Formalism for Internal Dosimetry

IAEA IDOS meeting Vienna

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Update on Medical Internal Radiation Dosimetry:

2009 MIRD Committee Recommendations for Unifying MIRD and ICRP Formulas, Quantities, and Units

HPS Continuing Education Lecture
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MIRD Committee

Absorbed dose in biological systems

General equation

$$D = \left(\frac{k\mathrm{AEf}}{m} \right) \int_{\mathrm{o}}^{t} \mathrm{B}(t)\, dt$$

Gy (J kg^{-1})

where k is a unit conversion constant

A is the activity in the organ (Bq)

E is the total energy emitted (J)

f is the fraction of energy that is absorbed

m is the mass of target tissue (g)

$\mathrm{B(t)}$ is the biological retention with time t

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Absorbed dose

Rearranged

$$D = A\int_{o}^{t} \mathrm{B}(t)dt\left(\frac{k\mathrm{Ef}}{m}\right)$$

MIRD Formula

$$D(r_k \leftarrow r_h) = \tilde{A}_h \ \Sigma_i \ \Delta_i \ \varphi_i(r_k \leftarrow r_h) \ / \ m_k$$

where $\tilde{A}_h$ is the cumulated activity, Δ_i is the mean energy emitted per unit cumulated activity, and $\varphi\ (r_k \leftarrow r_h)$ is the absorbed fraction of energy imparted by a source organ

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Absorbed dose

Rearranged

$$D = A\int_{o}^{t} \mathrm{B}(t)\,dt \left(\frac{k\mathrm{Ef}}{m}\right)$$

MIRD Formula

$$\mathrm{D}(\mathrm{r_k} \leftarrow \mathrm{r_h}) = \tilde{\mathrm{A}}_{\mathrm{h}} \Sigma_{\mathrm{i}}\, \Delta_{\mathrm{i}}\, \varphi_{\mathrm{i}}(\mathrm{r_k} \leftarrow \mathrm{r_h}) \,/\, \mathrm{m_k}$$

Total number of transformations

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Absorbed dose

Rearranged

$$D = A\int_{o}^{t} \mathrm{B}(t)dt\left(\frac{k\mathrm{Ef}}{m}\right)$$

MIRD Formula

$$\mathrm{D}(\mathrm{r_k} \leftarrow \mathrm{r_h}) = \tilde{\mathrm{A}}_{\mathrm{h}} \sum_{\mathrm{i}} \Delta_{\mathrm{i}}\, \varphi_{\mathrm{i}}(\mathrm{r_k} \leftarrow \mathrm{r_h}) / \mathrm{m_k}$$

Energy imparted

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Absorbed dose

Rearranged

$$D = A\int_{o}^{t} \mathrm{B}(t)dt\left(\frac{k\mathrm{Ef}}{m}\right)$$

MIRD Formula

$$\mathrm{D}(\mathrm{r_k} \leftarrow \mathrm{r_h}) = \tilde{\mathrm{A}}_{\mathrm{h}} \ \Sigma_{\mathrm{i}} \ \Delta_{\mathrm{i}} \ \varphi_{\mathrm{i}}(\mathrm{r_k} \leftarrow \mathrm{r_h}) \ / \ \mathrm{m_k}$$

Organ mass

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ICRP dosimetry formalism (ICRP-26)

Dose equivalent rate in a target organ or tissue:

$$\dot{H}_T = 1.6\text{x}10^{-10}\ \text{SEE}_{(T \leftarrow S)}\ A_S$$

where $\text{SEE}_{(T \leftarrow S)}$ is the specific effective energy deposited in the target organ or tissue per radionuclide transformation in source organ S (MeV g^{-1}),

A_S is the radioactivity present in the source organ or tissue (bequerel), and

the factor $1.6\text{x}10^{-10}$ is a unit conversion constant.

