[CANCER RESEARCH (SUPPL.) 50, 1039s–1042s, February 1, 1990]

Tumor, Red Marrow, and Organ Dosimetry for ^{131}I-labeled Anti-Carcinoembryonic Antigen Monoclonal Antibody[1]

Jeffry A. Siegel,[2] David A. Pawlyk, Robert E. Lee, Norma L. Sasso, Jo Ann Horowitz, Robert M. Sharkey, and David M. Goldenberg

Department of Diagnostic Imaging, Temple University Hospital, Philadelphia, Pennsylvania 19140 [J. A. S.], and Center for Molecular Medicine and Immunology, at the University of Medicine and Dentistry of New Jersey, Newark, New Jersey 07103 [D. A. P., R. E. L., N. L. S., J. A. H., R. M. S., D. M. G.]

Abstract

Tumor-, red marrow-, and organ-absorbed doses were calculated for patients receiving ^{131}I-labeled monoclonal antibodies against carcinoembryonic antigen for either diagnosis or therapy. Ten patients with confirmed liver tumors who received doses ranging from 10.79 to 200 mCi were evaluated. Urine and blood samples were taken in order to determine total body and red marrow activity, respectively. Anterior and posterior gamma camera images were obtained at multiple times postinjection in order to quantitate activity uptake using the conjugate view counting method for the following organs and regions: lungs, liver, spleen, kidneys, and the liver tumors. In addition, sacral regions of interest were drawn to generate red marrow-absorbed dose estimates for comparison to those obtained by blood sampling. Tumor volumes were obtained from volumetric analysis of the patient's computed tomographic study and tumor S values were obtained by assuming uniform distribution of the ^{131}I-labeled monoclonal antibody in spherical tumor regions considering all emitted electrons, β-particles, and photons. The following mean absorbed doses in rads/mCi injected were obtained: lungs, 2.3 ± 1.6 (SD); liver, 1.4 ± 0.7; spleen, 2.6 ± 1.4; kidneys, 3.1 ± 1.5; total body, 0.7 ± 0.5; red marrow from blood sampling, 2.9 ± 1.9; red marrow from sacral scintigraphy, 1.7 ± 1.2; and liver tumors, 69.3 ± 92.5. Tumor volumes ranged from 1 to 216 g and the percentage of uptake/g of monoclonal antibody into these tumors ranged from 0.0006 to 1.040. There was a statistically significant difference between the two techniques for estimation of red marrow dose ($P < 0.01$). This methodology permits calculation of tumor, red marrow, and organ dosimetry using planar gamma camera imaging.

Introduction

Radiolabeled antibody dose calculations have been reported for various organs and tumors (1–9) based on the medical internal radiation dose schema (10, 11). For the most part, these dose estimates were obtained by the method of conjugate view counting (12–14). Bone marrow was the critical normal tissue in these studies. Estimates of red marrow absorbed dose have been reported by a number of investigators based on: photon emissions only (2, 15), mean whole body dose (16), circulating blood mass of the red marrow (8, 17), equivalent red marrow and blood activity concentration (18), and sacral scintigraphy (19).

The current study uses the method of conjugate view counting to obtain the absolute activity measurements necessary for the dose calculation. The following organs and regions were included: lungs; liver; spleen; kidneys; red marrow; and liver tumors. This study also compares the red marrow dose estimates based on scintigraphy with those obtained by the blood-based methodology of Bigler *et al.* (18). In addition, a new method of tumor dosimetry is proposed utilizing S values obtained with the assumption of uniform antibody distribution within spherical tumor regions.

