20. 5. 2003

IAEA Training Course on Radiation Protection in Nuclear Medicine
GAEC, Athens 2003

Dose to the patient in Nuclear Medicine (Clinical Dosimetry)

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CLINICAL DOSIMETRY (BSS)

II.20. Registrants and licensees shall ensure that the following items be determined and documented:

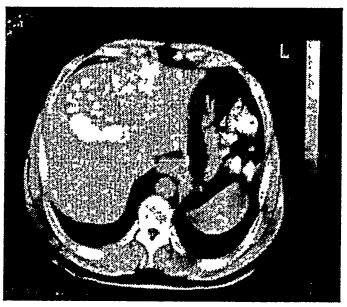
(d) In diagnosis or treatment with unsealed sources, representative absorbed doses to patients;

Conception of absorbed dose in NM

The calculation of the absorbed dose - a tricky problem, because of several factors:

- 1. the distribution of the radionuclide within the body and its uptake in certain critical organs
- 2. inhomogeneous distribution of the nuclide even within the critical organ
- 3. the biological half-life of the nuclide, which may vary with patients' ages and may be modified by disease or pathological conditions.

Treatment of Hepatocellular Carcinoma with ^{131}I-Lipiodol



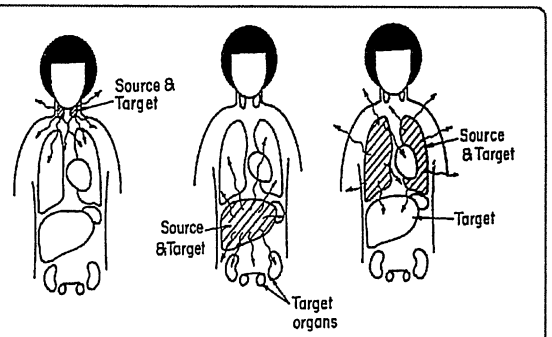
CT scan demonstrating non-homogeneous distribution of Lipiodol. Tumour can not be treated as a homogenous sphere.

Absorbed dose to an organ is determined by:

- Radionuclide
- Activity administered
- Activity in the organ
- Size and shape of the organ
- Activity in other organs
- Kinetics of radiopharmaceutical
- Quality of radiopharmaceutical

The MIRD System of Internal Absorbed Dose Calculation

- MIRD - Medical Internal Radiation Dosimetry developed by the Society of Nuclear Medicine
- The organ containing the radionuclide is called the *source* organ
- We wish to calculate the absorbed dose to the *target* organ
- The source and target organs may be the same
- The amount of radiation from the source reaching the target must be known



Derivation of the General MIRD Equation

- Let E be the mean energy per particle (photon or electron)
- If n is the number of particles emitted per disintegration
- then nE is the mean energy emitted per disintegration

Khorstek → stralo faktor na (yield) en torpad

Mean energy per nuclear transition

Type i radiation

$$\Delta_i = K \cdot n_i \cdot E_i$$

Total energy/disintegration

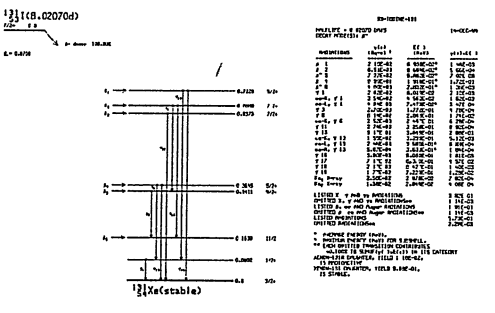
$$\Delta = \sum_i \Delta_i = K \sum_i n_i \cdot E_i$$

Emitted energy

Radionuclide	MeV/disintegration	
	particles	photons
Ga-67	0.0047	0.016
Se-75	0.0143	0.391
Tc-99m	0.0149	0.127
In-111	0.0030	0.405
I-123	0.0236	0.172
I-125	0.0045	0.042
I-131	0.1910	0.382
Tl-201	0.0303	0.093

