MIRD Dose Estimate No. 15: Radiation Absorbed Dose Estimates for Radioindium-Labeled Autologous Platelets

J.S. Robertson, M.D. Ezekowitz, M.K. Dewanjee, M.G. Lötter, and E.E. Watson

The MIRD Committee, Society of Nuclear Medicine, New York, New York

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The radiation absorbed dose estimates for radioindium-labeled autologous platelets are presented in Table 1. The data and assumptions used in the calculations of these estimates follow.

RADIOPHARMACEUTICAL

The data used in this report are based on studies in patients with autologous blood platelet fractions labeled with either ^{111}In-oxine (8-hydroxyquinoline) in acid-citrate-dextrose (ACD)-plasma (*1,2*), or ^{111}In-tropolone (2-hydroxy-2,4,6-cyclohepatatrienone) in ACD-plasma or ACD-saline (*3,4*). Studies using acetylacetone (2,4-pentanedione)-labeled platelets have also been reported (*5,6*). The labeling procedures varied somewhat among the different laboratories, and it now appears likely that variations in the contamination of the preparations with labeled red blood cells affected the results. At the time, only $^{111}InCl_3$ was commercially available. The methods used to convert this to the platelet-labeling agents are described in the articles on biologic data cited below. Because it is also possible to label platelets with ^{113m}In and ^{115m}In, and because commercially available ^{111}In is contaminated with ^{114m}In (<0.1% when shipped), the absorbed doses for these isotopes are also estimated. The presence of a small amount of ethanol (50 μl) or 100 μg of detergent (Tween-80) in commercial sources of ^{111}In-oxine did not affect platelet distribution, but at high levels these substances affected platelet survival times.

NUCLEAR DATA

The nuclear data for ^{111}In, ^{113m}In, ^{114m}In, ^{114}In, and ^{115m}In are given in Table 2. These are based on the data of Weber et al. (*7*).

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For reprints contact: David A. Weber, PhD, Chairman, MIRD Committee, Medical Department, Brookhaven National Laboratory, Upton, NY 11973.

BIOLOGIC DATA

The data used in this report are derived from studies by Scheffel et al. (*2*), Wahner et al. (*8*), Robertson et al. (*9*) and Dewanjee et al. (*10*). Some details of the platelet-labeling methods used in these studies and in one by Kotze et al. (*11*) are compared in Table 3. A discussion of methods used and results obtained by other investigators appears in the paper by Robertson et al. (*9*). Wahner et al. (*8*) studied the ^{111}In disappearance rate from blood and the organ distribution of ^{111}In-oxine-labeled platelets in ACD-saline administered intravenously in 28 healthy volunteer subjects (20 females, 8 males) and of ^{111}In-tropolone-labeled platelets in ACD-plasma in five normal male subjects. Robertson et al. (*9*) studied indium distribution and the rate of disappearance from blood in five normal males using ^{111}In-oxine-labeled platelets in ACD-saline. The mean platelet survival times were calculated by least squares fitting of linear, exponential and gamma function curves to the blood count rate data for each of the five subjects. Of these, the linear fit showed the least variation, and with this fit the platelet survival time was estimated as 8.3 ± 0.3 days. The time courses of the mean activity in the spleen, liver, heart, lung, kidneys and testes for the five subjects were analyzed by fitting the data with a single-exponential function plus a constant if needed.

Scheffel et al. (*2*) studied indium kinetics in nine normal male volunteers using ^{111}In-oxine-labeled platelets in ACD-plasma. They fitted their data with the linear and the gamma variate models, obtaining platelet survival times of 9.0 to 11.6 days and 6.4 to 9.9 days, respectively.

Dewanjee et al. (*10*) compared platelet survival times for ^{51}Cr-labeled platelets with those for ^{111}In-labeled platelets and found the survival times with ^{51}Cr to be slightly longer than those with ^{111}In.

In all of these studies, there is appreciable individual variation in the initial distribution of intravenously administered ^{111}In-labeled platelets, but the disappearance rates of ^{111}In from the blood are quite similar. For the first five days, the blood-activity curves were well described by single-exponential functions. At later times (up to 10 days), there was still no indication of a slower component. By

TABLE 1
Estimated Absorbed Doses from an Intravenous Administration of Indium-Labeled Platelets

	Absorbed dose per unit administered activity							
	rad/mCi				mGy/MBq			
Target organ	^{111}In	^{113m}In	^{114m}In + ^{114}In	^{115m}In	^{111}In	^{113m}In	^{114m}In + ^{114}In	^{115m}In
Blood	0.52	0.065	22	0.22	0.14	0.018	5.9	0.059
Surface of vena cava wall	0.54	0.047	15	0.13	0.15	0.013	4.0	0.035
Surface of aorta wall	0.46	0.042	14	0.13	0.12	0.011	3.8	0.035
Surface of capillary walls	0.014	0.0020	0.66	0.0030	0.0038	0.00054	0.18	0.00081
Kidneys	1.4	0.025	16	0.050	0.38	0.0065	4.2	0.014
Red marrow	1.1	0.016	530	0.040	0.29	0.0043	140	0.011
Liver	2.1	0.044	430	0.15	0.56	0.012	120	0.040
Spleen	30.0	1.3	7300	4.5	8.0	0.36	2000	1.2
Ovaries	0.46	0.012	11	0.032	0.12	0.0034	2.9	0.0086
Testes	0.25	0.0099	9.8	0.029	0.067	0.0027	2.6	0.0078
Remainder of body	0.58	0.016	48	0.047	0.16	0.0044	13	0.013