Materials and Methods

Ten patients with confirmed liver tumors receiving ^{131}I-labeled CEA[3] monoclonal antibody (NP-4) (20) for diagnosis and treatment were studied. Anterior and posterior gamma camera images of the chest, abdomen, and pelvis were acquired at multiple times, usually 24, 48, and 72 h after the injection of 25 mCi and at longer times after a therapy injection (>70 mCi). Images were acquired using a Gemini 700 scintillation camera equipped with a high energy collimator and interfaced to a Siemens Microdelta computer system. ROIs were drawn around the lungs, liver, spleen, kidneys, and liver tumors for both anterior and posterior views at all imaging times in order to obtain the counts within the ROI. In addition, ROIs were drawn around the sacrum to obtain RM counts as described previously (19, 21). Appropriate background regions were drawn for each of the ROIs. The patient anterior-posterior dimensions (T) through the chest, abdomen, and pelvis were determined in cm using calipers. A known activity of ^{131}I was then used to obtain the system calibration factor (C). The ^{131}I sample was first placed in a standard size Petri dish along with several ml of water to cover the bottom of the dish and then counted in air for 1 min at a distance of 10 cm from the collimator face of the same gamma camera that was used for the patient imaging studies. C was then determined by dividing the cpm by the known activity in mCi.

The absolute activity in each ROI at all imaging times was calculated (12) as:

$$A_{ROI} = (C_A \times C_P / e^{-\mu T})^{1/2} \times f/C \quad \text{(A)}$$

where A_{ROI} is absolute activity in μCi for the lungs, liver, spleen, kidneys, red marrow, and liver tumor ROIs; C_A is background-corrected anterior ROI cpm; C_P is background-corrected posterior ROI cpm; μ is the effective linear attenuation coefficient for ^{131}I (21); T is patient thickness measurement in cm across either chest, abdomen, or pelvis; f is self-attenuation correction = 1; and C is the system calibration factor in cpm/μCi.

Urine was collected from each patient in 8-h intervals up to 72 h and the total volume of each collection was recorded. Aliquots were counted in a calibrated automatic gamma well counter to obtain activity concentration in μCi/ml. The activity concentration in the urine was then converted to total activity in μCi eliminated per 8-h interval using the values of the sequential pooled total 8-h void volumes in ml. The total body retention (A_{TB}) in μCi at 8-h intervals was calculated as the difference between the administered activity and the cumulative decay-corrected activity in the sequential 8-h void volumes. Peripheral whole blood samples were also obtained from each patient at multiple times starting immediately after the 1 h infusion up to 72 h postinjection. Whole blood samples were counted in a calibrated concentration in μCi/ml as a function of time.

The time-activity curves obtained for the various ROIs, total body, and blood were fit to either a mono- or biexponential function which was then integrated to obtain the various cumulated activities; or, in the case of blood, the cumulated activity concentration. The cumulated activity in the RM was calculated according to the method of Bigler *et al.* (18) for the blood data and according to the method of Siegel *et al.* (21) for the scintigraphic data.

The mean dose in rads to the various target organs with the exception of the tumors was then obtained according to the equation (10, 11, 22,

[1] Presented at the "Second Conference on Radioimmunodetection and Radioimmunotherapy of Cancer," September 8–10, 1988, Princeton, NJ. Supported in part by USPHS Grant CA39841 from the NIH (D. M. G.).

[2] To whom requests for reprints should be addressed, at Center for Molecular Medicine and Immunology, 1 Bruce Street, Newark, NJ 07103.

[3] The abbreviations used are: CEA, carcinoembryonic antigen; ROI, region of interest; RM, red marrow.

23):

$$D_k = A_0[\Sigma_h(\tau_h - (m_h/m_{RB}\cdot\tau_{RB})\cdot S(r_k \leftarrow r_h) + (\tau_{RB}\cdot m_{TB}/m_{RB})\cdot S(r_k \leftarrow TB)] \quad (B)$$

where D_k is the mean absorbed dose in rads to the various target regions (r_k), A_0 is the injected activity in μCi; $\tau_.$ is the residence time in h in the various source regions (r_h) or remainder of body (RB); $m_.$ is the mass in g of the various source regions; and $S(r_k \leftarrow r_h)$ is the S value in rads/μCi/h from source region to target region.

