can be calculated**.

ϕ for photons are relatively constant, so **S_p can be scaled by mass**.

$$S = S_p + S_{np} = S_p + \frac{\Delta_{np}}{m}$$

$$S_p = \left(S - \frac{\Delta_{np}}{m}\right) \cdot \frac{m_{\text{phantom}}}{m_{\text{true}}}$$

$$S_{\text{recalculated}} = \left(S - \frac{\Delta_{np}}{m}\right) \cdot \frac{m_{\text{phantom}}}{m_{\text{true}}} + \frac{\Delta_{np}}{m}$$

ϕ for photons and electrons vary according to the initial energy and the target volume/mass, so the suitability of the recalculation will also vary.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

principle of reciprocity:

$$S(r_T \leftarrow r_S) \cong S(r_S \leftarrow r_T)$$

the S value is approximately the same for a given combination of source and target regions:

Valid under ideal conditions:

regions with a uniformly distributed radionuclide, within a material that is **infinite** and **homogenous** or absorbs the **radiation without scatter**.

Although the **ideal conditions** are not present in the human body, the reciprocity principle can be seen in **S value tables for human phantoms** as the numbers are almost **mirrored** along the diagonal axis of the table.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.3. Absorbed dose rate per unit activity (S value)

S values for a sphere of a certain **volume** and **material** should be **scaled according to density** if the material in the sphere is different from the material in the phantom:

$$S_{\text{volume, material X}} = S_{\text{volume, material Y}} \cdot \frac{\phi_{\text{material Y}}}{\phi_{\text{material X}}}$$

The technique can be applied when an *S* value for a unit density sphere is used for the **calculation of the absorbed dose to a tumour made up of bone or lung**.

However, it should be noted that an *S* value with the correct mass could be chosen instead of scaling the *S* value for the correct volume by the density.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4. Strengths and limitations inherent in the formalism

The MIRD formalism is based on two assumptions:

- ❑ (a) **Uniform activity distribution** in the source region;
- ❑ (b) Calculation of the **mean absorbed dose to the target** region

approximations

Strengths of MIRD: its **simplicity and ease** of use.

Limitations: the **absorbed dose may vary** throughout the region.

Absorbed dose D is defined by ICRU* as the ratio of the mean energy imparted and the mass dm

$$D = \frac{d\bar{\varepsilon}}{dm}$$

D is defined at a point, but it is determined from the mean specific energy and is, thus, a mean value

* ICRU: International Commission on Radiation Units and Measurements

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4. Strengths and limitations inherent in the formalism

In an older definition D is the limit of the mean specific energy as the mass approaches zero

$$D = \lim_{m \rightarrow 0} \bar{z}$$

The **specific energy z** is the dosimetric quantity that considers stochastic effects and is, thus, not based on mean values. It represents a **stochastic distribution** of individual **energy deposition events ε** divided by the mass **m** in which the energy was deposited:

$$z = \frac{\varepsilon}{m}$$

[J/kg = Gy]



→ especially important in **microdosimetry** (the study of energy deposition spectra within small volumes corresponding to the size of a cell or cell nucleus)

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4. Strengths and limitations inherent in the formalism

The **energy imparted** to a given volume is the sum of all energy **deposits** ε_i in the volume

$$\mathcal{E} = \sum_i \varepsilon_i$$

Each ε_i is the energy deposited in a single interaction, where:

ε_{in} is the **kinetic** energy of the **incident** ionizing particle

ε_{out} is the sum of the **kinetic** energies of all ionizing particles **leaving** the interaction

Q is the change in the rest energies of the nucleus and of all of the particles involved in the interaction

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

If the rest **energy decreases**, **Q** has a **positive** value; if the rest energy **increases**, it has a **negative** value. The unit of energy imparted/deposited is J or eV.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4. Strengths and limitations inherent in the formalism

The **absorbed dose is a macroscopic entity** - the mean value of the specific energy per unit mass - but is **defined at a point in space**.

For an extended volume (e.g. an organ in the body), containing a distributed radioactive source, the **mean absorbed dose** is a true **representation** of the **absorbed dose** to the target volume, if **radiation or charged particle equilibrium** exist.



i.e. the energy entering the volume equals the energy leaving the volume for both charged and uncharged radiation.

- The radioactive source must be **uniformly** distributed
- The **atomic** composition of the medium must be **homogeneous**
- The **density** of the medium must be **homogeneous**
- No electric or magnetic fields** may disturb the paths of the charged particle

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4. Strengths and limitations inherent in the formalism

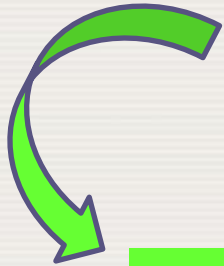
Charged particle equilibrium \leftarrow radiation equilibrium

but

Charged particle equilibrium $\not\rightarrow$ radiation equilibrium

If **only charged particles** are emitted from the radioactive source (e.g. ^{90}Y , ^{32}P), **charged particle equilibrium** exists if radiative **losses are negligible**.

