Internal Dosimetry: the MIRD Approach

Medical Internal Radiation Dose
Committee of the Society of Nuclear Medicine

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covering ABR Core Examination Guide sections 17.m.(i)-(iii)

Internal Dosimetry: the MIRD Approach

Background:

1. **Radiation absorbed dose, D,** is a measure of the energy deposited (Joules) per kilogram of absorber (e.g., an organ in the body). 1 Gray (Gy) = 1 Joule / kg

2. **Equivalent dose, H**, is related to absorbed dose by the radiation's "quality factor", Q:

$$H\ (Sv) = D\ (Gy) \times Q\ (unitless)$$

3. The MIRD formalism provides a procedure for calculating D to any "target organ" from any source organ by following a 3-step procedure:

   A. Estimate the amount of radioactivity and time spent by the radioactivity in one or more source organs.

   B. Determine the amount of radiation energy emitted by the radioactivity in the source organs (from the energy of the emissions and their relative abundance.)

   C. Determine the fraction of energy emitted by the source organ that is absorbed by the target organ (a function of particle energy and type, distance, density, etc.)

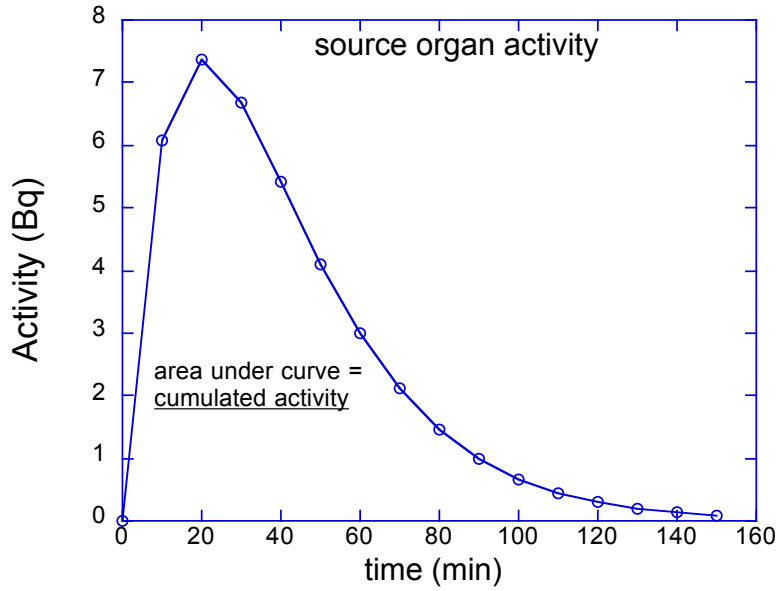
Internal Dosimetry: the MIRD Approach

A. Estimate the total number of nuclear decays expected to occur in a given source organ.

- The **cumulated activity** is the integral (sum) of the radioactivity (Bq) in the source organ from the time of initial administration of the radiopharmaceutical to infinity:

$$\tilde{A} = \int_0^\infty A(t)dt$$

The cumulated activity has units of Becquerel-seconds (Bq-s).



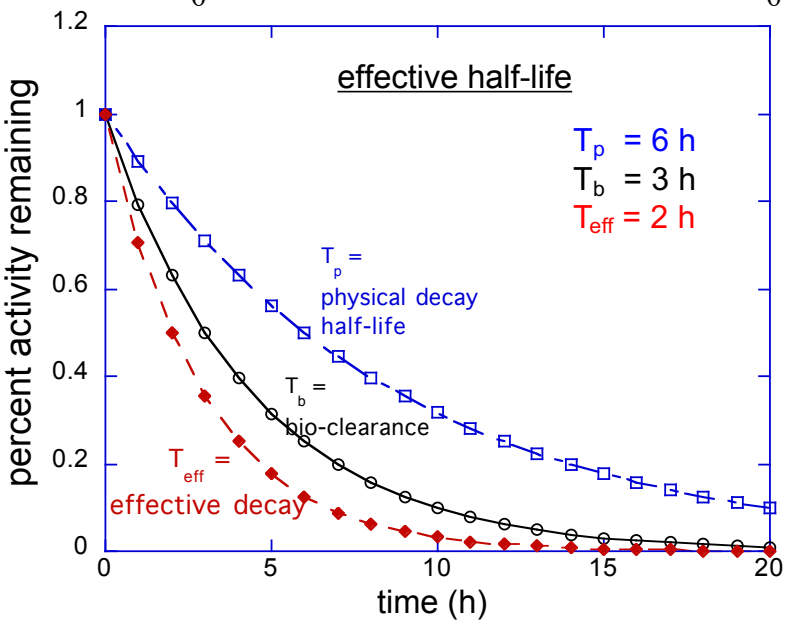
Internal Dosimetry: the MIRD Approach

A. Estimating the total number of nuclear decays expected to occur in a given source organ.

• The **effective half-life** of the radioactivity in an organ is based on two factors:

- the physical half-life, T_p
- the biological clearance half-time, T_b

$$\tilde{A} = \int_0^\infty A_0 e^{-\ln(2)t/T_p} e^{-\ln(2)t/T_b}\, dt = A_0 \int_0^\infty e^{-\ln(2)t\left[\frac{1}{T_p}+\frac{1}{T_b}\right]} dt$$



$$\frac{1}{T_{eff}} = \frac{1}{T_p} + \frac{1}{T_b}$$

Cumulated activity in organ:

$$\tilde{A} = \int_0^\infty A_0 e^{-\ln(2)t/T_{eff}}\, dt$$

$$\tilde{A} = 1.44\, A_0 T_{eff} = 1.44\, A_0 \frac{T_p T_b}{T_p + T_b}$$

Internal Dosimetry: the MIRD Approach

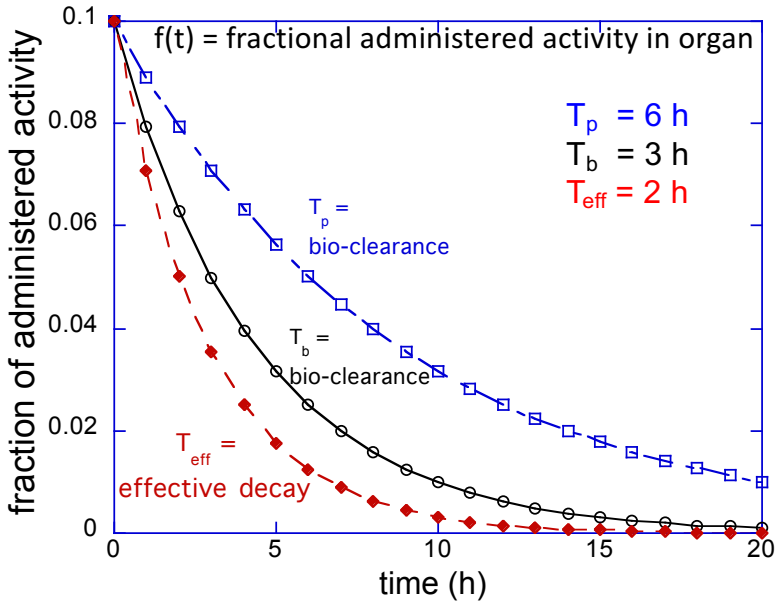
A. Estimating the total number of nuclear decays expected to occur in a given source organ.

- The **residence time** of the radioactivity in an organ is the ratio of the cumulated activity to the administered dose:

$$\tilde{A} = \int_0^\infty A(t)dt = A_0 \int_0^\infty f(t)dt$$, A_0 = administered total activity

f(t) = fraction of A_0 in organ at time, t

"Residence time", $\tau = \frac{\tilde{A}}{A_0} = \int_0^\infty f(t)dt$ = total decays per unit administered activity



Useful concept because it can be used to express dose in terms of dose per activity administered, **BUT**

Opinion:
# of decays per unit activity is not logically a measure of time, even though it has units of time.

Calling this quantity a "residence time" is a poor choice of terminology, as well as confusing and misleading!

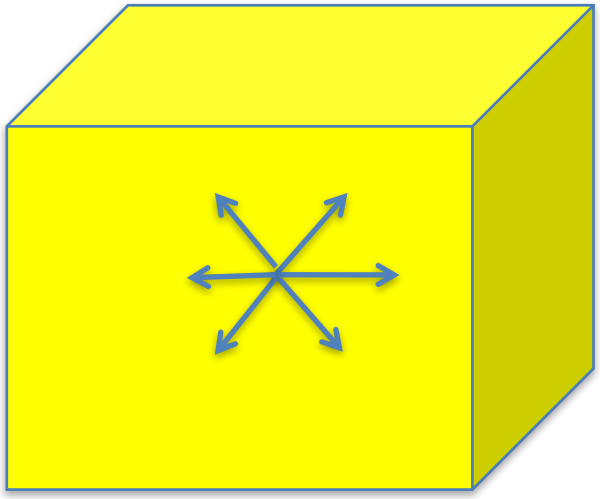
Internal Dosimetry: the MIRD Approach

B. Computing the energy emitted per decay

- The **equilibrium absorbed dose constant** of the radioactivity is the energy emitted per unit of cumulated activity. This is solely a property of the radionuclide in question. For the i'th emission:

$$\Delta_i = 1.6x10^{-13} N_i E_i \quad \text{, in units of Gy-kg / (Bq-sec)}$$

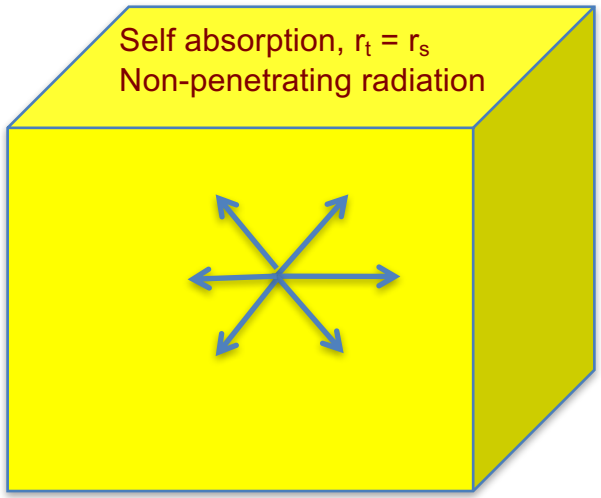
where N_i = the fraction of decays resulting in emission of the i'th particle
E_i = the mean energy of the i'th particle emitted
Δ_i = the equilibrium absorbed dose constant of the i'th particle



Equilibrium conditions exist near the center of a large absorber (large in comparison to the range of all particles emitted).