The mean dose in rads to the tumors (D_T) was obtained according to

$$D_T = A_0[\tau_T(\Sigma_{np}\Delta_{np}/m_T + \Sigma_p\Delta_p\phi_p/m_T)] + [\tau_h - (m_h/m_{RB}\cdot\tau_{RB})\cdot S_p(r_h \leftrightarrow r_h)] + \Sigma_h(\tau_h - (m_h/m_{RB}\cdot\tau_{RB})\cdot S(r_k \leftarrow r_h) + (\tau_{RB}\cdot m_{TB}/m_{RB})\cdot S(r_K \leftarrow TB) \quad (C)$$

where Δ_{np}, Δ_p are the mean energy emitted per unit cumulated activity for penetrating and nonpenetrating emissions, respectively (24), ϕ_p is the absorbed fraction for penetrating emissions (25, 26), m_T is mass of tumor in g obtained from volumetric analysis of patient's computerized tomographic scan, is represented by the tumor S value in rads/μCi/h $\Sigma_{np}\Delta_{np}/m_.$ $+\Sigma_p\Delta_p\phi_p/m_.$, and $S_p(r_h \leftrightarrow r_h) = S$ value for penetrating emissions from tumor host organ, *i.e.*, the liver.

Tumor dose estimates obtained with Equation C were compared to those obtained by the method of Wessels and Rogus (4) through the use of a Gedanken experiment in which liver tumors of 50, 100, 500, and 1000 g with uptake ratios of 1:1, 2:1, 5:1, and 10:1 were simulated for the comparison.

Results

The administered doses of ^{131}I-anti-CEA monoclonal antibody (NP-4) ranged from 10.79 to 200 mCi. The absorbed dose estimates (mean ± SD) in rads/mCi injected for the lungs, liver, spleen, kidneys, and total body are shown in Table 1. The red marrow doses based on blood sampling and sacral scintigraphy are compared in Table 2. The RM dose per injected activity was 2.9 ± 1.9 rads/mCi for the blood data and 1.7 ± 1.2 rads/mCi for the sacral data. The mean RM dose estimated by sacral scintigraphy was 38.2% less than that obtained by blood counting. The difference is statistically significant ($P < 0.01$). The mean initial (time zero) sacrum/blood red marrow cumulated activity concentration ratio was 0.57 ± 0.27.

The tumor S values required for equation C are shown in Table 3 for tumor masses ranging from 1 to 6000 g. Tumor absorbed dose estimates obtained with Equation C are compared to those calculated by the method of Wessels and Rogus (4) in Table 4. The total body and tumor plus liver cumulated activities were kept constant for these dose comparisons as shown in Table 4. The two methods were in good agreement.

Tumor weights, percentage of uptake/g of monoclonal antibody into the tumor, and tumor absorbed doses per injected activity are shown in Table 5. The tumors ranged in weight from 1 to 216 g and their percentage of uptake/g varied from 0.006 to 1.040. Fig. 1 shows a plot of tumor percentage of uptake/g *versus* tumor weight. Pseudolinear regression analysis (27) of these data with the function $y = A\exp(-kx)$ resulted in values of 0.3 and 0.0279 for A and k, respectively, with a correlation coefficient of −0.96. The patient with the high human anti-mouse antibody titer had a tumor percentage of uptake/g which, as expected, fell far below the regression line. As shown in Table 5, the mean tumor absorbed dose per injected activity was 69.3 ± 92.5 rads/mCi.

