5. Gullquist RR, Fleming JS. Error analysis by simulation studies in renography deconvolution. *Phys Med Biol.* 1987;32:383–395.

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REPLY: We wish to thank Dr. Fleming for his interest in our article and his constructive remarks. It is true that creatinine clearance has limited accuracy for estimating the glomerular filtration rate (GFR) but it is still the widely used method due to its availability. The overwhelming majority of clinical decisions are based on the creatinine clearance test (CCT) or simply the serum creatinine value. This is one of the reasons why Gates (*1*) and others compared gamma-camera-based GFR estimates to CCT and not to the gold standard methods, such as inulin or ^{51}Cr-ethylenediaminetetraacetic acid clearance. In our case, the choice of CCT as a reference was predetermined by the initial scope of the study: to validate Gates' method on Elscint gamma cameras and software.

Although we acknowledge that the standard error of estimate (Sy.x) is a more appropriate measure of correlation, it still can be misleading if reported alone. For example, in the simple linear regression procedure we performed comparing CCT with GFR (that we estimated with measured depth correction) in the 14 patients presented in Table 2 (*2*), we obtained a correlation coefficient of $r = 0.87$ with an Sy.x of 10.1 mL/min. When CCT is correlated with the GFR values obtained with the original Gates method (which doesn't measure renal depth, but only estimates it by Tonnesen's formula), $r = 0.51$ and Sy.x = 17.3 mL/min were obtained. This result is worse than the 7 mL/min value published by Gates (*1*). Thus, there is no doubt that the modifications we introduced improved the correlation with CCT, yet the Sy.x in our study has a higher value than in Gates' original study.

We agree that a GFR estimate based on diethylenetriamine pentaacetic acid (DTPA) renal uptake over a short period (between 2–3 min after injection) represents the GFR for only that point in time, but it has proven highly efficient and is widely accepted including in Gates' study—and may be potentially advantageous when studying GFR under pharmacologic interventions such as captopril.

The renal contour should be reliably depicted on lateral views by 20-min post-DTPA injection with some operator experience. The fact that the kidney outline is not the same as it would have been obtained at 2 min, doesn't actually affect locating the geometric center of the renal region of interest (ROI). Our precision of renal depth measurement in the supine position was better than ±1 cm (approximately ±0.5 cm). To obtain these results, certain hardware is required, and some rules are to be observed: lateral views should be acquired in a 256 × 256 matrix (1.6 mm/pixel for a 40-cm field-of-view camera), and the computer must have adequate contrast enhancement and zoom controls to adjust the picture quality so that renal contour and posterior body contour are well visualized. Before any renal depth measurement is performed, the posterior views in the last few frames of the renal dynamic scan should be examined for potential pitfalls as hydronephrosis, missing kidney, etc. Severe tracer retention in one kidney may appear on the lateral view of the other kidney and should be excluded from the lateral renal ROI.

We too believe that GFR determination by tracer disappearance using multiple blood samples is more precise than gamma camera-based methods. The statement that modifying Gates' technique improves its precision to the range of blood sample-based methods refers, rather, to other gamma camera-based methods, some of them using one blood sample at the end of acquisition (*3–5*). We appreciate Dr. Fleming's comments to clarify this point and to bring it to the attention of the journal's readers.

REFERENCES

1. Gates GF. Split renal function testing using Tc99m-DTPA. A rapid technique for determining differential glomerular filtration. *Clin Nucl Med.* 1983;8:400–407.
2. Steinmetz AP, Zwas ST, Macadziob S, Rotemberg G, Shrem Y. Renal depth estimates to improve the accuracy of glomerular filtration rate. *J Nucl Med.* 1998;39:1822–1825.
3. Ginjaume M, Casey M, Barker F, Duffy G. A comparison between four simple methods for measuring glomerular filtration rate using technetium-99m DTPA. *Clin Nucl Med.* 1986;11:647–650.
4. Waller DG, Keast CM, Fleming JS, Ackery DM. Measurement of glomerular filtration rate with technetium-99m DTPA: comparison of plasma clearance techniques. *J Nucl Med.* 1987;28:372–377.
5. Fleming JS, Keast CM, Waller DG, Ackery DM. Measurement of glomerular filtration rate with Tc99m-DTPA: a comparison of gamma camera methods. *Eur J Nucl Med.* 1987;13:250–253.

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Mouse Models for Internal Radiation Dosimetry

TO THE EDITOR: The article by Muthuswamy et al. (*1*), "A Mouse Bone Marrow Dosimetry Model," referred to prior work by Hui et al. (*2*) in ways that may have misinterpreted the purpose and discounted the usefulness of our earlier (and simpler) mouse dosimetry model. Muthuswamy et al. described our work as "a model . . . for ^{90}Y mouse bone marrow dosimetry that does not assume local energy deposition of β particles that are emitted inside the marrow . . . this model also computed the dose to marrow from the rest of the mouse body."