Radiative losses increase with increasing electron energy and with an increase in the atomic number of the medium.



The maximum β energy for pure β emitters commonly used in nuclear medicine (e.g. ^{90}Y , ^{32}P and ^{89}Sr) is < 2.5 MeV and the ratio of the radiative stopping power to the total stopping power is 0.018 and 0.028 for skeletal muscle and cortical bone, respectively, for an electron energy of 2.5 MeV.

Radiative losses could be neglected in internal dosimetry and charged particle equilibrium could be assumed

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

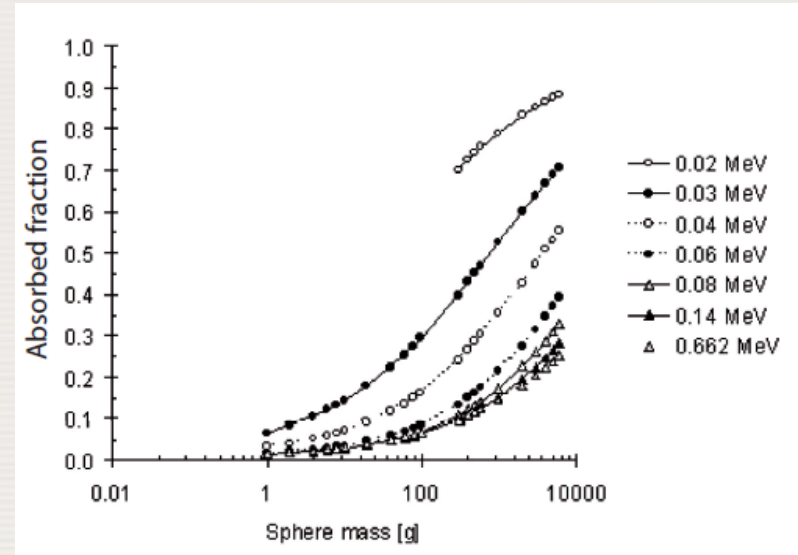
18.1.4. Strengths and limitations inherent in the formalism

If both charged and uncharged particles (photons) are emitted (as is the case with most radionuclides used in nuclear medicine),

charged particle equilibrium exists if the interaction of the uncharged particles within the volume is negligible

Negligible number of interactions

→ photon absorbed fraction is low.



The relative **photon contribution** for a radionuclide is also **dependent on the energy** and the **probability of emission of electrons**. For example, the photon contribution to the absorbed dose cannot be disregarded for ^{111}In in a 10 g sphere, where the photons contribute 45% to the total S value.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4.1. Non-uniform activity distribution

□ Activity distribution is not completely uniform over the whole tissue

→ The non-uniformity in the activity distribution can be overcome by redefining the source region into a smaller volume.

→ feasible until the activity per unit volume becomes small enough to cause a break-down of radiation and charged particle equilibrium

□ Redistribution of the radioactive atoms over time

→ non-uniformities of the absorbed dose distribution over time

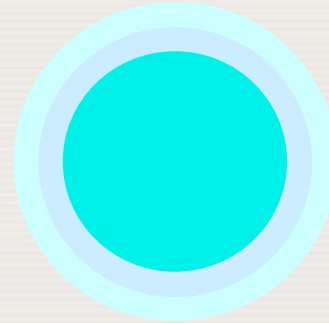
→ MIRDO formalism takes this into account by the concept of cumulated activity, i.e. the total **number of decays during the time of integration** (e.g. u. bladder).

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

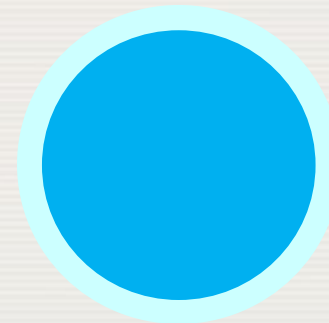
18.1.4.2. Non-uniform absorbed dose distribution

Activity of α or β emitting radionuclide uniformly distributed within a sphere of radius R

The **D distribution will be uniform** from the centre of the sphere out to a **distance from the rim** corresponding to the range of the most energetic particle emission.



