Quantification of Myocardial Blood Flow

TO THE EDITOR: I would like to point out an error in the abstract by Kuhle (*1*) published in the Proceedings of the 38th Annual Meeting of the Society of Nuclear Medicine. In the two-compartment model for quantification of myocardial blood flow (MBF) using ^{13}N-ammonia, the relationship K1 = 1-0.607exp(−1.25/MBF) is incorrect. Rather, this is the equation for the first-pass myocardial extraction fraction of 13N-ammonia (*2*). The forward rate constant between the two compartments can be shown to be K1 = E·MBF/(1-E), which reduces to K1 = MBF·[1.65exp(1.25/MBF)-1], where E is the extraction fraction. Curiously, I made the same error in my abstract submitted to the 35th annual meeting (*3*), which described the identical model for myocardial 13N-ammonia kinetics using a different set of animal data. The error was subsequently corrected in the poster presentation at the meeting.

Since my original abstract, the model has been validated using synthetic data to address errors in the calculated value of MBF due to inaccuracies in the assumed volume of distribution, reverse rate constant (k2), and noise (*4*). In addition, the clinical utility of the model was demonstrated both in my original abstract and in patients both using exercise and dipyridamole stress with ^{13}N-ammonia PET scanning (*3,5,6*). Methods to estimate k2 and internal myocardial dosimetry based on the model have also been described (*7,8*). Finally, comparison of calculated MBF from neural network analysis and from the two-compartment model have been reported (*9*). Further work on neural network correlation with the model was rejected by the SNM 1991 Scientific Program Committee.

Congratulations to Dr. Kuhle on his idea to reslice the image data into short-axis projections, obviously the inspiration of a Young Investigator. I look forward to the 39th Annual Society of Nuclear Medicine Meeting so we can "Play It Again, Sam" (*10*).

REFERENCES

1. Kuhle W, Porenta G, Buxton D, Huang SC, Hanson H, Phelps ME, Schelbert HR. Quantification of regional myocardial blood flow using N-13-ammonia and reoriented dynamic PET imaging. *J Nucl Med* 1991;32:909–910.
2. Schelbert HR, Phelps ME, Huang SC, et al. N-13-ammonia as an indicator of myocardial blood flow. *Circulation* 1981;63:1259–1272.
3. Smith GT, Huang SC, Nienaber CA, Krivokapich J, Schelbert HR. Non-invasive quantification of regional myocardial blood flow with N-13-ammonia and dynamic PET. *J Nucl Med* 1988;29:940.
4. Wu Y. Measurement of regional myocardial blood flow by compartment modeling method. Master of Science Thesis, University of Tennessee, Knoxville, TN, 1990.
5. Krivokapich J, Smith GT, Huang SC, et al. ^{13}N-ammonia myocardial imaging at rest and with exercise in normal volunteers. *Circulation* 1989;80:1328–1337.
6. Smith GT, Wu Y, Miller L. Quantification of myocardial blood flow with dynamic positron emission tomography. *Trans Am Nucl Soc* 1990;62:6.
7. Smith GT, Stubbs JB, Hubner K, Goodman M. Dynamic PET scanning and compartmental model analysis to determine cellular level radiotracer distribution in vivo. Presented at the Fifth International Radiopharmaceutical Dosimetry Symposium, sponsored by Oak Ridge Associated Universities, Oak Ridge, TN, May 9, 1991.
8. Stubbs JB, Smith GT, Stabin MG, Eckerman KF, Turner JE. An approach to cellular level dosimetry using compartmental analysis and dynamic PET. Paper presented at the Fifth International Radiopharmaceutical Dosimetry Symposium, sponsored by Oak Ridge Associated Universities, Oak Ridge, TN, May 9, 1991.
9. Smith GT, Liu Y, Upadhyaya BR. Quantitative myocardial blood flow determined with PET and neural network analysis. *Radiology* 1990;177:148.
10. Strauss HW. Play It Again, Sam [Editorial]. *J Nucl Med* 1991;32(7):3A.