Internal Dosimetry: the MIRD Approach

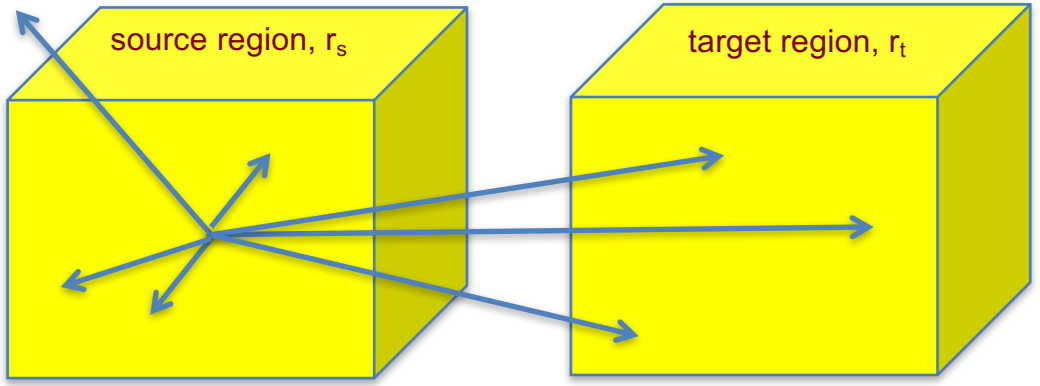
C. Computing the fraction of each particle energy from the source region absorbed in the target region, i.e., **the absorbed fraction,** $\phi_i(r_t \leftarrow r_s)$



Note 1: $\phi \sim 1.0$ for beta particle and low-energy x-ray emission within most organs.

Note 2: $\phi \sim 0.5$ near the organ surface

Penetrating radiation has both self-absorption and distant absorption

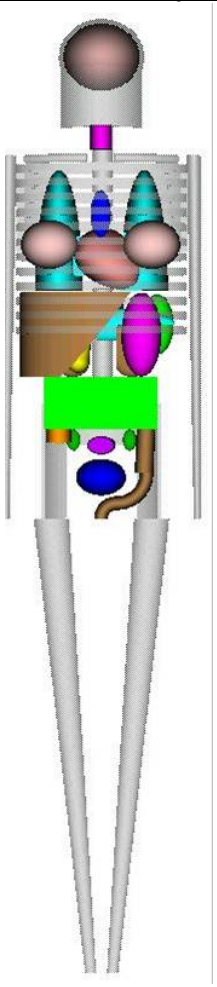


- calculated by Monte Carlo simulation for numerical phantoms

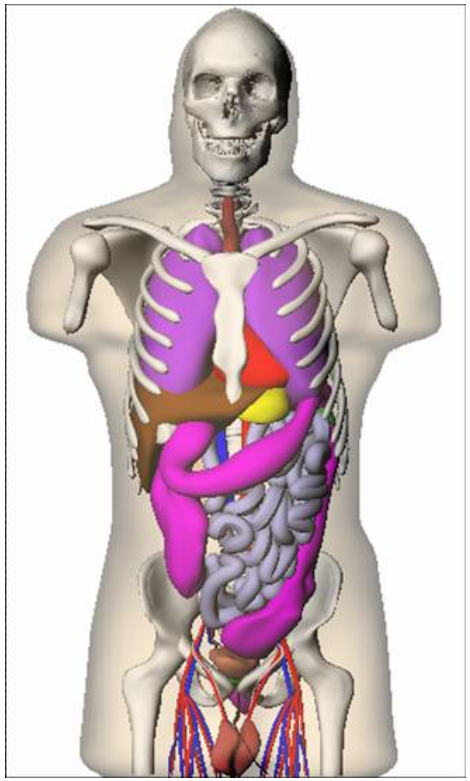
- **reciprocity theorem**: fraction of energy absorbed per gram is the same for radiation traveling from r_s to r_t as it is for radiation traveling from r_t to r_s. (Requires that attenuation be homogeneous.)

C. **Absorbed fractions** have been computed and tabulated for many different radionuclides and combinations of source and target organs using Monte Carlo simulation.

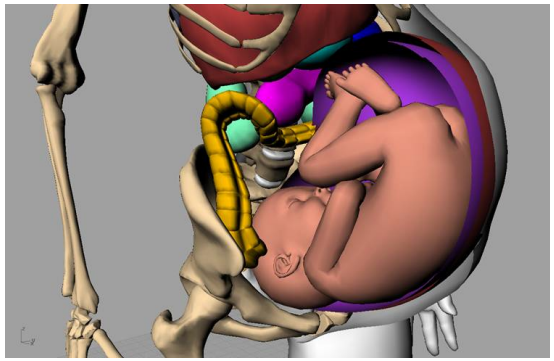
original MIRD phantom

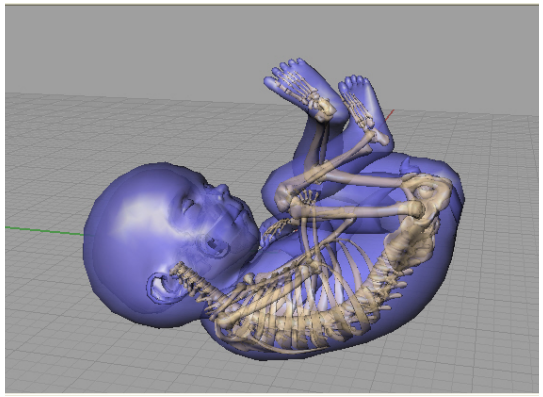


more realistic male phantom



pregnant female and fetal phantoms





Courtesy of: http://www.doseinfo-radar.com/RADARphan.html

D. **Average dose to target region from source region:**

$$D(r_t \leftarrow r_s) = \frac{\tilde{A}}{m_t} \sum_i \phi_i(r_t \leftarrow r_s)\Delta_i$$