Table 1 *Organ dosimetry*

Patient	Dose (rads/mCi)				
	Lungs	Liver	Spleen	Kidneys	Total body
1	4.2	2.1	1.5	2.8	0.7
2	3.0	1.6	1.0		0.4
3	2.2	1.4	4.7	5.3	0.3
4	0.2	0.2	0.7	0.5	0.2
5	1.3	2.1	4.4		0.8
6	0.5	0.9	3.0	2.8	0.8
7	3.1	1.7	2.1	3.6	1.7
8	3.4	1.3	2.9	2.6	0.6
9	0.5	0.5			0.4
10	4.4	2.4	2.8	4.3	1.4
Mean ± SD	2.3 ± 1.6	1.4 ± 0.7	2.6 ± 1.4	3.1 ± 1.5	0.7 ± 0.5

Table 2 *Red marrow dosimetry*

Patient	Dose (rads/mCi)	
	Blood	Sacrum
1	5.1	3.0
2	2.7	1.5
3	2.8	1.4
4	0.3	0.3
5	4.4	3.6
6	1.4	1.3
7	4.2	2.9
8	5.8	2.4
9	0.5	0.1
10	1.6	0.7
Mean ± SD	2.9 ± 1.9	1.7 ± 1.2

Table 3 *S values for spherical tumors*

Mass (g)	S (rads/μCi/h)
1	4.17×10^{-1}
2	2.10×10^{-1}
4	1.06×10^{-1}
6	7.07×10^{-2}
8	5.34×10^{-2}
10	4.28×10^{-2}
20	2.17×10^{-2}
40	1.10×10^{-2}
60	7.51×10^{-3}
80	5.76×10^{-3}
100	4.66×10^{-3}
300	1.62×10^{-3}
400	1.24×10^{-3}
500	1.00×10^{-3}
600	8.43×10^{-4}
1000	5.22×10^{-4}
2000	2.74×10^{-4}
3000	1.88×10^{-4}
4000	1.45×10^{-4}
5000	1.18×10^{-4}
6000	1.01×10^{-4}

Table 4 *Tumor dose comparison*[a]

Tumor wt (g)	Uptake ratio (tumor/liver)	Tumor dose (rads)	
		Wessels and Rogus (4)	Current study
50	1	16.5	17.2
	2	27.3	28.8
	5	56.2	60.2
	10	96.1	103.3
100	1	16.5	17.6
	2	26.7	29.0
	5	51.6	57.0
	10	80.8	89.8
500	1	16.5	17.7
	2	22.9	25.0
	5	32.1	35.4
	10	37.6	41.7
1000	1	16.5	17.4
	2	19.8	21.0
	5	22.8	24.3
	10	24.1	25.7

[a] Total body cumulated activity kept constant at 5×10^5 μCi/h. Tumor and liver cumulated activity kept constant at 5×10^4 μCi/h.

Table 5 *Tumor data*

Patient	Tumor wt (g)	% of uptake/g	Dose (rads/mCi)
1	77	0.023	7.7
2	1	0.941	217.8
3	39	0.058	19.7
4[a]	12.8	0.006	0.7
5	1	1.040	188.6
6	163	0.006	1.6
7	77	0.032	9.4
8	2	0.160	36.4
9	82	0.021	5.3
10	216	0.0006	3.0
Mean ± SD[b]			69.3 ± 92.5

[a] Patient 4 had a human anti-mouse antibody titer of 18,981.
[b] Excludes patients 4, 6, and 10.

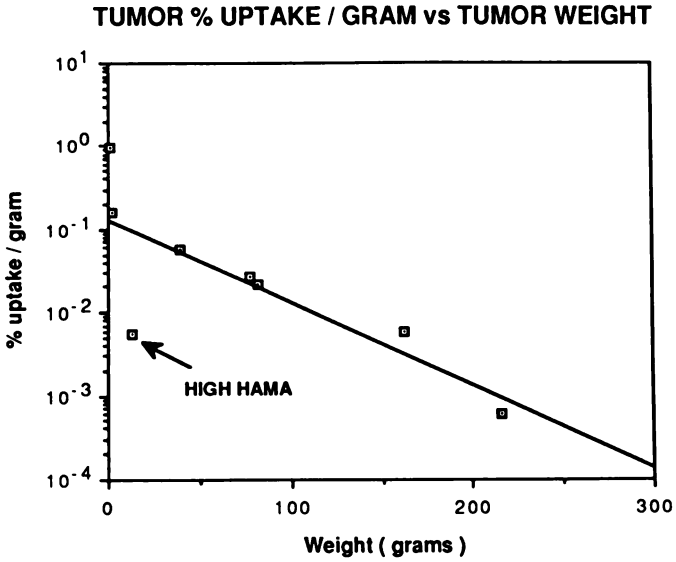

Fig. 1. Plot of tumor percentage of uptake/g *versus* tumor weight. *HAMA*, human anti-mouse antibody.

