The MIRD Schema for Radiopharmaceutical Internal Dose Calculation

Learning Objectives

- Describe the MIRD methodology for internal dosimetry
- Identify the similarities and differences between the MIRD and ICRP formalisms

MIRD Schema

- Developed by the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine
- Dose calculations needed to evaluate risks of radiopharmaceutical use for imaging, therapy, or noninvasive studies
- Standard methodology used in nuclear medicine, but not for occupational internal dosimetry

Reference Material

- The MIRD Primer (Lovinger, Budinger, and Watson, 1991)
- MIRD Pamphlets 1-14
  - published periodically in J. Nucl. Med.
- Radiation Dose Estimates for Radiopharmaceuticals (Stabin, Stubbs, and Toohey, 1996--NUREG/CR-6345)
- Fetal Dose Workbook (Stabin 1998)

Simplified MIRD Dose-rate Equation

- Consider a single radionuclide with a single type of radiation uniformly distributed in an almost infinitely large volume of tissue ("source organ")
- Define a "particle" as either a photon, an electron, an alpha or a beta (+ or -)
- Let E = the mean particle energy,

  n = the number of particles per decay,

  and k = a unit conversion constant

MIRD equation: energy emitted

- Let $\Delta = k\, E\, n$
  - mean energy emitted per decay
- Let A = activity (decay rate)
- Then $A\,\Delta$ = energy emitted in source organ per unit time
- For dose calculation, we need to know the energy absorbed

MIRD equation: energy absorbed

- In an infinite medium, all the energy is absorbed; in the body, it is not
- Let ϕ = the absorbed fraction =

$$\phi = \frac{\text{energy absorbed in the target organ}}{\text{energy emitted by the source organ}}$$

- The source organ is always a target organ, also, and $\phi = 1$ for e^-, α, β^-, β^+
- Energy deposited in target organ per unit time = $A \Delta \phi$

Table of ϕ values for liver as source organ

TARGET ORGAN	Photon Energy, E, (MeV) 0.100	0.200	0.500	1.00
Adrenals	1.61E-05	1.81E-05	1.68E-05	1.56E-05
Bladder wall	6.16E-07	5.60E-07	1.21E-06	5.80E-07
Bone (Total)	4.93E-06	3.17E-06	2.53E-06	2.30E-06
Stomach wall	7.07E-06	6.96E-06	6.50E-06	6.44E-06
SI + Contents	6.32E-06	6.01E-06	5.44E-06	5.16E-06

MIRD equation: dose rate

- Since absorbed dose is defined as energy deposited per unit mass, we need to divide by the mass of the target organ, m_T
- The dose rate is then $\dot{D} = A\,\Delta\,\phi/m_T$
- Define $\Phi = \phi/m_T$ = specific absorbed fraction
- Then the dose rate is $\dot{D} = A\,\Delta\,\Phi$

The “S” Factor

- Define $S = \Delta \Phi$
- S is the mean absorbed dose in the target organ per decay in the source organ
- Dose rate $\dot{D} = A\ S$
- Tables of S factors have been published for most radionuclides for all combinations of source and target organs

S-factor Units

- Traditional units:
  - rad / μCi-h
  - 1 μCi-hr = 1.332×10^8 disintegrations
- SI units:
  - Gy / Bq-s
  - 1 Bq-s = 1 disintegration
- 1 rad / μCi-h = 7.51×10^{-11} Gy/Bq-s

Table of S-values for Tc-99m (rad/μCi-hr)

TARGET ORGANS	SOURCE ORGANS				
	Adrenals	Kidneys	Liver	Lungs	Spleen
Adrenals	3.1E-03	1.1E-05	4.5E-06	2.7E-06	6.3E-06
Bladder wall	1.3E-07	2.8E-07	1.6E-07	3.6E-08	1.2E-07
Bone (total)	2.0E-06	1.4E-06	1.1E-06	1.5E-06	1.1E-06
Stomach wall	2.9E-06	3.6E-06	1.9E-06	1.8E-06	1.0E-05
Small Int.	8.3E-07	2.9E-06	1.6E-06	1.9E-07	1.4E-06

