for internal dosimetry in most cases, especially for radiolabeled antibody agents. Would "tumor-to-marrow" absorbed doses or some other ratio be more indicative of the efficacy from a dosimetry standpoint?

REFERENCES

1. Breitz H, Fisher DR, Weiden PL, et al. Dosimetry of rhenium-186-labeled monoclonal antibodies: methods, prediction from technetium-99m-labeled antibodies and results of phase I trials. *J Nucl Med* 1993;34:908–917.
2. Snyder W, Ford M, Warner G, Watson S. "S," absorbed dose per unit cumulated activity for selected radionuclides and organs. *MIRD pamphlet no. 11*. New York: Society of Nuclear Medicine; 1975.
3. Thomas S, Stabin M, Chen C-T, Samaratunga R. A dynamic urinary bladder model for radiation dose calculations. *MIRD pamphlet no. 14. J Nucl Med* 1992;33:783–802.

Michael Stabin
Radiation Internal Dose Information Center
Oak Ridge, Tennessee

REPLY: I reported tumor-to-whole-body dose ratios as a means of comparing relative cumulative activity of different radiolabeled antibodies in tumors, not as a direct measure of efficacy (*1*). Whole-body dose is the absorbed dose that is estimated most consistently by all investigators. I agree that whole-body dose does not correlate reliably with any radiobiological effect but the tumor-to-whole-body ratio does seem to be useful for comparing localization of different radiolabeled antibodies.

In my paper I reported the tumor-to-liver, tumor-to-lung and tumor-to-kidney dose ratios. However, derivation of data for these ratios varies regarding exactly how regions of interest are drawn and how background is subtracted. Tumor-to-marrow dose ratios are not an accurate assessment of efficacy, because even if the marrow dose is accurate, the patients' marrow reserve is also important in determining the therapeutic index. Tumor-to-marrow dose ratios seem to be the least valuable as a comparison at this stage, because the methods used to estimate marrow dose are continually changing as we learn more about marrow dosimetry.

Another reason for reporting tumor-to-whole-body dose ratios was to compare them with those derived from theoretical modeling of radiolabeled antibodies (*2*). These ratios have also been developed in animal models in an attempt to predict clinical results (*3*).

REFERENCES

1. Breitz HB, Fisher DR, Weiden PL, et al. Dosimetry of ^{186}Re-labeled monoclonal antibodies: methods, predictions from ^{99m}Tc-labeled antibodies and results of phase I trials. *J Nucl Med* 1993;34:908–917.
2. Wessels B, Rogus RD. Radionuclide selection and model absorbed dose calculations for radiolabeled tumor associated antibodies. *Med Phys* 1984; 11:638–675.
3. Yorke ED, Beaumier PL, Wessels BW, Fritzberg AR, Morgan AC. Optimal antibody-radionuclide combinations for clinical radioimmunotherapy: a predictive model based on mouse pharmacokinetics. *Nucl Med Biol* 1991;18: 827–835.

Hazel Breitz
Virginia Mason Medical Center
Seattle, Washington

Samarium-153-EDTMP Dosimetry

TO THE EDITOR: In a recent paper, Eary et al. (*1*) addressed the issue of the biodistribution and dosimetry of samarium-153-EDTMP. I would like to make a few comments about the dosimetry aspects of this article. In particular, I would like to comment on the statement reproduced below:

> Radiation dose estimates for soft tissues were similar to those estimated by Logan et al. (*2*) and Heggie (*3*), which were human doses scaled from rat biodistribution data. Skeletal doses were several-fold higher, ranging from 20,000 to 32,000 mrad/mCi (5300–8800 Gy/MBq).

