Whole-Body Effective Half-Lives for Radiolabeled Antibodies and Related Issues

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ABSTRACT

Radiolabeled antibodies (RABs) are being developed and used in medical imaging and therapy in rapidly increasing numbers. There are concerns about the radiation exposure of caregivers and the general public from treated patients. The magnitude of this hazard is closely related to the RABs' whole-body effective half-life (T_e). Data on whole-body effective half-lives were calculated from external dose rates obtained from attending physicians and radiation safety officers at participating institutions. Calculations of T_e s were made using exponential regression analyses of data from patients receiving single and multiple administrations.

These data were analyzed on the basis of age, sex, isotope label, radiation energy, antibody type, disease treated, method of administration, and number of administrations.

The effective half-life in the blood did not correlate with the T_e . Values of T_e varied by a factor of two for patients taking the same RAB. A single exponential clearance rate, compared with a bi-exponential clearance rate, provides an adequate fit for 95% of the data sets tested.

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EXECUTIVE SUMMARY

Whole-body effective half-life (T_e) for a radio-labeled antibody (RAB) is a primary factor in estimating the external dose deliverable to people near to a patient. The T_e also is required to estimate waste discharges and predict contamination levels.

External radiation doses from patients treated with RABs were investigated. Such information, expressed as a function of time after administration of RABs may be useful in supporting discussions on the criteria for discharging the patients.

Attending physicians, Radiation Safety Officers (RSOs), or medical health physicists at institutions participating in clinical trials with RABs were asked to provide whole-body clearance rate data for RABs. Staff extracted that data from the patients' files without patient identifiers to assure confidentiality. The following information was requested: age and sex of the patient; radionuclide and dose administered; type and form of antibody administered; route and method of administration; patient's disease; exposure rate one meter from the patient as a function of time; method of measurement; and number of surveyors who made the measurements. The data provided by respondents was for patients treated with RABs labeled with Tc-99m, I-131, Lu-177, Re-188, and Re-186.

External dose rates measured in air as a function of time at a specified distance from the patient were compiled. Whole-body effective half-lives for about 350 administrations were computed from exponential regressions of the dose rate with time post-administration; one hundred and four of these had six or more measurements. Time did not allow two-component regression analyses on all 104 data sets, so 11 that were identified visually as likely to follow a two-component elimination function were tested. All of them were identified visually to follow a bi-exponential clearance rate. For four of the treatments in these 11, a bi-exponential clearance rate was statistically significant at the 95% confidence level. Values of T_e for the longer lived component were factors of 1.3 to 2.2 greater than that determined using single exponential fits to the data; however, the standard deviation for the longest T_e for 2 of the 4 bi-exponential T_e s in-

cluded the T_e calculated using a single exponential. For 95% of clearance rates we analyzed, a single exponential adequately fit the data.

Clearance rates for the same RAB can vary by a factor of about two from patient to patient. Possible factors influencing this variation are the type of RAB, the disease treated and its stage, patient's well being, age, sex, and metabolism.

Dose received in one year by any member of the public, including members of the family, from a patient treated with RABs is strongly influenced by the associated T_e . Since some T_e values for RABs are greater than those of commonly used radiopharmaceuticals, there is a greater probability of exceeding the annual dose limits for members of the public.

Six clearance rate distributions were tested for normality. While all six had P-values greater than 0.05, four of the distributions had P-values less than 0.25.

Biological half lives for the identical antibody and antibody form using I-131 and Re-188 radiolabels were substantially different (a factor of about five greater for I-131). This finding suggests that knowing the biological clearance rate for one radiolabel does not provide accurate information to predict what the biological clearance rate will be for a different radionuclide label attached to the same antibody and antibody form.

Effective half life of the RAB in blood does not give an accurate measurement of T_e (whole body).

The ratio of integrated exposure and exposure rate of family members to the exposure of one meter from a RAB patient is denoted as the exposure factor. Exposure factors of greater than 100% were deduced from measured dose to family members of patients receiving non-RAB I-131, assuming the family members were at a distance of one meter from the patient. For these cases, family members apparently were at distances of less than one meter from the patient. Therefore, the use of exposure factors (or occupancy factors) for estimating dose from RABs may lead to underestimating the exposure of family

members.

If allowance is made for attenuation of photons by only 10 cm of tissue, and if caregivers of the patient minimize the time near the patient for the first week for RABs with $T_{1/2}$ s greater than 70 h (Table K.1), the current release criteria for a patient containing less than 1.11 GBq (30 mCi) or having a dose rate of less than 0.05 mSv h^{-1} (5 mrem h^{-1}) one meter from the patient should result in doses of less than 5 mSv (500 mrem) in one year to caregivers. Except for In-111, the activity required to produce 0.05 mSv h^{-1} at one meter from a patient is much larger than 1.11 GBq (30 mCi) (Table 3.11). However, for the patient containing high levels of activity, consideration should be given to the potential skin and internal dose to the family and to the public from the resulting contamination of the environment by the patient. This latter issue may require additional investigation.

The results of this work may apply only to the RABs identified in this report.

FOREWORD

The Nuclear Regulatory Commission (NRC) became aware some years ago that radiolabeled antibodies (RABS) were being developed for medical uses including cancer diagnosis and treatment. In order to develop a technical base to support licensing and regulatory decisions and to understand better the potential hazards associated with new biochemistry, larger quantities of radioactivity and the new uses of alpha and beta emitters, the NRC contracted BNL to develop a series of reports.

Two reports already published are NUREG/CR-4444, "Radiation Safety Issues Related to Radiolabeled Antibodies," and NUREG/CR-5877, "Aspects of Monitoring and Quality Assurance for Radiolabeled Antibodies." This report looks at data available on wholebody clearance rates for patients administered RABS. Doses to care-givers and the general public from released patients are related to the wholebody effective half-lives for elimination of the radioactive material. Thus, the data analysis provided here may prove useful in reviewing patient release criteria for medical use of RABS.

The results, approaches, and methods described in this NUREG/CR-6374 are provided for information only. Publication of this report does not necessarily constitute NRC approval of, or agreement with, the findings of the study.

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1 INTRODUCTION

Radiolabeled antibodies (RABs) are being developed and used in medical imaging and therapy. Technical aspects of this approach to imaging and therapy are somewhat different from more common radiopharmaceutical protocols (Barber et al, 1991), and include the types and levels of activity administered to the patient, the temporality of the administration and subsequent imaging, the labeling method, and the pharmacokinetics of the radiopharmaceutical. Tables 1.1 and 1.2 show the radionuclides (and some of their characteristics) presently used to label RABs.

Denardo et al. (1988) observed that the pharmacokinetic behavior of radioiodinated and radio-metal, chelated antibodies differ in humans and mice. Hence, the clearance of RABs from patients must be measured directly if T_e s applicable to humans are to be determined confidently.

The whole-body effective half-life (T_e), also called the effective half-life in this report, for a RAB is a primary factor in determining when it is acceptable to discharge a patient from a hospital because the external and internal doses deliverable to people who interact closely with a patient depend directly on this factor. The T_e also is required to estimate waste discharges, and predict levels of contamination.

Measurements of dose rates from patients as a function of time after administration provide the necessary information to determine T_e s (see Table 1.3). The values of T_e were calculated from data received from institutions carrying out RAB clinical trials. We determined if a bi-exponential function was statistically justified rather than a single exponential function for selected patients. The distributions of T_e for patients administered with the same protocol were investigated for statistical normality. The biological half-life calculated from T_e for two studies using identical antibodies but different radiolabels were compared. The dependence of T_e on patient disease was investigated for two groups of patients with different diseases who had been administered the same antibody. The use of measurements of radioactivity in the blood in determining T_e was evaluated.

External radiation doses from patients treated

with RABs were investigated. Also, some implications of the T_e s for contamination of the environment by patients are discussed. Information on the external dose rates from patients as a function of time after administering RABs was compiled and analyzed to provide a technical basis to support discussions of confinement limits.

1.1 Project Objectives

The following were the objectives of this project:

1. to compile and analyze information on the clearance of RABs from therapy patients,
2. to determine T_e s for different RABs and patients, and
3. to provide some technical basis to help determine if the release limits described in 10 CFR 35 are appropriate for RAB patients.

1.2 Project Benefits

The release limits for RAB patients must comply with NRC regulations for limiting dose to the public. This requires assessing T_e s to assure that patients are not hospitalized unnecessarily, and that dose limits for the public and family of patients are not exceeded.

The results of this study directly benefit patients, hospital staff, the families of patients, and the public by enabling release limits to be based on projected doses that are specific to nuclear medicine.

Table 1.1 Characteristics of radionuclides used to label RABs that emit photons^a

Radionuclide	Physical half-life, h	Exposure rate constant ^b		Principal (>1 %) photon energies, keV, and (percent abundance)
		$\mu\text{C kg}^{-1} \text{ cm}^2 \text{ MBq}^{-1} \text{ h}^{-1}$	$\text{R cm}^2 \text{ mCi}^{-1} \text{ h}^{-1}$	
Cu-67	61.8	4.04	0.58	184 (48), 92 (23)
Y-90	64.0	0.293	0.042 ^c	bremsstrahlung, E (max.) = 2.28 MeV
Tc-99m	6.01	4.39	0.63	141 (>99)
In-111 ^d	67.3	22.4	3.21	245 (94), 171 (90), 23.2 (44), 23.0 (24), 26.1 (8.1), 26.1 (4.2), 26.6 (2.4)
I-123	13.2	11.2	1.60	159 (83), 30.9 (4.5) 31.0 (8.7), 31.7 (2.7), 27.5 (46), 27.2 (25)
I-125	1430	9.97	1.43	31.7 (4.3), 31.0 (14), 30.9 (7.2), 27.5 (74), 27.2 (40)
I-131	192	15.3	2.20	637 (7.3), 365 (81), 284 (6.1)
Lu-177	161	0.63	0.09	208 (11), 113 (6.4), 63 (1.2), 56 (2.9), 55 (1.6), and bremsstrahlung, E (max.) = 0.497 MeV
Re-186	89.3 ^e	1.53	0.22 ^f	137 (9.0)
Re-188	17.0	2.72	0.39 ^f	155 (15), and bremsstrahlung, E (max) = 2.12 MeV
At-211	7.21	~0.21	~0.03 ^g	α -emitter, 900 (0.5), 570 (0.5)

^a After Barber et al., 1991; Barber, 1992; Coursey et al., 1991; Erdtmann and Soyka, 1979; Radiological Health Handbook, 1970; Stabin, 1991; Stabin and Stelson, 1991; Walker et al., 1989; Weber et al., 1989; Williams et al., 1989.

^b Excluding photons <20 keV.

^c Based on the exposure rate from bremsstrahlung (Williams et al., 1989).

^d Not a byproduct material.

^e Coursey et al., 1991.

^f Stabin, M., 1991, Dose Calculations, Radiopharmaceutical Internal Dose Information Center, Medical Sciences Division, Oak Ridge Associated Universities, Oak Ridge, TN, personal communication.

^g The approximation includes photons from the daughter of At-211 (Po-211, 0.52 s half-life).

Table 1.2 Characteristics of radionuclides used to label RABs that emit α - or β -radiation^a

Radionuclide	Physical half-life, h	Maximum beta-range, mg cm ⁻²	Equilibrium dose rate constant ^b Gy kg Bq ⁻¹ h ⁻¹
Cu-67	61.8	200	24.8 E-15
Y-90	64.0	1100	14.9 E-14
Tc-99m	6.01	19	25.8 E-16
In-111 ^c	67.3	48	55.6 E-16
I-123	13.2	29	45.1 E-16
I-125	1430	2	31.2 E-16
I-131	192	210	30.4 E-15
Lu-177	161	162	23.6 E-15
Re-186	89.3 ^d	440	54.9 E-15
Re-188	17.0	1050	12.5 E-14
At-211 ^c	7.21	α -emitter	α -emitter

- ^a After Barber et al., 1991; Walker et al., 1989; Coursey et al., 1991; Weber et al., 1989; Wolf and Shani, 1986; Volkert et al., 1991.
- ^b For electrons and beta particles (Weber et al, 1989). Divide by 7.51 E-14 to obtain rad g μ Ci⁻¹ h⁻¹.
- ^c Not a byproduct material.
- ^d Coursey et al., 1991.

Table 1.3 Published whole-body effective half-lives (T_e s) for RABs

Radionuclide	Antibody				Type of cancer	No. of patients	Reference
	Type	Use*	Dosage, GBq (mCi)	T_e (h)			
I-131	whole chimeric C-17-1A	R _x	0.19 (5)	58±7 T _e WB count 64±13 urine	colon, metastatic	6	Meredith et al., 1991
I-131	whole chimeric C-B72.3	R _x	1.3 - 2.0 (35 - 55)	87 - 110	colon, metastatic	6 ^b	Meredith et al., 1990
I-131	whole IgG2a 1F-5 anti-Cd-20 & IgG1 MB-1 anti-CD-37	R _x	0.32 - 0.81 (8.6 - 22)	17 - 30 19 - 46 37 - 47	B-cell lymphoma	5 ^c	Eary et al., 1990
In-111	F(ab') ₂ fragments to anti CA-19-9	D _x	0.037 (1.0) 0.074 (2.0)	160	colorectal, pancreatic, ovarian, small cell lung	14	Hnatowich et al., 1985
I-131	whole IgG2a Lym-1	R _x	0.074-2.4 (2-65) multiple 1.4-12 (37-324) total	22 - 38	lymphoma, leukemia	5	Denardo et al., 1988
I-131	whole polyclonal	R _x	1.1 (30) and 0.74 (20) on day 5	79 - 101	hepatoma	10	Leichner et al., 1983
I-131	anti-mucin 2G3	R _x	0.65 (15) - 5.5 (150)	95 - 250	ovarian and breast cancer	9	Buckman et al., 1992
In-111	Fragments (Fab') ₂ OV-TL3	D _x	0.15 (~4)	25	ovarian primary recurrent	9 19	Buist et al., 1992
I-131	B72.3 murine IgG ₁ monoclonal	D _x	0.03-0.37 (0.8-10)	82	colorectal carcinoma	35	Carrasquillo, 1992
I-131	monoclonal murine IgG ₁ Anti Breast B72.3	D _x	0.04-0.16 (1-4)	68.2 for plasma clearance no T _e given	colorectal	6 for kinetic studies	Stern et al., 1993
I-131	B72.3 (chimeric)	R _x		18 - 109 ^d	metastatic colorectal	9	Meredith et al., 1993
I-131	CC-49 CC-83 B72.3	D _x kinetics	Not given	44.9 53.6 48.3 - 50.2	metastatic colorectal	8 8	Gallinger et al., 1993
Re-186	NR-LU-13	D _x Ph. I clin. trl.	2 patients 0.93 (25) 7 patients 2.2 (60)	112	Adenocarcinoma: Colon - 4 Gastroesophageal - 2 Lung - 1 Breast - 1 Unknown - 1	9	Weiden et al, 1993

Table 1.3 (Continued)

Radionuclide	Antibody				Type of cancer	No. of patients	Reference
	Type	Use ^a	Dosage, GBq (mCi)	T _{1/2} (h)			
Re-186	NR-LU-10 Intact pancarcinoma antibody	D _x -R _x Ph. I	0.9 (25) - 4.4 (120)	Serum T _{1/2} 20 ± 3.7 ^a	Colorectal - 10 Lung - 2 Ovarian - 2 Renal - 1	15	Breitz et al., 1992
Re-186	Relabeled F(ab') ₂ fragment NR-CO-02 anti- CEA variant	D _x -R _x Ph. I	0.74 (20) - 7.4 (200)	12 ± 6 ^a	Colorectal - 27 Lung - 2 Gastric - 2	31	
Re-186 Tc-99m Re-186	NR-LU-10 F(ab') ₂ NR-CO-02	Dos. study	0.185 (5.0)	38 ^a 26 ^a	Refractory carcinomas	46	Breitz et al., 1993
I-131	Human IgM 16.88	Dist. study	0.3 (8)	Biol T _{1/2} 37.8	Advanced colorectal Men - 14 Women - 6	20	Roos et al., 1993
I-125 I-131	Chimeric IgG MOV 18	D _x Dist. Kin.	0.00185 (0.05)	Biol T _{1/2} 70	Ovarian cancer - 17 Benign - 3 no yes - 2 normal - 1	24	Buist et al., 1993
	F(ab') ₂	D _x Dist. Kin.	0.00185 (0.05)	20.3	Ovarian cancer - 17 Benign - 3 no yes - 2 normal - 1	23	
Tc-99m	IG6 F(ab') ₂	D _x	Not available	9.3	Advanced colorectal	8	Buist et al., 1993
In-111	B72.3	Blodist. imaging	0.1 (3) - 0.19 (5)	283 (11.8 days)	Colorectal	8	Yokoyama et al., 1989
I-131	B72.3	Blodist. imaging	0.04 (1) - 0.37 (10)	79 (3.3 days)	Colorectal	13	
I-111	B72.3	D _x	0.13 (3.5) - 0.2 (5)	α13.2±3.8 β65±5.8	Colorectal	11	Webster et al., 1992
Y-90	Biotin-LC-DOTA	R _x	1.85 (50) - 3.7 (100)	1.3±0.6 serum	Colon, breast	4	Paganelli et al., 1995
I-131		R _x	0.74 (20) - 5.85 (158)	1st treatment 50 2nd treatment HAMA 18	Ovarian	36	Stewart et al., 1989

Table 1.3 (Continued)

Radionuclide	Antibody				Type of cancer	No. of patients	Reference
	Type	Use ^a	Dosage, GBq (mCi)	T _e (h)			
In-111	B72.3 IgG	Kinetic study	0.20 (5.4)	Serum clearance α 6.6 $\pm$ 5.0 β 64.2 $\pm$ 14.2	Colon	5	Harwood et al., 1990
I-131 I-125	B72.3	Kinetic study	0.037 (~1.0) - 0.074 (~2.0)	α 3.7 β 62.4	Colorectal	16	Reilly et al., 1993
I-125	Chimeric 17-1A mAb	Kinetic study	Not expressed in activity units	See footnotes e and f	Colon Single Inj. - 4 3 infusions at 2-wk intervals - 6	10	LoBuglio et al., 1989

a R_x signifies therapy. D_x signifies diagnosis.

b Data provided by W. Bass and S. Richards, University of Alabama, for some of these patients.

c McBaugh (1990) included these patients.

d Varied greatly with HACA levels and 1st and 2nd treatments.

e Murine 17-1A mAb correlating T_e 15 h after single infusion and 16.2 h, after 1 to 24 infusions. Best fit by single exponents.

f Chimeric 17-1A mAb has plasma disappearance curve best fit by a 2-compartment model having a α T_{1/2} of 17.5 h and a β T_{1/2} of 100.5 h.

g Decay corrected clearance times

2 METHODS

During earlier work (Barber et al., 1991), organizations were identified that carried out external dose-rate measurements or imaging measurements that would enable the calculation of T_e s for RABs. Requests for information were sent to these and other organizations.

2.1 Collection of Data

Attending physicians, radiation safety officers, and medical health physicists at institutions participating in clinical trials with RABs were asked to provide data on whole-body clearance for RABs. The data were extracted from patient files by staff without patient identifiers to assure confidentiality. The information requested was the age and sex of the patient; the radionuclide and activity administered; the antibody type and form administered; the route and method of administration; the disease treated; the exposure rate 1 meter from the patient as a function of time; the method of measurement, and the number of people who made the measurements.

2.2 Calculation of Whole-Body Effective Half-Lives (T_e s)

2.2.1 Calculating T_e Assuming a Single-exponential or Bi-Exponential Clearance Rate Model

2.2.1.1. Single-Exponential

External dose rates measured in air at a specified distance from the patient were compiled as a function of time after the dose was administered. Single exponential regressions on dose rate as a function of time were prepared. The T_e was calculated by regressing the natural log of the dose rate (or number of counts per unit time if a sodium-iodide detector was used) from the patient as the dependent parameter, and the time-post-administration as the independent parameter. Dividing the natural log of 2 (0.693) by the regression slope gives T_e . The relative standard deviation of the regression slope (slope standard deviation divided by the slope) is the relative standard deviation of T_e ; from which the standard deviation of T_e was calculated. The latter mea-

sures the confidence of the T_e value. These calculations were carried out using a spreadsheet, but were verified manually using the procedures given by Walpole and Myers (1978).

The regression line was not forced through the initial measurement. Forcing the regression line through the first measurement appears to be justified because 100% of the activity should be present then. However, such forcing implies that there are no uncertainties associated with the first measurement. However, this is incorrect because the same uncertainties exist for the first measurement as for subsequent measurements, and thus, forcing the regression line through the first measurement may bias the calculation of T_e .

2.2.1.2 Bi-Exponential Clearance Rate Model

Bi-exponential regressions were calculated for selected data using the non-linear least squares regression procedure of the SAS/STAT family of computer programs (SAS Institute, 1989). The model equation used in the procedure was

$$\ln(y) = \ln(a e^{-\lambda_1 t} + b e^{-\lambda_2 t})$$

where,

$\ln(y)$ is the predicted dose rate from the patient at time t ,

a and b are the constants for the intercepts of the short and long term component, respectively,

λ_1 and λ_2 are the clearance rates for the short and long term components, respectively.

The procedure calculated which a , b , λ_1 , and λ_2 would best fit the external exposure (or dose) rate data.

As in the single-exponential clearance rate model case, dividing the natural logarithm of 2 by λ_1 , or λ_2 gives the effective half life for the short and long term component, respectively.

2 Methods

2.2.2 Investigation of Single- or Bi-Exponential Clearance Rate

To test if a single- or bi-exponential clearance rate was more suitable to determine $T_{0.5}$, two statistical tests were used. The first was the "runs test" (Walpole and Myers, 1978). If the data are adequately modeled by the regression line, then the measured values should be normally distributed about the predicted regression line. The test required that the number of "runs" be determined for the data set i.e., the number of times the measured data points shift from being either greater or less than the predicted value when the data are organized sequentially with respect to the independent parameter. A graphical interpretation of the number of runs would be the number of times a line connecting each measured data point to the next consecutive data point crosses the regression line, plus 1. The total number of runs for a sample of a certain size should be normally distributed, and tabular values were used to determine with 95% confidence whether or not the data were so distributed.

The second test used the F-test statistic (F_x) to determine if a bi-exponential fit was statistically justified over a single-exponential fit. This statistic is calculated using the following equation

$$F_x = \frac{\frac{\chi^2(n-2) - \chi^2(n)}{2}}{\frac{\chi^2(n)}{N-n-1}} = \frac{\Delta\chi^2_{df=2}}{\chi^2_{df=N-n-1}} \quad (1)$$

where,

- $\chi^2(n-2)$ = chi-squared statistic for the single-exponential regression fit to the data
- $\chi^2(n)$ = chi-squared statistic for the bi-exponential regression fit to the data
- n = 4 = the number of coefficients for the bi-exponential fit to the data
- N = the number of data points in the data set (must be greater than 6 for this comparison)
- df = number of degrees of freedom

The difference of the two chi-square terms for single- and bi-exponential clearance rate must follow a chi-square distribution with two degrees of freedom. Taking the ratio of this quantity with the chi-square per degree of freedom term for the two component exponential then follows the F_x distribution with 2 and $N-n-1$ degrees of freedom. If the calculated F_x value is greater than the 95% confidence tabular value of F_x , a bi-exponential fit is justified.

The F_x ratio is a measure of how much the additional term has improved the chi-square per degree of freedom value. This ratio will be small if the addition of the second term does not improve the fit of the function with one term; conversely, the ratio will be large if the second term improves the fit (Bevington 1969).

The chi-squared statistic for the single-exponential regression fit was calculated using

$$\chi^2 = \sum \left(\frac{1}{\sigma_i^2} (y_i - a e^{-\lambda_1 t_i})^2 \right) \quad (2)$$

where,

- y_i = the measured value for the i (th) data point at time t_i
- $a e^{-\lambda_1 t_i}$ = the predicted value for the i (th) data point based on a single-exponential regression at time t_i
- σ_i^2 = the variance or error of the i (th) data point which is assumed to be equal to y_i

The chi-squared statistic for the bi-exponential regression fit was calculated using

$$\chi^2 = \sum \left(\frac{1}{\sigma_i^2} (y_i - a e^{-\lambda_1 t_i} - b e^{-\lambda_2 t_i})^2 \right) \quad (3)$$

where,

- $a e^{-\lambda_1 t_i} + b e^{-\lambda_2 t_i}$ = the predicted value for the i (th) data point based on a bi-exponential regression at time t_i .