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ICRP dosimetry formalism

Integrating over time, the dose equivalent H_T is

$$H_T = 1.6\text{x}10^{-10}\ \text{SEE}_{(T \leftarrow S)}\ A_S \int_0 R(t)dt$$

where H_T is the dose equivalent in sievert (Sv),

and $R(t)$ is a retention function, and where $A_S \int_0 R(t)dt$ represents the total number of radioactive transformations in the source organ over time

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ICRP dosimetry formalism

The committed dose equivalent to an organ or tissue ($H_{T,50}$), a measure of long-term organ dose equivalent, was first defined in ICRP-26/30 as the dose equivalent that would be received from an intake of radioactive material by an individual during the 50-year period following the intake

Numerically, this quantity was defined as

$$H_{50,T} = 1.6\text{x}10^{-10} \sum A_S \; SEE_{(T \leftarrow S)}$$

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ICRP dosimetry formalism

The committed effective dose equivalent ($H_{E,50}$), a measure of total risk or detriment to the individual (sievert), was defined as the sum of the products of the weighting factors applicable to each of the body organs or tissues irradiated and the committed dose equivalent to those organs; thus

$$H_{E,50} = \sum W_T \, H_{T,50}$$

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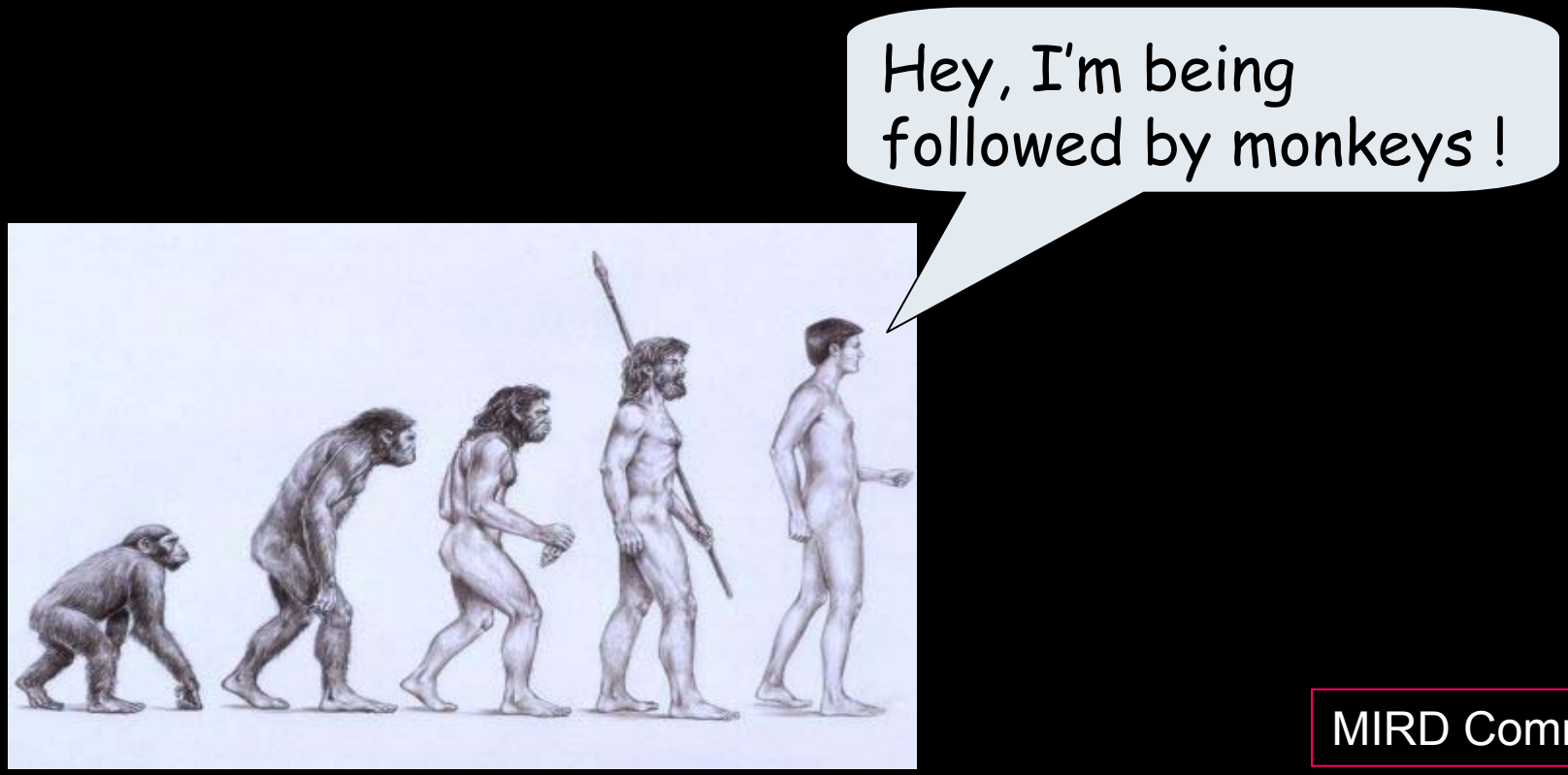
Evolution of ICRP quantities and units

From dose equivalent to equivalent dose!