MIRD equation: cumulated activity

- Since activity in the source organ is a function of time, so is the dose rate to the target organ
- To compute total dose, we need to integrate the activity
- $\tilde{A} = \int A(t)\, dt$ = cumulated activity

MIRD equation: absorbed dose

- Mean absorbed dose = cumulated activity (total number of decays) times mean absorbed dose per unit cumulated activity
- $D = \tilde{A}\, S$
- Remember at this point, this is the absorbed dose in a target tissue from activity in a single source organ

Alternate MIRD equation

- Let A_0 = the activity administered to the patient
- Divide both sides of the absorbed dose equation by A_0 : $D / A_0 = \tilde{A}\ S / A_0$
- Define the residence time, τ, of the radiopharmaceutical in the source organ as

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

- Then $D / A_0 = \tau\ S$ = mean dose per unit administered activity

Time-independent and time-dependent parameters

- The time-independent parameters are contained mostly in the S-factor
  - decay properties of the radionuclide
  - physical processes of radiation transport
  - anatomy of the reference individual
- The time-dependent parameters are contained mostly in the accumulated activity, $\tilde{A}$
  - uptake, retention, and loss (both physical and biological) of the radionuclide

Calculating S-factors

- The geometric properties (size, shape, location, orientation) of the organs relative to each other determine the value of Φ
- Anthropomorphic models of the human body, called phantoms, are used to calculate Φ for each radionuclide and each combination of source and target
- The calculations are performed by Monte Carlo methods

MIRD Phantoms

- The phantoms define the internal organs by using simplified shapes (cones, spheres, cylinders, ellipsoids, etc.) to identify the three-dimensional coordinates of every point in a given organ in relation to a standard coordinate system.

MIRD Phantoms

- There are nine standard phantoms used to compute S-factors in the MIRD schema
- Adult male and adult female
- Pediatric
  - 15, 10, 5, and 1 year-old
- Pregnant female
  - 3, 6, and 9 months gestation

The MIRD phantom

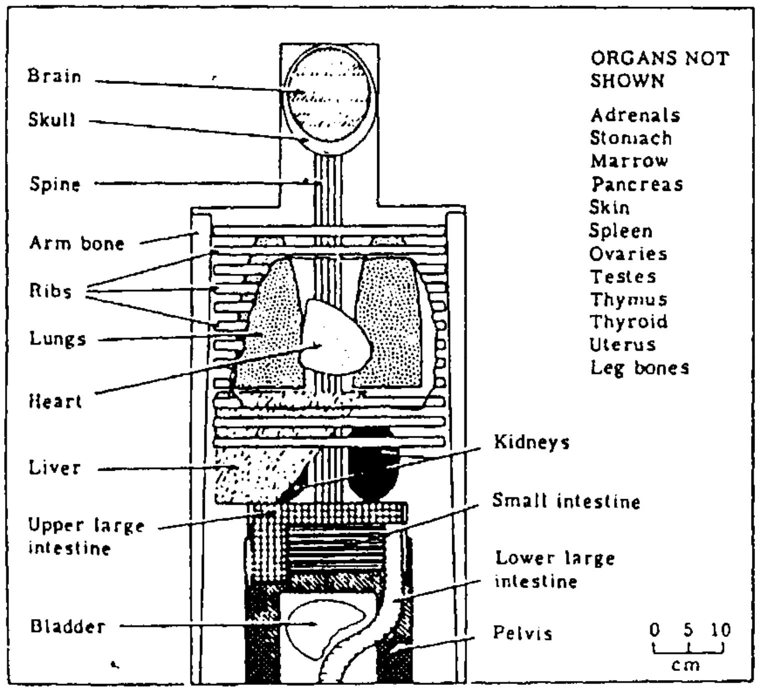
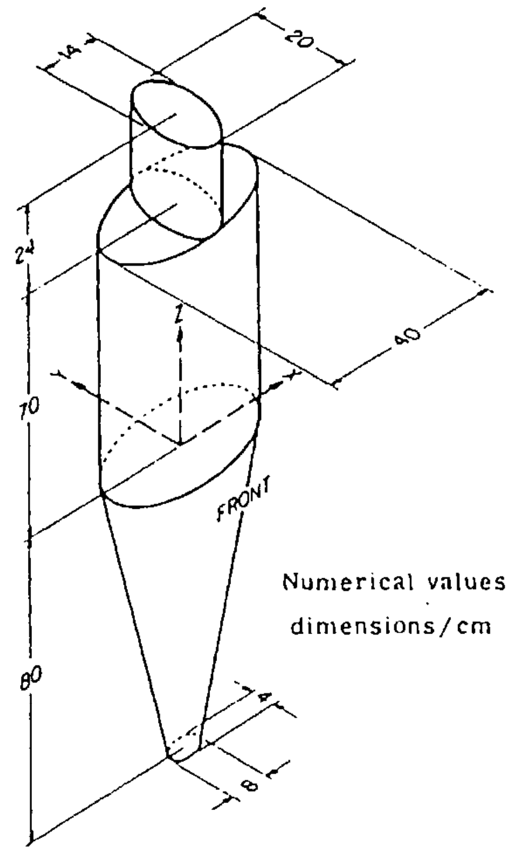