2.2.3 Calculation of Average T_e Values Assuming Patient Independence

The effective half-lives of the same RABs administered in the same form to different patients with the same disease were averaged together giving each patient's T_e equal weight, as shown in equation (4). This method assumes that each patient's T_e is an independent measurement of $\bar{T}_e$. This simple averaging technique is justified over a weighted average in which the weights are inversely proportional to the square of the variance because the uncertainty in the measured T_e may be a result of real biological processes, rather than error in measurement.

$$\bar{T}_e = \frac{\sum_{i=1}^n T_{e_i}}{n} \quad (4)$$

where,

$\bar{T}_e$ = average T_e for all patients at one institution receiving the same RAB treatment

T_{e_i} = the T_e for patient

n = number of patients

The standard deviation of this average also was calculated by treating each patient T_e with equal weight as given in equation 5.

$$SD_{T_e} = \sqrt{\frac{\sum_{i=1}^n (T_{e_i} - \bar{T}_e)^2}{n-1}} \quad (5)$$

2.2.4 Calculation of Average T_e s Assuming Independence of Each Measurement

The average T_e values for patients receiving the identical protocol calculated with equation (4) treats each patient as an independent measure-

ment of T_e . In addition to this method, another method was used. The data from each individual is normalized to the value of the initial measurement. The data from all patients receiving identical treatment protocols then are combined and a regression is carried out using the entire combined data set. The regression method, calculation of T_e from the slope, and standard deviation of T_e is identical to those discussed in Section 2.2.1 for an individual patient. This method assumes each measurement of any patient is an independent one which can be used to determine T_e .

This method gives greater weight to a data set from an individual patient that has the largest number of measurements. Patient to patient differences in clearance rate will be reflected in both the value of the calculated T_e value, as well as the standard deviation of T_e . The T_e determined this way will be similar to that determined using equation (4) if similar numbers of measurement of clearance rate are taken of each patient because each patient's data set then will have similar weight, which is the case when equation (4) is used. However, the standard deviations between the two methods of measurement will differ since the number of measurements is significantly increased for the combined patient regression and the error terms are calculated differently.

2.3 Calculation of Accumulated Dose

The dose (D_T) accumulated during time (t) in a radiation field is given by:

$$D_T = 1.44 T_e D_0 (1 - e^{-\lambda_e t}) \quad (6)$$

where,

T_e is the whole-body effective half-life for the radioactive material.

D_0 is the dose rate at $t = 0$.

λ_e is the effective decay constant for the radioactive material.

2 Methods

Equation (6) can be rewritten to calculate the dose rate (D_0) at the time of release of a patient from the hospital that will result in the delivery of a specified total dose (D_T), at a specified distance, i.e.:

$$D_0 = \frac{D_T}{1.44 T_e (1 - e^{-\lambda_e t})} \quad (7)$$

Equation (7) can be used to calculate dose rates at 1 meter which would assure that the public will not receive more than 5 mSv (500 mrem) in 1 y (8760 h) at a distance of 1 meter from the patient after discharge. Equation (7) is applicable if clearance from the whole body follows a single exponential function.

2.4 Calculation of the Activity Required to Produce a Specified Exposure Rate

The activity (A) required to produce a specified exposure rate (D_0) at 1 meter from a point source in a patient is given by:

$$A = \frac{10^4 D_0}{\Gamma F} \quad (8)$$

where,

A is the activity required to produce D_0 at 1 meter (MBq)

The constant corrects for inverse-square differences between 1 cm and 1 m.

D_0 is a specified exposure rate, $\mu\text{C kg}^{-1} \text{ h}^{-1}$ at 1 meter.

Γ is the exposure rate constant, $\mu\text{C kg}^{-1} \text{ cm}^2 \text{ MBq}^{-1} \text{ h}^{-1}$.

F is the attenuation factor for 10 cm of striated muscle, $F = e^{-10\mu\rho}$.

μ/ρ is the mass attenuation coefficient ($\text{cm}^2 \text{ g}^{-1}$).

If D_0 is taken to be $1.29 \mu\text{C kg}^{-1} \text{ h}^{-1}$ (5 mR h^{-1}) at 1 meter, equation (8) reduces to:

$$A = \frac{1.29 \times 10^4}{\Gamma F} \text{ (MBq)} \quad (9)$$

Attenuation factors were calculated for 10 cm of unit density tissue for the radionuclides in Table 1.1 using the attenuation coefficients for striated muscle reported by Hubbell (1982) and the photon abundances reported by Erdtmann and Soyka (1979). An attenuation thickness of 10 cm was chosen because the current release limit corresponds to the dose rate from a 1.11 GBq (30 mCi) point-source centered in the patient's torso. The assumption that the radius of a patient is 10 cm is conservative because most will have larger girths and greater attenuation characteristics. Tumor masses may be closer to the surface. However, current release limits do not consider the distribution of activity in the body. The assumption that sources are point-sources is conservative for a patient given radionuclides because the dose rate per unit activity for a given radionuclide at a given distance from a distributed source is less than that from a point source.

The attenuation factors were used in equation (9) to calculate the activity in a point-source required to produce 0.05 mSv h^{-1} (5 mrem h^{-1}) at 1 meter for the radionuclides of interest.

3 RESULTS

3.1 Description of Measurement Techniques

Ten of the organizations approached provided data on the clearance rate of RABs from patients. Seven of them gave results from measurements of dose rate at 1 meter from patients as a function of time using an ionization chamber. One respondent (University of Alabama, 1989-1990) made measurements at various distances; the measurements at 46 cm from one of the patients were used to determine the T_e because they appeared to be the most consistent. Studies during 1992-1993 at the University of Alabama at Birmingham Hospital employed a NaI(Tl) detector integrated with a multi-channel analyzer system at a distance of 13.5 feet from the patient. The researchers at Garden State Cancer Center at the Center for Molecular Medicine & Immunology used a hand-held ion chamber at one meter, urine bioassay, and a whole-body gamma camera. They provided T_e data for I-131 and Tc-99m RABs, and both T_e data and exposure rate data for Re-188 RAB patients. Researchers at Memorial Sloan-Kettering Cancer Center used an ionization chamber held at a distance of one meter and in contact with the patient, usually at the sternum. Respondents at the Neo Rx - Virginia Mason Clinical Research Unit measured dose rates with a whole-body gamma camera (Table 3.1). Additional information from each institution about the data that was collected is provided in the appendices.

Most administrations were made by intravenous infusion for as long as 4 h. Some intraperitoneal injections essentially instantaneous (2-3 s), also are given and are noted as such.

3.2 Regression of Clearance Rate Data

3.2.1 Calculation of T_e Assuming Single-Exponential Clearance Rate Models

Approximately 350 graphs of dose rate as a function of time post-administration of RABs were

prepared from the measurement data. Seven percent show two dose-rate measurements, one immediately following administration, and another just before the patient's release; these data are not presented graphically in this report. Regression plots are displayed for clearance rates from individual patients with four or more dose-rate measurements for all of them except for a data set sent by the Neo Rx - Virginia Mason Clinical Research Unit where clearance rates from four randomly selected patients are displayed for each of the four protocols. Twelve graphs of measurements on non-RAB patients receiving I-131 also were prepared for comparison.

A single-exponential clearance rate equation was used to fit all the radiation measurements provided. From the regression slopes, T_e and the standard deviation of T_e were calculated for each patient (Tables A.1, B.1, B.2, C.1, C.2, D.1, E.1, F.1, G.1, G.2, H.1, I.1, I.2, I.3, I.4, I.5, J.1, J.2, J.3, J.4, J.5). Visual examination of the plots of dose rate as a function of time indicated that for the majority of the treatment data, a single-exponential clearance rate model fits the data quite well (Figures A.5-A.11, B.5-B.19, C.5-C.28, D.2-D.5, E.2-E.5, F.2-F.11, G.3-G.25, H.4-H.7, I.12-I.63, J.7-J.26).

Averages for patients treated with the same protocol and having the same disease were averaged together in tabular format (Tables A.2, B.1, B.2, C.1, C.2, D.1, E.2, F.2, G.1, G.2, H.1, H.2, H.3, I.1, I.2, I.3, I.4, I.5, J.1, J.2, J.3, J.4, J.5). Values of T_e determined from two dose-rate measurements are included in estimating the average T_e values using equation (4). Averaging the T_e values obtained from two measurements is justified because for 95% of the patients in this report, a single-exponential fit to clearance rate data is justified (Section 3.2.2).

To better compare the different clearance rates of such patients, plots were made normalizing the dose rate measurements to the initial dose-rate measurement for each patient (Figures A.1-A.4, B.1-B.4, C.1-C.4, D.1, E.1, F.1, G.1-G.2, H.1-H.3, I.1-I.11, J.1-J.6). These figures show wide variability of the grouped data about the combined regression line, which contrasts with the typically small variability of the data about the

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regression line for individual patients. The larger error term for the grouped data compared with individual clearance rate data is shown in the tables at the beginning of each appendix. As an example, Figures I.12-I.28 for individual measurements for patients treated with CC-49, IgG, for colon cancer at Memorial Sloan-Kettering Cancer Center indicate that the errors of the regression line about the data are quite small for each patient compared to errors of the regression line about the combined data shown in Figure I.1. This is further borne out in Table I.1 for the same data set where values of T_e and the corresponding standard deviation are listed for the first administration. The standard deviation for the combined T_e for measurements made at 1 meter is 25% of T_e , whereas the average standard deviation for the 15 individual patient measurements is 11%.

Information provided by the Garden State Medical Center included calculations of T_e using a single exponential clearance rate model. The large quantity of data (600 administrations) from this institution made duplicate calculation of T_e values impractical. Rather, the results are averaged using equations (4) and (5). Measurements for several patients treated at this institution with Re-188 RABs were received, and these data are plotted as well (Figures H.4-H.7).

3.2.2 Comparisons of Single- or Bi-Exponential Clearance Rate

Several plots of the clearance rate suggest that a bi-exponential clearance rate model may be more appropriate than a single-exponential model. Both the "runs test" and the F_x test discussed in Section 2.2.2, were used to determine the suitability of each.

The number of clearance rate data sets collected were too large to assess every data set. Rather, selected ones for individual administrations were tested which appeared visually to follow a bi-exponential clearance rate.

A single-exponential fit to data exhibiting a two-component exponential clearance rate will underestimate both the initial and final measurements and overestimate the median measurements.

For the "runs test," this pattern requires three runs. The number of measurements required to reject the appropriateness of the single-exponential fit with 95% confidence for three runs is greater than eleven. Since many of these data sets have fewer than eleven measurements, the "runs test" was not sensitive enough to determine the inappropriateness of the single-exponential for all but the data shown in Figure I.38 for dose measurements made at 1 meter (Table 3.2). The measurements at 1 meter follow neither a single- nor a bi-exponential clearance rate; however, the pattern for the readings taken at the sternum of the patient (not displayed) appear to follow a single-exponential clearance rate.

The F_x test required a minimum of 6 measurements to determine the clearance rate, which eliminated a large portion of the data from the comparison. Eleven data sets with six or more measurements showed a possible bi-exponential clearance rate. A bi-exponential fit for four of these eleven was statistically justified with 95% confidence (Table 3.2 and Figures 3.1-3.4). For these four data sets, the whole-body effective half lives for the longer component are factors of 1.3 to 2.2 greater than that of the single exponential fit. It should be noted, however, that the standard deviation of the greater T_e for two of the four data sets includes the T_e for the single exponential fit. Many measurements taken after the shorter T_e component becomes insignificant would be required to minimize the standard deviation of the longer T_e component for the bi-exponential fit to the data.

Further analyses of the clearance rate of patients number 1 and 11 treated with 3F8 RAB were made on dose measurements taken at the sternum. Calculations of the F_x statistic verified that a bi-exponential component fit was justified for patient 1, but not for patient 11.

Five out of the eleven patient data sets that visually appear to have a bi-exponential clearance rate pattern were taken from data provided by Memorial Sloan-Kettering Cancer Center for 21 patients administered 3F8 RAB. To test the possibility that the entire treatment group exhibited a bi-exponential clearance rate, a bi-exponential fit was carried out for the entire group of patients receiving a first administration of 3F8 (data shown

in Appendix I Table I.4 and Figure I.6). The results showed that a single exponential clearance rate adequately fitted the data. This is noteworthy because a bi-exponential fit was justified for two of the patients. Hence, data from individual patients should not be combined to accurately represent the clearance rate function for all cases.

The F_x test demonstrated that a bi-exponential clearance rate was justified for only four out of eleven clearance rate plots that visually appeared to follow a bi-exponential clearance rate. Thus, we assume that data which visually appear to follow a single-exponential clearance rate will not be better fitted by a bi-exponential function.

Table 3.1 Listing of clearance rate measurement techniques for institutions providing data and appendix location of corresponding data.

Institution	Appendix	Method used to measure clearance rate		
		#1 ^a	#2 ^a	#3
NIH, Bethesda	A	IC at 1 m		
U of Alabama, Birmingham 1989-1990	B		IC at 0.46 m	
U of California, Davis	C	IC at 1 m		
U of Washington, Seattle	D	IC at 1 m		
VA Med Center, Minneapolis	E	IC at 1 m		
U of Minnesota, Minneapolis	F	IC at 1 m		
U of Alabama, Birmingham 1992-1993	G			Nal(Tl) at 4.1 m
Garden State Cancer Center at the Center for Molecular Medicine & Immunology, Newark	H	IC at 1 m	Urine	Whole-body γ camera
Memorial Sloan-Kettering Cancer Center, New York	I	IC at 1 m	IC at contact (sternum)	
Neo Rx - Virginia Mason Clinical Research Unit, Seattle	J			Whole-body γ camera

^a IC refers to hand-held ionization chamber.

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Figure 3.1 Single and bi-exponential fit to clearance rate for patient F administered with I-131 non-RAB. Data provided by the University of Minnesota.

Figure 3.2 Single and bi-exponential fit to clearance rate data for patient number 1 for the first administration of I-131 RAB CC-49 (IgG). Data provided by the University of Alabama (1992-1993).

Figure 3.3 Single and bi-exponential fit to clearance rate data for patient number 1 for the first administration of I-131 RAB 3F8 (IgG). Data provided by the Memorial Sloan-Kettering Cancer Center.

Figure 3.4 Single and bi-exponential fit to clearance rate data for patient number 11 receiving a third administration of I-131 RAB 3F8 (IgG). Data provided by Memorial Sloan-Kettering Cancer Center.

Table 3.2 Computations necessary to determine if a bi-exponential clearance rate is justified rather than a single-exponential clearance rate.

Figure Number	Patient ID	Anti-body	Adminis-tration #	# of Mea-sure-ments	T _e Single-exp Fit (h)	SD T _e Single-exp Fit (h)	Runs Test Single-exp Fit*	χ^2 Single-exp Fit	T _e #2 Great-est of Bi-exp Fit (h)	SD T _e #2 Great-est of Bi-exp Fit (h)	T _e #1 Least of Bi-exp Fit (h)	SD T _e #1 Least of Bi-exp Fit (h)	Runs Test of Bi-exp Fit*	χ^2 of Bi-exp Fit	F _x of Adding Second Term	95% Confidence F _x	Bi-exp Fit Justified?
A-7	J	B72.3	1	6	49	3.8	Ok	0.77	135	11	26	8.2	Ok	0.043	8.5	199	No
B-17	V	B72.3	1	6	60	16	Ok	11	1247	254	18	8.5	Ok	1.5	3.1	199	No
3.1.1,F-9	F	Non-Rab	1	7	58	8.8	Ok	0.32	104	16	6.4	4.1	Ok	0.010	30	19.0	Yes
3.1.2,G-12	1	CC-49	1	7	70	5.4	Ok	17	93	11	22	6.1	Ok	0.38	66	9.55	Yes
G-15	4	CC-49	1	8	44	7.3	Ok	3.1	45	1.6	0.32	0.041	Ok	5.0	-0.77	6.94	No
I-38	10	M-195	2	13	47	5.3	No	6.0	47	<1%	3.1	<1%	No	6.0	-0.006	4.46	No
3.1.3,I-43	1	3F8	1	8	23	2.3	Ok	0.89	51	52	11	4.3	Ok	0.066	19	9.55	Yes
I-49	8	3F8	4	9	36	6.1	Ok	0.99	73	57	25	6.6	Ok	0.75	0.48	6.94	No
I-51	10	3F8	3	10	45	4.0	Ok	2.9	49	5.6	15	21	Ok	1.1	3.9	5.79	No
3.1.4,I-52	11a	3F8	3	12	34	4.4	Ok	0.99	51	27	19	10	Ok	0.27	9.2	4.74	Yes
I-58	16	3F8	4	6	32	4.3	Ok	10	38	<1%	1.0	0.17	Ok	0.51	19	199	No

*"OK" indicates the deviations of the data about the regression line were not sufficiently significant to reject the single exponential fit hypothesis. "no" signifies a single exponential fit is not justified at the 95% level of significance.

3.3 Combining the T_e Data

3.3.1 Calculating Average T_e Values

We list the average values of T_e calculated by both using equation (4) treating each patient T_e as an independent measurement of T_e , and by carrying out a regression on the combined normalized data and corresponding standard deviations (Tables A.2, B.1, B.2, C.1, C.2, D.1, E.1, F.2, G.1, G.2, H.1, H.7, I.1-I.5, J.1-J.5).

The regressions of the combined data sets for each protocol are shown graphically (Figures A.1-A.4, B.1-B.4, C.1-C.4, D.1, E.1, F.1, G.1, G.2, H.1-H.3, I.1-I.11, J.1-J.6). They provide additional information on clearance rates for patients from whom only 2 or 3 measurements were taken.

The standard deviations for the method using equation (4) are typically larger than those determined from the combined regression; this is due to the latter having many data points as well as fundamental differences in the calculational methods. While this difference exists, it is reassuring to note that for many of the treatment protocols, the T_e values and corresponding standard deviations overlap for the two different methods (i.e., Tables I.4 and I.5).

We believe that while the combined regression method of calculating T_e yields a smaller error term than that calculated using equation (4), the data set is better represented by treating each patient's measurement as an independent measurement of T_e , rather than assuming all measurements of clearance rate are from the same distribution in the combined regression case. The rationale for this assertion is that the distribution of measurements for one patient may differ from that of another, and so each measurement is not an independent measurement of the same distribution. Also, since not all the patients in each treatment group had the same number of measurements taken, the combined regression gives greater undue weight to the clearance rates of a patient who had the greater number made.

3.3.2 Distribution of T_e Values

The distributions of T_e values were analyzed for statistical normality. Preliminary visual examination of frequency distributions of six treatment groups indicated that the T_e distributions were either Poisson or normal (Figures 3.5 - 3.10).

The Wilk-Shapiro test (SAS Institute, 1989) was used to calculate the probability (P-value) that the distributions were normally distributed (Table 3.3). Values of P can be interpreted as the probability that the sample came from a normal distribution. The level of significance (α) chosen for the test was 0.05. This gave a 5% chance of claiming the distribution was not normal, when, in fact, the true distribution was not normally distributed a Type II error was not considered.

While none of the distributions had P-values less than 0.05, the values for 4 of the 6 distributions were small (less than 25%) (Table 3.3). Since the numbers of samples in each distribution were small (9 to 21), deviations from normality would become apparent with larger samples. If the distributions are not normally distributed, then comparison of treatment groups should be made using non-parametric tests.

3.3.3 Evaluation of Multiple Administrations

Many patients received multiple RAB treatments. In some cases, a previous treatment influences the RAB clearance rate of the subsequent treatment. This is most evident with patients who develop human anti-mouse antibody (HAMA), in which subsequent T_e s can be factors of 2-10 less than previous ones. For patients not developing this antibody, the T_e may be constant (Figure 3.11). The T_e for this patient over the course of a year varied by less than 20% from the average for 13 treatments. Another example of similarities in T_e s for multiple treatments also is seen in Figures I.29-I.63 and in Tables I.2-I.5 in which average treatment T_e s are within one standard deviation of each other.

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Figure 3.5 Frequency distribution for patients treated with the first administration of I-131 RAB B72.3, chimeric, for colon cancer. Data provided by Bass and Richards (1992). See Table 3.3 and Appendix B for additional information.

Figure 3.6 Frequency distribution for patients treated with first administration of Lu-177 RAB CC-49, IgG, for ovarian cancer. Data provided by the University of Alabama for patients treated in 1992-1993. See Table 3.3 for additional information.

Figure 3.7 Frequency distribution for patients treated with the first administration of I-131 RAB CC-49, IgG, for prostate cancer. Data provided by the University of Alabama for patients treated in 1992-1993. See Table 3.3 for additional information.

Figure 3.8 Frequency distribution for patients treated with the first administration of I-131 RAB CC-49, IgG, for colon cancer. Data provided by Memorial Sloan-Kettering Cancer Center. See Table 3.3 for additional information.

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Figure 3.9 Frequency distribution for patients treated with the first administration of I-131 RAB M-195, IgG, for myelogenous leukemia. Data provided by Memorial Sloan-Kettering Cancer Center. See Table 3.3 for additional information.

Figure 3.10 Frequency distribution for patients treated with the first administration of I-131 RAB 3F8, IgG, for neuroblastoma. Data provided by Memorial Sloan-Kettering Cancer Center. See Table 3.3 for additional information.

Figure 3.11 Whole-body effective half-life for one patient receiving 13 administrations of I-131 RAB LL2 (Fab') for chronic lymphocytic leukemia. Data provided by Garden State Medical Center.

Figure 3.12 Whole-body effective half-life as a function of patient age for administrations of I-131 RAB 3F8 (IgG). Data provided by Memorial Sloan-Kettering Cancer Center.

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However, researchers at several of the institutions discouraged averaging of T_e s for repeated treatments administered to the same patient (e.g., the T_e determined from the first treatment should not be averaged with the T_e for the second treatment). For this reason, clearance-rate data for patients administered with the same RAB, RAB form, disease, and administration protocol are averaged for treatment number (e.g., first treatment T_e s for multiple patients are averaged together, second treatment T_e s are averaged together, but results from successive treatments are not averaged). In the future, it may be desirable to investigate the possibility of combining T_e s for repeated treatments.

3.3.4 Effects of Patient Gender on T_e

The gender of the patient was not thought to generally influence the clearance rates of RABs; this may not be true in certain situations when different hormones contribute to biological elimination processes affecting RABs. Therefore, when the patient's gender was given, males and females were treated separately. The average T_e s for both sexes were typically within one standard deviation of each other, indicating that averaging irrespective of sex may be permissible and should be further investigated.

3.3.5 Effects of Patient-Age on T_e

It was not within the scope of this study to fully investigate the dependence of the clearance rate on patient age. Figure 3.12 shows data for 21 patients age 3 - 27 y with neuroblastoma treated with 3F8 in the form of IgG. No relationship appears to exist between age and clearance rate; therefore, T_e s were averaged without regard to the patients' ages.

3.3.6 Listing of T_e Values

Values of T_e from data provided in Appendices A-J were summarized (Tables 3.4-3.9). The radiolabels include I-131, Tc-99m, Re-186, Re-188, and Lu-177. The values of T_e are alphabetized according to the patient's disease, antibody, antibody form, radiolabel, and sex. Also listed are the number of patients from which the T_e was calculated, the method of measurement (Table 3.1), and the corresponding table from which the information was extracted. Subsequent administrations are listed in subsequent tables.

Table 3.3 Probability of T_e responses following a normal distribution after one dose.

Corresponding Table	Corresponding Figure	Disease	Radio-label	Anti-body	Anti-body Form	Number of Patients	p-Value*
B.2	3.5	Colon Cancer	I-131	B72.3	IgG	13	0.24
G.1	3.6	Ovarian Cancer	Lu-177	CC-49	IgG	9	0.25
G.2	3.7	Prostate Cancer	I-131	CC-49	IgG	14	0.76
I.1	3.8	Colon Cancer	I-131	CC-49	IgG	15	0.73
I.2	3.9	Myelogenous Leukemia	I-131	M-195	IgG	13	0.06
I.4	3.10	Neuroblastoma	I-131	3F8	IgG	21	0.22

- * Values of p were calculated using the Wilk-Shapiro test. Results were considered significant (distributions were not normally distributed) if the P-value was less than 0.05.