If $R \gg$ **particle emission ranges**
→ radiation equilibrium except at the rim
→ **D mean** representative value of D



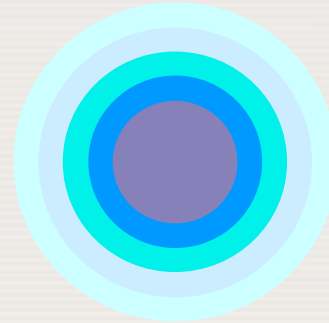
18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4.2. Non-uniform absorbed dose distribution

Activity of α or β emitting radionuclide **uniformly distributed** within a sphere of radius R

If $R \sim$ range of electrons
significant gradients in D at
the borders of the sphere

$$D_{\text{border}} \sim \frac{1}{2} D_{\text{centre}}$$



If $R <$ range of the electrons
never charged particle equilibrium
D distribution never uniform



For α emitting radionuclides, **D is uniform** for almost all sized spheres, **except within 70–90 μm from the rim**, corresponding to the α particle range.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4.2. Non-uniform absorbed dose distribution

Interfaces between media (e.g. soft tissue/bone or soft tissue/air)

will cause **non-uniform D distribution** due to differences in backscatter.

Significant when estimating the contribution of **absorbed dose to the stem cells** in the **bone marrow from backscatter off the bone surfaces**.

For **^{90}Y** and planar geometry, the maximum increase in D was **9%** (Monte Carlo simulations). Experimental measurements with **^{32}P** showed a maximal increase of **7%**. For a spherical interface with a 0.5 mm radius of curvature, the absorbed dose to the whole sphere showed a maximum increase **for 0.5 MeV electrons** of as much as **12%**.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4.2. Non-uniform absorbed dose distribution

Cross-absorbed doses

(e.g. lung and heart)

Non-uniform D distribution are caused when **one organ is next to another**. Cross-organ absorbed dose from high energy β emitters (e.g. ^{90}Y , ^{32}P), can be **significant in preclinical small animal studies**, but **in humans**, cross-absorbed dose occurs from **penetrating photon radiation only** (the separation between organs is sufficient).

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.1.4.2. Non-uniform absorbed dose distribution

To summarize, a number of **factors causing non-uniformity in the absorbed dose distribution** have been identified:

- ❑ **Edge effects** due to lack of radiation equilibrium;
- ❑ **Lack of radiation and charged particle equilibrium** in the whole volume (high energy electrons emitted in a small volume);
- ❑ **Few atoms** in the volume, causing a lack of radiation equilibrium and introduction of stochastic effects;
- ❑ **Temporal non-uniformity** due to the kinetics of the radiopharmaceutical;
- ❑ **Gradients** due to hot spots;
- ❑ **Interfaces** between media causing backscatter;
- ❑ **Spatial non-uniformity** in the activity distribution.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.1. Introduction

Internal dosimetry : different purposes → different levels of accuracy:

- ❑ Dosimetry for **diagnostic** procedures utilized in nuclear medicine;
- ❑ Dosimetry for **therapeutic** procedures (radionuclide therapy);
- ❑ Dosimetry in conjunction with **accidental intake** of radionuclides.

Dosimetry for diagnostic procedures

To optimize the procedure concerning **radiation protection** consistent with an **accurate diagnostic** test. The mean pharmacokinetics for the radiopharmaceutical should be utilized for the calculation of the time-integrated activity and S values based on a reference man phantom.

Absorbed dose / injected activity for most radiopharmaceuticals used for diagnostic procedures are in **ICRP 53**, updates in **ICRP 80** and **ICRP 106**.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.1. Introduction

Dosimetry for therapeutic procedures

To **optimize the treatment** so as to achieve the highest possible absorbed dose to the tumour, consistent with absorbed dose limiting toxicities.

Individualized treatment planning should be performed that takes into account the patient specific pharmacokinetics and biodistribution of the therapeutic agent.

Dosimetry in case of accidental intake of radionuclides

The procedure to apply after an accidental intake of radionuclides must be **decided on a case by case basis**, depending on: level of activity, radionuclide, number of persons involved, retrospective dosimetry or as a precaution, possibility to perform measurements after the intake.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level

Dosimetry on an organ level

Imaging: activity quantification using 2-D or 3-D images

2-D images: **whole body** scans or **spot views** covering the regions of interest

3D-SPECT: limited field of view including the essential structures of interest

3D-PET: is emerging due to greater ease and accuracy of radiotracer quantification with this modality

3-D tomographic methods **avoid problems** associated with corrections for activity in **overlying and underlying tissues** (e.g. muscle, gut and bone), and corrections for activity in partly **overlapping tissues** (e.g. liver and right kidney)