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ICRP dosimetry formalism (ICRP-60)

Equivalent dose, H_T

$$H_T = \sum w_R \, D_{T,R}$$

where $D_{T,R}$ is the absorbed dose (averaged over a tissue or organ T) due to radiations of type R, and w_R is the radiation weighting factor. $D_{T,R}$ can not be measured experimentally. The weighting factor is introduced to weight the absorbed dose for biological effectiveness

Unit: J kg^{-1}
Special name for the unit of equivalent dose is sievert (Sv)

ICRP dosimetry formalism

Effective dose, E

$$E = \sum w_T H_T = \sum w_T \sum w_R D_{T,R}$$

where $D_{T,R}$ is as above and w_T is a tissue weighting factor which reflects the total detriment to health. This is a doubly-weighted surrogate of risk based on physical quantities imparted (i.e., not a physical dose quantity)

Unit: J kg^{-1}
Special name for the unit of effective dose equivalent is sievert (Sv).

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Toward consistency

- In 2009, the MIRD Committee recommended a revised framework for unifying the ICRP and MIRD equations, models, and terminology

→ The result is a general schema for internal dosimetry, consistent for both nuclear medicine and radiation protection.

MIRD Committee

SPECIAL CONTRIBUTION

MIRD Pamphlet No. 21: A Generalized Schema for Radiopharmaceutical Dosimetry—Standardization of Nomenclature

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MIRD Pamphlet No. 21

Purpose:

- Provides standardized formulas, nomenclature, quantities, and units
- Clarifies the use of *equivalent dose* and *effective dose* for applications in nuclear medicine
- Presents the case for a new dosimetric quantity, based on absorbed dose, for deterministic effects associated with radionuclide therapy

MIRD Committee

Revised nomenclature, symbols

- Comparison of MIRD (old), MIRD (21, revised), and the ICRP quantities, parameters, symbols, and units

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MIRD Pamphlet No. 21 – Quantities and symbols

TABLE 1. Quantities, Parameters, Symbols, and Units Used in the MIRD and ICRP Dosimetry Schema (Listed in Order of Appearance in Equations 1–17)

Quantity or parameter	MIRD Pamphlet 21	MIRD Primer (1991) (4)	ICRP publications (7,8,18)	Units or special name
Source region (or tissue)	r_S	r_h	S	
Target region (or tissue)	r_T	r_k	T	
Absorbed dose rate to target region	$\dot{D}(r_T,t)$	$\dot{\bar{D}}(r_k)$ or $\dot{\bar{D}}_k$	$\dot{D}_{T,R}$	Gy s^{-1}
Activity in source region	$A(r_S,t)$	$A_h(t)$	$q_S(t)$	Bq
Absorbed dose rate per unit activity	$S(r_T \leftarrow r_S,t)$	$S(r_k \leftarrow r_h)$	Not defined	Gy $(\text{Bq s})^{-1}$
Dose-integration period	T_D	Assumed to be ∞	τ	s
Absorbed dose to target	$D(r_T,T_D)$	$\bar{D}(r_k)$ or $\bar{D}_k$	$D_{T,R}$	Gy
Administered activity	A_0	A_0	q_0	Bq
Fraction of administered activity in the source region	$a(r_S,t) = A(r_S,t)/A_0$	$f_h(t)$	Not defined	Unitless
Absorbed dose coefficient	$d(r_T,T_D)$	Not defined	$d_T(\tau)$	Gy Bq^{-1}
Mean energy of the ith transition	E_i	E_i	E_i	J or MeV
Number of ith transitions per nuclear transformation	Y_i	n_i	Y_i	$(\text{Bq s})^{-1}$
Mean energy of the i^{it} transition per nuclear transformation	Δ_i	Δ_i	Δ_i	J $(\text{Bq s})^{-1}$ or MeV $(\text{Bq s})^{-1}$

MIRD Pamphlet No. 21 – Quantities and symbols

TABLE 1. Quantities, Parameters, Symbols, and Units Used in the MIRD and ICRP Dosimetry Schema (Listed in Order of Appearance in Equations 1–17)