Table 3.4 Whole-body effective half-lives (T_{e} s) for various diseases, RABs, and radiolabels for first administrations.

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T_{e} Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Adenocarcinoma	B72.3		I-131	?	2	35			A.2
Appendix	NP4	Fab'	Tc-99m	M	1			5.6	H.2
Bartholin's Gland Tumor	G9	Fab'	Tc-99m	F	1			5.4	H.2
Biliary Tumor	G9	Fab'	Tc-99m	M	1		5.5	5.3	H.2
Bowel (small)	MN14	F(ab)2	I-131	M	1	49		54	H.2
Bowel (small)	NP4	Fab'	Tc-99m	M	1			5.2	H.2
Breast	chL-6		I-131	F	3	48			C.2
Breast	ml-6		I-131	F	1	36			C.2
Breast	LL2	Fab'	Tc-99m	F	1		5.9		H.2
Breast	MA5	F(ab')2	I-131	F	4			44	H.2
Breast	MA5	Fab'	Tc-99m	F	3		4.7	5.2	H.2
Breast	MA5	IgG	I-131	F	1			34	H.2
Breast	MN14	IgG	I-131	F	1			75	H.2
Breast	MN3	Fab'	Tc-99m	F	3		5.4	5.6	H.2
Breast	NP4	Fab'	Tc-99m	F	12		5.3	5.3	H.2
Breast	RINA	IgG	I-131	F	1			45	H.2
Breast	RS7	Fab	Tc-99m	F	2		3.2	5.4	H.2
Choriocarcinoma	IMMU8	IgG	I-131	F	4		5.6	55	H.2
Cirrhosis	IMMU31	Fab'	Tc-99m	F	1		5.7		H.2
Chron. Lym. Leuk.	LL2	Fab'	Tc-99m	F	2		5.5	5.5	H.2
Colon	B72.3		I-131	F	5		91		B.1
Colon	B72.3		I-131	M	13		67		B.2
Colon	CC-49	IgG	I-131	M/F	15	48	47		I.1

* Method #1, #2, #3 refers to measurement methods listed in Table 3.1. This list is alphabetized according to disease, antibody, antibody form, radiolabel, and sex.

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Table 3.4 (Continued)

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T _s Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Colon	G9	Fab'	Tc-99m	F	5		5.6	5.8	H.2
Colon	G9	Fab'	Tc-99m	M	3		5.3	5.3	H.2
Colon	MN14	F(ab')2	I-131	F	4	39		46	H.2
Colon	MN14	F(ab')2	I-131	M	3	31		35	H.2
Colon	MN14	IgG	I-131	F	2	2		68	H.2
Colon	MN14	IgG	I-131	M	10	30		39	H.2
Colon	MN14	IgG	Re-188	F	6		4.6	14	H.2
Colon	MN14	IgG	Re-188	M	3		4.3	14	H.2
Colon	MN3	Fab'	Tc-99m	M	3		5.3	5.5	H.2
Colon	MU9	F(ab')2	I-131	F	4	38		49	H.2
Colon	MU9	F(ab')2	I-131	M	3	45		43	H.2
Colon	MU9	F(ab')2	Tc-99m	F	2		5.6	5.5	H.2
Colon	MU9	F(ab')2	Tc-99m	M	4		5.6	5.7	H.2
Colon	MU9	Fab'	Tc-99m	F	4		5.5	5.3	H.2
Colon	MU9	Fab'	Tc-99m	M	9		5.5	5.4	H.2
Colon	MU9	IgG	I-131	F	5	58		55	H.2
Colon	MU9	IgG	I-131	M	1	43		51	H.2
Colon	NP4	F(ab')2	I-131	F	3	34		39	H.2
Colon	NP4	F(ab')2	I-131	M	3	33		43	H.2
Colon	NP4	Fab'	Tc-99m	F	15		5.4	5.1	H.2
Colon	NP4	Fab'	Tc-99m	M	25		5.4	5.1	H.2
Colon	NP4	IgG	Tc-99m	M	1		5.7	5.5	H.2
Colon	COL-1		I-131	F	3	20			A.2
Colon	COL-1		I-131	M	2	24			A.2
Colon, Lung, or Ovary	NR-LU-10	IgG	Re-186	F	5			40	J.1
Duodenal	MN14	IgG	I-131	M	1	45		73	H.2

Table 3.4 (Continued)

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T ₀ Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Elevated Marker	IMMU31	Fab'	Tc-99m	F	1		5.1	5.2	H.2
Elevated Marker	IMMU31	Fab'	Tc-99m	M	1		5.3	5.1	H.2
Elevated Marker	MN14	F(ab)2	I-131	M	2			69	H.2
Elevated Marker	NP4	Fab'	Tc-99m	F	1		4.9	5.3	H.2
Endometrial	NP4	Fab'	Tc-99m	F	1		5.7	6.0	H.2
Endometrial	RS7	Fab'	Tc-99m	F	1		5.7	5.9	H.2
Esophageal	MN14	F(ab)2	I-131	M	1	41		42	H.2
Germ Cell	IMMU31	Fab'	Tc-99m	M	1			4.8	H.2
Germ Cell	IMMU31	IgG	I-131	F	1			59	H.2
Germ Cell	IMMU8	IgG	I-131	M	1	37		36	H.2
Gest. Tropho. Dis.	IMMU8	IgG	I-131	F	2			52	H.2
Head/Neck	MN14	IgG	I-131	M	1			55	H.2
Hepatoblastoma	IMMU31	Fab'	Tc-99m	M	1			5.0	H.2
Hepatoma	IMMU31	F(ab')2	I-131	F	5	49		50	H.2
Hepatoma	IMMU31	F(ab')2	I-131	M	3	56		76	H.2
Hepatoma	IMMU31	Fab'	Tc-99m	M	6		5.6	5.4	H.2
Hepatoma	IMMU31	IgG	I-131	F	1	73		86	H.2
HIV (+)	7C5	Fab'	Tc-99m	F	2			5.6	H.2
HIV (+)	7C5	Fab'	Tc-99m	M	9			5.5	H.2
HIV (+)	LL2	Fab'	Tc-99m	M	1			5.5	H.2
Lung	MN14	F(ab)2	I-131	F	1	49		50	H.2
Lung	MN14	IgG	I-131	F	1	50		59	H.2
Lung	NP4	F(ab')2	I-131	F	1	45		46	H.2
Lung	NP4	F(ab')2	I-131	M	1	38		46	H.2
Lung	NP4	Fab'	Tc-99m	M	4		5.4	5.2	H.2
Lung	RS7	F(ab')2	I-131	F	1	41		37	H.2

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Table 3.4 (Continued)

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T _e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Lung	RS7	F(ab') ₂	I-131	M	1	51		48	H.2
Lung	RS7	Fab'	Tc-99m	F	2		1.0	5.2	H.2
Lung	RS7	Fab'	Tc-99m	M	3		3.0	5.3	H.2
Lung	RS7	IgG	I-131	F	1			58	H.2
Lung	RS7	IgG	I-131	M	1			53	H.2
Lung or Gastrointestinal	NR-LU-13	Chimeric	Re-186	F	8			50	J.2
Lymphoma	CD-37		I-131	?	4	42			D.1
Lymphoma	LYM-1		I-131	F	1	25			C.1
Lymphoma	LYM-1		I-131	M	9	28			C.1
Medullary Thyroid	MN14	F(ab) ₂	I-131	F	1	48		42	H.2
Medullary Thyroid	MN14	F(ab) ₂	I-131	M	3	56		62	H.2
Medullary Thyroid	MN14	IgG	I-131	F	2	62		66	H.2
Medullary Thyroid	NP4	F(ab') ₂	I-131	M	1	37		42	H.2
Medullary Thyroid	NP4	Fab'	Tc-99m	F	1		5.5	4.6	H.2
Medullary Thyroid	NP4	Fab'	Tc-99m	M	1		5.5	5.3	H.2
Medullary Thyroid	NP4	IgG	I-131	F	1	41		34	H.2
Mixed	B72.3		I-131	F	1	111			A.2
Myelogen. Leukemia	M-195	IgG	I-131	M/F	13	38	32		I.2
Neuroblastoma	3F8	IgG	I-131	M/F	21	26	23		I.4
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	F	2	35		36	H.2
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	M	1			23	H.2
Non-Hodg Lymphoma	LL2	Fab'	Tc-99m	F	1		5.3	4.7	H.2
Non-Hodg Lymphoma	LL2	Fab'	Tc-99m	M	6		5.5	5.3	H.2
Ovarian	B72.3		I-131	F	4	50			A.2
Ovarian	CC-49	IgG	Lu-177	F	9			76	G.1
Ovarian	MA5	Fab'	Tc-99m	F	1			6.2	H.2

Table 3.4 (Continued)

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T _e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Ovarian	MA5	IgG	I-131	F	1	66		73	H.2
Ovarian	NP4	Fab'	Tc-99m	F	1		5.6	5.5	H.2
Ovarian	RS7	Fab'	Tc-99m	F	1			5.4	H.2
Pancreatic	B72.3		I-131	?	1	48			A.2
Pancreatic	COL-1		I-131	M	1	35			A.2
Pancreatic	MN14	IgG	I-131	M	1			66	H.2
Pancreatic	MN14	IgG	Re-188	F	1		5.1	14	H.2
Pancreatic	NP4	Fab'	Tc-99m	F	1			5.1	H.2
Pancreatic	NP4	Fab'	Tc-99m	M	1			5.1	H.2
Pancreatic	PAM4	Fab'	Tc-99m	F	1		5.3	5.4	H.2
Pancreatic	PAM4	Fab'	Tc-99m	M	1		5.7	5.3	H.2
Pancreatic	PAM4	IgG	I-131	F	1			40	H.2
Pancreatic	PAM4	IgG	I-131	M	1		0.14	48	H.2
Prostate	CC-49	IgG	I-131	M	15			54	G.2
Prostate	NP4	Fab'	Tc-99m	M	1			5.1	H.2
Prostate	RS7	F(ab') ₂	I-131	M	1			61	H.2
Rectal	G9	Fab'	Tc-99m	M	1		5.6	5.5	H.2
Rectal	MN14	F(ab) ₂	I-131	F	1			48	H.2
Rectal	MN14	IgG	I-131	M	1			66	H.2
Rectal	MN14	IgG	Re-188	M	1			16	H.2
Rectal	MU9	F(ab') ₂	I-131	M	2	20		27	H.2
Rectal	MU9	F(ab') ₂	Tc-99m	F	1		5.6	5.5	H.2
Rectal	MU9	F(ab') ₂	Tc-99m	M	1		5.9	5.6	H.2
Rectal	MU9	Fab'	Tc-99m	F	1			5.5	H.2
Rectal	MU9	Fab'	Tc-99m	M	3		5.5	5.4	H.2
Rectal	MU9	IgG	I-131	M	4	52		49	H.2

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Table 3.4 (Continued)

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T _{1/2} Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Rectal	NP4	F(ab') ₂	I-131	M	1			63	H.2
Rectal	NP4	Fab'	Tc-99m	F	2			5.0	H.2
Rectal	NP4	Fab'	Tc-99m	M	10		5.3	5.2	H.2
Renal	A6H		I-131	F	1	36			E.1
Renal	A6H		I-131	M	4	53			E.1
Stomach	NP4	Fab'	Tc-99m	M	2		5.4	5.2	H.2
Testicular	IMMU31	F(ab') ₂	I-131	M	1	37		42	H.2
Testicular	IMMU31	Fab'	Tc-99m	M	1		5.7	5.7	H.2
Testicular	IMMU8	IgG	I-131	M	2			63	H.2
Thyroid	L-6		I-131	M	1	55			A.2
Thyroid	NON-RAB		I-131	F	6	26			F.2
Thyroid	NON-RAB		I-131	M	2	19			F.2
Thyroid	NP4	Fab'	Tc-99m	M	1			5.3	H.2
Unknown	B72.3		I-131	?	1	85			A.2
Unknown Primary	IMMU31	F(ab') ₂	I-131	M	1	62		68	H.2
Unknown Primary	IMMU31	Fab'	Tc-99m	M	1		5.2	5.1	H.2
Unknown Primary	LL2	Fab'	Tc-99m	M	1		5.8	5.9	H.2
Unknown Primary	MN14	IgG	I-131	F	1	61		66	H.2
Unknown Primary	MU9	IgG	I-131	F	1			54	H.2
Unknown Primary	NP4	Fab'	Tc-99m	F	2		5.4	5.0	H.2
Unknown Primary	PAM4	Fab'	Tc-99m	M	1		5.5	5.8	H.2
Unknown Primary	RS7	IgG	I-131	M	1	27			H.2

Table 3.5 Whole-body effective half-lives (T_{e} s) for various diseases, RABs, and radiolabels for second administrations.

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T _e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Breast	chL-6		I-131	F	3	36			C.2
Breast	ml-6		I-131	F	1	35			C.2
Chron. Lymph. Leuk.	LL2	F(ab') ₂	I-131	F	2			32	H.2
Colon	MN14	IgG	I-131	F	1	61			H.2
Colon	MN14	IgG	I-131	M	5	28		35	H.2
Colon	MN14	IgG	Re-188	F	5		4.1	14	H.2
Colon	MN14	IgG	Re-188	M	2		3.2	13	H.2
Colon	MU9	F(ab') ₂	I-131	F	1	33			H.2
Colon	MU9	F(ab') ₂	I-131	M	2	33		42	H.2
Colon	MU9	IgG	I-131	F	2	19		17	H.2
Colon	MU9	IgG	I-131	M	1	10		11	H.2
Colon	NP4	F(ab') ₂	I-131	F	2	30		30	H.2
Colon	NP4	F(ab') ₂	I-131	M	1		38	28	H.2
Colon	NP4	Fab'	Tc-99m	M	3		5.4	5.2	H.2
Colon	NP4	IgG	Tc-99m	F	1		5.6	5.1	H.2
Colon	NP4	IgG	Tc-99m	M	1		5.8	5.4	H.2
Colon	B72.3	Chimeric	I-131	F	3		64		B.1
Colon	B72.3	Chimeric	I-131	M	8		95		B.2
Colon	COL-1		I-131	F	1	16			A.2
Colon	CC-49	IgG	I-131	M/F	4	23	22		I.1
Colon	NR-CO-02	Fab' ₂	Re-186	F	1			31	J.5
Colon	NR-CO-02	Fab' ₂	Re-186	M	3			21	J.5
Colon, Lung, or Ovary	NR-LU-10	IgG	Re-186	F	10			47	J.3
Colon or Lung	NR-LU-10	IgG	Re-186	M	19			39	J.3
Duodenal	MN14	IgG	I-131	M	1	63		77	H.2

* Method #1, #2, #3 refers to measurement methods listed in Table 3.1. This list is alphabetized according to disease, antibody, antibody form, radiolabel, and sex.

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Table 3.5 (Continued)

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T _{1/2} Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Head/neck	MN14	IgG	I-131	M	1	47		54	H.2
Hepatoma	IMMU31	F(ab') ₂	I-131	F	4	39		52	H.2
Hepatoma	IMMU31	F(ab') ₂	I-131	M	1	46		51	H.2
Hepatoma	IMMU31	Fab'	Tc-99m	F	1		5.1	5.3	H.2
Lung	NP4	Fab'	Tc-99m	M	1		5.2	5.4	H.2
Lung	RS7	Fab'	Tc-99m	M	1		5.4	5.3	H.2
Lymphoma	Lym-1		I-131	M	7	31			C.1
Medullary Thyroid	MN14	F(ab) ₂	I-131	F	1	48		52	H.2
Medullary Thyroid	MN14	F(ab) ₂	I-131	M	1	10		8.9	H.2
Medullary Thyroid	NP4	F(ab') ₂	I-131	M	1	20			H.2
Myelogenous Leukemia	M-195	IgG	I-131	M/F	12	35	34		I.2
Neuroblastoma	3F8	IgG	I-131	?	20	25	23		I.4
Non-Hodg Lymphoma	LL2	F(ab') ₂	I-131	F	4	37		40	H.2
Non-Hodg Lymphoma	LL2	F(ab') ₂	I-131	M	6	31		56	H.2
Non-Hodg Lymphoma	LL2	Fab'	Tc-99m	M	1		5.5	5.6	H.2
Ovarian	MA5	F(ab') ₂	I-131	F	1	57		64	H.2
Pancreatic	MN14	IgG	I-131	M	1	49			H.2
Pancreatic	PAM4	IgG	I-131	M	1	46		46	H.2
Rectal	MN14	IgG	Re-188	M	1			14	H.2
Rectal	MU9	F(ab') ₂	I-131	M	1	39			H.2
Rectal	MU9	IgG	I-131	F	1			105	H.2
Rectal	MU9	IgG	I-131	M	1	16		20	H.2
Rectal	NP4	F(ab') ₂	I-131	M	1	51		48	H.2
Rectal	NP4	Fab'	Tc-99m	M	1		5.2		H.2
Rectal	NP4	IgG	Tc-99m	F	1			5.6	H.2
Testicular	IMMU31	F(ab') ₂	I-131	M	2	34		62	H.2
Thyroid	Non-RAB		I-131	F	1	41			F.2
Unknown Primary	MU9	IgG	Re-188	M	1		5.0	14	H.2

Table 3.6 Whole-body effective half-lives (T_e s) for various diseases, RABs, and radiolabels for third administrations

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T_e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Breast	chL-6		I-131	F	1	44			C.2
Breast	ml-6		I-131	F	1	33			C.2
Chron. Lymph. Leuk.	LL2	F(ab')2	I-131	F	1			44	H.4
Colon	B72.3	Chimeric	I-131	M	3		65		B.2
Colon	MN14	IgG	I-131	F	1	12		26	H.4
Colon	MN14	IgG	I-131	M	1	18		21	H.4
Colon	MN14	IgG	Re-188	F	2		3.8	13	H.4
Colon	MU9	F(ab')2	I-131	F	1	38		87	H.4
Colon	MU9	F(ab')2	I-131	M	1	60		81	H.4
Colon	NP4	F(ab')2	I-131	F	1	17		21	H.4
Colon, Lung, or Ovary	NR-LU-10	IgG	Re-186	F	1			24	J.4
Colon or Lung	NR-LU-10	IgG	Re-186	M	2			40	J.4
Colon, Lung, or Ovary	NR-CO-02	Fab'	Re-186	M	1			28	J.5
Hepatoma	IMMU31	F(ab')2	I-131	F	4	43		66	H.4
Lymphoma	Lym-1		I-131	M	5	32			C.1
Medullary Thyroid	MN14	F(ab)2	I-131	F	1	45		45	H.4
Myelogenous Leukemia	M-195	IgG	I-131	?	2	48	46		I.3
Neuroblastoma	3F8	IgG	I-131	?	20	27	27		I.4
Non-Hodg. Lymph.	LL2	F(ab')2	I-131	F	2	38		42	H.4
Non-Hodg. Lymph.	LL2	F(ab')2	I-131	M	4	26		63	H.4
Rectal	MU9	F(ab')2	I-131	F	1	45		48	H.4
Rectal	MU9	F(ab')2	I-131	M	1	34		22	H.4
Rectal	NP4	F(ab')2	I-131	M	1	37		33	H.4
Testicular	IMMU31	F(ab')2	I-131	M	1	34		52	H.4
Thyroid	Non-RAB		I-131	F	1	13			F.2
Unknown Primary	MU9	IgG	Re-188	M	1		4.3	14	H.4

* Method #1, #2, #3 refers to measurement methods listed in Table 3.1. This list is alphabetized according to disease, antibody, antibody form, radiolabel, and sex.

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Table 3.7 Whole-body effective half-lives (T_e s) for various diseases, RABs, and radiolabels for fourth administrations.

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Pa-tients	T_e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1			37	H.5
Colon	B72.3	Chimeric	I-131	F	1		24		B.1
Colon	B72.3	Chimeric	I-131	M	2		30		B.2
Colon or Lung	NR-LU-10	IgG	Re-186	M	3			36	J.4
Hepatoma	IMMU31	F(ab') ₂	I-131	F	1	29		44	H.5
Lymphoma	Lym-1		I-131	M	5	24			C.1
Myelogenous Leukemia	M-195	IgG	I-131	?	1	29	29		I.3
Neuroblastoma	3F8	IgG	I-131	?	14	29	28		I.5
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	F	1			37	H.5
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	M	1			38	H.5
Rectal	MU9	F(ab') ₂	I-131	F	1	59			H.5
Thyroid	Non-RAB		I-131	F	1	13			F.2

- Method #1, #2, #3 refers to measurement methods listed in Table 3.1. This list is alphabetized according to disease, antibody, antibody form, radiolabel, and sex.

Table 3.8 Whole-body effective half-lives (T_e s) for various diseases, RABs, and radiolabels for fifth administrations

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Pa-tients	T_e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1			37	H.6
Colon, Lung, or Ovary	NR-LU-10	IgG	Re-186	M	1			28	J.4
Lymphoma	Lym-1		I-131	M	1	23			C.1
Neuroblastoma	3F8	IgG	I-131	?	7	28	30		I.5
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	F	1			29	H.6
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	M	1			26	H.6
Thyroid	Non-RAB		I-131	F	1	19			F.2

- Method #1, #2, #3 refers to measurement methods listed in Table 3.1. This list is alphabetized according to disease, antibody, antibody form, radiolabel, and sex.

Table 3.9 Whole-body effective half-lives (T_e s) for various diseases, RABs, and radiolabels for sixth administrations

Disease	Anti-body name	Anti-body form	Radio-label	Sex	Number of Patients	T_e Average Values (h)			Table Source
						Avg* Method #1	Avg* Method #2	Avg* Method #3	
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1			32	H.7
Colon	B72.3	Chimeric	I-131	F	1		19		B.1
Neuroblastoma	3F8	IgG	I-131	?	4	31	32		I.5
Non-Hodg. Lymphoma	LL2	F(ab') ₂	I-131	M	1			17	H.7

* Method #1, #2, #3 refers to measurement methods listed in Table 3.1. This list is alphabetized according to disease, antibody, antibody form, radiolabel, and sex.

3.4 Radiolabel Biological Half-life

Knowing the biological half-life of a radiolabel attached to an antibody may not provide sufficient information to calculate the biological half-life of a different radiolabel with the same antibody. Because the radioisotope is bound to the antibody, it was initially believed that the biological half-life of the antibody and antibody form would dictate the biological clearance rate of the radiolabel. This was investigated for data from male and female colon cancer patients provided by the Garden State Medical Center using the MN14 antibody, IgG antibody form, for Re-188 and I-131 radiolabels. The biological half-life is calculated using;

$$T_b = \frac{T_e T_p}{T_p - T_e} \quad (10)$$

where,

T_b = whole-body biological half-life
 T_e = whole-body effective half-life
 T_p = physical decay half-life

Using parameters listed in Table H.2, the biological half-life for Re-188 tagged MN14 was 7.5 and 7.4 h for female and male patients, respectively. The biological half-life for I-131 tagged MN14 was 38 and 33 h for female and male patients,

respectively. This large discrepancy indicates that the RAB is being catabolized with the free radioisotopes having different residence times. The method by which the radioisotope is attached to the antibody plays a significant role in this process. Thus, the biological half-life of one radiolabel with an antibody should not be used to predict the biological clearance rate of a different radionuclide label attached to the same antibody for radiation protection purposes. This finding is similar to that of Naruki, et al. (1990).

3.5 Dependency of T_e on Disease

Since significant quantities of the RAB go to areas other than the tumor, it was considered that the T_e for a specific RAB may be the same regardless of the patient's disease. Table 3.10 lists the T_e s for different diseases treated with I-131 RAB MN14 in the form of F(ab')₂ and IgG. While there are not enough data in these 2 sets to reach any conclusion, the maximum difference between the smallest and largest clearance rates in both forms are within a factor of two, which is not unlike the variation of T_e values for different patients with the same disease receiving the same RAB. A more decisive result could be obtained if analysis of variance tests were carried out on T_e values for patients with different diseases treated with the same RAB; this is beyond the scope of the present work. As a preliminary

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test, frequency distributions for patients treated with the same RABs for different diseases were plotted for patients treated with I-131 labeled CC-49 in the form of IgG for prostate (University of Alabama at Birmingham Hospital) and colon (Memorial Sloan-Kettering Cancer Center, male

and female) cancer. We assumed that differences in treatment protocols had a negligible impact on T_e for these data. While the frequency distributions appear somewhat different (Figure 3.13) a non-parametric Wilcoxon Rank Sum Test (Walpole and Myers, 1978) shows that the two distributions are not statistically different. A Student t-test on the means also showed the distributions were not statistically different.