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level

S value tables for human phantoms

can be found in

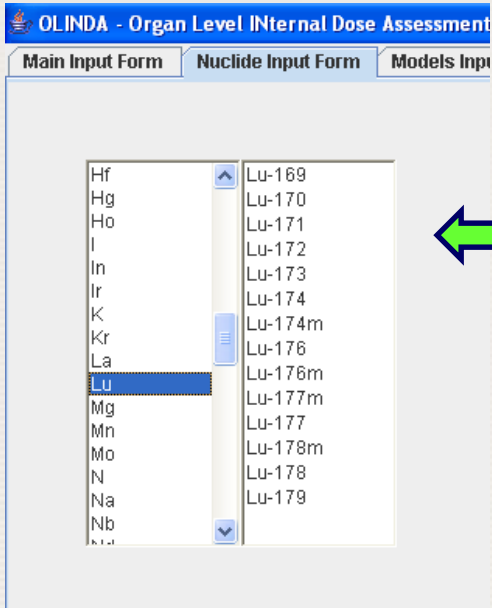
- **MIRD Pamphlet No. 11**
- in the **OLINDA/EXM** software
- on the **RADAR web site** (www.doseinfo-radar.com)



OLINDA/EXM: Organ Level Internal Dose Assessment/exponential modelling. Software for the calculation of absorbed dose to different organs in the body, being MIRDOSE 3.1 its predecessor.

OLINDA/EXM also includes a module **for biokinetic analysis**, allowing the user to fit an **exponential equation** to the data entered on the activity in an organ at different time points.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level



OLINDA includes S values 
 for most radionuclides (> 800)

Dose Conversion Factors:

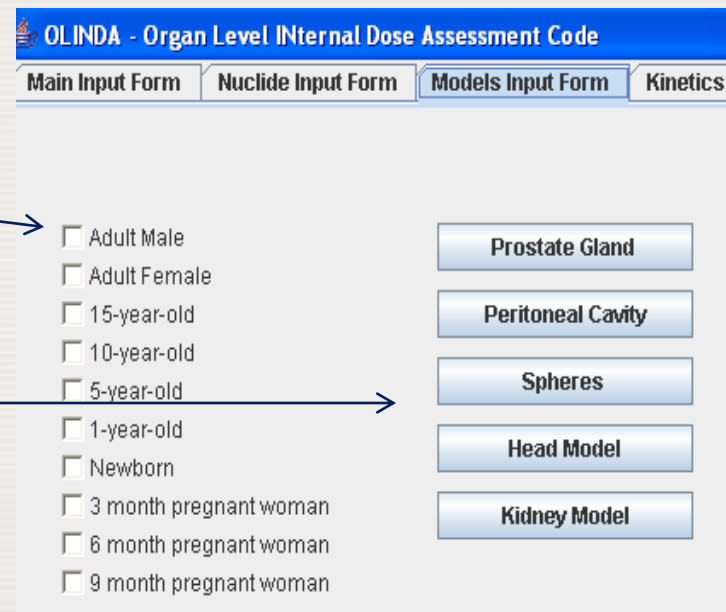
File View

OLINDA - Organ Level Internal Dose Assessment Code (Version 1.1, copyright Vanderbilt University, 2007)