Decay data

http://iaeand.iaea.or.at/formmird.html



OUTPUT DATA

43 TECHNETIUM 99M HALF LIFE = 6.03 HOURS

DECAY MODE- ISOMERIC LEVEL

RADIATION	MEAN NUMBER/ DISINTE- GRATION n_i	MEAN ENERGY/ PAR- TICLE $\bar{E}_i$ (MeV)	EQUI- LIBRIUM DOSE CONSTANT Δ_i (g-rad/ μCi-h)
GAMMA 1	0.0900	0.0021	0.0000
K INT CON ELECT	0.9840	0.0016	0.0035
GAMMA 2	0.8787	0.1405	0.2430
K INT CON ELECT	0.0913	0.1196	0.0232
L INT CON ELECT	0.0118	0.1377	0.0034
M INT CON ELECT	0.0039	0.1400	0.0011
GAMMA 3	0.0003	0.1426	0.0001
K INT CON ELECT	0.0088	0.1215	0.0022
L INT CON ELECT	0.0035	0.1398	0.0010
M INT CON ELECT	0.0011	0.1422	0.0003
K ALPHA-1 X-RAY	0.0441	0.0183	0.0017
K ALPHA-2 X-RAY	0.0221	0.0182	0.0008
K BETA-1 X-RAY	0.0105	0.0206	0.0004
KLL AUGER ELECT	0.0152	0.0154	0.0005
KLX AUGER ELECT	0.0055	0.0178	0.0002
LMM AUGER ELECT	0.1093	0.0019	0.0004
MXY AUGER ELECT	1.2359	0.0006	0.0011

^{99m}Tc

Required information for dosimetry calculations

Absorbed Dose

- Energy absorbed in a material per unit mass
- has unit of the gray (1 Gy = 1 J/kg)

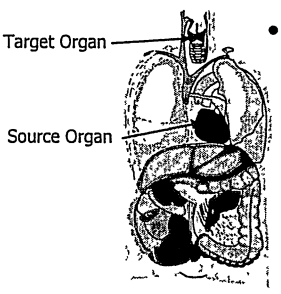
Absorbed Dose in the Target Organ

The **absorbed dose** will be equal to the **total amount of energy** that is **emitted** by the source organ X the **fraction** of that energy that is **absorbed** in the target organ **divided by the mass** of the target organ

Absorbed Fraction

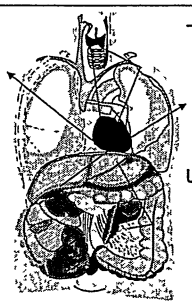
- The absorbed fraction, Φ, is the fraction of the energy emitted by the source organ that is absorbed in the target

Absorbed Fraction



- Depends on
  - the size of the source organ
  - the size of the target organ
  - the relative positions in the body of these organs
  - the energy of the photons
  - the attenuation properties of the tissues between the source and target organs

Determination of the Absorbed Fraction



The only method available is

CALCULATION

using Monte Carlo modelling

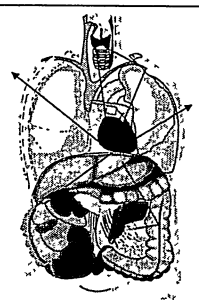
What is Monte Carlo Modelling?

- Essentially a ray tracing method, in which the fates of individual particles are determined
- The method is based on randomly sampling a probability distribution for each successive interaction
- Typically, the history of 10 million photons will be modeled