Discussion

Absorbed dose estimates have been presented for the lungs, liver, spleen, kidneys, red marrow, liver tumors, and total body in patients who have undergone radioimmunodetection and radioimmunotherapy with ^{131}I-anti-CEA monoclonal antibody.

At present, there is a controversy concerning red marrow dosimetry. The blood-based methodology of Bigler *et al.* (18) assumes equal marrow and blood activity concentration. However, other investigators have shown that the marrow/blood activity concentration varied between 0.05 and 0.62 (28–31). In addition, experience with ^{131}I for the treatment of thyroid carcinomas has shown that the RM/blood absorbed dose ranges from 0.44 to 0.79 (32–34). The current study based on sacral scintigraphy yields significantly lower RM absorbed dose estimates than those obtained by blood counting in agreement with the preceeding findings.

Tumor *S* values have been presented based on the assumption of uniform distribution of ^{131}I-labeled antibody in spherical regions varying in weight from 1 to 6000 g. The results of the tumor dosimetry indicated that the tumor percentage of uptake/g ranged from 0.0006 to 1.040, increasing with decreasing tumor weight. Surveys of the literature (35, 36) have concluded that the maximum possible tumor percentage of uptake/g was 0.005. However, these data were mainly from large bulk tumors. A tumor percentage of uptake/g of 0.038 for a 2.8-g tumor has recently been reported (37). It has also been concluded (38, 39) that there is an increase in per g % uptake of labeled monoclonal antibodies as tumors decrease in size.

In summary, a methodology for the calculation of tumor, red marrow, and organ dosimetry based on planar gamma camera imaging has been presented. None of the calculated absorbed doses to the lungs, liver, spleen, kidneys, and total body has resulted in toxicity. Dose estimation to the red marrow, the critical normal tissue in radioimmunotherapy, is still an area open to further research. Dose delivery to tumors has been found to increase with decreasing tumor mass.