Figure 3.13 Frequency distribution of prostate (University of Alabama) and colon (Memorial Sloan-Kettering Cancer Center) cancer patients treated with I-131 RAB CC-49 (IgG).

Table 3.10 Whole-body effective half-lives (T_{e} s) for patients receiving a first administration of I-131 labeled MN14 in the form of F(ab')₂ and IgG with different diseases

Disease	Sex	Anti-body form	# of Pat- ients	Avg Age (y)	S.D. Avg Age (y)	Avg Wt (kg)	S.D. Avg Wt (kg)	Avg Act (GBq)	S.D. Avg Act (GBq)	T_{e} (h)					
										Avg IC	S.D. Avg IC	Avg Scan	S.D. Avg Scan	Avg Blood	S.D. Avg Blood
Colon	M	F(ab) ₂	3	66	9	75	7.8	4.6	1.7	31	11	35	26	14	2.2
Elevated Marker	M	F(ab) ₂	2	66	13	87		0.38	0.12			69	27	30	7.7
Esophageal	M	F(ab) ₂	1	67		75		6.1		41		42		33	
Lung	F	F(ab') ₂	1	39		47		3.6		49		50		22	
Medullary Thyroid	M	F(ab') ₂	3	57	12	74	13	3.9	1.2			62	34	33	16
Medullary Thyroid	F	F(ab') ₂	1	72		60		1.8		48		42		20	
Rectal	F	F(ab) ₂	1	63		53		0.30				48		60	
Small Bowel	M	F(ab) ₂	1	66		76		4.9		49		54			
Breast	F	IgG	1	49		56		0.27				75		115	
Colon	M	IgG	10	65	7.3	83	8.6	1.5	1.3	30	6.3	39	18	25	10
Colon	F	IgG	2	57	26	63	4.2	0.31	0.033	2.5*		68		45	10
Duodenal	M	IgG	1	47		91		0.35		45		73		54	
Head/Neck	M	IgG	1	57		78		0.36				55		86	
Medullary Thyroid	F	IgG	2	57	23	45	5.7	2.8	0.10	62	8.6	66	10	45	17
Pancreatic	M	IgG	1	55		62		0.43				66		49	
Rectal	M	IgG	1	59		72		0.37				66		41	
Unknown Primary	F	IgG	1	60		80		2.7		61		66		43	

"Avg" refers to average, "S.D." refers to a sample standard deviation, "IC" refers to hand-held ionization chamber, "scan" refers to whole-body γ scan. Data were provided by Garden State Cancer Center at the Center for Molecular Medicine & Immunology

* The measurement is listed as received from the institution.

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3.6 Blood Clearance Rates

Blood effective half-lives, given in Tables H.2-H.7 (provided by the Garden State Cancer Center at the Center for Molecular Medicine & Immunology), are both single- and biphasic, but only the longer component of the biphasic clearance rate is shown if the clearance rate was biphasic. These are listed to demonstrate that blood clearance rates do not accurately measure T_e ; they typically are less than T_e . A correlation between T_e and blood clearance rates may exist, however, its determination is beyond the scope of the present work.

3.7 Dose to the Public from the Patient

The activity in a patient required to produce a dose rate of 0.05 mSv h^{-1} (5 mrem h^{-1}) at a distance of 1 meter is a function of the radionuclide under consideration, provided allowance is made for the attenuation of photons by 10 cm of striated muscle ($\rho = 1 \text{ g cm}^{-3}$).

Table 3.11 shows the effects of attenuation on the dose rate at 1 meter from a patient and the activity required to produce that dose rate for common RAB labels.

Table 3.11 Calculated activity of a point source which will produce $1.29 \mu\text{C kg}^{-1} \text{ h}^{-1}$ (5 mR h^{-1}) at 1 meter with and without attenuation by 10 cm of striated muscle having unit density (patient measurements).

Radionuclide	Attenuation factor (F) ^a	Activity, GBq ^b	
		without attenuation	with attenuation
Cu-67	0.17	3.2	19
Y-90	0.57 ^c	44	77
Tc-99m	0.20	2.9	15 (11) ^d
In-111	0.49	0.58	1.2
I-123	0.22	1.2	5.2
I-125	0.022	1.3	59
I-131	0.34 (0.42) ^e	0.84	2.5 (1.8) ^e
Re-186	0.035	8.4	241 (12.4) ^f (14) ^g
Re-188	0.066	4.7	72
At-211	0.0044	~61	~1.4 x 10 ⁴

a Based on the energies and abundances of photons published by Erdtmann and Soyka (1979) and attenuation coefficients published by Hubbell (1982).

b From equation (9). Multiply by 27.0 to obtain mCi.

c Based on a photon energy of 1500 keV (2/3 of E_{max}).

d An approximate average taken from a graph for 167 patients who received sodium pertechnetate Tc-99m (Hung *et al.*, 1992).

e The mean for 8 patients (Hammond *et al.*, 1984).

f The value for 1 patient (Breitz, 1995).

g Based on data for one patient provided by H. Breitz, personal communication, September 1995.

4 DISCUSSION

4.1 Release Limits

The physical and $T_{1/2}$ s of radionuclides used to label RABs presently are much less than 1 y. Hence, it is necessary to think in terms of both dose rate and accumulated dose over some specified time. The current release limits are 5 mrem/hr at one meter from a patient and the remaining activity is less than 30 mCi (NRC, 1991a)

4.1.1 Clearance Rate Model

The many compartments involved in the catabolism and elimination of RABs might be expected to result in multiphasic (or at least biphasic) clearance. Although vascular clearance is either monophasic or biphasic,¹ most whole-body clearance rates listed in the literature follows a single exponential (Meredith et al., 1991; Denardo et al., 1988; Hammond et al., 1984; Leichner et al., 1983). Castronovo et al. (1986) believe that whole-body clearance for NaI-131 (not a RAB) in thyroid cancer patients is best described by the sum of three exponential functions. However, their measurements for a single patient were only taken at 5 different times, which may not warrant a 3-component fit.

A single-exponential clearance rate model was justified for the large majority of patient data analyzed in this report. The exceptions were four patients in which a bi-exponential clearance rate was justified.

Figures for clearance rate measurements for several patients in Appendix I for RABs CC-49, M-195, and 3F8 follow single exponentials for data out to 7, 5, and 7 half-lives, respectively. The $T_{1/2}$ values shown have regression-slope standard errors (and thus, $T_{1/2}$ standard errors) of less than 15%, which is quite remarkable and lends much confidence to a single-exponential fit for these data. Any significant second-exponential component with a slower clearance rate would be evident within several half-lives and

certainly within seven half-lives of the shorter $T_{1/2}$ (Figure I.63).

A bi-exponential clearance rate may be justified for other treatment protocols. As examples, a biphasic clearance rate may occur if, after injecting the RAB, a substance is administered to remove the unattached RAB still circulating in the blood; or, the antibodies may be poorly labeled such that the clearance rate follows both the biological elimination rate of the antibody and the radionuclide.

4.1.2 Standard Deviation of $T_{1/2}$

Variations in measuring the dose rate or clearance rate from a patient associated with the standard deviation of $T_{1/2}$ in this report may be attributable to the following variables:

1. type of disease treated,
2. changes in RAB metabolism as a function of time.
3. stage of the disease in the patient,
4. variability in RAB labeling,
5. repeated administrations,
6. changes in the distribution of the activity in the patient as a function of time, leading to variability in measuring geometry
7. a full (as opposed to an empty) urinary bladder,
8. incomplete data due to death of the patient,
9. errors in meter calibration, reading errors, and statistical variation
10. variation in distances at which measurements were made,
11. errors in noting the time measurements were made, and
12. recording errors,

As an illustration, an error of 5 or 10 cm may not be unusual in estimating distances from a source to the center of the sensitive volume of an ionization chamber rate meter (item 9 above). An error of ± 5 cm would result in readings that are $\pm 10\%$ of the dose rate at 1 meter, and about $\pm 20\%$ for an error of ± 10 cm.

Under the best conditions, ionization chamber rate meters have an accuracy of about $\pm 15\%$. However, with care the repeatability of measure-

² Data received from University of Alabama at Birmingham Hospital and Garden State Cancer Center at the Center for Molecular Medicine and Immunology

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ments with such instruments is better than $\pm 10\%$.

The urinary bladder could easily be 20 cm below the center of a patient's torso. Therefore, a measurement made using an ionization chamber at 100 cm from the center of the torso could be 102 cm from most of the activity, depending on whether the bladder is full or empty. However, errors in measuring the distance from a patient to the point of measurement can introduce larger errors than changes in the distribution of activity in the body.

The standard deviation of the calculated T_e values for each administration is a measure of all of variations of the variables of the data points. As such, the standard deviations for the majority of the data given for individual patient administrations in Appendices A, D, F, G, I, and J are generally less than 15% of the measured T_e value. These variances demonstrate the quality of the data and the reproducibility of the measurement technique. Some of the larger standard deviations (up to 50% of the T_e value) for the individual patient data in Appendix C are seen in the data sets with only 3 measurements, and the standard deviations were improved significantly (to about 15% of the T_e value) with a fourth measurement.

The standard deviation of the greater T_e component for which a bi-exponential clearance rate is justified for a single patient is a measure of the uncertainty of that value, and was quite large for 2 of the 4 patients for which a biphasic clearance rate model was justified (Table 3.2). The standard deviation for the greater T_e component can be used to optimize the number of measurements required to bring uncertainty to an acceptable level.

The standard deviation of the T_e for multiple patients receiving the same treatment is a measure of patient-to-patient differences. The standard deviations of average T_e values are generally larger than the standard deviation of T_e for individual patients, indicating that there is a wider patient-to-patient response to the treatment than variations seen for an individual. Since the averages are made for patients having the same disease, similar radiolabeling protocols, and the same instrument in most cases, the standard deviation of the average T_e reflects differences in

clearance rate between patients.

While this study is a retrospective study, the standard deviations of the T_e values show that most data are of very high quality. A prospective study in which the health physics personnel exercise extreme care in measuring the dose rate from RAB patients may decrease the T_e standard deviation for individual patients. This could be accomplished through a protocol in which, for example, the measurement always is taken after the patient has emptied his/her bladder, making certain that possible radiation sources other than the patient (such as another patient or an unflushed toilet) are not in the area. Such measurements may have value in better predicting when an individual patient may be released and estimating dose to the patient's family. However, when these measurements with small standard deviations for individuals are averaged together to determine average clearance rates for multiple patients, the average standard deviation will most likely be as large as those given in this report because of the patient-to-patient differences in clearance rate.

4.1.3 Accumulated Dose

An exposure factor of .25 has been suggested for estimating the dose to members of the family from patients given radiopharmaceuticals (Schneider, 1994). This exposure factor, which accounts for the family member being within 1 meter of the patient about 6 hours per day, can apply for one year or until there is no detectable radiation from the radiopharmaceutical. It has been suggested that the estimate of the reduction in exposure from the patient be based on the physical half-life of the radionuclide to be conservative and allow values of T_e to be used for individual cases. More accurate estimated doses are likely when T_e is used to estimate the reduction in exposure rate.

Harbert and Wells (1974) and Jacobson et al. (1978) investigated doses to family members from patients undergoing thyroid treatment with non-RAB I-131. Harbert and Wells (1974) gave family members film badges to wear for 8 days at waist level with instructions to not sleep with the patient and for the patient to minimize contact

with infants. Jacobson et al. (1978) provided family members with wrist band TLD dosimeters to wear for 60 days, also instructing the patient to avoid close contact with children.

Measured doses from the two studies were compared with doses calculated at a distance of 1 meter from a point source with no attenuation. A T_e value of 1 d was used, which was calculated from averaging T_e values in the non-Rab I-131 administrations shown in Table F.2. For comparison, since the actual T_e value for these studies was not known, calculations also were carried out for a T_e value of 8 days, the physical half-life of I-131. Doses were calculated using the following equation.

$$D = 1.33 \times 10^{-4} F \Gamma Q T_e (1 - e^{-\frac{\ln 2}{T_e} t}) \quad (11)$$

where,

D = Whole-body dose to a family member continuously at a 1 meter distance from an unattenuated point source (mSv)

Γ = specific gamma ray constant
(15.3 for I-131) $\left(\frac{\mu C \text{ cm}^2}{kg \text{ h MBq}} \right)$

Q = activity of a point source (MBq)

T_e = Effective half-life of the isotope (h)

F = Exposure factor (=100% for continuous exposure at 1 meter)

Exposure factors for 7 of the 31 family members measured were greater than 25% when a T_e value of 1 d was used (Table 4.1 and Figure 4.1). Only one of the 31 family members had an exposure factor of greater than 25% when a T_e value of 8 days was assumed. This individual had exposure factors of 2,200% and 280% for T_e values of 1 and 8 days, respectively. This individual was the patient's spouse, and had accompanied the patient on a 2-week vacation, during which they spent several days together in a car. It should be noted that expected T_e values for these patients are most likely closer to 1 d, rather than 8 d.

Using the 8 d T_e value is of interest for this individual, because the exposure factor must be at least 280% even though the exact value of T_e for this patient is not known, since T_e must be equal to or less than the physical half-life of the isotope. For data in Table 4.1, the average T_e values, excluding the single highest dose family member, are $20\% \pm 25\%$ and $4\% \pm 4.1\%$ for T_e values of 1 and 8 d, respectively.

This analysis suggests that the assumed exposure factor of 25% is adequate to ensure that the average dose to family is less than 5 mSv. The seven cases in which the exposure factors exceeded 25% reflect the continuing need to stress the importance of family members limiting contact with the patient. With exception of the case which resulted in an exposure factor of 2,200%, none of the family members would have exceeded the recent NCRP guidance which permits up to 50 mSv (5 rem) annually for adult members of the family.

The family member with the exposure factor of 2,200% reflects a violation of good practice. This emphasizes the need for physicians and other medical personnel to counsel, train, and, perhaps, monitor family members who accept caregiving responsibilities for patients with large burdens of radiopharmaceuticals.

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Table 4.1 Calculation of family exposure factors by comparing measured whole-body dose to family members of patients receiving non-RAB I-131 treatment with dose calculated 1 meter from a point source assuming T_e values of 1 and 8 d. The T_e value of 1 d is taken from Table F.2 and the 8 d T_e value is the maximum possible value for I-131 (physical half life)

Reference	Patient Number	Body Burden at Discharge (MBq) ^d	Exposure Duration (d)	Measured Family Member Dose (mSv)	Calculated dose at 1 meter for exposure duration		Exposure Factor (F)	
					T_e : 1 d (mSv) ^c	T_e : 8 d (mSv) ^c	T_e : 1 d (%)	T_e : 8 d (%)
a	1	9.3E+02	8	0.3	2	8	16	4
a	1	9.3E+02	8	0.7	2	8	37	9
a	1	9.3E+02	8	0.8	2	8	42	11
a	2	1.6E+03	2	0.2	2	4	8	5
a	3	9.8E+02	8	0.2	2	8	10	3
a	3	9.8E+02	8	0.5	2	8	25	6
a	3	9.8E+02	8	0.2	2	8	10	3
a	4	6.8E+02	8	0.8	1	6	58	14
a	4	6.8E+02	8	0.4	1	6	29	7
a	4	6.8E+02	8	0	1	6	0	0
a	4	6.8E+02	8	0	1	6	0	0
a	5	1.1E+03	7	0.4	2	8	18	5
a	6	9.2E+02	6	0.4	2	6	22	7
a	7	9.3E+02	8	0	2	8	0	0
a	8	1.1E+03	8	0.3	2	9	13	3
a	8	1.1E+03	8	0.5	2	9	22	6
a	9	1.3E+03	7	0.3	3	10	11	3
a	9	1.3E+03	7	0	3	10	0	0
a	9	1.3E+03	7	0	3	10	0	0
a	10	1.1E+03	8	0	2	9	0	0
a	11	8.3E+02	8	0.2	2	7	12	3
b	1	3.0E+02	60	0.071	1	5	12	1
b	2	1.1E+03	60	0.19	2	18	8	1
b	2	1.1E+03	60	0.37	2	18	16	2
b	2	1.1E+03	60	1.4	2	18	63	8
b	3	5.1E+02	60	0.16	1	8	15	2
b	3	5.1E+02	60	0.11	1	8	11	1
b	4	7.3E+02	60	0.16	1	12	11	1
b	4	7.3E+02	60	0.059	1	12	4	0
b	6	6.5E+02	60	1.6	1	10	120	15
b	7	5.0E+02	60	22	1	8	2200	280

a = Harbert and Wells (1974); b = Jacobson et al. (1978); c = Calculated using equation (8); d = Multiply by 0.027 to obtain mCi.

Figure 4.1 Exposure factors calculated from measured doses of family members of patients administered with non-RAB I-131. Data taken from Harbert and Wells (1974) and Jacobson et al. (1978).

Except for In-111, the activity required to produce 0.05 mSv h^{-1} (5 mrem h^{-1}) 1 meter from a patient (assuming attenuation by 10 cm of tissue) is much larger than the current 1.11 GBq (30 mCi) limit for all radionuclides presently used to label RABs (Table 3.11). These activities would be sufficiently high that contamination control outside the hospital may be necessary.

Of the I-131 RABs listed in Tables 3.4-3.9, several groups have $T_{1/2}$ s greater than 70 h. Hence, some patients released from institutions with a dose rate of 0.05 mSv h^{-1} (5 mrem h^{-1}) could deliver a dose greater than 5 mSv (500 mrem) to caregivers over the course of 1 year if they were continuously 1 meter from the patient. Caregivers minimizing time near the patient, as given as an example in Table 4.2, should have adequate protection to keep doses below 5 mSv y^{-1} (500 mrem y^{-1}).

Another method that could minimize the chances of caregivers receiving doses exceeding the regulatory limits is to have the hospital's radiation safety officer issue self-reading dosimeters to be worn on a voluntary basis. Since the dosimeter may be a novelty, a large portion of people may

be willing to wear one. This would have several benefits. First, the family members would be monitoring themselves, and possibly changing routines to ensure doses are below the regulatory limits as well as ALARA. Second, the dosimeter would be an educational tool for those regulating the release of patients.

A patient would have to contain over 74 GBq (2 Ci) of Y-90 (a pure beta emitter) to produce an exposure rate of 0.05 mSv h^{-1} (5 mrem h^{-1}) at 1 meter. For pure alpha-, beta-, and low-energy photon-emitters, the activity in the patient may be governed more by the toxic dose to the patient than the external dose to others. However, this raises the questions of how much activity (irrespective of external exposure rate) is a reasonable limit for patients containing alpha- and beta-emitters. Such a limit could be based on contamination levels from the patient's secretions, which would give unacceptable external and internal doses to the public. These issues require additional investigation.

Factors that are important in estimating potential dose to caregivers include the following:

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1. the whole-body effective half-life of the labeled compound,
2. the amount of activity in the body,
3. the dose rate at 1 meter from the patient, and
4. the potential for increasing the internal and external dose to others from contamination of the environment by the patient.

Table 4.2 Example of a time schedule to achieve caregiver/public doses less than 5 mSv y⁻¹ (500 mrem y⁻¹) from a RAB patient released with an exposure rate of 50 μ Sv h⁻¹ (5 mrem h⁻¹) at 1 meter.^a

Whole-body Effective half-life (h)	Maximum time allowable for caregivers to be exposed 1 meter from patient ^b
80	16 h per day for first 3 days
90	16 h per day for first 7 days
100	12 h per day for first 6 days
110	12 h per day for first 10 days
120	8 h per day for first 8 days

^a This time schedule was generated using equation (6). It assumes the dose is negligible when the caregiver is at a distance of 1 meter or more from the patient.

^b After the specified period, the allowable time would be 24 hours per day.

4.2 Contamination Considerations

With RAB treatment, as with any other nuclear medicine procedure, there is a potential for contamination. Significant levels of surface contamination attributable to nuclear medicine patients are expected to be found in restrooms because much of the radioactivity is cleared via the urine. Ho and Shearer (1992) examined restroom contamination in a 700-bed hospital that carries out 25 to 30 nuclear medicine procedures per day. They concluded that for Tc-99m pertechnetate, about 10⁻⁴ times the injected dosage can be found there as surface contamination. Hence, if a patient were given 3.7 GBq (100 mCi), about 370 kBq (10 μ Ci) might be found as surface contamination in a restroom.

It generally is agreed that the most difficult radionuclides from the contamination standpoint are

the iodides. Iodine-131 is used in many radiopharmaceuticals including RABs. Although most of the I-131 is excreted via urine, significant quantities also are excreted via breath, saliva, and perspiration. Marshall et al. (1973) measured contamination from 5 patients receiving non-RAB I-131 treatment for thyroid carcinoma. Contamination on bedding and towels was about 8 x 10⁻⁴ times the administered activity each day for four days following the treatment. The highest contamination on the bedding was noted for a patient who had an enlarged prostate and suffered hesitancy in urinating and dribbled after urination. Contamination on dishes and utensils was about 6 x 10⁻⁴ times the administered activity each day for four days following treatment. The ranges for the contamination listed were within a factor of about 60 from the mean. It should be noted that this value did not necessarily decrease during the four days following the administration. One of these patients also deposited 1.7% of the administered activity in paper tissues from nasal dis-

charge in the first 4 days after treatment.

Total contamination for patients administered I-131 RAB treatment at the University of California at Davis was measured (Bushberg et al., 1991). The total contamination in the room determined from surface wipes, in which the wipe area was related to the entire surface area of the room, was about 2×10^{-5} times the administered activity for the 3 to 4 days during which the patient was in the room. The wipe samples were counted the same day the wipe was taken and were not corrected for decay to the time the activity was administered. The highest contamination levels were found near the toilet and sink.

A scenario with the potential to result in unacceptable exposure of family members is that due to incontinence of a patient with a large body burden of a radiopharmaceutical. Appendix K contains a calculation of the family member doses in such a "worst case scenario".

In addition to continuing the current practice of restricting the release of incontinent patients from the hospital, the family members may need to be specifically advised that the urine from the patient has significant contamination potential.

Contamination from the skin of the patient would result in activities much less than that calculated from urine contamination. Contamination previously described for I-131 non-RAB therapy of

patient's bedding and towels gave 8×10^{-4} times the administered activity. Skin wipe data of Re-188 labeled RABs was collected at the Garden State Cancer Center at the Center for Molecular Medicine and Immunology as part of the treatment protocol (Table 4.3). The decay-corrected contamination in a 10 cm² forearm wipe for all patients for the first 3 days is $6 \times 10^{-9} \pm 1 \times 10^{-8}$ times the administered activity. Assuming the same surface activity for the skin of the whole body, this gives $1 \times 10^{-5} \pm 2 \times 10^{-5}$ times the administered activity.

The importance of contamination will be a function of the amount of radioactive material administered to a patient, the $T_{1/2}$ of the RAB, the physical half-life, routes of excretion, and chemical form of the radionuclide administered. Radio-labeled antibodies have longer $T_{1/2}$ s than common radiopharmaceuticals. Therefore, they are eliminated slower and should produce less contamination per unit activity administered per unit time; however, the activities administered are much greater. The persistence of radioactivity in the environment from RABs, once eliminated from the patient, is no different from any other radiopharmaceutical because the physical half-life governs the rate once the radioactive material is expelled.