Quantity or parameter	MIRD Pamphlet 21	MIRD Primer (1991) (4)	ICRP publications (7,8,18)	Units or special name
Absorbed fraction	$\phi(r_T \leftarrow r_S, E_i, t)$	$\phi(r_k \leftarrow r_h)$	$AF(T \leftarrow S, E_i)$	Unitless
Mass of target region	$M(r_T, t)$	m_k	m_T	kg
Specific absorbed fraction	$\Phi(r_T \leftarrow r_S, E_i, t)$	$\Phi(r_k \leftarrow r_h)$	$SAF(T \leftarrow S, E_i)$	kg^{-1}
Time-integrated activity in source region*	$\tilde{A}(r_S, T_D)$	$\tilde{A}_h$	U_S	Bq s
Time-integrated activity coefficient†	$\tilde{a}(r_S, T_D)$	τ	Not defined	s
Equivalent dose to target	$H(r_T, T_D)$	Not defined	H_T	Sv
Radiation weighting factor	w_R	Not defined	w_R	Unitless
Absorbed dose to target by radiation type R	$D_R(r_T, T_D)$	Not defined	$D_{T,R}$	Gy
Radiation-weighted S	$S_w(r_T \leftarrow r_S, t)$	Not defined	$SEE(T \leftarrow S)$	Sv $(Bq\ s)^{-1}$
Equivalent dose coefficient	$h(r_T, T_D)$	Not defined	$h_T(\tau)$	Sv Bq^{-1}
Effective dose	E	Not defined	E	Sv

*This quantity was termed *cumulated activity* in 1991 MIRD Primer.

†This quantity was termed *residence time* in 1991 MIRD Primer.

Absorbed dose - time dependent equations

Mean absorbed dose rate at time *t*

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

Eq. 1

Mean absorbed dose

$$D(r_T,T_D) = \int_0^{T_D} \dot{D}(r_T,t)\,dt$$

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

Eq. 2

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Absorbed dose - time dependent equations

Mean absorbed dose rate at time *t*

Activity at time *t*

$$\dot{D}(r_T,t) = \sum_{r_S} A(r_S,t)\ \underbrace{S(r_T \leftarrow r_S\ ,t)}$$

Eq. 1

S value by radionuclide, target tissue, at time *t*

Mean absorbed dose

Dose-integration or dose commitment time period

$$D(r_T,T_D) = \int_0^{T_D} \dot{D}(r_T,t)\,dt$$

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

Eq. 2

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Absorbed dose - time dependent equations

Mean absorbed dose (Gy, J kg^{-1})

$$D(r_T, T_D) = \int_0^{T_D} \dot{D}(r_T, t)\, dt$$

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

Eq. 2

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Absorbed dose - time dependent equations

Absorbed dose coefficient

Fraction of administered activity

Eq. 3

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

Determined by direct measurements or compartment modeling

"S" - Absorbed dose to target per unit activity in source

$$S(r_T \leftarrow r_S, t) = \frac{1}{M(r_T, t)} \sum_i E_i\, Y_i\, \phi(r_T \leftarrow r_S, E_i, t)$$

Eq. 4

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

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Absorbed dose - time dependent equations

Absorbed dose coefficient

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

Eq. 3

"S" - Absorbed dose to target per unit activity in source

$$S(r_T \leftarrow r_S, t) = \frac{1}{M(r_T, t)} \sum_i E_i\, Y_i\, \phi(r_T \leftarrow r_S, E_i, t)$$

Eq. 4

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

Time-dependent mass

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Absorbed fraction

Absorbed fraction and specific absorbed fraction

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

Eq. 5

"S" - Absorbed dose to target per unit activity in source

$$S\left(r_T \leftarrow r_S\,, t\right) = \sum_i \Delta_i\, \Phi\left(r_T \leftarrow r_S\,, E_i\,, t\right)$$

Eq. 6

Restated in terms of a specific absorbed fraction

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Absorbed dose - time independent equations

Neglecting the time-dependence of S for lifetime doses, long-lived radionuclides

Mean absorbed dose

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

Eq. 7

Total nuclear transformations

where

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

Proposed quantity name: time-integrated activity

Previous quantity name: cumulated activity

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Absorbed dose - time independent equations

Per unit administered activity

Absorbed dose coefficient

$$d\left(r_T, T_D\right) = \sum_{r_S} \tilde{a}\left(r_S, T_D\right) S\left(r_T \leftarrow r_S\right)$$

Eq. 8

where

$$\tilde{a}\left(r_S, T_D\right) = \int_0^{T_D} a\left(r_S, t\right) dt = \frac{1}{A_0} \int_0^{T_D} A\left(r_S, t\right) dt$$

Eq. 9

Proposed quantity name: time-integrated activity coefficient

Previous quantity name: residence time τ

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Equivalent dose

Equivalent dose

For *stochastic* effects, replacing ICRP-103

$$H(r_T, T_D) = \sum_R w_R \, D_R(r_T, T_D)$$

Eq. 10

where W_R is the radiation-weighting factor for radiation type R, and $D_R(r_T, T_D)$ is the contribution of radiation type R to the mean absorbed dose in target tissue r_T.