Dose Conversion Factors (mSv/MBq-s), Nuclide: Lu-177 (6.73E00 day), Adult Male

| | Adrenals | Brain | Breasts | GB Cont | LLI Cont | SI Cont | StomCont | ULI Cont |
|----------------------|----------|----------|----------|----------|----------|----------|----------|----------|
| Adrenals | 1.46E-03 | 1.39E-10 | 1.35E-08 | 8.58E-08 | 6.60E-09 | 1.97E-08 | 7.50E-08 | 2.42E-0 |
| Brain | 1.39E-10 | 1.73E-05 | 9.72E-10 | 5.81E-11 | 6.70E-12 | 1.60E-11 | 1.78E-10 | 1.89E-1 |
| Breasts | 1.35E-08 | 9.72E-10 | 6.94E-05 | 8.69E-09 | 7.68E-10 | 2.24E-09 | 1.53E-08 | 2.50E-0 |
| Gallbladder Wall | 9.31E-09 | 5.68E-11 | 9.19E-09 | 2.15E-04 | 1.67E-08 | 1.19E-07 | 8.03E-08 | 2.00E-0 |
| LLI Wall | 5.95E-09 | 5.71E-12 | 6.08E-10 | 1.49E-08 | 8.35E-05 | 1.62E-07 | 2.40E-08 | 5.93E-0 |
| Small Intestine | 1.97E-08 | 1.60E-11 | 2.24E-09 | 1.25E-07 | 2.00E-07 | 2.82E-05 | 5.48E-08 | 3.49E-0 |
| Stomach Wall | 7.58E-08 | 9.23E-11 | 1.62E-08 | 8.03E-08 | 3.47E-08 | 5.82E-08 | 4.64E-05 | 7.79E-0 |
| ULI Wall | 2.93E-08 | 1.93E-11 | 2.27E-09 | 2.13E-07 | 8.33E-08 | 3.78E-07 | 7.17E-08 | 5.17E-0 |
| Heart Wall | 7.66E-08 | 8.55E-10 | 7.44E-08 | 2.75E-08 | 1.67E-09 | 5.69E-09 | 6.43E-08 | 8.21E-0 |
| Kidneys | 2.01E-07 | 5.71E-11 | 5.70E-09 | 1.03E-07 | 1.93E-08 | 5.77E-08 | 7.42E-08 | 5.72E-0 |
| Liver | 1.22E-07 | 2.65E-10 | 1.91E-08 | 2.25E-07 | 4.94E-09 | 3.14E-08 | 3.97E-08 | 5.07E-0 |
| Lungs | 6.42E-08 | 2.25E-09 | 6.52E-08 | 1.86E-08 | 1.42E-09 | 3.77E-09 | 2.97E-08 | 4.70E-0 |
| Muscle | 3.11E-08 | 6.15E-09 | 1.20E-08 | 3.18E-08 | 3.38E-08 | 3.08E-08 | 2.77E-08 | 2.93E-0 |
| Ovaries | 9.92E-09 | 6.67E-12 | 7.94E-10 | 2.84E-08 | 3.51E-07 | 2.54E-07 | 1.54E-08 | 2.11E-0 |
| Pancreas | 3.00E-07 | 1.62E-10 | 1.69E-08 | 1.83E-07 | 1.32E-08 | 3.77E-08 | 3.44E-07 | 4.37E-0 |
| Red Marrow | 6.85E-08 | 2.75E-08 | 1.57E-08 | 2.79E-08 | 5.67E-08 | 4.86E-08 | 2.89E-08 | 3.91E-0 |
| Osteogenic Cells | 6.88E-08 | 7.85E-08 | 2.00E-08 | 2.71E-08 | 4.59E-08 | 3.61E-08 | 2.50E-08 | 3.10E-0 |
| Skin | 9.53E-09 | 1.16E-08 | 2.15E-08 | 8.79E-09 | 1.00E-08 | 8.36E-09 | 9.58E-09 | 8.79E-0 |
| Spleen | 1.26E-07 | 2.24E-10 | 1.25E-08 | 3.41E-08 | 1.66E-08 | 2.70E-08 | 2.15E-07 | 2.74E-0 |
| Testes | 5.20E-10 | 7.62E-13 | 0.000000 | 2.14E-09 | 3.95E-08 | 7.00E-09 | 9.86E-10 | 5.70E-0 |
| Thyroid | 1.61E-08 | 2.15E-09 | 6.75E-08 | 4.20E-09 | 6.68E-10 | 1.46E-09 | 1.04E-09 | 1.74E-0 |
| Thyroid | 2.24E-09 | 3.69E-08 | 8.01E-09 | 8.10E-10 | 9.34E-11 | 1.55E-10 | 8.68E-10 | 2.72E-1 |
| Urinary Bladder Wall | 2.28E-09 | 2.82E-12 | 4.53E-10 | 1.24E-08 | 1.37E-07 | 5.77E-08 | 5.17E-09 | 4.31E-0 |
| Uterus | 5.88E-09 | 5.77E-12 | 8.93E-10 | 3.95E-08 | 1.42E-07 | 2.30E-07 | 1.32E-08 | 1.07E-0 |
| Total Body | 3.98E-07 | 3.45E-07 | 3.39E-07 | 6.64E-08 | 2.22E-07 | 2.92E-07 | 1.27E-07 | 1.88E-0 |

for **ten different human phantoms** (adult and children at different ages, pregnant and non-pregnant female phantoms) and for **5 specific models** (prostate, peritoneal cavity, spheres, head, kidney)



18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level

| | | | |
|----------|--------|-------------------|--------|
| Adrenals | 0.0000 | Ovaries | 0.0000 |
| Brain | 0.0000 | Pancreas | 0.0000 |
| Breasts | 0.0000 | Red Mar. | 0.30 |
| GB Cont | 0.0000 | CortBone | 0.0000 |
| LLI Cont | 0.0000 | TrabBone | 0.0000 |
| SI Cont | 0.0000 | Spleen | 1.9 |
| StomCont | 0.0000 | | |
| ULI Cont | 0.0000 | Thymus | 0.0000 |
| HeartCon | 0.0000 | Thyroid | 0.0000 |
| Hrt Wall | 0.0000 | UB Cont | 0.0000 |
| Kidneys | 2.1 | Uterus | 0.0000 |
| Liver | 1.6 | | |
| Lungs | 0.2 | | |
| Muscle | 0.0000 | Tot Body/Rem Body | 15 |