Table 4.3 Fraction of administered activity measured on a 10 cm² wipe of the inner forearm of a patient treated with Re-188 radiolabeled MN-14 (IgG) RAB

Day Post Administration	Number of Patients	Avg Fraction of Administered Activity	Std. Dev. of Avg Fraction of Administered Activity
0	14	9.9E-09	1.5E-08
1	8	1.4E-09	1.1E-09
2	3	1.3E-09	2.0E-09
3	1	5.2E-09	
4	1	0.0	

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Table 4.3 Fraction of administered activity measured on a 10 cm² wipe of the inner forearm of a patient treated with Re-188 radiolabeled MN-14 (IgG) RAB

Day Post Administration	Number of Patients	Avg Fraction of Administered Activity	Std. Dev. of Avg Fraction of Administered Activity
0	14	9.9E-09	1.5E-08
1	8	1.4E-09	1.1E-09
2	3	1.3E-09	2.0E-09
3	1	5.2E-09	
4	1	0.0	

5 CONCLUSIONS

It was found that a single exponential model describes the clearance rate of RABs from the whole body for the majority (about 95%) of the patients in this study, determined by a ratio of χ^2 statistics for single- and bi-exponential fits to selected data with tabular F statistics for 95% confidence. These findings apply only to the RABs identified in this report. The clearance pattern for about 5% of the patients and protocols were not adequately described by a single exponential function.

Radiolabeled antibodies have longer T_e s than NaI-131, which commonly has a T_e of about 20 h. The T_e s for I-131 RABs in this study range from about 20 to 100 h depending on the antibody used, the disease treated, and the stage of the disease. In addition, the use of one radiolabeled antibody to predict behavior using another radiolabel is appropriate. The ligand system used the labeling method and the localization of the radiolabel are relevant.

Hospital physicists and radiation safety officers should be encouraged to measure exposure rate or clearance rate at least daily to ensure accurate T_e determinations, particularly for undocumented RABs. The measurements should be made consistently and systematically to minimize the uncertainty estimating T_e , and the uncertainty in estimates of doses delivered to others.

We considered more comprehensive, radio-nuclide-specific limits based on the radionuclide in question, the nuclear medicine procedure involved, the patient's disease, and the RAB administered. It is suggested that confinement limits for patients be based on T_e s, and also that the type and energy of radiation emitted be considered.

The external dose in one year to a member of the public from a patient containing RABs depends on T_e . Since some T_e values for RABs are greater than that of common radiopharmaceuticals, there is a larger probability of exceeding the yearly dose limit. Assuming a patient is a point source and neglecting attenuation, a dose of 5 mSv (500 mrem) will be exceeded for individuals continually at a distance of 1 meter from the patient if the T_e is greater than 70 h. Caregivers

minimizing time near the RAB patient, as shown by the example in Table K.1 for RABs with T_e s greater than 70 h, should receive doses less than 5 mSv y^{-1} (500 mrem y^{-1}). Patients released with exposure rates of less than 0.05 mSv h^{-1} (5 mrem h^{-1}) at 1 meter treated with Cu-67, Tc-99m, In-111, I-123, and Re-188 should result in external whole-body doses to members of the public of less than 5 mSv y^{-1} (500 mrem y^{-1}).

If a T_e determined from a single exponential clearance model is used to assess the dose or dose rate from a patient, the result may underestimate the dose delivered if the clearance rate is represented better by a bi-exponential function. This is because the second component will have a longer T_e than that deduced from a single exponential.

Six clearance rate distributions were tested for normality. While all six had P-values greater than 0.05, four of the distributions had P-values less than 0.25. With larger samples, departures from normality may become evident. If the latter is true, comparisons between treatment groups should be made using non-parametric tests.

Based on a limited sample of RAB clearance rates listed in this report, the age of the patient does not seem to be a determining factor.

The biological half-life of the radiolabel may not be the same as that of the antibody. The biological clearance rate of the radiolabel is a function of the method by which it is attached to the antibody and subsequent biological clearance rate of the elemental processes once the radiolabel is no longer attached to the antibody. Accordingly, the T_e for each RAB must be measured rather than estimated from biological half-lives measured for the same antibody with a different radiolabel.

The half-life of the RAB in blood is not a good measure of T_e .

An exposure factor greater than 100% can be deduced if a family member spends a significant portion of time during activity decay less than the assumed 1 meter distance from the patient. It is for this reason that family members should be

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counceled on their responsibility for controlling their exposure.

If allowance is made for attenuation of photons by only 10 cm of tissue, current activity limits for determining when a patient can be released from confinement are adequate for patients containing currently available RABs. From the standpoint of external dose, the intent of the current regulations could have been met for patients containing much higher levels of activity even if lower population-dose limits were applied. It may be desirable to use I-131 as a standard of reference for measurements of external dose rate, and consider releasing patients containing activities that produce dose rates comparable to that from a patient containing 1.11 GBq (30 mCi) of I-131.

Doses to the skin were investigated for caregivers and members of the public. Contamination to the skin of patients administered RABs generally has been found to be less than 10^{-6} of the administered activity. Thus, skin doses to caregivers from patient skin contamination is not thought to be a significant hazard. Caregiver skin doses from contaminated urine may result in substantial skin doses (Appendix K), however, incontinent patients are not generally released.

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APPENDIX A

Data provided by the National Institutes of Health, Bethesda, MD

These data were provided by the National Institutes of Health, Bethesda MD. Clearance rate was measured using a hand-held ionization chamber at a distance of 1 meter. Table A.1 summarizes data on individual patients, and Table A.2 gives T_e averages of Table A.1.

Graphs of individual patient's clearance rate with four or more measurements also are shown (Figures A.5-A.11). Data for patients of the same gender receiving the same treatment were combined (Figures A.1-A.4).

Table A.1 Whole-body effective half-lives (T_e s) computed from regressions of relative dose rate as a function of time post-administration for patients treated with I-131 labeled antibodies for the disease indicated. Patient A received two administrations; all others received one. The abbreviation "SD" refers to standard deviation.

Patient Number	Gender	Number of data points	T_e (h)	SD T_e (h)	RAB	Type of cancer
A (1st)	F	2	28		Col-1	colon
A (2nd)	F	2	16		Col-1	colon
B	M	2	29		Col-1	colon
C	F	2	16		Col-1	colon
D	F	2	15		Col-1	colon
G	M	2	19		Col-1	colon
E	M	3	35	5.2	Col-1	pancreatic
J	?	6	49	3.9	B72.3	pancreatic
H	?	4	34	5.1	B72.3	adeno
K	?	4	36	2.2	B72.3	adeno
I	F	5	54	2.6	B72.3	ovarian
L	F	3	53	0.21	B72.3	ovarian
N	F	5	40	3.9	B72.3	ovarian
O	F	5	51	5.5	B72.3	ovarian
M	F	4	111	9.7	B72.3	mixed
P	?	2	85		B72.3	unknown
F	M	2	55		L-6	thyroid

Appendix A

Table A.2 Summary of Table A.1 including average T_e s. Radiolabel was I-131

Disease	Sex	Anti-body name	No. of Patients	T _e Method 1 First Administration		T _e Method 1 Second Administration		T _e Method 2 First Administration	
				Avg (h)	SD Avg (h)	Avg (h)	SD Avg (h)	Avg (h)	SD Avg (h)
Adeno	?	B72.3	2	35	1.4			69	8.5
Colon	F	COL-1	3	20	7.2	16		23	5.3
Colon	M	COL-1	2	24	7.1			21	4.2
Mixed	F	B72.3	1	111					
Ovarian	F	B72.3	4	50	6.6			49	2.5
Pancreatic	M	COL-1	1	35					
Pancreatic	?	B72.3	1	48					
Thyroid	M	L-6	1	55					
Unknown	?	B72.3	1	85					

T_e Method 1: T_e was calculated by treating each patient independently and averaging the T_e values with other patients (Equations 4 and 5).

T_e Method 2: T_e was calculated by regressing the normalized data points, treating each data point independently (Figures A.1-A.4).

Figure A.1. Clearance rate for female patients administered I-131 RAB Col-1 for colon cancer.

Figure A.2. Clearance rate for male patients administered I-131 RAB Col-1 for colon cancer.

Figure A.3. Clearance rate for patients administered I-131 RAB B72.3 for adeno cancer.

Figure A.4. Clearance rate for female patients administered I-131 RAB B72.3 for ovarian cancer.

Figure A.5 Clearance rate for patient H administered I-131 RAB B72.3 for adeno cancer.

Figure A.6 Clearance rate for patient I administered I-131 RAB B72.3 for ovarian cancer.

Figure A.7 Clearance rate for patient J administered I-131 RAB B72.3 for pancreatic cancer.

Figure A.8 Clearance rate for patient K administered I-131 RAB B72.3 for adeno cancer.

Figure A.9 Clearance rate for female patient M administered I-131 RAB B72.3 for mixed cancer.

Figure A.10 Clearance rate for patient N administered I-131 RAB B72.3 for ovarian cancer.

Figure A.11 Clearance rate for patient O administered I-131 RAB B72.3 for ovarian cancer.

APPENDIX B

Data Provided by the University of Alabama, Birmingham, AL, From Studies Carried out in 1989-1990

These data were provided by the University of Alabama at Birmingham. Clearance rate was measured using a hand-held probe at variable distances. The most consistent measurements were made at about 18 inches (46 cm).

Tabulated values of T_e are listed for females and males (Tables B.1 and B.2, respectively).

Data on the clearance rate combined for each administration for females and males are shown graphically (Figures B.1-B.4).

Table B.1 Whole-body effective half-lives (T_e s) based on a single exponential model for B72.3 chimeric antibodies labeled with I-131 to treat colon cancer for females.

	1st Administration			2nd Administration			4th Administration			6th Administration		
Patient ID	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)
A	3	99	32									
B	2	110		4	107	26						
E	3	95	31	2	12							
L				3	72	2	2	24		2	19	
R	7	72	13									
U	6	80	29									
Mean		91			64			24			19	
SD		15			48							
Combined Mean *		75			101							
Combined SD *		12			20							

- These mean T_e s were calculated by regressing the normalized data points (Figures B.1 and B.2).

Appendix B

Table B.2 Whole-body effective half-lives (T_e s) based on a single exponential model for B72.3 chimeric antibodies labeled with I-131 to treat colon cancer for males.

Patient ID	1st Administration			2nd Administration			3rd Administration			4th Administration		
	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)
C	5	35	11									
D	2	35										
H	3	70	47	2	17							
I	3	110	89	4	51	13						
J	3	77	150	4	-1499 ^a	-3976 ^a						
K				2	21							
M				3	49	3	2	24				
N	3	107	34	4	72	18						
O	3	42	21	4	63	32	2	37		2	10	
P	2	33		5	222 ^b	198	3	135	56	4	50	8
Q	2	27		3	261 ^b	226						
S	6	134	44									
T	5	54	27									
V	6	60	13									
W	6	81	16									
Mean		67			95			65			30	
SD		34			93			61			28	
Combined Mean ^c		68			145			68			61	
Combined SD ^c		12			64			33			57	

^a Positive slope

^b T_e is greater than the physical half-life (192 h).

^c These mean T_e s were calculated by regressing the normalized data points (Figures B.3 and B.4).

Figure B.1 Clearance rate for female patients receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.2 Clearance rate for female patients receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.3 Clearance rate for male patients receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.4 Clearance rate for male patients receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.5 Clearance rate for female patient B receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.6 Clearance rate for male patient C receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.7 Clearance rate for male patient I receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.8 Clearance rate for male patient J receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.9 Clearance rate for male patient N receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.10 Clearance rate for male patient O receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.11 Clearance rate for male patient P receiving the second administration of I-131 RAB B72.3 for colon cancer.

Figure B.12 Clearance rate for male patient P receiving the fourth administration of I-131 RAB B72.3 for colon cancer.

Figure B.13 Clearance rate for female patient R receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.14 Clearance rate for male patient S receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.15 Clearance rate for male patient T receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.16 Clearance rate for female patient U receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.17 Clearance rate for male patient V receiving the first administration of I-131 RAB B72.3 for colon cancer.

Figure B.18 Clearance rate for male patient W receiving the first administration of I-131 RAB B72.3 for colon cancer.

1. *Chlorophyll a* (Chl *a*)

APPENDIX C

Data Provided by the University of California, Davis, CA

These data were provided by the University of California at Davis. Clearance rate was measured using a hand-held ion chamber at 1 meter from the patient. Tables C.1 and C.2 summarize individual patient data and $T_{1/2}$ averages.

Clearance rate data for combined patient $T_{1/2}$ values for each administration are shown graphically (Figures C.1-C.4).

Graphs of individual patient clearance rate having four or more measurements (Figures C.5-C.28) also are shown.

Table C.1 Whole-body effective half-lives (T_e s) computed from regressions on relative dose rate as a function of time post-administration for lymphoma patients treated with I-131 labeled Lym-1 antibody.

Patient ID	Sex	1st Administration			2nd Administration			3rd Administration			4th Administration			5th Administration		
		Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)
B	M	3	41	1.1	3	49	20									
C	F	3	25	3.0												
F	M	3	18	9.2	4	19	2.0									
H	M	4	23	2.5				3	21	3.5	3	14	3.3			
I	M	4	20	2.2	5	30	3.4	4	23	1.4	4	23	1.8			
M	M	3	30	1.9	3	33	0.42	2	38		3	19	3.6	3	23	2.4
O	M	4	29	1.7	5	42	9.8	4	54	6.7	5	42	1.7			
V	M	4	25	5.2	4	21	1.4									
W	M	5	37	3.4	4	21	9.2	4	23	2.9	4	22	1.7			
AA	M	4	26	6.1												
Male Average			28			31			32			24			23	
Male SD of Average			7.7			12			14			11				
Female Average			25													
Combined Mean*			28			29			28			30				
SD Combined data mean*			2.2			3.3			4.0			4.6				

* The T_e was calculated by treating each data measurement independently and regressing the normalized data points (Figures C.1-C.4)

Table C.2 Whole-body effective half-lives (T_{e} s) computed from regressions of relative dose rate as a function of time post-administration for breast cancer patients treated with I-131 labeled antibodies. Patient E was treated with ml-6 antibody, and patients G, L, and CC were treated with chL-6 antibody.

Patient ID	Sex	Anti-body	1st Administration			2nd Administration			3rd Administration		
			Number of Data Points	T_{e} (h)	SD T_{e} (h)	Number of Data Points	T_{e} (h)	SD T_{e} (h)	Number of Data Points	T_{e} (h)	SD T_{e} (h)
E	F	ml-6	4	36	4.9	3	35	0.14	3	33	4.6
G	F	chL-6	4	49	6.1	4	39	5.9			
L	F	chL-6	5	47	3.3	4	33	4.3	4	44	12.6
CC	F	chL-6	7	47	1.8	7	36	3.3			
Average ml-6 antibody				36			35			33	
Average chL-6 antibody				48			36			44	
SD of chL-6 Average				1.2			2.6				

Figure C.1 Clearance rate for male patients receiving the first administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.2 Clearance rate for male patients receiving the second administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.3 Clearance rate for male patients receiving the third administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.4 Clearance rate for male patients receiving the fourth administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.5 Clearance rate for female patient E receiving the first administration of I-131 RAB mI-6 for breast cancer.

Figure C.6 Clearance rate for male patient F receiving the second administration of I-131 RAB Lym-1 for lymphoma cancer

Figure C.7 Clearance rate for female patient G receiving the first administration of I-131 RAB chL-6 for breast cancer.

Figure C.8 Clearance rate for female patient G receiving the second administration of I-131 RAB chL-6 for breast cancer.

Figure C.9 Clearance rate for male patient H receiving the first administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.10 Clearance rate for male patient I receiving the second administration of I-131 RAB Lym-1 for lymphoma cancer

Figure C.11 Clearance rate for male patient I receiving the third administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.12 Clearance rate for male patient I receiving the fourth administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.13 Clearance rate for female patient L receiving the first administration of I-131 RAB chL-6 for breast cancer.

Figure C.14 Clearance rate for female patient L receiving the second administration of I-131 RAB chL-6 for breast cancer.

Figure C.15 Clearance rate for female patient L receiving the third administration of I-131 RAB chL-6 for breast cancer

Figure C.16 Clearance rate for male patient O receiving the first administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.17 Clearance rate for male patient O receiving the second administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.18 Clearance rate for male patient O receiving the third administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.19 Clearance rate for male patient O receiving the fourth administration of I-131 RAB Lym-1 for lymphoma cancer

Figure C.20 Clearance rate for male patient V receiving the first administration of I-131 RAB Lym-1 for lymphoma cancer

Figure C.21

Clearance rate for male patient V receiving the second administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.22

Clearance rate for male patient W receiving the first administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.23

Clearance rate for male patient W receiving the second administration of I-131 RAB Lym-1 for lymphoma cancer

Figure C.24

Clearance rate for male patient W receiving the third administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.25 Clearance rate for male patient W receiving the fourth administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.26 Clearance rate for male patient AA receiving the first administration of I-131 RAB Lym-1 for lymphoma cancer.

Figure C.27 Clearance rate for female patient CC receiving the first administration of I-131 RAB chL-6 for breast cancer.

Figure C.28 Clearance rate for female patient CC receiving the second administration of I-131 RAB chL-6 for breast cancer.

APPENDIX D

Data Provided by the University of Washington, Seattle, WA

These data were provided by the University of Washington at Seattle. Clearance rate was measured using a hand-held ion chamber. Table D.1 summarizes the individual patient data and gives the average T_e .

Combined clearance rate data are shown graphically (Figure D.1); graphs of individual clearance rate also are given (Figures D.2-D.5).

Table D.1 Whole-body effective half-lives (T_e s) computed from regressions of relative dose rate as a function of time post-administration for lymphoma patients treated with I-131 labeled anti CD-37 antibody. Each patient received one administration. The patients' sex was not specified.

Patient ID	Number of Data Points	T_e (h)	SD T_e (h)
A	13	50	1.4
B	10	48	1.3
C	8	46	0.90
D	5	26	0.50
Mean		42	
SD of Mean		11	
Combined Measurements*		48	
SD of Combined Measurements*		2.9	

- The T_e was calculated by treating each measurement independently and regressing the normalized data points. The SD is the standard deviation of the regression slope (Figure D.1).

Appendix D

Figure D.5

Clearance rate for patient D (sex unknown)
receiving the first administration of I-131 RAB
CD-37 for lymphoma cancer

APPENDIX E

Data Provided by the VA Medical Center, Minneapolis, MN

These data were provided by the V.A. Medical Center in Minneapolis. Measurements of clearance rate were taken using a hand-held ion chamber at of 1 meter. Table E.1 summarizes individual patient data and T_e averages for all patients.

Combined clearance rate data are displayed graphically (Figure E.1); graphs of individual clearance rate having more than four measurements also are provided (Figures E.2-E.4).

Table E.1 Whole-body effective half-lives (T_e s) computed from regressions of relative dose rate as a function of time post-administration for renal cancer patients treated with I-131 labeled A6H antibody. Each patient received one administration.

Patient ID	Sex	Number of Data Points	T_e (h)	SD T_e (h)
A	F	5	36	8.3
B	M	5	80	9.9
C	M	5	35	8.1
D	M	3	56	7.5
E	M	2	41	
Male Mean			53	
SD of Male Mean			20	
Female Mean			36	
Combined M&F Measurements*			50	
SD of Combined Measurements*			7.0	

* The T_e was calculated by treating each measurement independently and regressing the normalized data points (Figure E.1).

Figure E.1 Clearance rate for male and female patients receiving the first administration of I-131 RAB A6H for renal cancer.

Figure E.2 Clearance rate for female patient A receiving the first administration of I-131 RAB A6H for renal cancer.

Figure E.3 Clearance rate for male patient B receiving the first administration of I-131 RAB A6H for renal cancer.

Figure E.4 Clearance rate for male patient C receiving the first administration of I-131 RAB A6H for renal cancer.

APPENDIX F

Data Provided by the University of Minnesota, Minneapolis, MN

These data were provided by the University of Minnesota. Clearance rate was measured with a hand-held ion chamber at 1 meter from the patient. Table F.1 summarizes individual patient data and Table F.2 provides T_e averages of Table F.1.

Combined clearance rate data are displayed graphically (Figure F.1); graphs of individual clearance rate having more than four measurements also are shown (Figure F.2-F.11).

Table F.1 Whole-body effective half-lives (T_e s) computed from regressions of relative dose rate as a function of time post-administration for common (non-RAB) thyroid cancer therapy with I-131.

Patient ID	Sex	Administration Number	Number of Data Points	T_e (h)	SD T_e (h)
A	F	2	4	41	7.2
A	F	3	3	13	3.1
A	F	4	4	13	0.26
A	F	5	5	19	1.1
B	F	1	9	23	1.3
C	M	1	5	19	1.0
D	F	1	5	15	0.33
E	F	1	9	32	4.6
F	F	1	7	104 ^a	16 ^a
G	F	1	4	16	3.4
H	F	1	2	14	
I	M	1	5	20	1.2

- A bi-exponential fit was justified for this patient. The value of T_e given is the largest component of the two-component fit.

Appendix F

Table F.2 Summary of Table F.1 including averaged T_s s. Headings "Avg" and "SD" refer to average and standard deviation of T_s . The disease involved the thyroid gland, the radiolabel was I-131, and the antibody was non-RAB.

Sex	Administration Number	Number of Patients	T _s Method 1		T _s Method 2	
			Avg T _s (h)	SD Avg T _s (h)	Avg T _s (h)	SD Avg T _s (h)
F	1	6	27	26	26	2.1
F	2	1	41			
F	3	1	13			
F	4	1	13			
F	5	1	19			
M	1	2	19	0.71	19	0.69

T_s Method 1: T_s was calculated by treating each patient independently and averaging the T_s values with other patients (Equations 4 and 5).

T_s Method 2: T_s was calculated by carrying out a regression on the normalized data points, treating each data point independently. The SD is the standard deviation of the regression slope (Figure F.1).

Figure F.1 Clearance rate for male and female patients receiving the first administration of I-131 non-RAB for thyroid cancer.

Figure F.2 Clearance rate for female patient A receiving the second administration of I-131 non-RAB for thyroid cancer

Figure F.3 Clearance rate for female patient A receiving the fourth administration of I-131 non-RAB for thyroid cancer.

Figure F.4 Clearance rate for female patient A receiving the fifth administration of I-131 non-RAB for thyroid cancer.

Figure F.5 Clearance rate for female patient B receiving the first administration of I-131 non-RAB for thyroid cancer

Figure F.6 Clearance rate for male patient C receiving the first administration of I-131 non-RAB for thyroid cancer.

Figure F.7 Clearance rate for female patient D receiving the first administration of I-131 non-RAB for thyroid cancer

Figure F.8 Clearance rate for female patient E receiving the first administration of I-131 non-RAB for thyroid cancer.

Figure F.9 Clearance rate for female patient F receiving the first administration of I-131 non-RAB for thyroid cancer.

Figure F.10 Clearance rate for female patient G receiving the first administration of I-131 non-RAB for thyroid cancer.

Figure F.11 Clearance rate for male patient I receiving the first administration of I-131 non-RAB for thyroid cancer.

APPENDIX G

Data Provided by the University of Alabama, Birmingham, AL from Studies Carried out in 1992-1993

These data were provided by University of Alabama at Birmingham Hospital. These measurements were made using a NaI(Tl) crystal integrated with a multichannel analyzer system. The patient sat in a chair 4.1 meters (13.5 feet) from the detector. All patients received one treatment. Patients were given Lu-177 RABs via intraperitoneal injection. Tables G.1 and G.2 summarize the individual data as well as the average $T_{\frac{1}{2}}$ data.

Combined clearance rate data are displayed graphically (Figures G.1 and G.2); graphs of individual patient's clearance rate also are shown (Figures G.3-G.25).

Table G.1 Whole-body effective half-lives ($T_{\frac{1}{2}}$ s) of Lu-177 RAB CC-49, IgG, for ovarian cancer patients receiving a single treatment. "SD" denotes the sample's standard deviation. Ovarian Cancer patients were treated with intraperitoneal injected Lu-177 RABs; the patients were older than 35 years.

Patient Number	Activity Administered (GBq) ^b	Number of Data Points	$T_{\frac{1}{2}}$ (h)	SD $T_{\frac{1}{2}}$ (h)
1	0.62	6	67	3.8
2	0.68	5	89	2.6
3	0.69	5	75	12
4	1.2	4	82	2.0
5	1.3	4	76	13
6	1.2	4	89	12
7	1.4	7	87	13
8	1.7	6	50	7.3
9	1.6	6	71	11
Mean			76	
SD Mean			13	
Combined Measurements ^a			75	
SD Combined Measurements ^a			4.1	

^a The $T_{\frac{1}{2}}$ was calculated by treating each measurement independently and regressing the normalized data points. The SD is the standard deviation of the regression slope (Figure G.1).