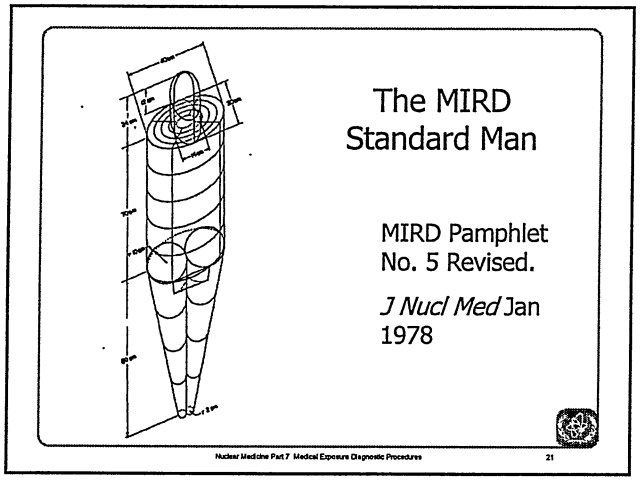
Monte Carlo Modelling

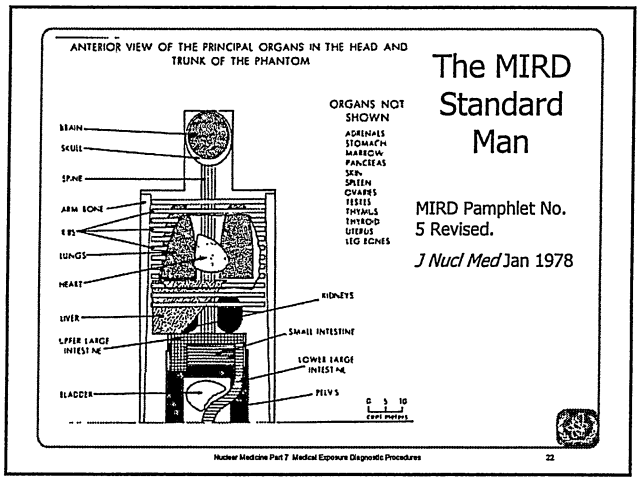
- Requires detailed knowledge of the absorption and scattering coefficients for the specific energies and for the various types of tissues.
- The name *Monte Carlo* was invented in 1947 by mathematicians Ulam and von Neumann who were working on nuclear weapons.

Determination of the Absorbed Fraction



- Radiation will be emitted randomly by the source in all directions
- Some photons will escape from the body without interaction
- Some photons will deposit their energy by photo electric interactions
- Some photons will undergo Compton scattering


The MIRD
Standard Man
MIRD Pamphlet
No. 5 Revised.
J Nucl Med Jan
1978
Nuclear Medicine Part 7 Medical Exposure Diagnostic Procedures
21


ANTERIOR VIEW OF THE PRINCIPAL ORGANS IN THE HEAD AND TRUNK OF THE PHANTOM
ORGANS NOT SHOWN
ADRENALS
STOMACH
MARROW
PANCREAS
SKIN
SPLEEN
OVARIES
TESTES
THYMUS
THYROID
UTERUS
LEG BONES
BRAIN
SKULL
SPINE
ARM BONE
RIBS
LUNGS
HEART
LIVER
UPPER LARGE INTESTINE
BLADDER
KIDNEYS
SMALL INTESTINE
LOWER LARGE INTESTINE
PELVIS
The MIRD
Standard
Man
MIRD Pamphlet No.
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J Nucl Med Jan 1978
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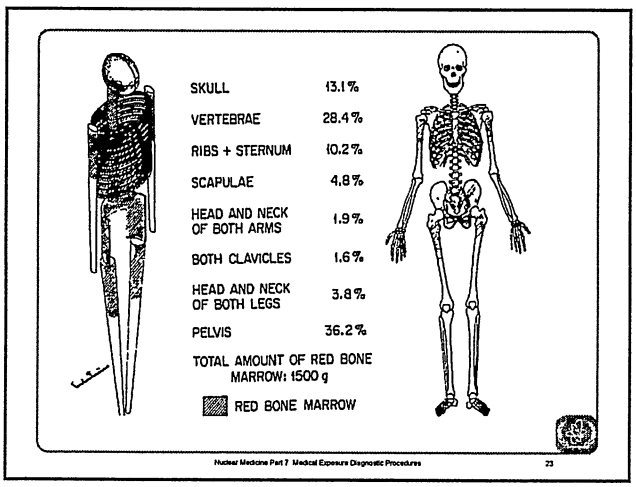
22


SKULL 13.1%
VERTEBRAE 28.4%
RIBS + STERNUM 10.2%
SCAPULAE 4.8%
HEAD AND NECK OF BOTH ARMS 1.9%
BOTH CLAVICLES 1.6%
HEAD AND NECK OF BOTH LEGS 3.8%
PELVIS 36.2%
TOTAL AMOUNT OF RED BONE MARROW: 1500 g
RED BONE MARROW
Nuclear Medicine Part 7 Medical Exposure Diagnostic Procedures
23

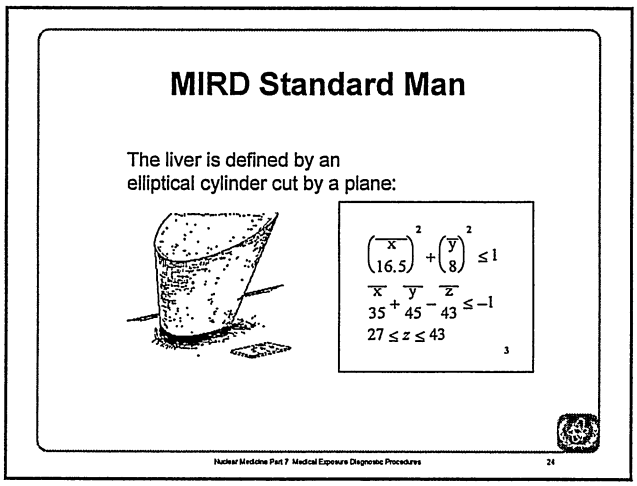

MIRD Standard Man
The liver is defined by an elliptical cylinder cut by a plane:
$\left(\frac{x}{16.5}\right)^2 + \left(\frac{y}{8}\right)^2 \le 1$
$\frac{x}{35} + \frac{y}{45} - \frac{z}{43} \le -1$
$27 \le z \le 43$
3
Nuclear Medicine Part 7 Medical Exposure Diagnostic Procedures
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TABLE 1. ELEMENTAL COMPOSITION OF DIFFERENT TISSUES OF THE PHANTOM* (% BY WEIGHT)