Fig. B.9. (a) Disposition of organs in human phantom of Snyder *et al.* (1969). This shows the anterior view of principal organs in head and trunk of phantom.



MIRD pediatric phantoms

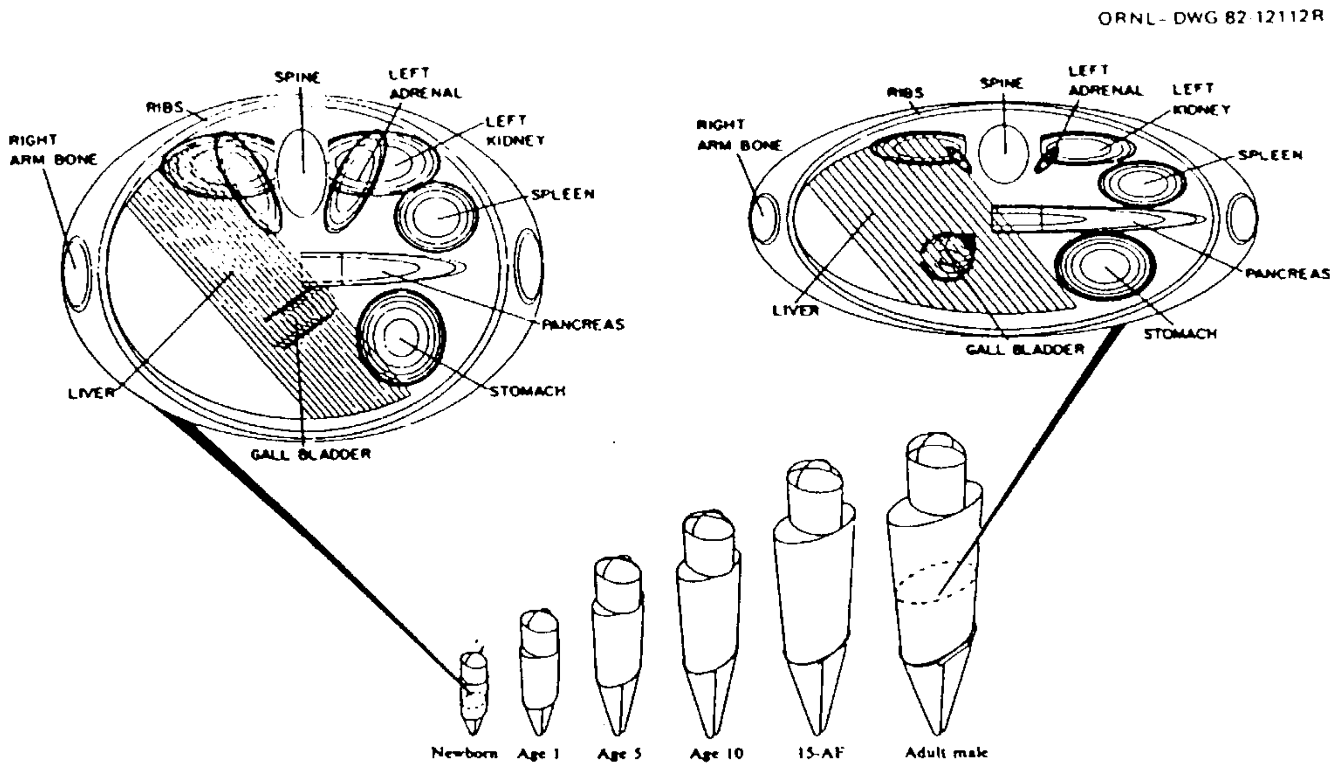


Fig. A-2. External views of the phantoms and superimposed cross-sections within the middle trunk of the newborn and adult male phantoms, depicting the space from the bottom of the liver to the top of the liver. In the younger phantoms, the head is relatively larger, the legs are relatively smaller, and the trunk is relatively thicker. The geometry of the organs may change dramatically from birth to adulthood. The "15-AF" and the "Adult male" phantoms have breasts appropriate for a reference adult female, which are not shown.

ORNL/TM-8381/V1

Monte Carlo Calculations

- The Monte Carlo method follows millions of photons from the points of origin in the source organ to the points of absorption in the target organ
- The average energy absorbed in the target organ per decay in the source organ is ϕ
- Remember $\Phi = \phi/m_T$

Full MIRD Equation

- Consider:
  - a single radiopharmaceutical
  - emitting multiple radiation types
  - depositing in multiple source organs
  - irradiating multiple target organs
- Subscripts
  - radiation type i
  - source organ h
  - target organ k

Mean energy emitted per decay