W_R = 1 for photons, electrons, positrons, and beta-particles; and = 20 for alpha particles

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Equivalent dose

Equivalent dose

For *stochastic* effects, replacing ICRP-103

$$H(r_T, T_D) = \sum_R w_R \, D_R(r_T, T_D)$$

Eq. 10

where W_R is the radiation-weighting factor for radiation type R, and $D_R(r_T, T_D)$ is the contribution of radiation type R to the mean absorbed dose in target tissue r_T.

! !

Applicable to a defined population, not the individual

W_R = 1 for photons, electrons, positrons, and beta-particles; and = 20 for alpha particles

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Equivalent dose

Equivalent dose

$$H(r_T, T_D) = \sum_R w_R \, D_R(r_T, T_D)$$

Eq. 10

Units of J kg-1, with special name sievert (Sv)

MIRD Committee

Radiation-weighted S

Rewritten: Radiation-weighted S

$$S_w\left(r_T \leftarrow r_S\,,t\right) = \sum_R w_R \sum_i E_{R,i}\, Y_{R,i}\, \Phi\left(r_T \leftarrow r_S\,, E_{R,i}\,,t\right)$$

$$= \sum_R w_R \sum_i \Delta_{R,i}\, \Phi\left(r_T \leftarrow r_S\,, E_{R,i}\,,t\right)$$

Eq. 11

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Equivalent dose and dose rate

Equivalent dose rate

After intake, in the target tissue, at time *t*

$$\dot{H}(r_T, t) = \sum_{r_S} A(r_S, t)\, S_w(r_T \leftarrow r_S, t)$$

Eq. 12

Equivalent dose

Integrated over a time period T_D

$$H(r_T, T_D) = \int_0^{T_D} \dot{H}(r_T, t)\, dt$$

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

Eq. 13

$$H(r_T, T_D) = \sum_{r_S} \tilde{A}(r_S, T_D)\, S_w(r_T \leftarrow r_S)$$

Eq. 14

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Equivalent dose

Per unit intake

Equivalent dose coefficient – time dependent

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

Eq. 15

Equivalent dose coefficient – time independent

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

Eq. 16

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Equivalent dose in medical internal dosimetry

- Since the radiation-weighting factors are developed by committee (ICRP) for stochastic effects (cancer), they are not applicable to deterministic biological effects represented by the concept of relative biological effectiveness (RBE)

- W_R values should not be used to predict deterministic effects

  - Not for evaluating toxicity or for treatment planning

  - Not for individual patients

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Effective dose: an ICRP construct of risk

Effective dose

A hybrid reference (50th percentile) person

$$E = \sum_T w_T \left[\frac{H(r_T, T_D)^{Male} + H(r_T, T_D)^{Female}}{2} \right]$$

Eq. 17

A radiation protection quantity for establishing annual limits to workers and members of the general public

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Effective dose

- In radiation protection, used for comparing patient exposures that might result from different procedures, and for conveying a measure of future risk
- Appropriate for use by institutional review boards and radiation safety committees
- But this quantity is not patient-specific
- And it should not be used as a measure of individual risk or for expressing deterministic effects
- Not an organ or tissue dose

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Quantities relevant to deterministic effects

MIRD Pamphlet No. 21 concludes with a discussion of deterministic effects

- RBE-weighted absorbed dose – D
- Biologically effective dose – BED
- Equivalent uniform dose – EUD
- Isoeffective dose – D_{IsoE}

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How do we deal with high absorbed doses in radionuclide therapy?