E. **Computations simplified further by tabulating "S-factors":**

$$S(r_t \leftarrow r_s) = \frac{1}{m_t} \sum_i \phi_i(r_t \leftarrow r_s)\Delta_i$$

$$D(r_t \leftarrow r_s) = \tilde{A} \cdot S(r_t \leftarrow r_s)$$

F. **Distribution Mass: Effect of body size**

$$D(r_t \leftarrow r_s) = \tilde{A} \cdot S(r_t \leftarrow r_s) \cdot \frac{m_{t,phantom}}{m_{t,patient}}$$

For constant cumulated activity in a source region, if a patient's target-organ mass is bigger than that of the phantom's target organ, the target-organ dose will be correspondingly less.

• Final dose to each target organ obtained by summing over all source organs:

$$D(r_t) = \sum_s A_s \cdot S(r_t \leftarrow r_s)$$

• Administered activity is often limited by the dose to one or more **critical organs**, e.g.:

- renal clearance can affect dose to kidney, urinary bladder, and/or whole body
- GI clearance of activity can increase dose to other abdominal organs and GI tract

• **Whole-body dose** (also called **total-body dose**) is the total energy deposited in the body, divided by the total mass of the body

• The **effective dose equivalent**, $H_E = \sum_{organs} D_{organ} \cdot Q \cdot W_{organ}$

• Different organ weighting factors, W_{organ}, described in ICRP reports from 1977 to 1990.

• Useful data and tables compiled in many MIRD and ICRP reports, and various dose-calculation programs, e.g., OLINDA / EXM, Radar software, etc.

Examples: treatment planning for I-131 thyroid therapy

- Patients considered likely to have high lung uptake or prolonged blood or whole-body clearance are candidates for image-based dosimetry treatment planning.

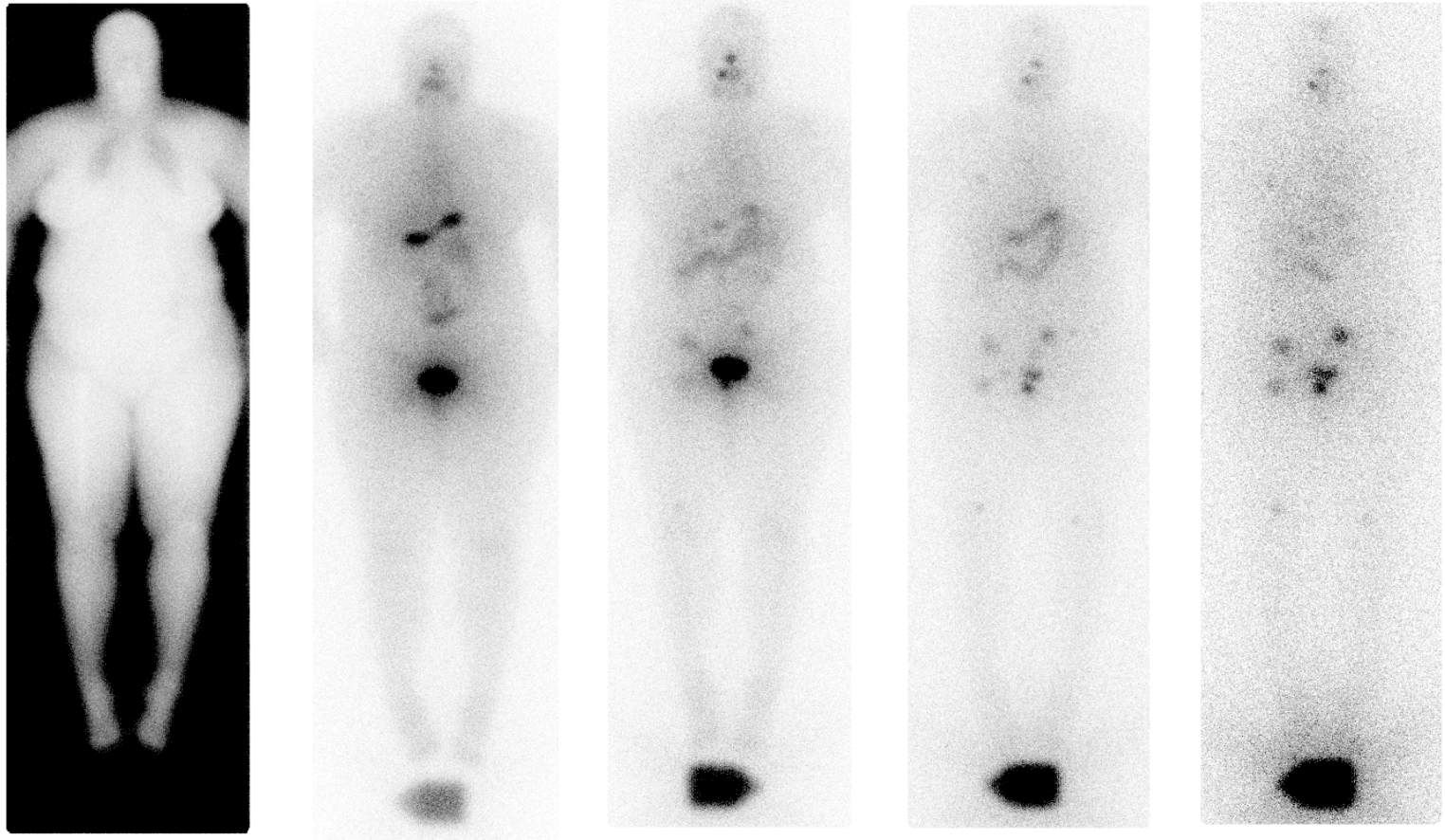
- Benua and Leeper, 1962 described two approaches for limiting therapy doses:

  1. Safety limit of 200-rad dose to blood (as a surrogate for bone marrow)

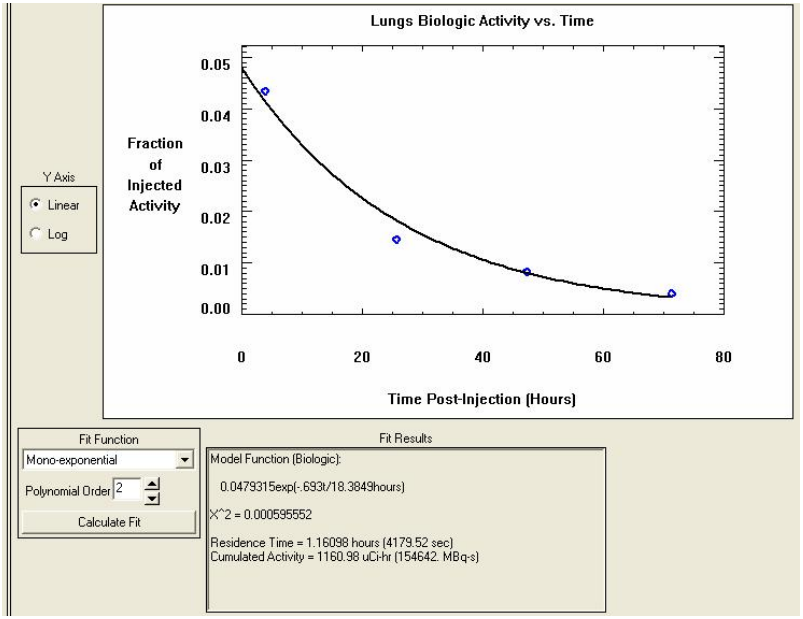
  2. For patients with extensive lung involvement, maximum activity in whole-body 48 hours after administration should be ≤80 mCi to avoid pulmonary fibrosis (or 120 mCi if no lung involvement).

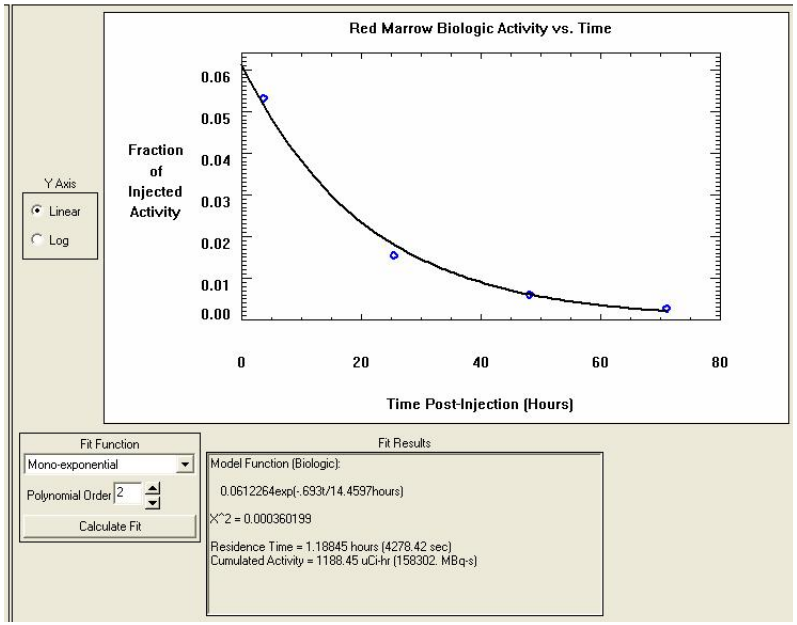
- More recent image-based program ("Nuclidose") includes tools for drawing regions on repeated whole-body scans (after administration of a planning dose of I-131), analysis of blood activity levels, data tables with necessary S-factors, mathematical models of bladder voiding, and a GI tract model.