^b Multiply by 27 to convert to mCi.

Appendix G

Table G.2 Whole-body effective half-lives (T_e s) of I-131 RAB CC-49, IgG, for prostate cancer patients receiving a single treatment. Measurements were made using a NaI(Tl) detector at 4.1 meters. The headings "SD" and "Blood" refer to sample standard deviation and half-life of the RAB in blood.

Patient Number	Age (y)	Wt (kg)	Activity (GBq)	Number of Data Points	Effective T_e (h)	SD T_e (h)	Blood T_e (h)
1	59	180	4.5	7	93 ^b	11	45.6
2	62	189	6.1	6	56	1.9	63.8
3			5.9	6	53	1.8	
4			6.0	8	44	1.4	
5			5.4	6	56	0.67	
6			6.6	6	58	1.8	
7			5.7	8	50	1.7	
8			6.6	6	51	1.3	
9			5.1	7	59	4.5	
10			4.7	6	54	1.1	
11			6.4	8	42	1.6	
12			7.2	6	53	0.73	
14			5.5	6	47	1.7	
15			5.1	6	61	0.80	
Average					56		
SD Average					12		
Combined Measurements ^a					52		
SD of Combined Measurements ^a					1.2		

^a The T_e was calculated by treating each measurement independently and regressing the normalized data points. The SD is the standard deviation of the regression slope (Figure G.2).

^b A bi-exponential fit was justified for this patient. The T_e value given is the greater of the two components.

^c Multiply by 27 to convert to mCi.

Figure G.1 Clearance rate for several female patients receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.2 Clearance rate for several male patients receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.3 Clearance rate for female patient 1 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer

Figure G.4 Clearance rate for female patient 2 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer

Figure G.6 Clearance rate for female patient 4 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.8 Clearance rate for female patient 6 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.5 Clearance rate for female patient 3 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.7 Clearance rate for female patient 5 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.9

Clearance rate for female patient 7 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.10

Clearance rate for female patient 8 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.11

Clearance rate for female patient 9 receiving the first administration of Lu-177 RAB CC-49 for ovarian cancer.

Figure G.12

Clearance rate for male patient 1 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.13 Clearance rate for male patient 2 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.14 Clearance rate for male patient 3 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.15 Clearance rate for male patient 4 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.16 Clearance rate for male patient 5 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.19 Clearance rate for male patient 8 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.20 Clearance rate for male patient 9 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.21 Clearance rate for male patient 10 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.22 Clearance rate for male patient 11 receiving the first administration of I-131 RAB CC-49 for prostate cancer

Figure G.23 Clearance rate for male patient 12 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.24 Clearance rate for male patient 14 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

Figure G.25 Clearance rate for male patient 15 receiving the first administration of I-131 RAB CC-49 for prostate cancer.

APPENDIX H

Data Provided by the Garden State Cancer Center, Newark, NJ

These data were provided by Garden State Cancer Center at the Center for Molecular Medicine & Immunology. Effective half-life measurements ($T_{1/2}$ s) were made using 1) a Keithley Model 36155 hand-held ionization chamber, referred to as a "probe," at 1 meter from the side of the patient using the highest measured dose rate; 2) urine bioassay results; 3) a whole-body gamma camera, Sopha Model DSX and Model DS7. The probe measurements were suggested to be the most reliable. Effective half-life of blood data are listed for the greater component if the clearance rate is biphasic. Typically, only 3 or 4 measurements were performed per patient using the gamma camera whereas probe measurements were made daily. An Eberline E520 with a compensated GM probe is used when the Keithley Model 36155 is being calibrated (once per year).

Clearance-rate data for Re-188 injections were provided, and the results are shown for combined data from four patients having three or more measurements (Table H.1 and Figures H.1-H.3). Individual patient regressions are shown in Figures H.4-H.7. The standard deviations are very small, indicating high precision in the whole-body gamma scans. Measurements were taken 3 to 4 times in one day, which was about 2 $T_{1/2}$ s.

The values of $T_{1/2}$ for a similar disease, RAB, and administration number were averaged together (Tables H.2-H.7). The first administration includes the first time a patient is treated with a specific antibody, regardless of the radiolabel or form. The rationale behind this choice is that the patient's immune system may respond similarly to the antibody, regardless of its form. Examples of this selection are for lung cancer and for non-Hodgkins lymphoma. Several lung cancer patients were first treated with Immu31 antibody form of F(ab')₂ labeled with I-131, then with Immu31 antibody in the form of Fab' labeled with Tc-99m, then again treated using the same protocol as the first administration. Similarly, 9 patients treated for non-Hodgkins lymphoma were first treated using LL2 Fab' labeled with Tc-99m, and subsequently with LL2 F(ab')₂ labeled with I-131.

This data set is the most comprehensive one obtained and is suggested for those carrying out future research in this field.

Appendix H

Table H.1 Whole-body effective half-lives (T_e s) for MN14 (IgG) labeled with Re-188 administered to patients. The T_e values were determined using a whole-body gamma scan.

Patient Number	First Administration			Second Administration			Third Administration		
	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)	Number of Data Points	T_e (h)	SD T_e (h)
1	4	14	0.37	4	13	1.2	4	14	0.12
2	3	14	0.33	3	13	0.38	3	14	0.005
3	3	12	0.23	3	12	1.5	3	14	0.14
4	3	12	2.3	4	13	0.39	4	12	0.093
Mean		13	0.99		13	0.56		13	0.059
Combined Measurements ^a		14	0.40		12	0.60		13	0.23

- ^a The T_e was calculated by treating each measurement independently and regressing the normalized data points (Figures H.1-H.3).

Table H.2

Average T_e s for diseases and RABs listed for first administrations. The headings "Avg," "SD," "Wt," refer to average, standard deviation, and weight. The headings "Urine," "IC," and "Scan" refer to the effective half-life calculations based on measurements using urine bioassay, ionization chamber at 1 meter, and whole-body gamma camera scan measurements.

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Pat-lents	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T _e Average (h)						Avg Blood T ½ (h)	S.D. Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Appendix	NP4	Fab'	Tc-99m	M	1	44		109		1.1						5.6		4.1	
Bartholin's Gland	G9	Fab'	Tc-99m	F	1	49		97		0.78						5.4		3.8	
Biliary Tumor	G9	Fab'	Tc-99m	M	1	54		73		1.1				5.5		5.3		5.3	
Breast	LL2	Fab'	Tc-99m	F	1	59		57		0.95				5.9					
Breast	MA5	F(ab')2	I-131	F	4	51	8.6	72	14	0.30	0.005					44	5.4	32	5.6
Breast	MA5	Fab'	Tc-99m	F	3	55	13			0.91	0.069			4.7	1.3	5.2	0.24	4.4	0.49
Breast	MA5	IgG	I-131	F	1	64		65		0.29						34		21	
Breast	MN14	IgG	I-131	F	1	49		56		0.27						75		115	
Breast	MN3	Fab'	Tc-99m	F	3	54	4.4	62	7.2	1.0	0.019			5.4	0.17	5.6	0.11	4.1	
Breast	NP4	Fab'	Tc-99m	F	12	56	7.3	66	10	0.94	0.088			5.3	0.22	5.3	0.15	4.4	0.66
Breast	RINA	IgG	I-131	F	1	46		62		0.28						45			
Breast	RS7	Fab'	Tc-99m	F	2	46	7.8	57	2.8	0.88	0.25			3.2	3.6	5.4	0.078	3.7	
Choriocarcinoma	IMMU8	IgG	I-131	F	4	36	2.5	56	4.2	0.28	0.017			5.6 ^b		55	25	30	14
Cirrhosis	IMMU31	Fab'	Tc-99m	F	1	55		47		0.89				5.7					
Chron. Lym. Leuk.	LL2	Fab'	Tc-99m	F	2	57	2.8	51	1.4	0.98	0.005			5.5		5.5	0.021	4.5	0.36
Colon	G9	Fab'	Tc-99m	F	5	51	10	69	10	0.98	0.12			5.6	0.18	5.8	0.73	4.0	0.23
Colon	G9	Fab'	Tc-99m	M	3	62	12	89	12	1.0	0.060			5.3	0.057	5.3	0.15	3.9	0.60
Colon	MN14	F(ab)2	I-131	F	4	60	10	83	0.58	1.6	1.5	39	10			46	3.8	16	8.9
Colon	MN14	F(ab)2	I-131	M	3	66	9.0	75	7.6	4.6	1.7	31	11			35	26	14	2.2

a Multiply by 27 to convert to mCi.

Table H.2 (Continued)

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T ₁ Average (h)						Avg Blood T ½ (h)	S.D. Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Colon	MN14	IgG	I-131	F	2	57	25	63	4.2	0.31	0.033	2				68		45	10
Colon	MN14	IgG	I-131	M	10	65	7.3	83	8.6	1.5	1.3	30	6.3			39	18	25	10
Colon	MN14	IgG	Re-188	F	6	53	16	67	15	1.7	0.72			4.6	1.0	14	1.2	7.8	3.0
Colon	MN14	IgG	Re-188	M	3	67	8.7	81	10	1.5	0.53			4.3	1.6	14	1.3	4.9	2.1
Colon	MN3	Fab'	Tc-99m	M	3	66	8.1	88	10	0.91	0.069			5.3	0.32	5.5	0.14	4.2	0.28
Colon	MU9	F(ab') ₂	I-131	F	4	60	12	58	12	3.8	0.97	38	3.0			49	11	24	13
Colon	MU9	F(ab') ₂	I-131	M	3	62	16	95	34	2.0	1.4	45	17			43	11	23	5.1
Colon	MU9	F(ab') ₂	Tc-99m	F	2	43	2.8	89		0.91	0.003			5.6	0.31	5.5	0.15	3.7	
Colon	MU9	F(ab') ₂	Tc-99m	M	4	66	8.0	73	7.2	0.85	0.15			5.6	0.15	5.7	0.40	3.7	0.53
Colon	MU9	Fab'	Tc-99m	F	4	66	2.5	68	16	0.96	0.029			5.5		5.3	0.31	4.2	0.035
Colon	MU9	Fab'	Tc-99m	M	9	68	7.6	88	7.9	0.99	0.10			5.5	0.12	5.4	0.22	4.2	0.76
Colon	MU9	IgG	I-131	F	5	47	13	64	8.3	2.3	1.2	58	4.9			55	13	44	6.0
Colon	MU9	IgG	I-131	M	1	61		76		3.6		43				51		34	
Colon	NP4	F(ab') ₂	I-131	F	3	54	5.0	88		1.8	1.3	34	0.22			39	11	45	21
Colon	NP4	F(ab') ₂	I-131	M	3	61	17	91	15	1.9	1.3	33	3.7			43	5.2	30	6.5
Colon	NP4	Fab'	Tc-99m	F	15	52	11	65	13	0.94	0.092			5.4	0.060	5.1	0.21	4.1	0.42
Colon	NP4	Fab'	Tc-99m	M	25	68	8.0	87	11	0.99	0.054			5.4	0.22	5.1	0.24	4.3	0.44
Colon	NP4	IgG	Tc-99m	M	1	76		98		0.80				5.7		5.5		4.8	
Duodenal	MN14	IgG	I-131	M	1	47		91		0.35		45				73		54	
Elevated Marker	IMMU31	Fab'	Tc-99m	F	1	64		67		0.91				5.1		5.2			
Elevated Marker	IMMU31	Fab'	Tc-99m	M	1	30		71		1.0				5.3		5.1		4.1	
Elevated Marker	MN14	F(ab') ₂	I-131	M	2	66	13	87		0.38	0.12					69	27	30	7.7

Table H.2 (Continued)

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Pat- ients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T ₁ Average (h)						Avg Blood T ½ (h)	S.D. Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Elevated Marker	NP4	Fab'	Tc-99m	F	1	64		57		0.77				4.9		5.3		4.3	
Endometrial	NP4	Fab'	Tc-99m	F	1	62		49		1.0				5.7		6.0		4.5	
Endometrial	RS7	Fab'	Tc-99m	F	1	62				1.0				5.7		5.9		4.7	
Esophageal	MN14	F(ab)2	I-131	M	1	67		75		6.1		41				42		33	
Germ Cell	IMMU31	Fab'	Tc-99m	M	1	5		14		0.26						4.8		3.8	
Germ Cell	IMMU31	IgG	I-131	F	1	3		29		0.11						59		50	
Germ Cell	IMMU8	IgG	I-131	M	1	24		70		2.5		37				36		24	
Gest.tropho.dise	IMMU8	IgG	I-131	F	2	30	7.8	63	2.1	0.27	7.3					52	5.8	45	5.1
Head/neck	MN14	IgG	I-131	M	1	57		78		0.36						55		86	
Hepatoblastoma	IMMU31	Fab'	Tc-99m	M	1	2		14		0.26						5.0		4.5	
Hepatoma	IMMU31	F(ab')2	I-131	F	5	40	25	59	26	1.6	1.2	49	26			50	27	49	15
Hepatoma	IMMU31	F(ab')2	I-131	M	3	54	20	76	18	1.9	0.009	56	10			76	28	45	21
Hepatoma	IMMU31	Fab'	Tc-99m	M	6	55	12	79	17	0.96	0.11			5.6	0.12	5.4	0.25	4.8	0.54
Hepatoma	IMMU31	IgG	I-131	F	1	58		89		2.0		73				86		62	
HIV (+)	7C5	Fab'	Tc-99m	F	2	29	7.8	54		0.90	0.063					5.6	0.32		
HIV (+)	7C5	Fab'	Tc-99m	M	9	33	5.9	62	6.6	0.94	0.066					5.5	0.28		
HIV (+)	LL2	Fab'	Tc-99m	M	1	37		58		1.1						5.5			
Lung	MN14	F(ab)2	I-131	F	1	39		47		3.6		49				50		22	
Lung	MN14	IgG	I-131	F	1	52		52		2.8		50				59		36	
Lung	NP4	F(ab')2	I-131	F	1	71		68		3.3		45				46		34	
Lung	NP4	F(ab')2	I-131	M	1	77		68		3.0		38				46		34	
Lung	NP4	Fab'	Tc-99m	M	4	60	8.2	87	4.7	0.92	0.17			5.4		5.2	0.24	4.2	0.071

Table H.2 (Continued)

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act ^a (GBq)	SD Avg Act ^a (GBq)	T _{1/2} Average (h)					Avg Blood T _{1/2} (h)	S.D. Avg Blood T _{1/2} (h)
												IC	SD IC	Urine	SD Urine	Scan		
Lung	RS7	F(ab') ₂	I-131	F	1	42		49		2.5		41				37	18	
Lung	RS7	F(ab') ₂	I-131	M	1	81		75		1.9		51				48	33	
Lung	RS7	Fab'	Tc-99m	F	2	67	7.8	52		1.1	0.010			1.0		5.2	4.2	
Lung	RS7	Fab'	Tc-99m	M	3	58	6.4	88	1.4	1.0	0.059			3.0	3.5	5.3	4.5	0.071
Lung	RS7	IgG	I-131	F	1	69		49		0.32						58		
Lung	RS7	IgG	I-131	M	1	65		75		0.31						53	38	
Medullary Thyroid	MN14	F(ab') ₂	I-131	F	1	72		60		1.8		48				42	20	
Medullary Thyroid	MN14	F(ab') ₂	I-131	M	3	57	12	74	13	3.9	1.2	56	27			62	34	16
Medullary Thyroid	MN14	IgG	I-131	F	2	57	23	45	5.7	2.8	0.10	62	8.6			66	10	17
Medullary Thyroid	NP4	F(ab') ₂	I-131	M	1	40		87		4.1		37				42	42	
Medullary Thyroid	NP4	Fab'	Tc-99m	F	1	21		73		1.0				5.5		4.6	4.9	
Medullary Thyroid	NP4	Fab'	Tc-99m	M	1	36				1.1				5.5		5.3	4.6	
Medullary Thyroid	NP4	IgG	I-131	F	1	60		56		2.5		41				34	30	
Non-hodg Lymph	LL2	F(ab') ₂	I-131	F	2	59	22	58	5.7	0.48	0.30	35				36	11	2.0
Non-hodg Lymph	LL2	F(ab') ₂	I-131	M	1	64		83		0.28						23	28	
Non-hodg Lymph	LL2	Fab'	Tc-99m	F	1	55		58		1.0				5.3		4.7	3.6	
Non-hodg Lymph	LL2	Fab'	Tc-99m	M	6	62	8.4	78	7.9	1.0	0.067			5.5	0.20	5.3	3.6	0.64
Ovarian	MA5	Fab'	Tc-99m	F	1	78		69		0.85						6.2	4.3	
Ovarian	MA5	IgG	I-131	F	1	74		76		0.36		66				73	49	
Ovarian	NP4	Fab'	Tc-99m	F	1	48		69		1.0				5.6		5.5	4.0	
Ovarian	RS7	Fab'	Tc-99m	F	1	78				1.0						5.4	4.1	
Pancreatic	MN14	IgG	I-131	M	1	55		62		0.43						66	49	

Table H.2 (Continued)

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T ₁ Average (h)						Avg Blood T _{1/2} (h)	S.D. Avg Blood T _{1/2} (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Pancreatic	MN14	IgG	Re-188	F	1	75		66		0.76				5.1		14		7.3	
Pancreatic	NP4	Fab'	Tc-99m	F	1	55		50		1.1						5.1		4.1	
Pancreatic	NP4	Fab'	Tc-99m	M	1	66		65		0.78						5.1		4.3	
Pancreatic	PAM4	Fab'	Tc-99m	F	1	80				0.85				5.3		5.4		4.1	
Pancreatic	PAM4	Fab'	Tc-99m	M	1	59		77		0.94				5.7		5.3		3.8	
Pancreatic	PAM4	IgG	I-131	F	1	74		60		0.27						40		25	
Pancreatic	PAM4	IgG	I-131	M	1	75				0.31				0.14		48		33	
Prostate	NP4	Fab'	Tc-99m	M	1	74		68		1.1						5.1		4.8	
Prostate	RS7	F(ab') ₂	I-131	M	1	58		88		0.30						61		13	
Rectal	G9	Fab'	Tc-99m	M	1	65		92		1.1				5.6		5.5		4.2	
Rectal	MN14	F(ab') ₂	I-131	F	1	63		53		0.30						48		60	
Rectal	MN14	IgG	I-131	M	1	59		72		0.37						66		41	
Rectal	MN14	IgG	Re-188	M	1	52				2.9						16		4.8	
Rectal	MU9	F(ab') ₂	I-131	M	2	53	0.71	84	3.5	1.6	1.7	20	0.81			27	12	19	12
Rectal	MU9	F(ab') ₂	Tc-99m	F	1	64				0.93				5.6		5.5		3.6	
Rectal	MU9	F(ab') ₂	Tc-99m	M	1	71		75		0.78				5.9		5.6		4.2	
Rectal	MU9	Fab'	Tc-99m	F	1	60				1.1						5.5			
Rectal	MU9	Fab'	Tc-99m	M	3	63	9.3	74	2.1	1.0	0.10			5.5	0.22	5.4	0.24	4.2	0.26
Rectal	MU9	IgG	I-131	M	4	59	9.1	85	18	2.9	0.49	52	15.2			49	19	39	11
Rectal	NP4	F(ab') ₂	I-131	M	1	40		83		0.28						63		25	
Rectal	NP4	Fab'	Tc-99m	F	2	68	4.2	76	5.7	0.76	0.042					5.0	0.028	3.5	
Rectal	NP4	Fab'	Tc-99m	M	10	64	6.1	88	18	0.99	0.087			5.3	0.078	5.2	0.20	4.3	0.65

Table H.2 (Continued)

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Pat-ients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T, Average (h)						Avg Blood T ½ (h)	S.D. Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Small Bowel	MN14	F(ab)2	I-131	M	1	66		76		4.9		49				54			
Small Bowel	NP4	Fab'	Tc-99m	M	1	60		77		0.99						5.2			
Stomach	NP4	Fab'	Tc-99m	M	2	47	4.2	76	24	0.93	0.20			5.4	0.042	5.2		3.8	
Testicular	MMU31	F(ab)2	I-131	M	1	34		84		1.8		37				42		38	
Testicular	MMU31	Fab'	Tc-99m	M	1	33		72		0.99				5.7		5.7		4.5	
Testicular	MMU8	IgG	I-131	M	2	38	16	77	17	0.27	0.029					63		26	23
Thyroid	NP4	Fab'	Tc-99m	M	1	7		19		0.21						5.3		4.2	
Unknown Primary	MMU31	F(ab)2	I-131	M	1	61		68		1.9		62				68			
Unknown Primary	MMU31	Fab'	Tc-99m	M	1	66		74		1.0				5.2		5.1		3.4	
Unknown Primary	LL2	Fab'	Tc-99m	M	1	54		64		0.86				5.8		5.9		4.4	
Unknown Primary	MN14	IgG	I-131	F	1	60		80		2.7		61				66		43	
Unknown Primary	MU9	IgG	I-131	F	1	74				0.28						54		109	
Unknown Primary	NP4	Fab'	Tc-99m	F	2	69	11	55		0.94	0.092			5.4		5.0	0.45	4.0	
Unknown Primary	PAM4	Fab'	Tc-99m	M	1	67		71		1.0				5.5		5.8		3.4	
Unknown Primary	RS7	IgG	I-131	M	1	36				2.7		27						12	

Table H.3 Average T_s for diseases and RABs listed for second administrations. The headings "Avg," "SD," "Wt," refer to average, standard deviation, and weight. The headings "Urine," "IC," and "Scan" refer to the effective half-life calculations based on measurements using urine bioassay, ionization chamber at 1 meter, and whole-body gamma camera scan measurements.

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Pat-ients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T _s Average (h)						Avg Blood T ½ (h)	SD Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	2	57	2.8	56	2.1	0.91	0.18					32	3.5	28	5.5
Colon	MN14	IgG	I-131	F	1	39		67		3.9		61						82	
Colon	MN14	IgG	I-131	M	5	66	5.7	82	6.8	8.3	1.4	28	14			35	10	24	6.9
Colon	MN14	IgG	Re-188	F	5	47	8.4	59	6.4	1.1	0.30			4.1	2.0	14	0.80	7.5	2.2
Colon	MN14	IgG	Re-188	M	2	64	9.9	73	2.1	1.2	0.11			3.2	1.9	13	1.3	4.9	0.49
Colon	MU9	F(ab') ₂	I-131	F	1	69		53		7.1		33						33	
Colon	MU9	F(ab') ₂	I-131	M	2	68	16	107	37	8.8	0.33	33	24			42	24	31	18
Colon	MU9	IgG	I-131	F	2	39	4.2	61	4.2	1.9	1.4	19	2.5			17		13	
Colon	MU9	IgG	I-131	M	1	61		80		5.5		10				11		7.2	
Colon	NP4	F(ab') ₂	I-131	F	2	52	2.8	89	0.71	7.3	1.7	30	24			30	23	27	19
Colon	NP4	F(ab') ₂	I-131	M	1	65		110		9.4		30				38		28	
Colon	NP4	Fab'	Tc-99m	M	3	68	17	86	13	1.0	0.054			5.4		5.2	0.28	4.0	0.28
Colon	NP4	IgG	Tc-99m	F	1	46		63		0.85				5.6		5.1		4.7	
Colon	NP4	IgG	Tc-99m	M	1	70		92		0.78				5.8		5.4		4.7	
Duodenal	MN14	IgG	I-131	M	1	47		90		2.2		63				77		41	
Head/neck	MN14	IgG	I-131	M	1	57		78		5.5		47				54		38	
Hepatoma	IMMU31	F(ab') ₂	I-131	F	4	51	18	71	13	3.4	0.82	39	22			52	26	44	16
Hepatoma	IMMU31	F(ab') ₂	I-131	M	1	33		59		4.6		46				51		53	
Hepatoma	IMMU31	Fab'	Tc-99m	F	1	64		78		1.0				5.1		5.3		4.6	

^a Multiply by 27 to convert to mCi.