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Can Iodine-131 Whole-Body Scan Be Replaced by Thyroglobulin Measurement in the Post-Surgical Follow-up of Differentiated Thyroid Carcinoma?

TO THE EDITOR: The study of Ronga et al. (*1*) warrants some comments.

The early discovery of metastases at a stage when x-rays are still normal, is the main prognostic factor for cure (*2*). In a given patient, the increase in Tg level is related to the size of the metastases (*3*) and Tg assays should be sensitive enough to reliably detect low Tg levels (> 1 ng/ml). This has been made possible by the use of IRMA systems using monoclonal antibodies directed against Tg (*4*).

Following total thyroid ablation, Tg is be undetectable in the absence of normal or neoplastic thyroid tissue and any detectable Tg level warrants further investigation, even if there is no other evidence of disease. A whole-body scan (WBS) with a therapeutic dose (100 mCi) of radioiodine permitted the discovery of unknown metastases in a large proportion of patients with detectable Tg levels (*3,5,6*). In the others in whom neoplastic tissue did not take up radioiodine, Tg level was elevated long before metastases became detectable on x-rays (*3,4*). In the series of Ronga et al. (*1*), 9 of the 14 patients with absence of thyroid activity had a significant increase in Tg level following suppression of therapy, which was similar to that of 3 patients with proven metastases. However no post-therapy WBS was performed and it is likely that these patients were misclassified.

In 7 of the 17 patients with residual thyroid tissue, Tg level

TABLE 1
Ultrasound of Residual Thyroid Tissue as a Function of Tg Level

Ultrasound Tg (ng/ml)	Normal	Nodules
≤1	18	0
2–5	3	6
≥6	0	5

Tg was measured during LT_4 treatment at suppressive doses with the Dynotest Tg kit (Henning, Berlin) (*4*).

was equal or above 10 ng/ml during T4 treatment at suppressive doses (*1*). In these patients, infraclinical thyroid abnormalities should be sought by neck ultrasound, as shown in our series (Table 1). These infraclinical nodules may be benign or malignant, but their high incidence argues for performing initially at total thyroidectomy.

Finally, the conclusion that Tg determination cannot replace the WBS is based on the use of a given commercial kit and may be not valid for other methods of Tg measurement (*2–4*). In fact, these two methods of follow-up should be combined (*2–6*).

REFERENCES

1. Ronga G, Fiorentino A, Paserio E, et al. Can iodine-131 whole-body scan be replaced by thyroglobulin measurement in the post-surgical follow-up of differentiated thyroid carcinoma? *J Nucl Med* 1990;31:1766–1771.
2. Schlumberger M, Tubiana M, De Vathaire F, et al. Long-term results of treatment of 283 patients with lung and bone metastases from differentiated thyroid carcinoma. *J Clin Endocrinol Metab* 1986;63:960–967.
3. Schlumberger M, Tubiana M. Serum Tg measurements and total-body ^{131}I scans in the follow-up of thyroid cancer patients. In: Hamburger JI ed. *Diagnostic methods in clinical thyroidology*. New York: Springer-Verlag, 1989:147–157.
4. Schlumberger M, Fragu P, Gardet P, Lumbroso J, Violot D, Parmentier C. A new immunoradiometric assay (IRMA) system for thyroglobulin measurement in the follow-up of thyroid cancer patients. *Eur J Nucl Med* 1991;18:153–157.
5. Pacini F, Lippi F, Formica N, et al. Therapeutic doses of iodine-131 reveal undiagnosed metastases in thyroid cancer patients with detectable serum thyroglobulin levels. *J Nucl Med* 1987;28:1888–1891.
6. Schlumberger M, Arcangioli O, Piekarski JD, Tubiana M, Parmentier C. Detection and treatment of lung metastases of differentiated thyroid carcinoma in patients with normal chest x-ray. *J Nucl Med* 1988;29:1790–1794.