Patient #1: 44-year-old female, preparing for 2’nd I-131 treatment



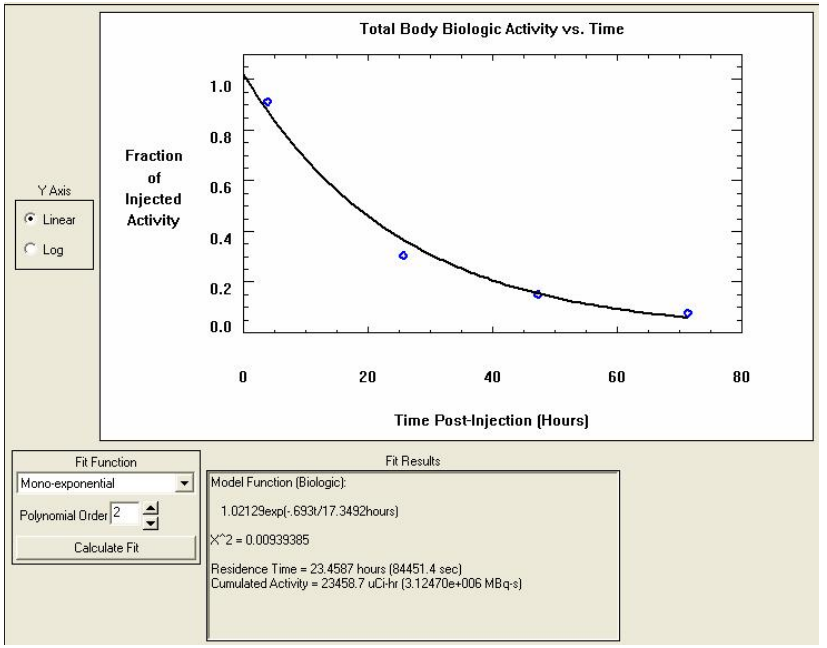
transmission 4 h 24 h 48 h 72 h





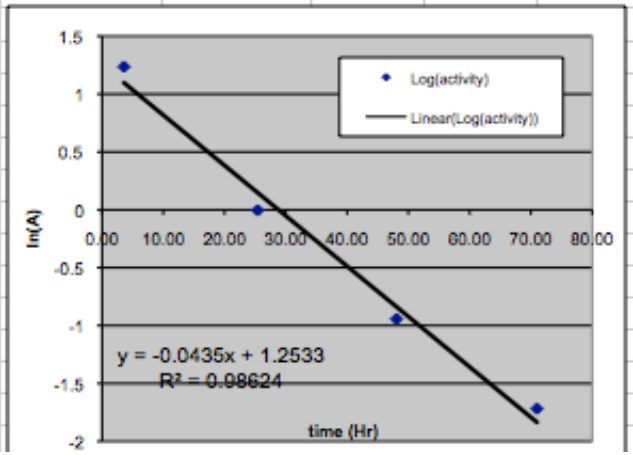
Patient #1: Time-activity curves for lungs, red marrow and whole body, obtained from ROIs drawn on whole-body images.

Measured data fitted to exponential decay functions and used in MIRD-based dosimetry calculations.



Patient #1: Spread-sheet analysis of blood-sample data.

Administered Activity	3.27	mCi	3270	uCi						
Administered Time	3/28/11 8:00									
Bloods counted (Thursday)	3/31/11 7:18									
Age	44	yrs								
body weight	220	lb	100.00	kg						
								4.3% TB = blood vol(mass)		
	time	elapsed time	decay corr. uCi/cc	%ID/cc	%ID/L	ln	fit	calculated %ID/l	act. in blood uCi/cc	
administered time	3/28/11 8:00	0.00					1.25	3.50		
day 1	3/28/11 11:35	3.58	0.1125	0.0034	3.4397	1.2354	1.10	3.00	**483.66**	
day 2	3/29/11 9:25	25.42	0.0326	0.0010	0.9958	-0.0042	0.15	1.16	**140.02**	
day 3	3/30/11 8:05	48.08	0.0127	0.0004	0.3894	-0.9431	-0.84	0.43	**54.76**	
day 4	3/31/11 7:00	71.00	0.0059	0.0002	0.1794	-1.7179	-1.84	0.16	**25.23**	
Tbio	15.93	h								
slope (from the fit)	-0.043509727									
intercept (from the fit)	1.25331375									



NucliDose Quantitative Imaging and MIRD Dosimetry Thu Mar 31 11:09:09 2011

Name: Patient #1 data. Study: Thyroid Scan Date: 2011:03:

Radiation Dose Estimates for the Adult Female - Nonpregnant
for 131 I 53

TARGET ORGAN	TOTAL DOSE mGy/MBq	TOTAL DOSE rad/mCi	PRIMARY CONTRIBUTOR	%	SECONDARY CONTRIBUTOR	%
1) Adrenals	7.17E-02	2.65E-01	Rem. Body	84.0%	Red Marrow	4.8%
2) Brain	5.26E-02	1.94E-01	Rem. Body	96.6%	Red Marrow	3.0%
3) Breasts	5.43E-02	2.01E-01	Rem. Body	90.3%	Lungs	5.7%
4) Gallbladder Wall	7.27E-02	2.69E-01	Rem. Body	81.1%	ULI Conten	7.1%
5) LLI Wall	5.49E-01	2.03E+00	LLI Conten	86.0%	Rem. Body	11.0%
6) Small Intestine	1.17E-01	4.31E-01	Rem. Body	49.7%	Sm Int Con	28.1%
7) Stomach	3.49E-01	1.29E+00	Stomach Co	80.9%	Rem. Body	16.9%
8) ULI Wall	2.60E-01	9.64E-01	ULI Conten	70.7%	Rem. Body	23.4%
9) Heart Wall	7.01E-02	2.59E-01	Rem. Body	84.6%	Lungs	8.5%
10) Kidneys	6.78E-02	2.51E-01	Rem. Body	85.4%	Stomach Co	4.1%
11) Liver	6.68E-02	2.47E-01	Rem. Body	87.2%	Lungs	4.3%
12) Lungs	2.00E-01	7.40E-01	Lungs	87.6%	Rem. Body	10.6%
13) Muscle	6.23E-02	2.31E-01	Rem. Body	85.7%	Urin Bl Co	3.7%
14) Ovaries	9.81E-02	3.63E-01	Rem. Body	62.3%	LLI Conten	17.2%
15) Pancreas	8.18E-02	3.02E-01	Rem. Body	75.7%	Stomach Co	15.7%
16) Red Marrow	1.78E-01	6.57E-01	Red Marrow	59.8%	Rem. Body	35.6%
17) Bone Surfaces	9.59E-02	3.55E-01	Rem. Body	61.1%	Red Marrow	34.0%
18) Skin	5.06E-02	1.87E-01	Rem. Body	92.5%	Urin Bl Co	1.7%
19) Spleen	7.12E-02	2.63E-01	Rem. Body	81.8%	Stomach Co	9.8%
21) Thymus	6.24E-02	2.31E-01	Rem. Body	90.7%	Lungs	6.0%
22) Thyroid	5.57E-02	2.06E-01	Rem. Body	95.1%	Lungs	2.3%
23) Urin Bladder Wall	6.80E-01	2.52E+00	Urin Bl Co	94.1%	Rem. Body	4.7%
24) Uterus	9.28E-02	3.44E-01	Rem. Body	65.1%	Urin Bl Co	20.3%
27) Total Body	7.06E-02	2.61E-01	Rem. Body	75.8%	Red Marrow	5.6%