Table H.3 (Continued)

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T, Average (h)						Avg Blood T ½ (h)	SD Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Lung	NP4	Fab'	Tc-99m	M	1	70		85		0.97				5.2		5.4		4.3	
Lung	RS7	Fab'	Tc-99m	M	1	81				1.1				5.4		5.3		4.1	
Medullary Thyroid	MN14	F(ab')2	I-131	F	1	72		59		7.2		48				52		25	
Medullary Thyroid	MN14	F(ab')2	I-131	M	1	45		88		8.8		10				8.9		7.5	
Medullary Thyroid	NP4	F(ab')2	I-131	M	1	40		87		9.0		20						20	
Non-hodg Lymph	LL2	F(ab')2	I-131	F	4	67	8.2	57	4.0	1.1	0.05	37	5.9			40	14	28	7.2
Non-hodg Lymph	LL2	F(ab')2	I-131	M	6	66	4.9	77	12	1.0	0.17	31				56	62	22	5.6
Non-hodg Lymph	LL2	Fab'	Tc-99m	M	1	49		98		0.92				5.5		5.6		3.7	
Ovarian	MA5	F(ab')2	I-131	F	1	78		69		2.5		57				64		20	
Pancreatic	MN14	IgG	I-131	M	1	65		63		4.5		49						53	
Pancreatic	PAM4	IgG	I-131	M	1	59		76		2.8		46				46			
Rectal	MN14	IgG	Re-188	M	1	52				1.5						14		4.4	
Rectal	MU9	F(ab')2	I-131	M	1	52		80		9.4		39						24	
Rectal	MU9	IgG	I-131	F	1	57				0.30						105		39	
Rectal	MU9	IgG	I-131	M	1	63		78		6.6		16				20		11	
Rectal	NP4	F(ab')2	I-131	M	1	67		84		2.3		51				48		34	
Rectal	NP4	Fab'	Tc-99m	M	1	62		72		0.96				5.2				3.9	
Rectal	NP4	IgG	Tc-99m	F	1	65		79		0.85						5.6		4.5	
Testicular	IMMU31	F(ab')2	I-131	M	2	48	19	77	11	6.1	2.3	34	7.4			62	4.7	31	
Unknown Primary	MU9	IgG	Re-188	M	1	67				1.4				5.0		14		7.9	

Table H.4 Average T_s for diseases and RABs listed for third administrations. The headings "Avg," "SD," "Wt," refer to average, standard deviation, and weight. The headings "Urine," "Probe," and "Scan" refer to the effective half-life calculations based on measurements using urine bioassay, probe ionization chamber at 1 meter, and whole-body gamma camera scan measurements.

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Pat-ients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T _s Average (h)						Avg Blood T ½ (h)	SD Avg Blood T ½ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1	59		55		0.8						44		21	
Colon	MN14	IgG	I-131	F	1	40		67		3.0		12				26		11	
Colon	MN14	IgG	I-131	M	1	74		87		7.4		18				21		17	
Colon	MN14	IgG	Re-188	F	2	44	4.2	67	9.9	1.1	0.026			3.8	0.38	13	0.91	6.3	0.25
Colon	MU9	F(ab') ₂	I-131	F	1	69		51		7.5		38				87		36	
Colon	MU9	F(ab') ₂	I-131	M	1	57		129		10.0		60				81		52	
Colon	NP4	F(ab') ₂	I-131	F	1	50		89		8.9		17				21		14	
Hepatoma	IMMU31	F(ab') ₂	I-131	F	4	59	13	75	10	6.8	2.7	43	20			66	26	51	18
Medullary Thyroid	MN14	F(ab') ₂	I-131	F	1	72		54		5.4		45				45		33	
Non-hodg Lymph	LL2	F(ab') ₂	I-131	F	2	65	13	58	4.9	1.3	0.77	38	7			42	2.8	30	3.3
Non-hodg Lymph	LL2	F(ab') ₂	I-131	M	4	69	2	80	13	0.8	0.019	26	29			63	62	25	4.8
Rectal	MU9	F(ab') ₂	I-131	F	1	57		104		5.5		45				48		27	
Rectal	MU9	F(ab') ₂	I-131	M	1	61		97		3.8		34				22		13	
Rectal	NP4	F(ab') ₂	I-131	M	1	67		86		8.5		37				33		29	
Testicular	IMMU31	F(ab') ₂	I-131	M	1	34		66		3.6		34				52		57	
Unknown Primary	MU9	IgG	Re-188	M	1	67				1.4				4.3		14		7.1	

a Multiply by 27 to convert to mCi.

Table H.5 Average $T_{1/2}$ s for diseases and RABs listed for fourth administrations. The headings "Avg," "SD," "Wt," refer to average, standard deviation, and weight. The headings "Urine," "IC," and "Scan" refer to the effective half-life calculations based on measurements using urine bioassay, ionization chamber at 1 meter, and whole-body gamma camera scan measurements.

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T, Average (h)						Avg Blood $T_{1/2}$ (h)	SD Avg Blood $T_{1/2}$ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1	59		54		1.0						37		23	
Hepatoma	IMMU31	F(ab') ₂	I-131	F	1	65		73		4.5		29				44		26	
Non-Hodg Lymph	LL2	F(ab') ₂	I-131	M	1	70		97		1.0						38		33	
Non-Hodg Lymph	LL2	F(ab') ₂	I-131	F	1	55		59		1.1						37		21	
Rectal	IMMU31	F(ab') ₂	I-131	F	1	57		101		9.0		59						32	

a Multiply by 27 to convert to mCi.

Table H.6 Average $T_{1/2}$ s for diseases and RABs listed for fifth administrations. The headings "Avg," "SD," "Wt," refer to average, standard deviation, and weight. The headings "Urine," "IC," and "Scan" refer to the effective half-life calculations based on measurements using urine bioassay, ionization chamber at 1 meter, and whole-body gamma camera scan measurements.

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T, Average (h)						Avg Blood $T_{1/2}$ (h)	SD Avg Blood $T_{1/2}$ (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1	59		54		0.77						37		23	
Non-Hodg Lymph	LL2	F(ab') ₂	I-131	M	1	70		96		0.80						26		20	
Non-Hodg Lymph	LL2	F(ab') ₂	I-131	F	1	55		60		0.77						29		16	

a Multiply by 27 to convert to mCi.

Table H.7 Average $T_{1/2}$ s for diseases and RABs listed for sixth administrations. The headings "Avg," "SD," "Wt," refer to average, standard deviation, and weight. The headings "Urine," "IC," and "Scan" refer to the effective half-life calculations based on measurements using urine bioassay, ionization chamber at 1 meter, and whole-body gamma camera scan measurements.

Disease	Anti-body name	Anti-body form	Isotope	Sex	No. of Patients	Avg Age (y)	SD Avg Age (y)	Avg Wt (kg)	SD Avg Wt (kg)	Avg Act (GBq) ^a	SD Avg Act (GBq) ^a	T _{1/2} Average (h)						Avg Blood T _{1/2} (h)	SD Avg Blood T _{1/2} (h)
												IC	SD IC	Urine	SD Urine	Scan	SD Scan		
Chron. Lym. Leuk.	LL2	F(ab') ₂	I-131	F	1	59		57		1.0						32		22	
Non-Hodg Lymph	LL2	F(ab') ₂	I-131	M	1	70		99		1.1						17		13	

a Multiply by 27 to convert to mCi.

Figure H.1 Clearance rate for one male and three female patients receiving the first administration of Re-188 RAB Mn-14 (IgG) for colon cancer.

Figure H.2 Clearance rate for one male and three female patients receiving the second administration of Re-188 RAB Mn-14 (IgG) for colon cancer.

Figure H.3 Clearance rate for one male and three female patients receiving the third administration of Re-188 RAB Mn-14 (IgG) for colon cancer.

Figure H.4 Clearance rate for female patient number 1 receiving three administrations of Re-188 RAB Mn-14 (IgG) for colon cancer.

Figure H.5 Clearance rate for female patient number 2 receiving three administrations of Re-188 RAB Mn-14 (IgG) for colon cancer.

Figure H.6 Clearance rate for male patient number 3 receiving three administrations of Re-188 RAB Mn-14 (IgG) for colon cancer.

Figure H.7 Clearance rate for female patient number 4 receiving three administrations of Re-188 RAB Mn-14 (IgG) for colon cancer.

APPENDIX I

Data Provided by the Sloan Kettering Memorial Cancer Center, New York, NY

These data were provided by Sloan Kettering Memorial Cancer Center. The combined data on clearance rate for each administration are displayed graphically (Figures I.1 - I.11). Tables I.1 - I.5. summarize individual patient data as well as averages of RAB T_0 .

Effective half-life measurements were made using a hand held ion chamber, Keithley Model 361100, at 1) a distance of 1 meter from the torso of the patient and 2) at contact, usually the sternum, where the highest reading was found. Exposure rate measurements for clearance rates in Figures I.43 - I.63

Graphs of individual patient clearance rates are shown (Figures I.12 - I.63).

Table I.1 Whole-body effective half-lives (T_{e} s) of I-131 RAB CC-49, IgG, for colon cancer patients receiving first and second treatments. The heading "at Strn" and "at 1m" refer to T_{e} s determined from measurements taken at the sternum and at 1 meter, respectively. "SD" refers to standard deviation.

Patient Number	Age	First Administration						Second Administration					
		Act-ivity (GBq) ^a	Number of Data Points	at Strn T_{e} (h)	SD at Strn T_{e} (h)	at 1m T_{e} (h)	SD at 1m T_{e} (h)	Act-ivity (GBq)	Number of Data Points	at Strn T_{e} (h)	SD at Strn T_{e} (h)	at 1m T_{e} (h)	SD at 1m T_{e} (h)
1	56	2.6	7	56.0	1.82	57	3.1						
2	30	2.4	4	18.2	1.45	26	6.7						
3	63	4.2	5	48.3	4.08	68	4.8	3.7	2	24.3		22.0	
4	?	4.6	7	44.5	1.68	45	2.6						
5	55	5.4	5	54.7	8.63	50	2.5						
6	60	5.7	7	49.7	2.04	52	2.5						
7	61	4.2	5	50.4	5.61	43	9.8						
8	74	5.2	6	57.1	5.30	64	2.6						
9	56	6.7	6	31.4	0.91	43	2.9	6.9	2	11.0		11.7	
10	81	4.8	4	34.5	8.07	28	5.5						
11	49	4.6	6	47.8	3.11	46	2.1	4.3	5	11.6	0.538	16	0.42
12	73	1.7	7	51.8	4.26	36	4.3	1.7	4	39.0	0.162	43	4.3
13	71	3.3	6	51.8	7.16	51	7.7						
14	38	2.2	4	48.5	1.98	49	7.3						
15	39	2.2	7	63.1	3.28	63	8.6						
Average				47.2		48.0				21.5		23.1	
SD Average				11.3		12.2				13.2		13.9	
Combined Measurements ^b						51.0						23.0	
SD Combined ^b						2.1						4.9	

^a Multiply by 27 to obtain mCi

^b The T_{e} was calculated by treating each data measurement independently and regressing the normalized data points. (Figures I.1 - I.2).

Table I.2 Whole-body effective half-lives (T_{e} s) of I-131 RAB M-195, IgG, for myelogenous leukemia patients with receiving first and second treatments. The heading "at Strn" and "at 1m" refer to T_{e} s determined from measurements taken at the sternum and at 1 meter, respectively; "SD" refers to sample standard deviation.

Patient Number	Age	First Administration						Second Administration					
		Act-ivity (GBq) ^c	Number of Data Points	at Strn T_{e} (h)	SD at Strn T_{e} (h)	at 1m T_{e} (h)	SD at 1m T_{e} (h)	Act-ivity (GBq)	Number of Data Points	at Strn T_{e} (h)	SD at Strn T_{e} (h)	at 1m T_{e} (h)	SD at 1m T_{e} (h)
1	45	1.4	7	22	0.61	25	3.0	1.8	6	28	1.6	26	3.0
2	19	1.7	7	26	1.8	28	1.6	1.7	7	31	1.7	34	0.78
3	37	1.9	6	32	2.4	29	9.3	1.9	7	33	2.8	28	1.6
4	52	2.8	4	30	4.8	35	3.7	2.9	6	49	4.8	47	1.4
5	76	2.3	5	26	4.0	30	4.2	2.4	6	36	2.4	37	2.3
6	36	2.2	4	34	3.1	48	3.7	2.4	9	44	1.8	45	2.5
7	70	2.8	3	28	0.61	34	2.5	2.7	8	35	0.65	37	1.2
8	53	2.6	5	12	1.6	14	1.1	2.8	5	13	1.6	11	0.34
9	62	2.8	4	32	0.61	34	0.41	2.7	3	35	0.10	38	2.6
10	74	2.7	6	46	5.4	79	13	2.6	13	60	1.8	47 ^a	5.3 ^b
11	71	2.2	8	55	3.7	44	4.0						
12	45	3.1	5	30	1.8	45	5.0	2.6	4	23	1.5	34	4.6
13	68	2.6	5	38	4.3	45	8.7	2.6	3	27	5.7	30	4.5
Average				32		38				34		34	
SD Average				11		16				12		10	
Combined Measurements ^a						46						49	
SD of Combined Measurements ^a						3.8						4.0	

^a The T_{e} was calculated by treating each data measurement independently and regressing the normalized data points (Figures I.3 - I.4).

^b A runs test described in Section 3.2.2 indicated that neither a single- nor a bi-exponential clearance rate was statistically justified for the T_{e} value.

^c Multiply by 27 to obtain mCi.

Table I.3 Whole-body effective half-lives (T_{e} s) of I-131 RAB M-195, IgG, for myelogenous leukemia patients receiving third and fourth treatments. The heading "at Strn" and "at 1m" refer to T_{e} s determined from measurements taken at the sternum and at 1 meter, respectively. "SD" refers to sample standard deviation.

Patient Number	Age	Third Administration						Fourth Administration					
		Act-ivity (GBq) ^a	Number of Data Points	at Strn T_{e} (h)	SD at Strn T_{e} (h)	at 1m T_{e} (h)	SD at 1m T_{e} (h)	Act-ivity (GBq)	Number of Data Points	at Strn T_{e} (h)	SD at Strn T_{e} (h)	at 1m T_{e} (h)	SD at 1m T_{e} (h)
12	45	2.7	7	42	2.3	48	2.0	2.6	7	29	1.4	29	2.2
13	68	2.7	5	50	2.2	48	1.7						
Average				46		48				29		29	
SD Average				6.0		0.13							
Combined Measurements ^a						48							
SD of Combined Measurements ^a						1.3							

a The T_{e} was calculated by treating each data measurement independently and regressing the normalized data points (Figure I.5).

b Multiply by 27 to obtain mCi.

Table I.4 Whole-body effective half-lives (T_e s) of I-131 RAB 3F8, IgG, for neuroblastoma patients receiving first, second, and third treatments. The heading "at Strm" and "at 1m" refer to T_e s determined from measurements taken at the sternum and at 1 meter, respectively. "SD" refers to sample standard deviation.

Pat- ient Num- ber	Age	First Administration						Second Administration						Third Administration					
		Act- ivity (GBq)	Number of Data Points	at Strm T_e (h)	SD at Strm T_e (h)	at 1m T_e (h)	SD at 1m T_e (h)	Act- ivity (GBq)	Number of Data Points	at Strm T_e (h)	SD at Strm T_e (h)	at 1m T_e (h)	SD at 1m T_e (h)	Act- ivity (GBq)	Number of Data Points	at Strm T_e (h)	SD at Strm T_e (h)	at 1m T_e (h)	SD at 1m T_e (h)
1	3	1.1	8	21	1.5	51 ^b	52												
2	5	1.1	7	21	1.8	23	1.4	1.1	6	14	0.79	12	1.1	1.1	4	12	1.6	9.7	1.5
3	5	1.1	4	14	1.7	16	3.7	1.1	4	17	2.3	17	2.5	1.1	5	23	1.8	23	1.3
4	4	1.1	6	24	4.2	32	4.0	1.1	4	24	0.42	20	1.4	1.1	5	26	2.5	29	2.7
5	4	1.0	4	13	0.85	12	2.3	1.0	4	20	1.2	22	3.8	1.1	4	31	5.6	28	5.1
6	3	1.1	5	22	2.3	39	6.5	1.1	7	22	1.3	25	1.4	1.2	6	26	1.9	28	1.8
7	26	1.1	7	16	0.90	14	1.2	1.1	5	16	2.7	10	0.50	1.1	3	6	0.30	7.6	0.33
8	7	1.1	6	31	1.7	36	6.0	1.1	3	27	1.6	29	11	1.1	4	25	1.5	27	3.1
9	25	3.7	9	32	2.2	27	1.7	3.8	5	34	2.8	42	3.8	3.7	8	39	2.0	32	2.0
10	4	3.0	7	28	0.67	28	0.51	3.0	5	29	2.8	35	11	3.0	10	41	3.0	45	4.0
11	3	1.9	6	22	1.9	24	2.9	1.9	5	22	1.5	21	0.34	1.9	12	32	1.4	51 ^b	27 ^b
12	5	2.7	9	29	1.2	25	1.2	2.7	4	25	3.5	22	0.42	2.8	8	31	1.9	30	1.4
13	3	2.2	5	23	3.6	21	0.87	2.2	6	20	0.60	22	0.65	2.1	3	20	0.83	19	3.3
14	8	2.6	5	31	5.6	42	7.2	2.7	6	27	1.7	24	2.3	2.6	5	29	1.2	24	0.51
15	3	2.5	5	22	0.42	21	2.4	2.4	4	21	3.2	20	0.73	2.4	5	24	1.7	25	1.8
16	4	2.7	5	19	0.66	23	2.6	2.7	4	19	0.33	22	3.2	2.7	3	23	1.1	33	9.5
17	3	2.4	5	25	2.0	25	2.3	2.2	4	23	3.6	37	4.0	2.4	4	35	2.4	38	8.4
18	3	2.6	4	24	1.6	25	1.2	2.5	4	24	1.3	24	2.2	2.6	4	27	1.0	23	1.1
19	11	4.1	3	23	3.6	27	7.8	4.0	4	24	1.1	30	5.5	3.9	4	30	0.91	31	5.8
20	6	2.8	5	20	0.40	23	1.5	3.0	5	29	1.3	29	1.4	2.9	5	21	1.7	27	2.8
21	17	4.4	4	24	1.4	33	4.2	4.4	3	21	4.3	31	3.9	4.0 & 3.9	3	39	14	35	7.3
Average				23		27				23		25				28		27	
SD Average				5.2		9.3				4.8		7.9				10		8.6	
Combined Measurements ^a						24						21						34	
SD of Combined Measurements ^a						1.0						1.6						1.6	

^a The T_e was calculated by treating each data measurement independently and regressing the normalized data points (Figures I.6 - I.8).

^b A bi-exponential fit was justified for this patient. The T_e given is for the greater of the two components.

Table I.6 Whole-body effective half-lives (T_e s) of I-131 RAB 3F8, IgG, for neuroblastoma patients receiving fourth, fifth, and sixth treatments. The heading "at Strn" and "at 1m" refer to T_e s determined from measurements taken at the sternum and at 1 meter, respectively. "SD" refers to sample standard deviation.

Patient Number	Age	Fourth Administration						Fifth Administration						Sixth Administration					
		Activity (GBq) ^a	Number of Data Points	at Strn T_e (h)	SD at Strn T_e (h)	at 1m T_e (h)	SD 1m T_e (h)	Activity (GBQ)	Number of Data Points	at Strn T_e (h)	SD at Strn T_e (h)	at 1m T_e (h)	SD 1m T_e (h)	Activity (GBQ)	Number of Data Points	at Strn T_e (h)	SD at Strn T_e (h)	at 1m T_e (h)	SD 1m T_e (h)
3	5	1.2	6	19	1.4	20	1.0	1.1	6	23	2.3	21	1.1	1.1	6	27	3.9	30	3.8
5	4	1.1	5	26	3.2	28	2.6												
6	3	1.1	4	21	0.88	23	1.5												
8	7	1.1	9	47	3.4	36	2.0												
11	3	1.9	5	23	0.67	26	2.4	2.2	5	26	7.3	34	5.0	2.3	7	31	3.3	30	2.7
13	3	2.2	9	33	2.7	25	1.9												
14	8	2.6	8	31	1.7	32	1.5												
15	3	2.3	4	26	0.79	24	1.7												
16	4	2.7	6	24	2.0	32	4.3												
17	3	2.4	4	26	1.2	36	2.2	2.5	5	29	1.3	26	0.68						
18	3	2.4	6	34	1.7	32	2.5	2.6	4	34	5.6	23	4.2						
19	11	4.0	4	28	7.2	38	2.0	4.0	8	40	3.6	36	1.8						
20	6	2.9	3	22	3.7	24	4.7	2.8	4	27	0.66	28	1.9	2.9	6	29	2.0	29	1.7
21 ^c	17	4.1 & 4.3	4	31	2.0	34	7.4	4.2 & 4.1	3	30	2.9	30	4.5	8.0 & 7.3	13	40	1.8	34	0.44
Average				28		29				30		28				32		31	
SD Average				7.1		5.6				5.7		5.7				5.8		2.2	
Combined Measurements ^a						33						34						35	
SD of Combined Measurements ^a						1.1						1.8						1.1	

a The T_e was calculated by treating each data measurement independently and regressing the normalized data points (Figures I.9 - I.11).

b Multiply by 27 to obtain mCi.

c This patient received an administration in the morning and a second administration in the early afternoon for the administrations shown.

Figure I.1 Clearance rate for male and/or female patients receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer.

Figure I.2 Clearance rate for male and/or female patients receiving the second administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer.

Figure I.3 Clearance rate for male and/or female patients receiving the first administration of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia.

Figure I.4 Clearance rate for male and/or female patients receiving the second administration of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia.

Figure I.5

Clearance rate for male and/or female patients receiving the third administration of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia.

Figure I.6

Clearance rate for male and/or female patients receiving the first administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma.

Figure I.7

Clearance rate for male and/or female patients receiving the second administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma.

Figure I.8

Clearance rate for male and/or female patients receiving the third administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma.

Figure I.9 Clearance rate for male and/or female patients receiving the fourth administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma.

Figure I.10 Clearance rate for male and/or female patients receiving the fifth administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma.

Figure I.11 Clearance rate for male and/or female patients receiving the sixth administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma.

Figure I.12 Clearance rate for patient number 1 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 2.6 GBq (70 mCi).

Figure I.13 Clearance rate for patient number 2 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 2.4 GBq (64 mCi).

Figure I.14 Clearance rate for patient number 3 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 4.2 GBq (110 mCi).

Figure I.15 Clearance rate for patient number 4 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 4.6 GBq (130 mCi).

Figure I.16 Clearance rate for patient number 5 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 5.4 GBq (150 mCi).

Figure I.17

Clearance rate for patient number 6 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 5.7 GBq (150 mCi).

Figure I.18

Clearance rate for patient number 7 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 4.2 GBq (120 mCi).

Figure I.19

Clearance rate for patient number 8 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 5.2 GBq (140 mCi).

Figure I.20

Clearance rate for patient number 9 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 6.7 GBq (180 mCi).

Figure I.21

Clearance rate for patient number 10 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 4.8 GBq (130 mCi).

Figure I.23

Clearance rate for patient number 11 receiving the second administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 4.3 GBq (117 mCi).

Figure I.22

Clearance rate for patient number 11 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 4.6 GBq (124 mCi).

Figure I.24

Clearance rate for patient number 12 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 1.7 GBq (45 mCi).

Figure I.25

Clearance rate for patient number 12 receiving the second administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 1.7 GBq (46 mCi).

Figure I.26

Clearance rate for patient number 13 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 3.3 GBq (88 mCi).

Figure I.27

Clearance rate for patient number 14 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 2.2 GBq (58 mCi).

Figure I.28

Clearance rate for patient number 15 receiving the first administration of I-131 RAB CC-49 (IgG) for the treatment of colon cancer. The activity administered was 2.2 GBq (58 mCi).

Figure I.29

Clearance rate for patient number 1 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for consecutive treatments was 1.4 and 1.8 GBq (39 and 48 mCi).

Figure I.30

Clearance rate for patient number 2 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for consecutive treatments was 1.7 and 1.7 GBq (46 and 46 mCi).

Figure I.31

Clearance rate for patient number 3 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for consecutive treatments was 1.9 and 1.9 GBq (51 and 51 mCi).

Figure I.32

Clearance rate for patient number 4 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for subsequent treatments was 2.8 and 2.9 GBq (77 and 79 mCi).