- The mean energy emitted per nuclear decay for radiation type i = $\Delta_i = k\, n_i\, E_i$
- Then $\Delta = \Sigma_i\, \Delta_i$
- Values of Δ are published for each radionuclide

Unit conversion constant, k

- Values of the unit conversion constant, k
- SI units:
  - if E is in Joules, m_T is in kg, and $\tilde{A}$ is in Bq-sec, then k = 1 Gy-kg/Bq-sec
- Conventional (traditional, old) units:
  - if E is in MeV, m_T is in g, and $\tilde{A}$ is in μCi-h, then k = 2.13 g-rad/μCi-h

Absorbed fraction ϕ_i

- Let r = an anatomic region (organ)
  - r_h = the source region or organ
  - r_k = the target region or organ
- Then $\phi_i(r_k \leftarrow r_h) =$

$$\frac{\text{(i-type radiation energy emitted in } r_h \text{ and absorbed in } r_k)}{\text{(i-type radiation energy emitted in } r_h)}$$

Penetrating and non-penetrating radiation

- For penetrating radiation (photons of energy > 10-20 keV), $0 < \phi_i(r_k \leftarrow r_h) < 1$
- For non-penetrating radiation (photons of energy < 10-20 keV, e^-, α, β^-, β^+):
  - when $h = k$, $\phi_i(r_k \leftarrow r_h) = 1$
  - when $h \neq k$, $\phi_i(r_k \leftarrow r_h) = 0$

Specific absorbed fraction and S-factor

- The specific absorbed fraction $\Phi_i = \phi_i(r_k \leftarrow r_h)/m_k$
- The mean dose per unit cumulated activity $S(r_k \leftarrow r_h) = \Sigma_i \Delta_i \Phi_i(r_k \leftarrow r_h)$