RESIDENCE TIMES:

LLI Contents**	1.05E+00 hr
Sm Int Contents**	1.99E-01 hr
Stomach Contents**	9.96E-01 hr
ULI Contents**	6.18E-01 hr
Lungs	1.16E+00 hr
Red Marrow	1.19E+00 hr
Urin Bl Cont*	1.50E+00 hr
Rem. Body	1.67E+01 hr

* Dynamic Bladder Model Used (Voiding Interval = 4.00 hr)
80.0% with Tbio = 1.73E+01 hr

** ICRP 30 GI Tract Model for the Adult Female - Nonpregnant used,
100.00% input to the Stomach, 95.00% absorbed by the Small Intestine

Patient #1: Results and conclusions for referring endocrinologist

Summary of dose estimates (organ dose in rads)

Patient info.	Administered Time	age	weight (lb)
	3/28/11 8:00	44	220

Organ		Administered dose (mCi)															
		20	40	60	80	100	120	140	160	180	200	220	240	260	280		limit
MIRD:	rad/mCi																
Lungs	0.74	15	30	44	59	74	89	104	118.4	133.2	148	163	178	192	207	rad	2000 rad
Red Mar	0.66	13	26	39	53	66	79	92	105	118	131	145	158	171	184		200rad
T.Body	0.26	5	10	16	21	26	31	37	42	47	52	57	63	68	73	rad	
Bladder	2.52	50	101	151	202	252	302	353	403	454	504	554	605	655	706	rad	
Benua:																	
Bld(Marrow)	0.32	6	13	19	26	32	39	45	51	58	64	71	77	83	90	rad	623mCi
48hr retain (mCi)	0.15	3	6	9	12	15	18	21	24	26	29	32	35	38	41	mCi	544mCi

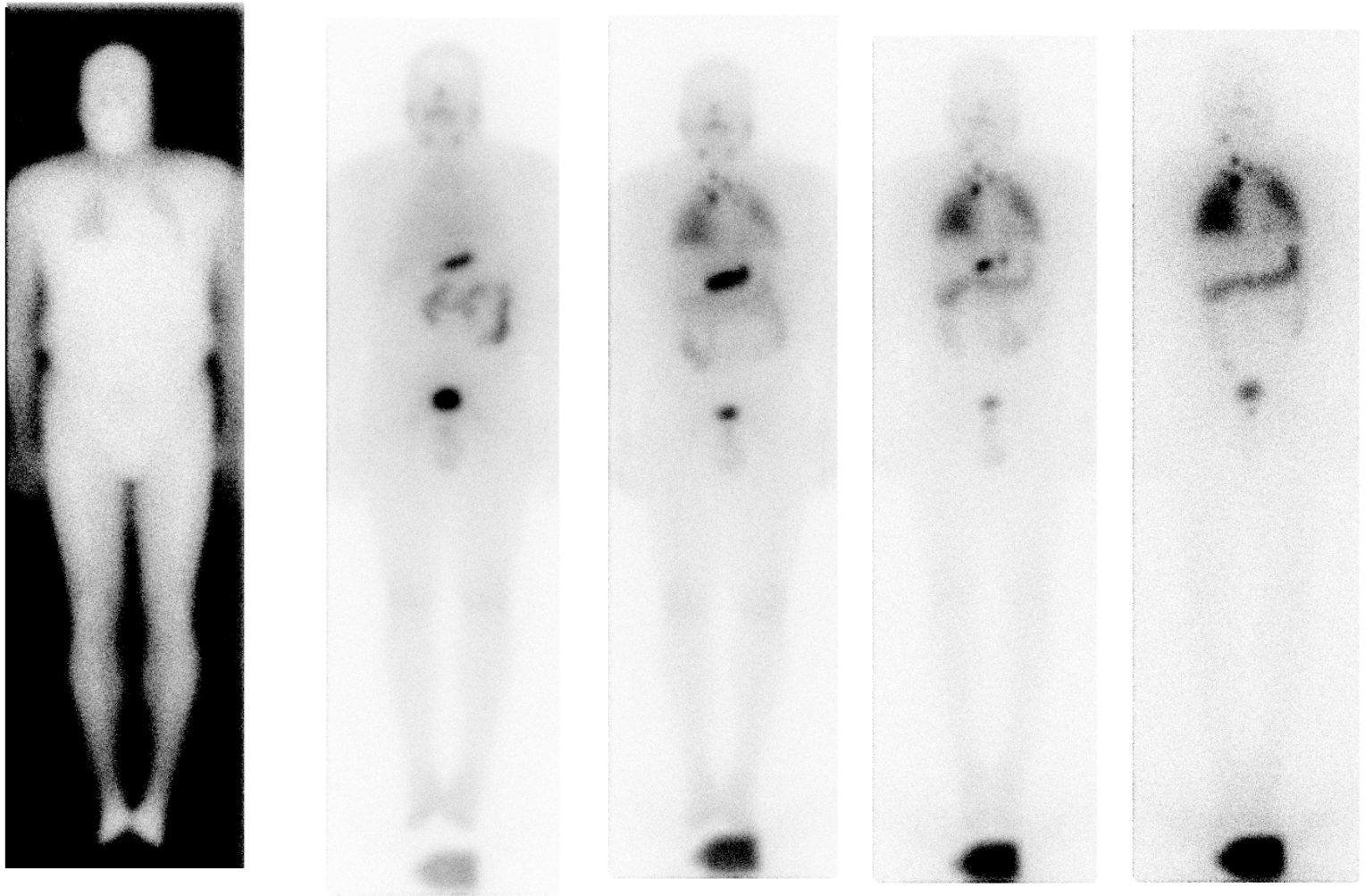
The amount retained at 48 hr should be <80 mCi