Get setup (stp) file

Bone Activity on Bone Surfaces

Bone Activity in Bone Volume ← \tilde{a} (input)

Voiding Bladder Model

ICRP GI Model

Fractions and Half-times

Fit data to Model

absorbed
doses
(output) ←

Organ doses

Organ Doses (mSv/MBq), Nuclide: Y-90 (6.41E01 hr), Adult Male

| Target Organ | Alpha | Beta | Photon | Total | EDE Cont. | ED Cont. |
|------------------|----------|----------|----------|----------|-----------|----------|
| Adrenals | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 6.75E-03 | 2.81E-04 |
| Brain | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 2.81E-04 |
| Breasts | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 1.69E-02 | 5.63E-03 |
| Gallbladder Wall | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 0.00E000 |
| LLI Wall | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 1.35E-02 |
| Small Intestine | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 2.81E-04 |
| Stomach Wall | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 1.35E-02 |
| ULI Wall | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 2.81E-04 |
| Heart Wall | 0.00E000 | 1.13E-01 | 0.00E000 | 1.13E-01 | 0.00E000 | 0.00E000 |
| Kidneys | 0.00E000 | 3.69E000 | 0.00E000 | 3.69E000 | 2.21E-01 | 9.22E-03 |
| Liver | 0.00E000 | 4.79E-01 | 0.00E000 | 4.79E-01 | 2.88E-02 | 2.40E-02 |
| Lungs | 0.00E000 | 1.08E-01 | 0.00E000 | 1.08E-01 | 1.29E-02 | 1.29E-02 |

Modify Input Data
Next Phantom
Previous Phantom
Main M

See Source Organ Contributions
Mult. Doses by (MBq):

Exit

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level

OLINDA – Specific models

Output:

absorbed doses
mGy/MBq; cGy/mCi

brain model

Input: \tilde{a}
(MBq-h / MBq)

kidney model

MIRD Head and Brain Model

Enter the number of disintegrations/A0 (uCi-h/uCi or MBq-h/MBq) for:

| | |
|---------------------|-----|
| Whole Brain: | 0 |
| Caudate Nucleus: | 1 |
| Cerebellum: | 0 |
| Cerebral Cortex: | 0 |
| Cranial CSF: | 3 |
| Cranium: | 0 |
| Lateral Ventricles: | 0 |
| Lentiform Nuclei: | 0 |
| Spinal CSF: | 2 |
| Spinal Skeleton: | 0 |
| Thalami: | 0 |
| Third Ventricle: | 0 |
| Thyroid: | 1.2 |
| White Matter: | 0 |

Doses from Nuclide: Lu-177 in Head Model, Adult

| Target Organ | Dose (mGy/MBq) |
|---------------|----------------|
| Brain | 6.86E-02 |
| Caud. Nucl. | 7.78E000 |
| Cerebellum | 1.26E-02 |
| Cereb. Cort. | 1.67E-02 |
| Cranium | 2.43E-02 |
| Eyes | 2.96E-03 |
| Lent. Nucl. | 2.33E-02 |
| Mandible | 4.02E-03 |
| Other Tissues | 5.90E-03 |
| Skin | 3.01E-03 |
| Spinal Col. | 1.69E-01 |
| Spinal Skel. | 3.78E-02 |
| Thalami | 1.17E-02 |
| Thyroid | 4.93E000 |

Adult

- 15-Yr-Old
- 10-Yr-Old
- 5-Yr-Old
- 1-Yr-Old
- Newborn

Calculate Doses DONE

MIRD Multipart Kidney Model

Enter the Number of disintegrations/A0 (uCi-h/uCi or MBq-h/MBq) for:

| | |
|-----------------|------|
| Renal Cortex: | 1.62 |
| Renal Medulla: | 0.65 |
| Renal Pelvis: | 0.18 |
| Renal Papillae: | 0 |

Adult

- 15-Yr-Old
- 10-Yr-Old
- 5-Yr-Old
- 1-Yr-Old
- Newborn

Doses from Nuclide: Lu-177 in Kidney Model 15-yr-old

| Target Organ | Dose (mGy/MBq) |
|--------------|----------------|
| Cortex | 8.02E-01 |
| Medulla | 9.13E-01 |
| Pelvis | 1.44E000 |
| Papillae | 1.78E-01 |