First, although the absorbed dose data of Logan et al. (*2*) is based on the rat model, the dosimetry in my article (*3*) makes no assumptions about biodistribution. Indeed, I calculated the bone and red marrow absorbed doses with respect to unit activity taken up by the *bone surfaces*. In that respect, it is not clear whether the bone dosimetry results of Eary et al. (*1*) refer to *administered* unit activity or unit activity on the bones. I suspect the former but it is not clear from their Table 4. In the absence of data reflecting the uptake to bone, direct comparison between my data and theirs is difficult. Assuming a bone uptake of 50% of injected dose (in line with data in Eary et al., Table 2), my calculations would suggest values of 0.93 mGy/MBq and 2.43 mGy/MBq for the absorbed dose to the red marrow and endosteal surfaces, respectively. These values are indeed lower, but not *severalfold lower*, than those estimated by Eary et al. (*1*). Incidentally, the SI dosimetry values shown in Table 4 and throughout the text of their work have been erroneously converted from traditional units; they are shown as being approximately a factor of a million larger than they should be.

The reason for the absorbed dose discrepancy between their work and my own is undoubtedly due to their adoption of the ICRP model of bone. As previously noted (*3*), the validity of the ICRP-30 dosimetry model for bone must be questioned on two counts. First, it was developed for *radiation protection* purposes and not accurate dosimetry. As such, it overestimates the absorbed fractions for electrons to the red bone marrow and the endosteal layer. Second, it uses bone structural data that is at odds with the work of Beddoe et al. (*4*) and others. Specifically, the adopted model underestimates the area of the endosteal surface layer associated with trabecular bone.

In the context of therapeutic treatment of bone metastes with ^{153}Sm-EDTMP, the success or failure of the treatment hinges on an accurate determination of the absorbed dose to the red bone marrow, since it is the red bone marrow absorbed dose which limits the amount of radioactivity that can be safely administered. In view of this, it would be instructive to use the biodistribution data of Eary et al. (*1*) with my previously published S-factors (*3*).

REFERENCES

1. Eary JF, Collins C, Stabin M, et al. Samarium-153-EDTMP biodistribution and dosimetry estimation. *J Nucl Med* 1993;35:1031–1036.
2. Logan K, Volkert W, Holmes R. Radiation dose calculations in persons receiving injection of Sm-153-EDTMP. *J Nucl Med* 1987;28:505–509.
3. Heggie JCP. Radiation absorbed dose calculations for samarium-153-EDTMP localized in bone. *J Nucl Med* 1991;32:840–844.
4. Beddoe AH, Darley PJ, Spiers FW. Measurements of trabecular bone structure in man. *Phys Med Biol* 1976;21:589–607.

John C.P. Heggie
St. Vincent's Hospital
Fitzroy, Australia

REPLY: We appreciate Dr. Heggie's (*1*) comments about our paper on ^{153}Sm distribution and dosimetry. He makes several

good points about the dosimetry, and we agree with his evaluation of the differences between the estimates in his earlier paper (*2*) and ours (*3*). We have the following responses to his points:

1. Our dose estimates are given per unit of injected activity, as is traditional and as is implied by the use of the quantity resident time (*4*). But this was not explicitly stated in the text or in the heading of Table 4.
2. We agree that the estimates of Dr. Heggie are lower because of our use of the ICRP 30 dose conversion factors for bone and marrow, which are conservatively high, having been designed for use in radiation protection programs (which operate at or below the 50-mGy level). We chose to use this system, as previous S-values contained a systemic error for low energy photon absorption (*5*), and because it is questionable to interpolate between mean energies and spectral shapes. Recent efforts by researchers at ORNL (*6*) have updated the photon *and* electron dosimetry and represent a more accurate dosimetry system. In this system, absorbed fractions (and thus dose estimates) will be provided for marrow and bone surfaces in seven bone groups, with explicit treatment of the beta spectra. We are currently in the process of implementing these values in our standard methods. We agree with Dr. Heggie that a recalculation of these dose estimates will be in order when these better dose conversion factors are available.
3. We agree that the values given for absorbed dose in SI unites are misstated. They should all be "μGy/MGq" not "Gy/MGq." The SI units were added during the review process, at the suggestion of a reviewer, and without the oversight of the main authors responsible for the dosimetry (Stabin).