Figure I.33 Clearance rate for patient number 5 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for subsequent treatments was 2.3 and 2.4 GBq (39 and 48 mCi).

Figure I.34 Clearance rate for patient number 6 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for subsequent treatments was 2.2 and 2.4 GBq (61 and 65 mCi).

Figure I.35 Clearance rate for patient number 7 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for subsequent treatments was 2.8 and 2.7 GBq (77 and 73 mCi).

Figure I.36 Clearance rate for patient number 8 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for subsequent treatments was 2.6 and 2.8 GBq (71 and 75 mCi).

Figure I.37

Clearance rate for patient number 9 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for consecutive treatments was 2.8 and 2.7 GBq (76 and 74 mCi).

Figure I.38

Clearance rate for patient number 10 receiving two administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for consecutive treatments was 2.7 and 2.6 GBq (74 and 70 mCi).

Figure I.39

Clearance rate for patient number 11 receiving one administration of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered was 2.2 GBq (58 mCi).

Figure I.40

Clearance rate for patient number 12 receiving four administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for subsequent treatments was 3.1, 2.6, 2.7, and 2.6 GBq (84, 70, 74, and 71 mCi).

Figure I.41 Clearance rate for patient number 13 receiving three administrations of I-131 RAB M-195 (IgG) for the treatment of myelogenous leukemia. The activity administered for consecutive treatments was 2.6, 2.6 and 2.7 GBq (71, 71 and 73 mCi).

Figure I.42 Clearance rate for patient number 1 receiving the first administration of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered was 1.1 GBq (30 mCi).

Figure I.43 Clearance rate for patient number 2 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.1, 1.1, and 1.1 GBq (29, 30, and 30 mCi).

Figure I.44 Clearance rate for patient number 3 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.1, 1.1, 1.1, 1.2, 1.1, 1.1 GBq (30, 30, 30, 31, 31, 30 mCi).

Figure I.45 Clearance rate for patient number 4 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.1, 1.1, and 1.1 GBq (30, 30, and 30 mCi).

Figure I.46 Clearance rate for patient number 5 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.0, 1.0, 1.1 and 1.1 GBq (28, 28, 30, 29 mCi).

Figure I.47 Clearance rate for patient number 6 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.1, 1.1, 1.2, and 1.1 GBq (29, 31, 31, and 31 mCi).

Figure I.48 Clearance rate for patient number 7 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.1, 1.1, and 1.1 GBq (29, 30, and 29 mCi).

Figure I.49

Clearance rate for patient number 8 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.1, 1.1, 1.1, and 1.1 GBq (29, 30, 30, and 31 mCi).

Figure I.50

Clearance rate for patient number 9 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 3.7, 3.8, and 3.7 GBq (100, 100, and 100 mCi).

Figure I.51

Clearance rate for patient number 10 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 3.0, 3.0, and 3.0 GBq (80, 81, 82 mCi).

Figure I.52

Clearance rate for patient number 11 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 1.9, 1.9, and 1.9 GBq (50, 50, and 50 mCi).

Figure I.53

Clearance rate for patient number 11 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma 1 year after first treatment regiment (Figure I.52). The activity administered for consecutive treatments was 1.9, 2.2, and 2.3 GBq (50, 60, and 62 mCi).

Figure I.54

Clearance rate for patient number 12 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.7, 2.7, and 2.8 GBq (72, 73, and 76 mCi).

Figure I.55

Clearance rate for patient number 13 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.2, 2.2, 2.1, and 2.2 GBq (58, 60, 58, and 60 mCi).

Figure I.56

Clearance rate for patient number 14 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.6, 2.7, 2.6, and 2.6 GBq (70, 72, 69, and 71 mCi).

Figure I.57

Clearance rate for patient number 15 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.5, 2.4, 2.4, and 2.3 GBq (68, 64, 64, and 62 mCi).

Figure I.58

Clearance rate for patient number 16 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.7, 2.7, 2.7, and 2.7 GBq (73, 72, 73, and 73 mCi).

Figure I.59

Clearance rate for patient number 17 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.4, 2.2, 2.4, 2.4, and 2.5 GBq (64, 60, 65, 64, and 69 mCi).

Figure I.60

Clearance rate for patient number 18 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.6, 2.5, 2.6, 2.4, and 2.6 GBq (70, 66, 70, 66, and 71 mCi).

Figure I.61

Clearance rate for patient number 19 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 4.1, 4.0, 3.9, 4.0, and 4.0 GBq (110, 110, 110, 110, and 110 mCi).

Figure I.62

Clearance rate for patient number 20 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 2.8, 3.0, 2.9, 2.9, 2.8, and 2.9 GBq (76, 81, 78, 78, 75, and 79 mCi).

Figure I.63

Clearance rate for patient number 21 receiving multiple administrations of I-131 RAB 3F8 (IgG) for the treatment of neuroblastoma. The activity administered for consecutive treatments was 4.4, 4.4, 4.0 in the morning and 3.9 the same afternoon, 4.1 in the morning and 4.3 the same afternoon, 4.2 in the morning and 4.1 the same afternoon, and 8.0 in the morning and 7.3 the same afternoon GBq (120, 120, 110 plus 110, 110 plus 120, 110 plus 110, and 220 plus 200 mCi).

APPENDIX J

Data Provided by the Neo Rx - Virginia Mason Clinical Research Unit, Seattle, WA

These data were provided by the Neo Rx Virginia Mason Clinical Research Unit. All measurements of clearance rate were determined using a gamma camera. A summary of the effective half-lives for each study is given in Tables J.1-J.5. All patients were treated with Re-186 RABs.

Figures J. 1-J.6 are graphs of all patients in each treatment group. Randomly selected graphs for individual patients are shown in Figures J.7-J.24.

Table J.1 Whole-body effective half-lives (T_e s) for female patients treated with Re-186 radiolabeled NR-LU-10, whole antibody administered via an intraperitoneal injection. The patients had ovarian cancer. Data were provided by Neo Rx - Virginia Mason Clinical Research Unit.

Patient Number	Activity (GBq) ^a	Wt (kg)	Number of Data Points	T_e (h)	SD T_e (h)
1	1.5	66	5	48	4.0
3	3.3	50	5	40	2.1
12	8.0	73	5	31	1.6
13	8.5	92	5	39	3.2
17	9.4	65	5	35	1.9
Average				39	
SD of Average				6.4	
Combined Measurements ^b				37	
SD of Combined Measurements ^b				1.8	

a Multiply by 27 to obtain mCi.

b The T_e was calculated by treating each measurement independently and regressing the normalized data points (Figure J.1).

Appendix J

Table J.2 Whole-body effective half-lives (T_e s) for female patients administered Re-186 radiolabeled NR-LU-13, mouse/human chimeric, administered via an intravenous injection. Data were provided by Neo Rx - Virginia Mason Clinical Research Unit.

Patient Number	Activity (GBq) ^a	Wt (kg)	Tumor Location	Primary Cancer	Number of Data Points	T_e (h)	SD T_e (h)
2	1.5	53	Abdomen	Esophagus	5	48	0.95
3	4.1	79	Lungs	Breast	5	41	0.78
4	4.0	68	Liver	Colon	5	57	1.8
5	4.4	80	Axilla	Lung	5	55	2.2
6	4.3	72	Liver	GE Junction	5	55	1.8
7	4.8	89	Liver	Rectal	6	41	1.4
8	3.7	61	Liver	Rectal	6	48	0.68
9	3.5	54	Neck	Unknown	6	52	2.1
Average						50	
SD of Average						6.0	
Combined Measurements ^b						48	
SD of Combined Measurements ^b						1.5	

a Multiply by 27 to obtain mCi.

b The T_e was calculated by treating each data measurement independently and regressing the normalized data points (Figure J.2).

Table J.3

Whole-body effective half-lives (T_e s) for patients administered Re-186 radiolabeled NR-LU-10 whole antibody administered via an intravenous injection. All patients had previously received Tc-99m radiolabeled NR-LU-10 Fab', thus, this data is considered to be the second administration. The patients had solid tumors metastasis of the colon, lung, and/or ovary. Data were provided by Neo Rx - Virginia Mason Clinical Research Unit.

Patient Number	Sex	Activity (GBq) ^a	Wt (kg)	Tumor Location	Primary Cancer	Number of Data Points	T_e (h)	SD T_e (h)
18	M	2.2		Liver	Colon	6	30	0.93
28	F	2.9	40	Right Axilla	Ovary	6	37	1.3
43	M	4.6	86		Colon	6	38	3.2
46	M	6.6	92	Axilla	Renal	6	40	1.3
48	M	5.4	81	Liver	Colon	6	38	1.0
49	M	5.4	69	Liver	Lung	6	48	3.5
50	F	7.9	77	Left Lung	Colon	6	39	1.0
51	M	8.8	89	Liver	Ovary	5	48	2.1
54	F	6.7	52	Liver & Lung	Colon	6	47	3.8
55	M	9.6	104	Liver	Colon	6	32	0.44
73	M	3.9	103	Liver & Lung	Colon	5	35	0.94
77	M	3.5	93	Liver	Colon	5	37	0.81
82	F	2.6	54	Lungs	Colon	5	42	1.1
83	M	3.2	68	Lungs	Lung	5	46	2.9
84	M	3.3	80	Left Lung	Lung	4	37	0.43
85	M	3.3	71	Right Axilla	Esophagus	4	44	0.04
86	F	2.9	61	Abdomen	Ovary	4	42	0.32
87	M	3.4	92	Lungs	Lung	4	46	1.9
88	M	2.9	61	Liver	Ampulla Vater	5	34	0.37
89	M	3.8	104	Liver Lt Lobe	Colon	4	31	1.4
90	M	3.2	73	Lt Lung	Lung	4	42	0.97
95	F	1.5	60	Liver	Colon	4	48	4.0
96	F	1.6	62	Liver	Colon	4	46	0.66
97	F	1.6	65	Liver	Colon	5	55	3.1
99	M	1.6	66		Colon	3	37	0.18
100	M	1.8	76	Liver	Colon	4	41	0.41
Female Average							44	
SD of Female Average							5.7	
Male Average							39	
SD of Male Average							5.7	
Combined Female Measurements ^b							41	
SD of Combined Measurements ^b							1.1	
Combined Male Measurements ^b							38	
SD of Combined Measurements ^b							0.88	

^a Multiply by 27 to obtain mCi.

^b The T_e was calculated by treating each data measurement independently and carrying out a regression on the normalized data points (Figure J.3).

Appendix J

Table J.4 Whole-body effective half-lives (T_e s) for patients administered Re-186 radiolabeled NR-LU-10 whole antibody via an intravenous injection for 3-4 administrations. The administration number includes Tc-99m radiolabeled NR-LU-10 Fab' as the first treatment. The patients had solid tumors metastasis of the colon, lung, and/or ovary. Data were provided by Neo Rx - Virginia Mason Clinical Research Unit.

Patient Number	Sex	Administration #	Activity (GBq) ^a	Wt (kg)	Tumor Location	Primary Cancer	Number of Data Points	T_e (h)	SD T_e (h)
77	M	3	3.6	93	Liver	Colon	5	37	0.46
77	M	4	3.7	93	Liver	Colon	5	40	0.60
81	F	3	3.1	68	Liver	Breast	5	24	2.7
87	M	3	3.5	92	Lungs	Lung	5	43	0.66
87	M	4	3.6	92	Lungs	Lung	4	39	2.2
89	M	4	3.7	104	Liver Lt	Colon	4	27	3.3
Female Third Administration Average								24	
Male Third Administration Average								40	
SD of Third Administration Average								3.9	
Combined Male Third Measurements ^b (Figure J.4)								40	
SD of Combined Third Measurements ^b								1.5	
Male Fourth Administration Average								36	
SD of Fourth Administration Average								7.2	
Combined Male Fourth Measurements ^b (Figure J.5)								37	
SD of Combined Fourth Measurements ^b								3.9	

a Multiply by 27 to obtain mCi.

b The T_e was calculated by treating each data measurement independently and regressing the normalized data points.

Table J.5 Whole-body effective half-lives (T_e s) for patients administered Re-186 radiolabeled NR-CO-02, Fab'2 via an intraarterial injection. All patients received Tc-99m radiolabeled NR-CO-02 Fab'2 within 15 days preceding the Re-186 RAB, which is considered the first administration. No patients developed human antimouse antibody. The patients had colon cancer.

Patient Number	Sex	Administration #	Activity (GBq) ^a	Wt (kg)	Tumor Location	Primary Cancer	Number of Data Points	T_e (h)	SD T_e (h)
4	M	2	5.2	64	Liver	Colon	6	24	1.7
4 ^c	M	4	5.4	64	Liver	Colon	6	28	0.41
7	F	2	7.5	64	Liver Lt Lobe	Colon	5	31	5.9
14	M	2	9.4	91	Liver	Colon	5	24	0.83
Male Average (second treatment only)								24	
SD of Male Average								0.36	
Male Average (fourth treatment only)								28	
Female Average								31	
Combined M&F Second Administration Measurements ^b								26	
SD of Combined Measurements ^b								1.7	

a Multiply by 27 to obtain mCi.

b The T_e was calculated by treating each data measurement independently and regressing the normalized data points (Figure J.6).

c This patient had a Tc-99m radiolabeled NR-CO-02 Fab'2 prior to the second Re-186 treatment.

Figure J.1

Clearance rate for female patients receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intraperitoneal injection for the treatment of ovarian cancer.

Figure J.2

Clearance rate for female patients receiving the second administration of RAB NR-LU-13 (first use of Re-186 radiolabel) mouse/human chimeric via intravenous injection for the treatment of colon, lung, or breast cancer.

Figure J.3

Clearance rate for male and female patients receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel)) via intravenous injection for the treatment of solid tumor metastases of the colon, lung, or ovary.

Figure J.4

Clearance rate for male patients receiving the third administration of RAB NR-LU-10 whole antibody (second use of Re-186 radiolabel) via intravenous injection for the treatment of solid tumor metastases of the colon or lung.

Figure J.5 Clearance rate for male patients receiving the fourth administration of RAB NR-LU-10 IgG (third use of Re-186 radiolabel) via intravenous injection for the treatment of solid tumor metastases of the colon or lung.

Figure J.6 Clearance rate for male and female patients receiving the second administration of NR-CO-02, Fab'2, (first use of Re-186 radiolabel) via intraarterial injection for treatment of colon cancer

Figure J.7 Clearance rate for female patient number 1 receiving the first administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intraperitoneal injection for the treatment of ovarian cancer.

Figure J.8 Clearance rate for female patient number 3 receiving the first administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intraperitoneal injection for the treatment of ovarian cancer.

Figure J.9 Clearance rate for female patient number 12 receiving the first administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intraperitoneal injection for the treatment of ovarian cancer.

Figure J.10 Clearance rate for female patient number 13 receiving the first administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intraperitoneal injection for the treatment of ovarian cancer.

Figure J.11 Clearance rate for female patient number 2 receiving the first administration of Re-186 RAB NR-LU-13 mouse/human chimeric via intravenous injection for the treatment of cancer of the esophagus.

Figure J.12 Clearance rate for female patient number 3 receiving the first administration of Re-186 RAB NR-LU-13 mouse/human chimeric via intravenous injection for the treatment of breast cancer.

Figure J.13 Clearance rate for female patient number 7 receiving the first administration of Re-186 RAB NR-LU-13 mouse/human chimeric via intravenous injection for the treatment of rectal cancer.

Figure J.14 Clearance rate for female patient number 8 receiving the first administration of Re-186 RAB NR-LU-13 mouse/human chimeric via intravenous injection for the treatment of rectal cancer.

Figure J.15 Clearance rate for male patient number 18 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of colon cancer.

Figure J.16 Clearance rate for female patient number 28 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of ovarian cancer.

Figure J.17 Clearance rate for male patient number 37 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of colon cancer.

Figure J.18 Clearance rate for female patient number 39 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of colon cancer.

Figure J.19 Clearance rate for female patient number 40 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of colon cancer.

Figure J.20 Clearance rate for male patient number 43 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of colon cancer.

Figure J.21

Clearance rate for male patient number 46 receiving the second administration of RAB NR-LU-10 whole antibody (first use of Re-186 radiolabel) via intravenous injection for the treatment of renal cell carcinoma.

Figure J.22

Clearance rate for male patient number 4 receiving the second administration of RAB NR-CO-02, Fab'2, (first use of Re-186 radiolabel) via intraarterial injection for treatment of colon cancer.

Figure J.23

Clearance rate for male patient number 4 receiving the fourth administration of RAB NR-CO-02, Fab'2, (second use of Re-186 radiolabel) via intraarterial injection for treatment of colon cancer.

Figure J.24

Clearance rate for female patient number 7 receiving the second administration of RAB NR-CO-02, Fab'2, (first use of Re-186 radiolabel) via intraarterial injection for treatment of colon cancer.

APPENDIX K

Family Doses Resulting from an Incontinent Patient

A possible event that would release the largest activity to family members would occur if a patient urinated on the bed sheets. The potential skin dose was calculated from a patient receiving RAB therapy being released from the hospital at 5 p.m., clearing bladder at 9 p.m., and then urinating on the bed sheets after a 6-hour accumulation at 3 a.m. on the following day (Table K.1). A 6-hour accumulation gives approximately 350 ml of urine for standard man (ICRP, 1974). It is assumed that a plastic cover is placed over the mattress, a 0.3-cm-thick cloth pad is placed over the plastic, and 200- μ m-thick sheets are placed over the cloth pad. The density of the pad and sheets is assumed to be 0.3 g/cc and 0.5 g/cc, respectively. Based on this, the urine will be deposited in a 1,600 cm² area, or a circular diameter of 45 cm, assuming that the bed is flat.

It is assumed that all biological elimination of the radiolabel occurs via the urine (97% according to Bushberg et al. (1991) for a I-131 RAB). The skin dose rates calculated for the urine contamination are for either the patient, or bedside companion who may be sleeping with the patient. The possibility of someone, such as a spouse, sleeping with the patient should be considered, as many people may be unwilling to adjust living habits, including sexual contact, because of radiation therapy (Buchan and Brundle, 1970; Jacobson et al., 1978).

While the radiolabels listed in Table K.1 are used currently in RAB therapy, the authors were not able to obtain data for Y-90 and I-111 radiolabels. The activity chosen for I-131, Re-186, and Re-188 at the time of patient release was suggested as the maximum activity below which a patient may be released in the Nuclear Regulatory Commission Draft Regulatory Guide 8015 (Schneider, 1994). It is proposed to release patients with activities that will result in a whole-body dose of less than 5 mSv y⁻¹ (500 mrem y⁻¹), where dose is calculated for an individual spending six hours per day (25%) at 1 meter from the patient for the entire physical decay of the isotope. The activity chosen for Lu-177 was the maximum activity listed in the Draft Regulatory Guide for Re-188, which results in a whole-body dose of less than 5 mSv y⁻¹ (500 mrem y⁻¹) as previously specified. The activity used for In-111 would deliver a dose of 5 mSv y⁻¹ (500 mrem y⁻¹) calculating dose at 1 meter with 25% exposure factor during the entire physical decay of the radionuclide. The activity used for Y-90 was the maximum activity used for therapy listed in the literature with no toxic effects (Paganelli et al., 1995). The biological half lives were calculated from T_e measurements given in tables cited under "Justification for Clearance Rate Used" (Table K.1).

The largest contamination in this specified scenario occurs for Re-186, in which 2.9 GBq (78 mCi) is deposited on the bed sheets and would give a dose of 0.46 Gy h⁻¹ (46 rad h⁻¹), where dose is averaged over 1 cm² at 70 μ m depth to a person laying in the urine. Doses were calculated using VARSKIN MOD2 (Durham, 1992). The current skin dose limit for radiation workers is 0.5 Gy y⁻¹ (50 rad y⁻¹). This limit would be exceeded for this Re-186 contamination scenario in about an hour. Assuming skin dose to the public should be a factor of 10 less than radiation workers, a dose of 0.05 Gy h⁻¹ would be exceeded in 6 minutes. The dose rate is constant over the area of the sheets, so exposure to a one cm² area of Re-186 contaminated urine will give about the same dose rate per cm² as the entire 1600 cm² contaminated area. Skin dose rates were similar to those for Re-186.

To equate skin dose with that from other sources, the effective dose from these contamination events was calculated using ICRP 60 (1991) methodology as follows: the skin dose rate is multiplied by the ratio of the area of the contamination divided by the area of the whole body (18,000 cm²) and multiplied by the tissue weighing factor (0.01). Since the concern is with dose to individuals other than the patients, it is assumed that a sleeping companion is in contact with 100 cm² of the urine-contaminated bed sheets. The results show the highest doses are for Re-186 and Re-188, which are about 0.025 mSv h⁻¹. A 5 mSv y⁻¹ (500 mrem y⁻¹) dose limit could be exceeded in 8 days.

Table K.1 Skin dose and effective dose from urine-contaminated bed sheets.^j

Radio-label	Activity At Time of Release (GBq) ⁱ	Whole-body Dose ^a (mSv)	Specific Gamma Ray Constant ($\mu\text{C kg}^{-1} \text{cm}^2 \mu\text{Bq h}^{-1}$)	Physical Half-life (h)	Biological Whole-body Half-life (h)	T_e (h)	Justification for Clearance Rate Used	Activity of Contaminated Urine 10 h after Patient Release (GBq)	VARSKIN ^b MOD2 Skin Dose From Urine at 70 μm , 1 cm^2 (cGy h^{-1})	ICRP 60 Effective Dose 100 cm^2 ICRP (1991) ($\mu\text{Sv h}^{-1}$)
Y-90	3.7 ^h	0.097	0.293	64	73	34	Selected ^f	0.18	7.6	4.2
I-131	1.2 ^d	5.0	15.3	192	62	47	Table I.1	0.073	0.43	0.24
In-111	2.4 ^e	5.0	22.4	67	73	35	Selected ^g	0.12	0.0033	0.0018
Lu-177	29 ^c	4.1	0.63	161	129	72	Table G.1	0.90	3.4	1.9
Re-186 ^k	29 ^d	5.0	1.53	89	33	24	Table J.5	2.9	46	25
Re-188	29 ^d	1.9	2.72	17	68	14	Table H.1	1.1	42	24

- a Estimates of whole-body dose calculated using methodology of Draft Regulatory Guide, DG-8015, (Schneider 1994) assuming 25% of the external dose at 1 meter is received and no biological elimination occurs.
- b Skin doses were calculated using VARSKIN MOD2 (Durham 1992).
- c Not listed in the Draft Regulatory Guide, Task DG-8015; however, the listed activity is the maximum activity of any isotope listed.
- d Maximum activity for this isotope suggested for release of patients receiving radiation therapy in the Draft Regulatory Guide, Task DG-8015 (Schneider, 1994).
- e Maximum activity at the time of patient release such that a person who is at one meter from the patient 25% of the time will receive 5 mSv (500 mrem).
- f Whole-body clearance rate is not available. A biological half-life of 73 h was chosen, which is the average for the known biological half-lives listed in this table, as an example.
- g Taken from the long-term component of the biological clearance rate for the whole-body (ICRP, 1987).
- h Maximum activity listed in literature with no toxic effects (Paganelli et al., 1995).
- i Multiply by 27 to obtain mCi.
- j The activities excreted via urine are based on a 6-hour accumulation period. Other parameters are listed in the text.
- k Recent data suggests that 85%, rather than 100%, is cleared via the urine and the contamination level should be reduced by 15%.

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11. ABSTRACT (200 words or less)

Radiolabeled antibodies (RABs) are being developed and used in medical imaging and therapy in rapidly increasing numbers. There are concerns about the radiation exposure of caregivers and the general public from treated patients. The magnitude of this hazard is closely related to the RABs' whole-body effective half-life (T_e). Data on whole-body effective half-lives were calculated from external dose rates obtained from attending physicians and radiation safety officers at participating institutions. Calculations of T_e s were made using exponential regression analyses of data from patients receiving single and multiple administrations. These data were analyzed on the basis of age, sex, isotope label, radiation energy, antibody type, disease treated, method of administration, and number of administrations. The effective half-life in the blood did not correlate with the T_e . The values of T_e varied by a factor of two for patients taking the same RAB. A single exponential clearance rate, compared with a bi-exponential clearance rate, provides an adequate fit for 95% of the data sets tested.

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