Conclusion:

The blood cleared with Tbio of 15.93 h
The WB cleared exponentially with Tbio of 17.35 h.
The overall lung uptake was relatively low (not dose limiting).
The marrow dose limit (200 rad) would be reached with a 300 mCi administration, based on MIRD image-based dosimetry. .

A 530 mCi administration would yield 80 mCi whole-body retained activity at 48 hours and 170 rads to the marrow by the Benua method.

Patient #2: 55-year-old male, preparing for 1’st I-131 treatment



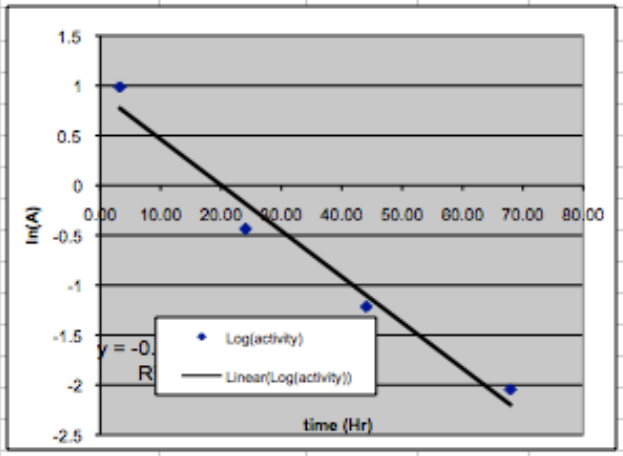
transmission 4 h 24 h 48 h 72 h

Patient #2: Spread-sheet analysis of blood-sample data.

Administered Activity	4.04	mCi	4040	uCi
Administered Time	2/23/09 12:20			
Bloods counted (Thursday)	2/26/09 9:17			
Age	53	yrs		
body weight	230	lb	104.55	kg

	time	elapsed time	decay corr. uCi/cc	%ID/cc	%ID/L	ln	4.3% TB = blood vol(mass) fit	calculated %ID/l	act. in blood uCi/cc
administered time	2/23/09 12:20	0.00					0.92	2.51	
day 1	2/23/09 15:35	3.25	0.1083	0.0027	2.6796	0.9857	0.77	2.17	**486.65**
day 2	2/24/09 12:25	24.08	0.0261	0.0006	0.6468	-0.4357	-0.18	0.83	**117.47**
day 3	2/25/09 8:25	44.08	0.0120	0.0003	0.2964	-1.2161	-1.10	0.33	**53.83**
day 4	2/26/09 8:16	67.93	0.0052	0.0001	0.1294	-2.045	-2.20	0.11	**23.50**

Tbio	**15.09**	h
slope (from the fit)	-0.045928677	
intercept (from the fit)	0.922259027	



Patient #2: Results and conclusions for referring endocrinologist

Summary of dose estimates (organ dose in rads)

	Administered Time	age	weight (lb)
Zuniga, Mateo	2/23/09 12:20	53	230

Organ		Administered dose (mCi)															
		20	40	60	80	100	120	140	160	180	200	220	240	260	280		limit
MIRD:	rad/mCi																
Lungs	2.20	44	88	132	176	220	264	308	352	396	440	484	528	572	616	rad	2000 rad
Red Mar	0.49	10	20	30	40	49	59	69	79	89	99	109	119	128	138		200 rad
T.Body	0.18	4	7	11	14	18	22	25	29	33	36	40	43	47	51	rad	
Bladder	1.80	36	72	108	144	180	216	252	288	324	360	396	432	468	504	rad	
Benua:																	
Bld(Marrow)	0.22	4	9	13	17	22	26	31	35	39	44	48	52	57	61	rad	916 mCi
48hr retain (mCi)	0.19	4	8	12	15	19	23	27	31	35	39	43	46	50	54	mCi	414 mCi
The amount retained at 48 hr should be <80 mCi																	

Conclusions:

The blood cleared with Tbio of 15.1 h
The WB cleared exponentially with Tbio of 20.2 h.

The marrow dose limit (200 rad) would be reached with a 408 mCi administration, using MIRD image-based dosimetry

A 414 mCi administration would yield 80 mCi whole-body retained activity at 48 hours and 91 rads to the marrow by the Benua method.

The lungs cleared slowly (Tbio=170 hr); however, the dose would not exceed the maximum limit of 2000 rad. A 400 mCi administration would yield a lung dose of 880 rad.