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Single Plasma GFR in Children

TO THE EDITOR Ham and Piepsz (*1*) showed in their recent article that measurement of glomerular filtration rate (GFR) from a single sample taken 2 hr after ^{51}Cr-EDTA injection correlated very closely with the value calculated from the slope/intercept method using samples at 2 and 4 hr. Since they expressed clearance without scaling for body surface area, it is not clear from their population of children how many had poor renal function, although they made the point that single sample techniques have usually not performed well at low renal function.

This question of function is rather critical because if the value of the rate constant of the slope (i.e., "α") is between about 0.005 min^{-1} and 0.012 min^{-1}, then the 2-hr single-sample clearance *automatically* correlates closely with the double-sample clearance. In other words, it does not really matter where the second point lies in relation to the first point if the y-axis value of the second point is between values that would give an α of between about 0.005 and 0.012 min^{-1}. This is because any error in α is counterbalanced by the resulting zero time plasma concentration. This is illustrated in Figure 1. By fixing the 2-hr plasma concentration at a nominal constant value, a set of clearances can be calculated by varying the second point to give a range of slope rate constants. The subsequent relationship between the calculated clearances and α is shown in Figure 2.

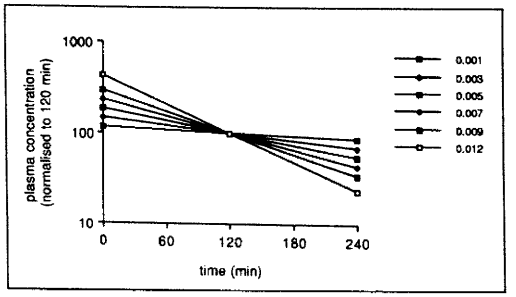

FIGURE 1. Range of values of zero time plasma concentration, which is the denominator in clearance calculation (Equation 1), corresponding to a range of values of α (min^{-1}), which is the numerator. As α increases, the zero time concentration decreases.

It can be seen from Figure 2 that with the two-sample slope/intercept method and the first sample taken at 2 hr, the maximum clearance is obtained when α is 0.0083 min^{-1}; any value of α above or below this figure gives a lower clearance. For values of α lower than about 0.005 min^{-1}, calculated clearance falls appropriately, and the tendency for automatic correlation between single sample and double sample clearances disappears. Hence the critical nature of reduced renal function.

The relationship between clearance and α, as shown in Figure 2, has previously been intimated by Waller et al. (*2*) and by Fawdry and Gruenewald(*3*). Both these groups demonstrated, on theoretical grounds, that the relationship between clearance and the 2-hr apparent, time-dependent, volume of distribution was almost linear at values of t chosen to suit the range of encountered

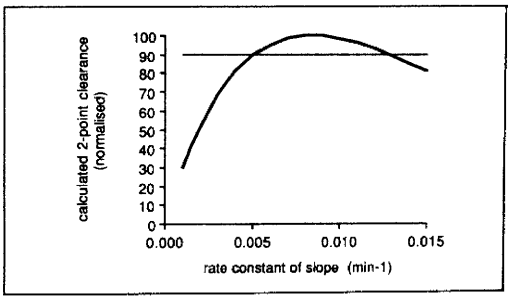

FIGURE 2. Relationship between clearance (C), calculated from the 2-point slope/intercept method, and the rate constant, α, of the slope. The y-axis has been normalized to the maximum value. The horizontal line defines the values of α which give a calculated clearance to within 10% of the maximum. The curve defined by the bold line is given by:

$$C = k \cdot \alpha \cdot e^{-\alpha t} \quad \text{Eq. 1}$$

where

$$k = \text{constant} \times \text{dose} \quad \text{Eq. 2}$$

Therefore

$$dC/d\alpha = k \cdot e^{-\alpha t} - k \cdot \alpha \cdot t \cdot e^{-\alpha t} \quad \text{Eq. 3}$$

when

$$dC/d\alpha = 0, \text{ C is maximal, whereupon } \alpha = 1/t \quad \text{Eq. 4}$$

So, for t = 120 min, maximal calculated two-point clearance is obtained when $\alpha = 0.0083$ min^{-1}.