REFERENCES

1. Heggie J. Samarium-153-EDTMP dosimetry. *J Nucl Med* 1994;35:194.
2. Heggie J. Radiation absorbed dose calculation for samarium-153-EDTMP localized in bone. *J Nucl Med* 1991;32:840–844.
3. Eary JF, Collins C, Stabin M, et al. Samarium-153-EDTMP biodistribution and dosimetry evaluation. *J Nucl Med* 1993;34:1031–1036.
4. Loevinger R, Budinger T, Watson E. MIRD primer for absorbed dose calculations. New York: Society of Nuclear Medicine; 1988.
5. Snyder W, Ford M, Warner G, Watson S. "S" absorbed dose per unit cumulated activity for selected radionuclides and organs. *MIRD pamphlet no. 11*, New York: Society of Nuclear Medicine; 1975.
6. Eckerman K. Aspects of the dosimetry of radionuclides within the skeleton with particular emphasis on the active marrow. In: Watson EE, Schlafke-Stelson AT, eds. *Fourth International Radiopharmaceutical Dosimetry Symposium*, Oak Ridge, Tennessee, November 58, 1985, CONF-851113 Oak Ridge Associates Universities, Oak Ridge, TN; 1986.

Janet F. Eary
University of Washington Medical Center
Seattle, Washington

Michael Stabin
Radiation Internal Dose Information Center
Oak Ridge, Tennessee

Current Status of Clinical PET

TO THE EDITOR: The editorial (*1*) by Dr. Edward Deutsch is an insightful analysis of aspects of the current status of clinical PET relating to generator-produced radionuclides. There is no doubt that a good generator-produced radiopharmaceutical for PET use, whatever its application, has a useful niche in clinical PET due to ready commercial availability and lack of dependence on local radiopharmaceutical production.

Dr. Deutsch points out that the FDA seems uncomfortable with PET radiopharmaceuticals because their production does not fit into existing regulatory cubbyholes. The agency is reacting with indecision and long delay. Therefore, the medical and financial benefits of a unique and well-proven subset of clinical nuclear medicine remain largely untapped. However, the concept that FDA approval could be obtained only by concentrating on tracers which fit existing regulatory mechanisms is cause for alarm. Is the solution to our dilemma that we should abandon the organic radiopharmaceuticals which are the mainstay of PET? Should we give up ^{18}F-2-fluoro-2-deoxyglucose now that FDG is almost a household word? Should we even replace cheap (when the cyclotron is already there), easy and effective ^{13}N-ammonia with a generator method and its associated added costs and procedures? The inorganic chemistry of metabolic or functional radiopharmaceuticals is very difficult. There are some impressive instances which demonstrate that generator-produced nuclides are not limited to perfusion and blood pool markers, but at best we have many years of work to match the current array of PET metabolic and receptor agents.

I do not believe that we will benefit as practitioners of PET, or as health care *consumers*, by restricting medical tools to fit bureaucratic preconceptions. This is not the path of innovation along which nuclear medicine has grown, nor is it a path to cost-effective health care. Drugs were once things we isolated from plants. Somehow a mechanism arose that allowed them to be synthesized and distributed. Now we must hope that there is still some room for original thought in government and that we will someday have regulations for PET materials which protect without stifling. Let us not propose abandoning an entire class of valuable diagnostic tools and the decades of government-funded work which produced it. Instead, we can work with the FDA to create understanding and sensible regulations, and let them know in increasingly urgent terms that these materials will continue to be needed regardless of the number of generators which are produced.

REFERENCE

1. Deutsch E. Clinical PET: its time has come? [Editorial]. *J Nucl Med* 1993;34:1132–1133.

Marc S. Berridge
University Hospitals of Cleveland
Cleveland, Ohio