Element	Skeletal tissue[a]	Lung tissue[b]	Total body minus skeleton and lungs[c]
H	7.04	10.21	10.47
C	22.79	10.01	23.02
N	3.87	2.80	2.34
O	48.56	73.96	63.21
Na	0.32	0.19	0.13
Mg	0.11	7.4×10^{-3}	0.015
P	6.94	0.081	0.24
S	0.17	0.23	0.22
Cl	0.14	0.27	0.14
K	0.15	0.20	0.21
Ca	9.91	7.0×10^{-3}	0
Fe	8.0×10^{-3}	0.037	63×10^{-4}
Zn	4.8×10^{-3}	1.1×10^{-3}	32×10^{-4}
Rb	0	3.7×10^{-3}	37×10^{-4}
Sr	3.2×10^{-3}	3.9×10^{-4}	3.4×10^{-4}
Zr	0	0	8.0×10^{-4}
Pb	1.1×10^{-4}	4.1×10^{-4}	1.4×10^{-4}

* Reference 13 and 14.
[a] Density 1.412 g/cm³.
[b] Density 0.296 g/cm³.
[c] Density 0.969 g/cm³.

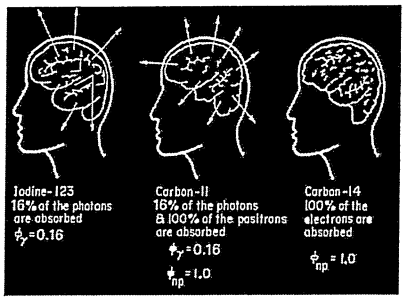
The MIRD Standard Man

Mird Pamphlet No. 5 Revised.

J Nucl Med Jan 1978

Examples of Absorbed Fractions

Note: $\phi = 1$ for charged particles



Derivation of the General MIRD Equation

- If A is the activity of the source, the *cumulated activity* Ã is the sum, or accumulation, of all the nuclear transitions occurring in the source over a period of time
- then ÃnE is the total radiation energy emitted by the source

Derivation of the General MIRD Equation

- ÃnEϕ is the energy absorbed in the target during the time interval of interest (ϕ is the absorbed fraction)
- D = ÃnEϕ/m is the absorbed dose, where m is the mass of the target organ

Derivation of the General MIRD Equation

$D = \tilde{A}S \quad (S = nE\phi/m)$

S is dependent on the radionuclide and the geometry. S-values for different radionuclides and source/target organs can be found in MIRD publications

Derivation of the General MIRD Equation

Generally each radionuclide will emit more than one type of "particle"

$D = \tilde{A}\Sigma S_i$ where S_i is the S factor of the ith particle

Derivation of the General MIRD Equation

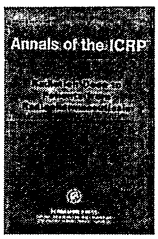
Generally there will be many source organs r_h contributing to the target organ r_k, and all these contributions must be added to give the total dose to the target organ.

$$D(r_k) = \Sigma D(r_k \Leftarrow r_h)$$

TARGET SOURCE ORGAN

ICRP

ICRP publications 53, 62 & 80 give the absorbed dose per unit activity administered (mGy/MBq) for different radiopharmaceuticals and different organs as well as the effective dose.



Calculation of the cumulated activity

The Cumulated Activity, $\tilde{A}_h$ is simply the sum of all the nuclear transitions in organ h during the time interval of interest. Therefore

$$\tilde{A}_h = \int A_h(t)\, dt$$

Determination of cumulated activity

- Numerical integration of time-activity curves
- Assuming exponential outflow from an organ
- Using a biokinetic model

Use of the General MIRD Equation

- Often the activity function $A_h(t)$ can be approximated by a sum of exponentials

$$A_h(t) = \Sigma A_j e^{-\lambda t}$$

where λ is the "effective" clearance constant, combining both the physical decay constant and the biological clearance constant.

