6. Jain D, Burg M, Soufer R, Kerns R, Zaret BL. Silent left ventricular dysfunction during routine structured interveiw and induced mental stress in coronary patients: impact of type A behavior. 40th Annual Scientific Session, American College of Cardiology, Atlanta, GA, March, 1991.
7. Carey J, Stewart J, Merrill W, et al. Continuous radionuclide monitoring of left ventricular systolic performance in postoperative cardiac surgery patients: validation of the Capintec-VEST. 39th Annual Scientific Session, American College of Cardiology, New Orleans, March, 1990.

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Reconstitution and Fractionation of Radiopharmaceutical Kits

TO THE EDITOR: Several reports have appeared in the literature describing cost-saving measures by which radiopharmaceutical kits are reconstituted with saline, divided into portions in separate vials and refrigerated or frozen. These vials are thawed at a later time (hours to days) after which [^{99m}Tc]-pertechnetate is added. Piera et al. (*1*) and Ballinger (*2*) were able to demonstrate sustained stability of ^{99m}Tc-HMPAO kits prepared from divided, reconstituted fractions, particularly if the kits were reconstituted with nitrogen-purged saline and subsequently frozen at −10°C. We have extended this approach to two of the newer radiopharmaceutical kits ^{99m}Tc-sestamibi (DuPont/Merck, Billerica, MA) and ^{99m}Tc-mertiatide (Mallinckrodt, St. Louis, MO).

The kits were initially reconstituted with 2 ml of low-dissolved-oxygen (LDO) saline and divided into four aliquots of 0.5 ml and placed in sterile vials. Three of the vials were frozen, while 20 mCi of ^{99m}Tc-pertechnetate (obtained 1 hr after elution of a generator) was added to the other vial using the procedure recommended by the manufacturer. The radiochemical purity of the kits was also determined according to the manufacturer's instructions (ITLC for the sestamibi kit; a Sep-Pak cartridge for the mertiatide kit). The frozen kits were thawed 1–5 days after the initial reconstitution, and [^{99m}Tc]pertechnetate was added as described above. This procedure was repeated several times for each kit.

The ^{99m}Tc-sestamibi kits exhibited excellent stability, even for the reconstituted aliquots that had been frozen for five days. A 90%–96% radiochemical purity was observed for all samples tested. However, the radiochemical purity of the mertiatide kits was unacceptably low for frozen aliquots stored for longer than one day.

The mertiatide kit is supplied as a lyophilized powder stored under argon gas. The instructions for the preparation of this kit call for the removal of this argon layer and replacing it with air in the vial. When the vials were reconstituted with LDO saline, the stored, frozen vials no longer had this argon layer. Thus, the low radiochemical purity observed for the frozen, reconstituted aliquots may have been due to the oxidation of the stannous chloride in the kit. This is apparently the same phenomenon observed by Ballinger during the preparation of reconstituted ^{99m}Tc-HMPAO kits (*2*). Therefore, an adjustment was made in which the reconstituted aliquots were added to sterile vials that were purged with argon gas. The argon was added using a pressurized tank and an in-line 0.22 micron filter. These vials were then treated similarly to the other ^{99m}Tc-mertiatide preparations and subjected to the same quality control procedures. A radiochemical purity of greater than 97% was observed for all aliquots, including one that had been frozen for 21 days.

These procedures are easily performed in a nuclear medicine department and can lead to substantial savings. By using the appropriate reconstitution procedures, the stability of the kits can be maintained for a time to sufficiently maximize the utility of the kit. While we have not evaluated the effect of the reconstitution, freezing and thawing of the kits on the quality of the scan, we assume that as long as the number of doses extracted from one kit does not exceed the manufacturer's recommendations, this should not be a problem.

REFERENCES

1. Piera C, Pavia A, Bassa P, Garcia J. Preparation of ^{99m}Tc-HMPAO [Letter]. *J Nucl Med* 1990;31:127–128.
2. Ballinger J. Preparation of technetium-99m-HMPAO [Letter]. *J Nucl Med* 1990;31:1892.

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Calculation of the Radiation Dose at a Bone-to-Marrow Interface

TO THE EDITOR: With great interest, we read the article by Johnson et al. (*1*). This article proposes a simple anatomical model and uses straightforward calculations to improve understanding of the absorbed dose distribution in bone marrow. The presentation of the results as a dose profile may enhance our understanding of the myelotoxicity of high activity doses of radionuclides. However, we would like the authors' comment on the following items:

1. Is the proposed anatomical model applicable to humans, in whom the marrow is always embedded in trabecles, even in the mid-femur (*2*)?
2. Do the authors expect a homogeneous absorbed dose in marrow cavities in humans, where the trabecle distances [± 1000 μm (*3,4*)] are comparable to the percentile distances X_{90} [1000 μm for ^{153}Sm and 1800 μm for ^{186}Re (*5*)]?
3. Do the authors expect the results to change significantly because of possible deviations from the planar source approximation? Why is application of the lateral correction algorithm (LCA) not required?
4. With the EGS4 code, electrons less than 10 keV are neglected. However, these electrons do occur in the decay spectrum (*1,6,7*) of ^{153}Sm and ^{186}Re (Table 1) and may be

TABLE 1

	β constant (g-cGy/μCi-hr)		Electron constant (g-cGy/μCi-hr)	
Isotope	Johnson	MIRD	All E	E < 10 keV
^{153}Sm	0.48	0.48	0.089	0.0083
^{186}Re	0.69	0.70	0.031	0.0022

essential to the endosteal dose, considering the small volume and the short range of these electrons (*8*).