References

1. Leicher, P. K., Klein, J. L., Garrison, J. B., *et al.* Dosimetry of I-131-labeled anti-ferritin in hepatoma: a model for radioimmunoglobulin dosimetry. Int. J. Radiat. Oncol. Biol. Phys., *7:* 323–333, 1981.
2. Larson, S. M., Carrasquillo, J. A., Kroh, K. A, *et al.* Localization of I-131 labeled p97-specific Fab fragments in human melanoma as a basis for radiotherapy. J. Clin. Invest., *72:* 2101–2114, 1983.
3. Leichner, P. K., Klein, J. L., Siegelman, S. S., Ettinger, D. S., and Order, S. E. Dosimetry of I-131-labeled antiferritin in hepatoma: specific activities in the tumor and liver. Cancer Treat. Rep., *67:* 647–658, 1983.
4. Wessels, B. W., and Rogus, R. D. Radionuclide selection and model absorbed dose calculations for radiolabeled tumor associated antibodies. Med. Phys., *11:* 638–645, 1984.
5. Myers, M. J., Epenetos, A. A., and Hooker, G. Practical assessment of radiation doses using radiolabeled antibodies for therapy. Nucl. Med. Biol., *13:* 437–446, 1986.
6. Doherty, P., Schwinger, R., King, M., and Gionet, M. Distribution and dosimetry of indium-111 labeled F(ab')$_2$ fragments in humans. *In:* Proceedings of the Fourth International Radiopharmaceutical Dosimetry Symposium, p. 464–475. Oak Ridge, TN: Oak Ridge Associated Universities, 1986.
7. Lashford, L., Jones, D., Pritchard, J., *et al.* Therapeutic application of radiolabeled monoclonal antibody UJ13A in children with disseminated neuroblastoma. Natl. Cancer Inst. Monogr., *3:* 53–57, 1987.
8. Leichner, P. K., Yang, N., Frenkel, T. L., *et al.* Dosimetry and treatment planning for Y-90-labeled antiferritin in hepatoma. Int. J. Radiat. Oncol. Biol. Phys., *14:* 1033–1042, 1988.
9. Siegel, J. A., Pawlyk, D. A., Lee, R. E., *et al.* Organ and tumor dosimetry for I-131 labeled monoclonal antibodies (MAbs) in patients with liver and lung tumors. J. Nucl. Med., *29:* 874–875, 1988.
10. Snyder, W. S., Ford, M. R., Warner, G. G., and Watson, S. B. "S" absorbed dose per unit cumulative activity for selected radionuclides and organs. MIRD phamphlet No. 11. New York: Society of Nuclear Medicine, 1975.
11. Loevinger, R., and Berman, M. A revised scheme for calculating the absorbed dose from biologically distributed radionuclides. MIRD Pamphlet No. 1, revised. New York: Society of Nuclear Medicine, 1976.
12. Thomas, S. R., Maxon, H. R., and Kereiakes, J. G. *In vivo* quantitation of lesion radioactivity using external counting methods. Med. Phys., *3:* 253–255, 1976.
13. Hammond, N. D., Moldofuky, R. J., Beardsley, M. R., and Mulhern, C. B. External imaging techniques for quantitation and distribution of I-131 F(ab')$_2$ fragments of monoclonal antibody in humans. Med. Phys., *11:* 778–783, 1984.
14. Wu, R. K., and Siegel, J. A. Absolute quantitation of radioactivity using the buildup factor. Med. Phys., *11:* 189–192, 1984.
15. Carrasquillo, J. A., Krohn, K. A., Beaumier, P., *et al.* Diagnosis and therapy for solid tumors with radiolabeled antibodies and immune fragments. Cancer Treat. Rep., *68:* 317–328, 1984.
16. Rosen, S. T., Zimmer, M., Goldman-Leiken, R., *et al.* Radioimmunodetection and radioimmunotherapy of cutaneous T cell lymphomas using an I-131-labeled monoclonal antibody: an Illinois cancer council study. J. Clin. Oncol., *5:* 562–573, 1987.
17. Cloutier, R. J., and Watson, E. E. Radiation dose from radioisotopes in the blood. *In:* Medical Radionuclides: Radiation Dose and Effects. AEC Symposium Series No. 20, pp. 325–346. Oak Ridge, TN: CONF 691212, 1970.
18. Bigler, R. E., Zanzonico, P. B., Leonard, R., *et al.* Bone marrow dosimetry for monoclonal antibody therapy. *In*: Proceedings of the Fourth International Radiopharmaceutical Dosimetry Symposium, pp. 535–544. Oak Ridge, TN: Oak Ridge Associated Universities, 1986.
19. Siegel, J. A., Lee, R. E., Pawlyk, D. A., *et al.* Red marrow dosimetry in radiolabeled monoclonal antibody therapy: a new approach using the sacrum. J. Nucl. Med., *29:* 858, 1988.
20. Primus, F. J., Newell, K. D., Blue, A., and Goldenberg, D. M. Immunological heterogeneity of carcinoembryonic antigen distinguished by monoclonal antibodies. Cancer Res., *43:* 686–692, 1983.
21. Siegel, J. A., Lee, R. E., Pawlyk, D. A., *et al.* Sacral scintigraphy for bone marrow dosimetry in radioimmunotherapy. Nucl. Med. Biol., *16:* 553–559, 1989.
22. Cloutier, R. V., Watson, E. E., Rohrer, R. H., and Smith, E. M. Calculating the radiation dose to an organ. J. Nucl. Med., *14:* 53–55, 1973.
23. Coffey, J. L., and Watson, E. E. Calculating dose from remaining body activity: a comparison of two methods. Med. Phys., *6:* 307–308, 1979.