- For deterministic effects, ICRP recommends using an RBE-weighted absorbed dose to the organ or tissue
  - Relative to a specific tissue and endpoint
  - Measured under well-defined conditions

- Failure to recognize this difference between radiation-weighting factors for stochastic effects and RBE values for deterministic effects has led to confusion regarding which value is appropriate

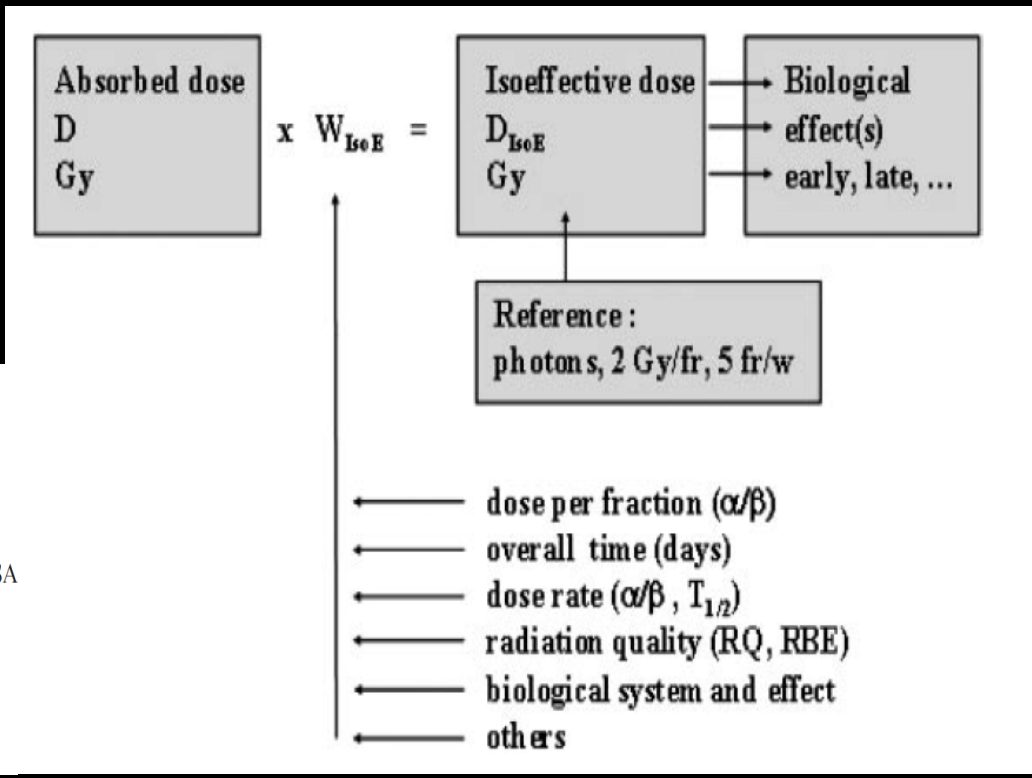
For alphas, the RBE is usually observed to be 3-6 for cell killing, not 20

MIRD Committee

Quantities relevant to deterministic effects

The ICRU has already described a weighted absorbed dose quantity: the equivalent absorbed dose of low-LET radiation that, would produce the same clinical effects as the high-LET radiation, all other conditions being equal

$$D_{IsoE}(r_T) = w_{IsoE} D(r_T)$$



THE RBE ISSUES IN ION-BEAM THERAPY: CONCLUSIONS OF A JOINT IAEA/ICRU WORKING GROUP REGARDING QUANTITIES AND UNITS

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MIRD Committee

New MIRD recommendation

The MIRD Committee proposes* that the barendsen (Bd) be defined as the special named unit for the product of deterministic RBE and absorbed dose.

The resulting quantity is "isoeffective dose" (D_{isoE}). In addition to relative biological effectiveness, the term D_{isoE} also accounts for dose rate and other modifying effects.

$$D_{isoE}(r_T, T_D) = RBE_\alpha \cdot D_\alpha(r_T T_D) \qquad \text{J kg}^{-1}$$

*Sgouros G, Howell RW, Bolch WE, Fisher DR. MIRD Commentary: Proposed Name for a Dosimetry Unit Applicable to Deterministic Biological Effects—The Barendsen (Bd). *J Nucl Med.* 2009; 50(3):485-487.

MIRD Committee

Summary

- The MIRD Committee of the Society of Nuclear Medicine has developed standardized nomenclature for harmonizing the ICRP and MIRD systems,
- ....has clarified the use of equivalent dose and effective dose in radiopharmaceutical dosimetry,
- ....and has proposed a new quantity (the barendsen, Bd) for describing the RBE-weighted absorbed dose for applications in high-LET radionuclide therapy

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http://www.snm.org/MIRD