A particular result of the study was that the backscatter at the bone-to-bone marrow interface increased the absorbed dose maximally 10%. Besides this "anatomical heterogeneity," "radionuclide distribution heterogeneity" is an important issue, for which, for example, a point kernel approach can be applied. So far, it does not seem possible to design models that account for both heterogeneities. Perhaps future dosimetric models will be able to do so or may indicate which issue has the most profound effect on the absorbed dose distribution.

REFERENCES

1. Johnson JC, Langhorst SM, Loyalka SK, et al. Calculation of radiation dose at a bone-to-marrow interface using Monte Carlo modeling techniques (EGS4). *J Nucl Med* 1992;33:623–628.
2. Voegeli E. *Grundelemente der Skeletradiologie.* Bern, Stuttgart, Wien: Verlag Hans Huber, 1981.
3. Jensen KS, Mosekilde L, Mosekilde L. A model of the vertebral trabecular bone architecture and its mechanical properties. *Bone* 1990;11:417–423.
4. Eckermann KF. Aspects of the dosimetry of radionuclides within the skeleton with particular emphasis on the active marrow. *Proc Fourth Int Radiopharm Dosimetry Symp* [CONf-851113-DE86010102], 1985:514–534.
5. Simpkin DJ, Mackie TR. EGS4 Monte Carlo determination of the beta dose kernel in water. *Med Phys* 1990;17:179–186.
6. *MIRD: radionuclide data and decay schemes.* New York: The Society of Nuclear Medicine. 1989.
7. Dillman LT, Von der Lage FC. MIRD Radionuclide decay schemes and nuclear parameters for use in radiation dose estimation. *MIRD pamphlet no. 10.* New York: The Society of Nuclear Medicine, 1975.
8. Cole A. Absorption of 20 eV to 50,000 eV electron beams in air and plastic. *Radiat Res* 1969;38:7–30.

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REPLY: Thank you for the opportunity to respond to the questions posed by Dr. van Dieren and his colleagues at the Free University Hospital, Amsterdam. Their questions address two issues. The first is the applicability of our model to trabecular bone in humans, while the second is our implementation of the EGS4 radiation transport algorithms.

Our results will have limited application to dose distributions in small trabecular cavities with thin walls. Our model described the backscatter dose enhancement near a cortical bone wall that was thick compared to the range of the electrons of interest. We did not address the potential for a buildup of dose across a comparatively thin trabecular structure. We did calculate dose factors in cortical bone at depths corresponding to the mean thickness of the trabecular structures (200–300 μm) (*1,2*). Those dose factors could be used to estimate the dose to endosteal tissue on the far side of a thin trabecular wall, but it would be better to modify the geometry of the model and calculate them directly.

It is unlikely that the marrow dose across trabecular cavities would be uniform because of significant contributions of atomic electrons near the source. This would be particularly true for ^{153}Sm because of its relatively large atomic electron component and low mean beta energy. We have calculated dose factors for ^{166}Ho using a cylindrical geometry. The source was deposited on the inside wall of a marrow-filled cylinder of cortical bone having an inside radius of 2000 μm (*3*). Our finding was that the dose distribution across the cavity becomes roughly uniform (within ±20%) beginning 75 μm from the cylindrical wall and extending through the center of the cylinder. We have not yet determined dose factors for ^{153}Sm or ^{186}Re in this geometry.

In our implementation of EGS4, we included source radiations having electrons of energy less than 10 keV. As Dr. van Dieren and his colleagues noted, the model does not transport these electrons. Neither does it summarily discard them. Instead, it allows the user to decide their fate (*4*). In our model, once the energy of an electron fell below 10 keV, we deposited the residual energy in the current dose region. Only then did we discard the particle. For an electron that started below the 10 keV threshold, we deposited its energy in the dose region of the source.

The lateral correlation algorithm (LCA) improves computing efficiency by allowing for long electron transport steps along a boundary (*5*). When a computer model transports an electron in a long, straight step near a boundary, it may incorrectly deposit all expended energy in a single region. In reality, the electron represented by the model may wander back and forth across that boundary, depositing energy on both sides. In EGS4, the LCA compensates for that wandering. In our implementation, the dose regions are very thin (10 μm thick near the source), and we limit the maximum transport step (ESTEP in Table 1) (*6*) so that LCA is not required.

Although we have not addressed heterogeneity of radionuclide distribution in our model, it could be added. We are also considering extending our model to calculate dose factors for sensitive tissues in complex irregular structures, such as nerve tissue in the vertebral column. The versatility of models like EGS4 makes them attractive tools for a variety of complex dosimetry calculations. The increased availability of fast and relatively inexpensive computer hardware makes direct dosimetry calculations in complex circumstances both efficient and affordable.

REFERENCES

1. Spiers FW, Beddoe AH. Radial scanning of trabecular bone: consideration of the probability distributions of path lengths through cavities and trabeculae. *Phys Med Biol* 1977;22:670–680.
2. Beddoe AH. Measurements of the microscopic structure of cortical bone. *Phys Med Biol* 1976;22:298.
3. Johnson JC. Determination of dose factors at a bone to marrow interface using Monte Carlo methods. Ann Arbor, MI: University Microfilms International; Dissertation No. 90-10570; 1990:100.
4. Nelson WR, Hirayama H, Rogers DWO. The EGS4 code system. Stanford, CA: Stanford Linear Accelerator Center; Report No. SLAC-265; 1985.
5. Bielajew AF, Rogers DWO. PRESTA: the parameter reduced electron-step transport algorithm for electron Monte Carlo transport. *Nucl Meth Phys Res* 1987;B18:165–181.
6. Johnson JC, Langhorst LM, Loyalka WA, Volkert WA, Ketring AR. Calculation of radiation dose at a bone-to-marrow interface using Monte Carlo modeling techniques (EGS4). *J Nucl Med* 1992;33:623–628.

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