Note: 1 mGy/MBq = 3.7 rad/mCi. However, because the values in the two sections of this table were calculated separately before rounding off to two significant figures, the corresponding numbers do not always have the exact ratio of 3.7.

pooling the data from these studies by averaging the means weighted by the number of subjects in each study, a composite mean lifetime of platelets in the blood of about 154 hr was yielded. Activities in the liver and spleen typically have early (first hour) values of about 8% and 30% of the injected activity, respectively, as determined by quantitative single-view gamma camera imaging. During the next 10 days, activity (corrected for decay) in these organs rises asymptotically to about 25% in the liver and 40% in the spleen. At 1 hr, 98% of the injected activity is accounted for in the blood, liver and spleen. However, at 200 hr, only 65% is found in these organs. The location of the other 35% has not been determined. Kotze (*11*) cites studies that indicate that 13%–16% of the injected activity is not in the liver, spleen or bone marrow. Therefore, for the present dosimetry purposes, 19% has been assumed to be in the bone marrow, and the remaining 16% has been assumed to be uniformly distributed in the remainder of the body. The liver and spleen data for each subject were fitted by functions of the type

$$A = \alpha_1 e^{-\lambda_1 t} + \alpha_2,$$

where A is activity, α_n is the y-axis intercept of the nth component, λ_1 is the biological disappearance constant, and t is time postinjection of labeled platelets. The averaged results and the residence times, which are calculated from the biological parameters and the physical decay scheme constant, are shown in Table 4.

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TABLE 2. NUCLEAR DATA

Radionuclide		Indium-111				Indium-113m				Indium-115m			
Physical half-life		2.83 d				1.658 h				4.486 h			
Decay constant (λ)		0.0102 h^{-1}				0.418 h^{-1}				0.155 h^{-1}			
Mode of decay		Electron capture				Isomeric transition				Isomeric transition (95%)			
Decay product		Cadmium-111 (stable)				Indium-113 (stable)				Indium-115 (4.41x10^{14}y) and β^- (5%) Tin-115 (stable)			
Principal Radiations	Type	E_i (keV)	n_i	Δ_i (rad·g/µCi·h)	Δ_i (Gy·kg/Bq·s)	E_i (keV)	n_i	Δ_i (rad·g/µCi·h)	Δ_i (Gy·kg/Bq·s)	E_i (keV)	n_i	Δ_i (rad·g/µCi·h)	Δ_i (Gy·kg/Bq·s)
Photons	γ	171.3	0.902	0.329	2.48x10^{-14}	391.7	0.642	0.536	4.04x10^{-14}	336.2	0.454	0.325	2.45x10^{-14}
	γ	245.3	0.940	0.491	3.70x10^{-14}								
	x-rays	23-27	0.826	0.042	3.13x10^{-15}	24-27	0.237	0.012	9.37x10^{-16}	24-28	0.334	0.018	1.32x10^{-15}
Nonpenetrating				0.074	5.56x10^{-15}			0.283	2.13x10^{-14}			0.364	2.74x10^{-14}

E_i Energy per particle or photon.
n_i Mean number of particles or photons per transition.
Δ_i Mean energy emitted per nuclear transition.
"Nonpenetrating" includes photons having E<10 keV, beta particles, and electrons.

TABLE 2 (CONTINUED). NUCLEAR DATA

Radionuclide	Indium-114m				Indium-114			
Physical half-life	49.51 d				71.9 s			
Decay constant (λ)	$5.8\text{x}10^{-4}$ h^{-1}				34.7 h^{-1}			
Mode of decay	IT		EC, β^{+}		β^{-}		EC, β^{+}	
	95.7%		4.3%		99.46%		0.54%	
Decay product	In-114 (71.9s)		Cadmium-114 (stable)		Tin-114 (stable)		Cadmium-114 (stable)	
Principal Radiations								
Type	E_i (keV)	n_i	Δ_i (rad·g/µCi·h)	Δ_i (Gy·kg/Bq·s)	Ei (keV)	n_i	Δ_i (rad·g/µCi·h)	Δ_i (Gy·kg/Bq·s)
Photons								
γ	190.3	0.154	0.0625	$4.69\text{x}10^{-15}$	1300	0.0014	0.00388	$2.92\text{x}10^{-16}$
γ	558.4	0.044	0.0522	$3.92\text{x}10^{-15}$				
γ	725.2	0.043	0.0669	$5.03\text{x}10^{-15}$				
x-rays	23-28	0.363	0.0190	$1.43\text{x}10^{-15}$	23-27	0.00361	0.00018	$1.367\text{x}10^{-17}$
Nonpenetrating			0.303	$2.27\text{x}10^{-14}$			1.65	$1.24\text{ x}10^{-13}$