It would have been more correct to describe our mouse model (*2*) as a useful tool for calculating β-particle doses to the relatively small volumes of mouse organs and tissues. Our mouse model accounts for β energy absorbed fractions from the activity in small organs and tissues, as well as from the cross-organ β irradiation of organs or tumors by activity residing in adjacent tissues. It also accounts for changes in organ mass over time. The cross-organ dose component in the mouse is particularly important for the high-energy β emitter ^{90}Y, as shown by Beatty et al. (*3*). For example, a substantial contributor to marrow dose is the β-particle dose from ^{90}Y activity deposited on adjacent bone surfaces (*2*). Our model also was extended to other radionuclides, such as ^{131}I and ^{186}Re. These features make our mouse model well suited for experimental radioimmunotherapy studies (*4*).

Muthuswamy et al. attempted to improve on one aspect of our approach by calculating the dose to various regions of the total-body marrow, rather than to merely femoral marrow, as in Hui et al. (*2*). However, Muthuswamy et al. did not show how one would actually determine activity concentrations in those various marrow regions. In addition, they did not include the cross-organ

irradiation component for marrow, which for small marrow masses will be much more important than the marrow self-irradiation dose.

We chose to include only femoral marrow because it is the femoral marrow that is usually obtained and counted to determine the percentage injected dose per gram (%ID/g) and for correlating dose and effect. It may not be practical to obtain all %ID/g data for each marrow site and for every point in time.

Although Muthusawamy et al. provided a more detailed calculation for various marrow locations in the mouse, they then assumed that these different regions may be represented by a single average value. Although they applied S values for a 20-g human thyroid to estimate the total-body gamma contribution to marrow, they did not incorporate the important cross-organ β dose contributions (*4*).

In accordance with Fisher's Last Theorem, which states that "every dosimetry model may be improved on by someone else in the future," we recognize the importance of calculating dose to marrow in sites other than the femur. However, the prior mouse dosimetry model of Hui et al. (*2*) may have the advantage of being less complicated, more complete in terms of small organ dosimetry and more applicable to real animal experiments.

REFERENCES

1. Muthuswamy MS, Roberson PL, Buchsbaum DJ. A mouse bone marrow dosimetry model. *J Nucl Med.* 1998;39:1243–1247.
2. Hui TE, Fisher DR, Kuhn JA, et al. A mouse model for calculating cross-organ beta doses from yttrium-90-labeled immunoconjugates. *Cancer.* 1994;73:951–957.
3. Beatty BG, Kuhn JA, Hui TE, et al. Application of the cross-organ beta dose method for tissue dosimetry in tumor-bearing mice treated with a ^{90}Y-labeled immunoconjugate. *Cancer.* 1994;73:958–965.
4. Badger CC, Fisher DR. The importance of accurate radiation dosimetry in radioimmunotherapy of cancer. *J Nucl Med.* 1994;35:300–302.

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REPLY: In their letter, Fisher and Hui point out that their work could have been described in a better manner. This is not contested. However, their work was correctly described in the context of our article.

Our model (*1*) makes it possible to compare the impacts of relative bone marrow dosimetry of various radionuclides. Specifically, we published these comparisons for ^{131}I, ^{186}Re and ^{90}Y radionuclides. Contrary to the claims of Fisher and Hui, no such comparisons were published by their group (*2,3*). In our model, average measured activity concentration can be input as a parameter.

The purpose of the marrow calculations presented by Hui et al. (*2*) was different from our purpose. Hui et al. limited their calculations to the bone marrow contributor that can be relatively easily verified within current experimental practice (the femur). Our purpose was to be more complete in incorporating the various marrow dose contributors (ribs, vertebrae, skull, etc.) to improve estimates of the correlation between dose calculation and organ function failure.

The work of Hui et al. (*2*) correctly calculated the dose to marrow using the known finite range of β particles resulting in a self-absorbed fraction of less than 1. The matrix of cross-organ absorbed fractions compiled for the mouse model by Hui et al. is reasonably extensive. Because of the assumptions made for their calculations, only the bone contributed as a source organ to the marrow dose. Nonetheless, in the simplest model of cross-organ dosimetry, as used by us, all nonmarrow organs are lumped together to represent the "rest of the body." We also discussed the meaningfulness of this approach compared to the approach used by Hui et al.

Both are, admittedly, only a part of the desired complete calculation, as pointed out by Fisher and Hui. A more complete calculation would include: (a) uptake in each marrow organ separately with properly registered heterogeneity of uptake and tissue density nonuniformity; (b) dose calculation including self-absorption and cross-organ dosimetry; and (c) dose response of each marrow dose contributor correlated with organ function as a whole. Attention to each piece of the puzzle may be of value as the pieces are assembled slowly.

We conclude that our discussion of the work of Hui et al. met the purpose of relating our results to their results while illustrating the effect of including a more representative bone marrow geometry and relative dosimetric impact of different radionuclides.

REFERENCES

1. Muthuswamy MS, Roberson PL, Buchsbaum DJ. A mouse bone marrow dosimetry model. *J Nucl Med.* 1998;39:1243–1247.
2. Hui TE, Fisher DR, Kuhn JA, et al. A mouse model for calculating cross-organ beta doses from yttrium-90-labeled immunoconjugates. *Cancer.* 1994;73:951–957.
3. Beatty BG, Kuhn JA, Hui TE, et al. Application of the cross-organ beta dose method for tissue dosimetry in tumor-bearing mice treated with ^{90}Y-labeled immunoconjugate. *Cancer.* 1994;73:958–965.

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