Doses from Nuclide: Lu-177 in Kidney Model 15-yr-old

| Target Organ | Dose (rad/mCi) |
|--------------|----------------|
| Cortex | 2.97E000 |
| Medulla | 3.38E000 |
| Pelvis | 5.33E000 |
| Papillae | 6.59E-01 |

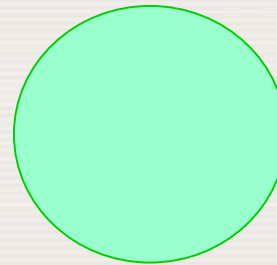
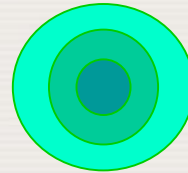


18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level

Tumours are not included in the phantoms, although the **S values for unit density spheres** could be applied for the calculation of the **self-absorbed dose to the tumour**.

The drawback is that neither the contribution from the cross-absorbed dose from activity in normal organs to the tumour nor the cross-absorbed dose from activity in the tumour to normal organs can be included in the calculations.



Doses from Nuclide: I-131
in Spheres:

Sphere Mass (g) Dose
(mGy/MBq)

| | |
|--------|----------|
| 0.01 | 9.68E03 |
| 0.1 | 1.04E03 |
| 0.5 | 2.14E02 |
| 1.0 | 1.11E02 |
| 2.0 | 5.62E01 |
| 4.0 | 2.85E01 |
| 6.0 | 1.92E01 |
| 8.0 | 1.45E01 |
| 10.0 | 1.17E01 |
| 20.0 | 5.94E00 |
| 40.0 | 3.03E00 |
| 60.0 | 2.05E00 |
| 80.0 | 1.56E00 |
| 100.0 | 1.26E00 |
| 300.0 | 4.43E-01 |
| 400.0 | 3.39E-01 |
| 500.0 | 2.75E-01 |
| 600.0 | 2.31E-01 |
| 1000.0 | 1.44E-01 |
| 2000.0 | 7.63E-02 |
| 3000.0 | 5.29E-02 |
| 4000.0 | 4.10E-02 |
| 5000.0 | 3.34E-02 |
| 6000.0 | 2.84E-02 |

self-doses

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.2. Dosimetry on an organ level

Modify input data

| Masses (g) for the Adult Female | | ** = Modified by user | |
|---------------------------------|--------------------|---|----------------------|
| Previous Phantom | | Hit <ret> to see changes immediately, or just | |
| 14.0 | Adrenals | 85.0 | Pancreas |
| 1200.0 | Brain | 1300.0 | Red Marrow |
| 360.0 | Breasts | 90.0 | Osteogenic Cells |
| 8.0 | Gallbladder Wall | 1790.0 | Skin |
| 160.0 | LLI Wall | 150.0 | Spleen |
| 600.0 | Small Intestine | 0.0 | Testes |
| 140.0 | Stomach Wall | 20.0 | Thymus |
| 200.0 | ULI Wall | 17.0 | Thyroid |
| 240.0 | Heart Wall | 35.9 | Urinary Bladder Wall |
| 275.0 | Kidneys | 80.0 | Uterus |
| 1400.0 | Liver | 0.0 | Fetus |
| 800.0 | Lungs | 0.0 | Placenta |
| 17000.0 | Muscle | 56912.0 | Total Body |
| 11.0 | Ovaries | | |
| Alpha Weight Factor | Beta Weight Factor | Photon Weight Factor | Reset organ v |
| 5.0 | 1.0 | 1.0 | DONE |
| Multiply all masses by: | 1.0 | | |

S values can be scaled by mass, allowing for a more patient specific dosimetry.

Owing to the inverse relation between the absorbed dose and the mass of the target region, scaling can have a considerable influence on the result.

$$S_{\text{patient}} \approx S_{\text{phantom}} \cdot \frac{m_{\text{phantom}}}{m_{\text{patient}}}$$

Alternatively, it was suggested to **scale the S values to the total mass** of the patient, assuming that the organ size follows the total body mass. The lean body weight should be used to avoid unrealistic organ mass values (S values due to obese or very lean patients).

$$S_{\text{patient}} \approx S_{\text{phantom}} \cdot \frac{m_{\text{TB,phantom}}}{m_{\text{TB,patient}}}$$

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.3. Dosimetry on a voxel level

- ❑ The activity in an image could be **quantified on a voxel level**.
- ❑ **Images** that display the activity distribution at **different points in time** after injection may be **co-registered** → exponential fit on a voxel by voxel basis.
- ❑ A **parametric image** that gives the **time-integrated activity** (the total number of decays) on a voxel level can be calculated
- ❑ A **parametric image** that gives the **biological half-life** for each voxel could also be produced

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.3. Dosimetry on a voxel level

Essential for accuracy

In the calculation of the time-integrated activity on a voxel level and, thus, in the absorbed dose:

- ❑ **registration of the images**
- ❑ acquired number of **counts per voxel** - random error
- ❑ **attenuation correction** - systematic error
- ❑ **calibration factor** (number of counts to activity) – random/systematic errors

Multimodality imaging such as **SPECT/CT** and **PET/CT** facilitates the interpretation of the images: as the **CT** will provide anatomical **landmarks** to support the functional images, which could change from one acquisition to the next.