24. Dillman, L. T., and Von der Lage, F. C. Radionuclide decay scheme and nuclear parameters for use in radiation-dose estimation. MIRD Pamphlet No. 10. New York: Society of Nuclear Medicine, 1975.
25. Brownell, G. L., Ellett, W. H., and Reddy, A. R. Absorbed fractions for photon dosimetry. MIRD Pamphlet No. 3. New York: Society of Nuclear Medicine, 1968.
26. Ellett, W. H., and Humes, R. M. Absorbed fractions for small volumes containing photon-emitting radioactivity. MIRD Pamphlet No. 8. New York: Society of Nuclear Medicine, 1971.
27. Remington, R. D., and Schork, M. A. Statistics with Applications to the Biological and Health Sciences. New York: Prentice-Hall, 1970.
28. Matthews, C. M. E., and Freeman, T. The albumin pool. *In:* Compartments, Pools, and Spaces in Medical Physiology. pp. 299–319. AEC Symposium Series No. 11, 1967.
29. Trunnel, J. B., Duffy, J. B., Godwin, J. T., *et al.* The distribution of radioactive iodine in human tissues: necropsy study in nine patients. J. Clin. Endocrinol., *10:* 1007–1021, 1950.
30. Klein, J. L., Ling, M. N., Leichner, P. K., *et al.* A model system that predicts effective half-life for radiolabeled antibody therapy. Int. J. Radiat. Oncol. Biol. Phys., *11:* 1489–1494, 1985.
31. Badger, C. C., Krohn, K. A., Peterson, A. V., Shulman, H., and Berstein, I. D. Experimental radiotherapy of murine lymphoma with ^{131}I-labeled anti-Thy 1.1 monoclonal antibody. Cancer Res., *45:* 1536–1544, 1985.
32. Robertson, J. S., and Godwin, J. T. Calculation of radioactive iodine β radiation dose to the bone marrow. Br. J. Radiol., *27:* 241–242, 1954.
33. Lewallen, C. G. Some observations on radiation dose to bone marrow during I-131 therapy of thyroid cancer. Am. J. Roentgenol., *89:* 618–623, 1963.
34. McEwan, A. C. Absorbed doses in the marrow during I-131 therapy. Br. J. Radiol., *50:* 329–331, 1977.
35. Dykes, P. W., Bredwell, A. R., Chapman, C. E., and Vaughan, A. T. M. Radioimmunotherapy of cancer: clinical studies and limiting factors. Cancer Treat. Rev., *14:* 87–106, 1987.
36. Vaughan, A. T. M., Anderson, P., Dykes, P. W., Chapman, C. E., and Bradwell, A. R. Limitations to the killing of tumors using radiolabeled antibodies. Br. J. Radiol., *60:* 567–578, 1987.
37. Macey, D. J., Denardo, S. J., Denardo, G. L., Goodnight, J. K., and Unger, M. W. Uptake of indium-111-labeled monoclonal antibody ZME-018 as a function of tumor size in a patient with melanoma. Am. J. Physiol., Imag., *3:* 1–6, 1988.
38. Hagan, P. L., Halpern, S. E., Dillman, R. O., *et al.* Tumor size: effect on monoclonal antibody uptake in tumor models. J. Nucl. Med., *27:* 422–427, 1986.
39. Williams, L. E., Duda, R. B., Proffitt, R. T., *et al.* Tumor uptake as a function of tumor mass: a mathematic model. J. Nucl. Med., *29:* 103–109, 1988.

Tumor, Red Marrow, and Organ Dosimetry for ^{131}I-labeled Anti-Carcinoembryonic Antigen Monoclonal Antibody

Jeffry A. Siegel, David A. Pawlyk, Robert E. Lee, et al.

Cancer Res 1990;50:1039s-1042s.