tion (*12*) derived the residence times for ^{111}In-labeled platelets listed in column (a) of Table 4, assuming that fractions of 0.30 and 0.1 are immediately deposited in the spleen and liver, respectively, and that the remaining fraction (0.60) is cleared from the blood with a half-time of 4 days. For adults, these assumptions yield the following absorbed dose estimates (mGy/MBq): adrenals 0.37, bladder wall 0.066, bone surface 0.23, breast 0.10, stomach wall 0.35, small intestine 0.14, upper large intestine wall 0.14, lower large intestine wall 0.097, heart 0.39, kidneys 0.41, liver 0.37, lungs 0.28, ovaries 0.098, pancreas 0.66, red marrow 0.36, spleen 7.5, testes 0.043, thyroid 0.0881, uterus 0.095, other tissue 0.12. For kidneys, red marrow and liver, these estimates are 7%–30% higher than the present estimates listed in Table 1, but are lower for other organs. The ICRP publication also lists absorbed dose estimates for 1-, 5-, 10-, and 15-yr-old individuals.

TABLE 3
Comparison of Platelet-Labeling Methods

	Scheffel et al. (*2*)	Robertson et al. (*9*)	Dewanjee* et al. (*10*)	Kotze et al. (*11*)
Reagents	Oxine	Oxine	Tropolone	Oxine
Amount (µg)	10–15	50	20	50
Ethanol (µl)	75	50	0	50
ACD-saline (ml)	4	4	4	4
ACD-plasma (ml)	2	2	2	0
Incubation time (min)	60	20	25	30
^{111}In-chloride (µCi)	740–1150	500–1000	200–300	740–1150
Blood/ACD	425/75	43/7	43/7	50/8.5
Platelets Inj'd (× 10^9)	100–200	2–4	3–5	NA
RBC contaminant (%)	NA	3–5	2–4	NA
Labeling eff %	40–60	45–55	70–80	NA
Harvest eff %	NA	40–45	40–45	NA

NA = not available.

* Wahner et al. (*8*) used essentially the same method as Dewanjee et al. (*10*).

DATA ANALYSIS

Murphy and Francis (*13*) present a general discussion of the problem of estimating platelet survival times in the circulating blood. It is generally agreed that the mean survival time is less than 12 days, and some studies indicate that it is only 1–4 days. In part, the problem is a lack of agreement on a mathematical function to describe platelet survival. The principal functions that have been used are the linear function, the exponential function, and the multiple-hit function. These are derived from different models. Use of the linear model is equivalent to the assumption that survival depends upon the age of the platelet, whereas the exponential model implies that platelets are removed from the circulation by some random process that is independent of how long the platelet has been in the circulation. The multiple-hit model (*13*) assumes that platelets sustain a number of injuries or "hits", the cumulative effects of which lead to their destruction. The exponential model is the special case of the multiple-hit model for which the number of hits is one. As the

TABLE 4
Biologic Parameters and Residence Times (τ) for Indium-Labeled Autologous Platelets

Organ	α_1	$\lambda_1(h^{-1})$	α_2	τ(h) ^{111}In (a)	^{111}In (b)	^{113m}In	$^{114}In + ^{114m}In$	^{115m}In
Blood	0.60	0.0069	0	34.4	35.0	1.41	80.2	3.73
Liver	−0.17	0.0069	0.25	17.2	14.5	0.20	408	0.57
Spleen	−0.10	0.0069	0.40	30.3	33.4	0.72	676	1.98
Red marrow	−0.18	0.0069	0.19	9.76	8.1	0.03	304	0.11
Remainder of body	−0.15	0.0069	0.16	3.9	6.9	0.03	256	0.11

$$\tau = \frac{\alpha_1}{\lambda_1 + \lambda} + \frac{\alpha_2}{\lambda}$$

For λ values, see Table 2.
(a) ICRP 53 values (*12*).
(b) MIRD values (this report).

number of hits increases, the multiple-hit function approaches the normal, or Gaussian, distribution function.

ABSORBED DOSE

The residence times listed in Table 3 and the S values from MIRD Pamphlet No. 11 (*14*) were used to calculate the mean absorbed dose per unit administered activity according to the method described in the MIRD Primer (*15*), except that the blood and blood vessel doses were calculated according to the method of Akabani and Poston (*16*). The results are shown in Table 1.

The problems encountered in considering nonuniform distribution of activity within tissues and the associated nonuniform absorbed dose patterns are discussed in the accompanying editorial (*17*).

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