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.3. Dosimetry on a voxel level

Dose point kernels (DPK)

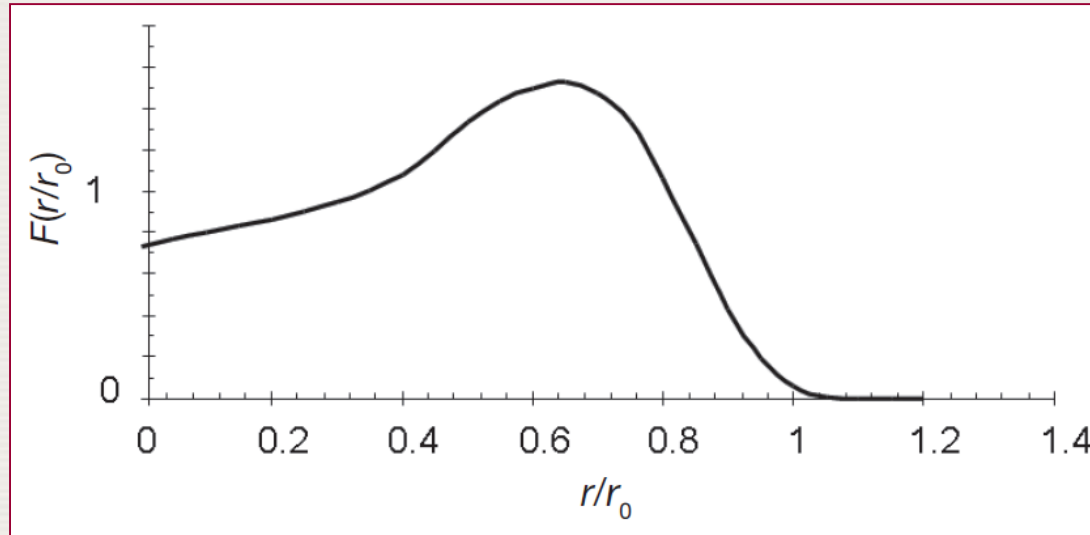
- ❑ describe the **deposited energy** as a function of **distance** from the site of emission of the radiation
- ❑ **convolution** of a dose point **kernel** and the **activity distribution** from an image acquired at a certain time after the injection gives the absorbed dose rate
- ❑ provide a **tool** for fast calculation of the **absorbed dose on a voxel level**
- ❑ main **drawback** is that a DPK is **only valid in a homogenous medium**, where it is commonly assumed that the body is uniformly unit density soft tissue

Monte Carlo simulations

- ❑ use the **activity distribution** from a functional image (PET or SPECT) and the **density distribution** (CT), avoiding the problem of non-uniform media
- ❑ full Monte Carlo simulations are **time consuming**
- ❑ **EGS** (Electron Gamma Shower), **MCNP** (Monte Carlo N-particle transport code), **Geant** and **Penelope** are commonly used Monte Carlo codes

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.3. Dosimetry on a voxel level



A scaled dose point kernel for 1 MeV electrons. r/r_0 expresses the distance scaled to the continuous slowing down approximation range of the electron and

$$\int_0^{\infty} F(r/r_0, E_0) d(r/r_0) = 1$$

18.1 THE MEDICAL INTERNAL RADIATION DOSE FORMALISM

18.2.3. Dosimetry on a voxel level

Dose–Volume Histograms (DVHs)

- ❑ extensively used to describe the **tumour and organ dose distribution** in **EBRT**
- ❑ can be used to display the **non-uniformity** in the absorbed dose distribution from **radionuclide procedures**.
- ❑ **Differential DVH**: shows the volume% that has received a certain absorbed dose as a function of the absorbed dose
- ❑ **Cumulative DVH** shows the volume% that has received an absorbed dose less than the figure given on the x axis.
- ❑ A truly **uniform absorbed dose** distribution would produce a differential DVH that shows a single sharp (**δ function**) peak and a **step function** on a cumulative DVH.
- ❑ **DVHs** might be used to assist the **correlation** between **absorbed dose** and **biological effect** (the mean absorbed dose in internal dosimetry may be a poor representation of the D distributed to the tissue)

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