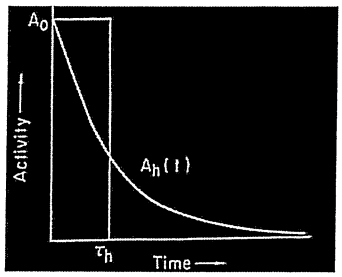
$$\frac{1}{T_{eff}} = \frac{1}{T_{phys}} + \frac{1}{T_{biol}}$$

Cumulated Activity

- Usually the integration limits for the calculation of the cumulated activity are zero to infinity.
- In which case:

$$\tilde{A} = \Sigma A_j / (\lambda_j)_e = 1.443 \Sigma A_j (T_j)_e$$

Example Plasma Clearance Curve showing Residence Time



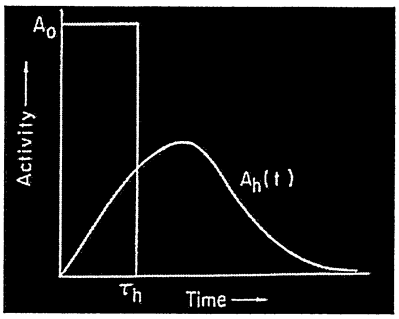
The Residence Time

The ratio τ in a source organ

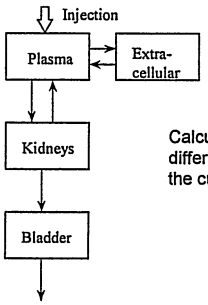
$$\tau = \tilde{A}_h / A_0$$

is defined as the residence time, where A_0 is the administered activity at zero time.

Example Organ Activity-Time Curve showing Residence Time



Biokinetic models



Calculate time-activity curves for the different compartments and calculate the cumulated activity.

Data Acquisition for Radiopharmaceutical Dosimetry (Biodistribution) Studies.

To determine the time-activity profile of the radioactivity in the source regions, four questions must be answered:

- What regions are source regions?
- How fast does the radioactivity accumulate in these source regions?
- How long does the activity remain in the source regions?
- How much activity is in the source regions?

Details of the appropriate measurement techniques can be found in MIRD Pamphlet No. 16 (J Nucl Med 1999, 40:37S-61S)

Data Acquisition for Radiopharmaceutical Dosimetry (Biodistribution) Studies.

Pharmacokinetics – biodistribution in humans and animals (when insufficient human data)

1. Human studies limited number of measurements, biodistribution and elimination only for few organs and tissues

   Methods -whole body measurements. sample collection (blood, urine, feaces..)

   Equipment – scintillation camera. SPECT

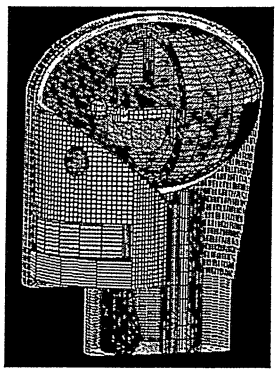
2. Animal studies – whole body activity retention (blood samples, urine) dissection of the body and collection of organs and tissues

Data Acquisition for Radiopharmaceutical Dosimetry (Biodistribution) Studies.

3. Compartmental analysis – mathematical models for describing the biokinetics of RF , transfer coefficients between compartments, calculation of residence time and cumulated activities

Assumptions in Standard MIRD Dosimetry

- Entire organs taken as sources and targets
- Homogeneous absorbing material
- Uniform activity distribution
- Constant mass
- Edge effects are negligible



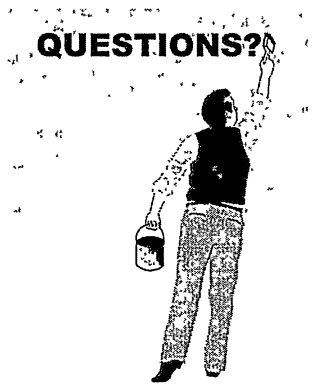
MIRD Pamphlet No. 15

J Nucl Med 1999, 40:62S-101S

Improved mathematical model of the brain and skull.

Patient-Specific Dosimetry

- The MIRD approach provides estimates of organ doses and Effective Dose to the standard phantoms. This can be used for dosimetry of diagnostic radiopharmaceuticals.
- For radionuclide therapy, a patient-specific approach must be taken to determine the tumour and non-tumour tissue doses.



DISCUSSION

Discuss the different factors that will affect the magnitude of the uncertainty between the equivalent dose to an organ and the effective dose calculated according to MIRD and the doses actually received by the patient.

Is it important if the uncertainty is e.g. a factor of 2?