Activity retention

- Typically, the retention of activity in an organ can be described by a simple exponential function: $A(t) = A_0e^{-\lambda t}$
- The decay constant λ, usually called the effective decay constant, λ_e, is composed of two terms representing physical (radioactive) decay and biological clearance: $\lambda_e = \lambda_p + \lambda_b$

Integrating the activity

- Cumulated activity is the integral of A(t):
$\tilde{A} = \int A(t)\,dt = \int A_0 e^{-\lambda t}\,dt = A_0/\lambda_e$
- The effective half-life, T_e is defined as:
$T_e = 0.693/\lambda_e$
- Therefore $\tilde{A} = 1.44\ A_0\ T_e$
- For each source organ, $\tau_h = \tilde{A}_h/A_0$

The full MIRD equation

- Putting it all together, the mean absorbed dose to a target organ k is:

$$D_k = \Sigma_h \tilde{A}_h \, \Sigma_i \, \Delta_i \, \Phi_i(r_k \leftarrow r_h)$$

$$= \Sigma_h \tilde{A}_h \, S(r_k \leftarrow r_h)$$

- Alternately:

$$D_k / A_0 = \Sigma_h \tau_h \, S(r_k \leftarrow r_h)$$

Whole-body dose

- So far, we have calculated doses to individual target organs; we also need a parameter describing dose to the body as a whole
- Whole-body (or total-body) dose is simply the total radiation energy absorbed ÷ 70 kg
- Whole-body dose is usually a small fraction of the maximum organ dose

Effective dose equivalent (EDE)

- Developed by the ICRP for occupational radiation protection, the EDE enables us to compare radiation detriment from a uniform external dose and a (highly) non-uniform internal dose
- EDE is a weighted sum of organ doses:

$$H_E = \Sigma_T \, w_T \, H_T \quad (H_T = D_k)$$

Some typical nucl. med. doses

Agent	A_0 mCi	Organ doses rad	WB dose rad	EDE rem
^{99m}Tc-DTPA	20	brain 0.09, bladder 5.6	0.30	0.60
^{99m}Tc-MDP	25	bone 3.3, marrow 0.5	0.17	0.55
^{99m}Tc-SC	3	liver 1.0, spleen 0.6	0.06	0.15
^{123}I-NaI	0.2	thyroid 2.6, bladder 0.1	0.01	0.09
^{99m}Tc-O4	10	thyroid 0.9, bladder 1.3	0.15	0.39
^{131}I-NaI	10	thyroid 13k, bladder 23	7.1	390
^{201}Tl-Cl	3	heart 3.0, colon 5.1	0.63	1.8
^{99m}Tc-MIBI	25	heart 0.12, colon 1.0	0.33	0.33

Special considerations: pregnancy

- Watson & Stabin (1991) developed pregnancy phantoms for 3, 6, and 9 months
- The embryo/fetus is a single target organ
- Russell (1997) published fetal dose tables for most radiopharmaceuticals, including fetal self-dose contributions from activity crossing the placenta
- Fetal thyroids are still occasionally ablated

Special Considerations: lactating patients

- NRC regulations limit maximum dose to a member of the public to 500 mrem from a released nuclear medicine patient
- Many radiopharmaceuticals are excreted in breast milk
- Cessation of breast feeding is indicated for I-131 NaI, and Ga-67 citrate
- Interruption for 1-2 days indicated for :

  Tc-99m MAA, TcO_4, SC, RBC's, & WBC's
  I-123 mIBG, In-111 WBC's; 7 days for Tl-201

Special considerations: patient-specific dosimetry

- For therapy applications, we need a more accurate assessment of organ doses, especially red marrow and tumor-containing organs, e.g., liver
- Can derive patient-specific biokinetics from administration of tracer amounts (routine)
- Can create a patient-specific voxel (3-D) mathematical phantom from CT/MRI scans
- Will be able to calculate patient-specific S-factors by computer