categorically, "that the steady-state $^{15}O_2$ method cannot provide quantitative values of regional oxygen utilization" (*5*), but we did indeed state that such measurements may be possible to carry out with reasonable accuracy for tissues that exchange water slowly.

The theoretical model using the Fick principle (*6–8*) suggested by Jones et al. (*9*) for measurement of regional cerebral blood flow (rCBF) and oxygen extraction (OER), has been applied, in conjunction with quantitative positron emission tomography, to in vivo studies as well as extended to regional cerebral oxygen consumption rates ($rCMRO_2$) (*10*) by means of their product, i.e., $rCMRO_2 = rCBF \times OER \times$ (total blood oxygen content). We use a compartmental-model approach (11) to analyze the possibility of the direct measurement of regional oxygen utilization by quantitative methods, e.g., our earlier two-dimensional (*12,13*) approach or now the more powerful three-dimensional approach provided by positron tomography. The clinical value of the steady-state technique will depend upon an understanding of the nature and magnitude of the uncertainties associated with the measurements and approximations used. In our opinion this understanding is facilitated by our work (*1*) and that of others (*14–16*), as well as by the material referred to by Jones et al. (*5*). One of us (REB) plans to carry out an error analysis similar to that for rCBF by SC Jones, JH Greenberg and M Reivich (*15*) in order to provide a more thorough understanding of the errors associated with the measurement of regional oxygen metabolism and OER in humans by the approach detailed by Frackowiak et al. (*10*).

RODNEY E. BIGLER
JOHN GILLESPIE
JEFFREY KOSTICK
Sloan-Kettering Institute
for Cancer Research
New York, New York

REFERENCES

1. BIGLER RE, KOSTICK JA, GILLESPIE JR: Compartmental analysis of the steady-state distribution of $^{15}O_2$ and $H_2{}^{15}O$ in the total body. *J Nucl Med* 22:959-965, 1981
2. BIGLER RE, KOSTICK JA, LAUGHLIN JS, et al: Compartmental analysis of the steady-state distribution of oxygen-15 labeled oxygen and water. *J Nucl Med* 20:606, 1979 (abst)
3. RUSS GA, BIGLER RE, TILBURY RS, et al: Whole body scanning and organ imaging with oxygen-15 at the steady-state. World Federation of Nuclear Medicine and Biology, First World Congress of Nuclear Medicine, Tokyo, Japan, Sept. 30-Oct. 5, 1974, pp 904-906
4. RUSS GA, BIGLER RE, MCDONALD JM, et al: Oxygen-15 scanning and gamma camera imaging in the steady-state. *J Nucl Med* 15:529-530, 1974 (abst).
5. JONES T, FRACKOWIAK RSJ, LAMMERTSMA AA, et al: Letter to the Editor, 1982
6. FICK A: Über die messung des blutquantums in den Herzventrikeln. Verhandl. d. phys med. Ges zu Würzlurg 2, XVI 1870 (Quoted in its entirety by Hoff HE and Scott HJ Physiology 120-126: *New Engl J Med* 239, 122-123 1948)
7. KETY SS: The theory and applications of the exchange of inert gas at the lungs and tissues. *Pharmacol Rev* 3:1-41, 1951
8. KETY SS: Theory of blood-tissue exchange and its application to measurement of blood flow. *Meth Med Res* 8:223-227, 1960
9. JONES T, CHESLER DA, Ter-Pogossian MM: The continuous inhalation of oxygen-15 for assessing regional oxygen extraction in the brain of man. *Br J Radiol* 49:339-343, 1976
10. FRAKOWIAK RSJ, LENZI GL, JONES T, et al: Quantitative measurement of regional cerebral blood flow and oxygen metabolism in man using ^{15}O and positron emission tomography: Theory, Procedure and Normal Values. *J Comput Assist Tomogr* 4(6):727-736, 1980
11. SHIPLEY RA, CLARK RE: *Tracer Methods for In Vivo Kinetics Theory and Applications*, New York, Academic, 1974
12. CLARK LP, LAUGHLIN JS, MAYER K: Quantitative organ-uptake measurement. *Radiology* 102:375-382, 1972
13. BIGLER RE, KOSTICK RA, DAVIS DC, et al: The use of $C^{15}O$ and $^{15}O_2$ steady-state imaging to monitor radiation treatment effects. *IEEE Trans Nucl Sci* NS-25:174-179, 1978
14. HUANG SC, PHELPS ME, HOFFMAN EJ, et al: A theoretical study of quantitative flow measurements with constant infusion of short-lived isotopes. *Phys Med Biol* 24:1151-1161, 1979
15. JONES SC, GREENBERG JH, REIVICH M: Error analysis for the determination of cerebral blood flow with the continuous inhalation of ^{15}O-labeled carbon dioxide and positron tomography. *J Comput Assist Tomogr* 6(1):116-124, 1982
16. SUBRAMANYAM R, ALPERT NM, HOOP B, et al: A model for the regional cerebral oxygen distribution during continuous inhalation of $^{15}O_2$, $C^{15}O$ and $C^{15}O_2$. *J Nucl Med* 19:48-53, 1978

Free Thyroxine RIA Concentration (GammaCoat) Is Spuriously Elevated in Blood Collected in Silicon-Coated Vacutainer Tubes

An unusual finding was observed when five radioimmunoassay (RIA) kits were used to measure the serum free thyroxine concentration (FT_4) in euthyroid subjects during a study to evaluate the serum FT_4 in patients with familial dysalbuminemic hyperthyroxinemia (FDH) (*1–3*). This syndrome is characterized by elevations in the serum T_4 concentration and free thyroxine index due to the presence of an abnormal serum albumin that preferentially binds T_4. However, these patients are euthyroid and the serum T_3 and FT_4 concentrations are normal when measured by equilibrium dialysis.

FT_4 concentrations in serum samples from 20 normal, euthyroid subjects were measured by RIA. The following methods were used: I-125-labeled T_4 analog, antibody-coated tube (GammaCoat, one-step)*; antibody-coated tube (GammaCoat, two-step)*; antibody-coated microfine silica (Immo Phase†); microencapsulated antibody (Liquisol)‡; and I-125-labeled T_4 analog (Amerlex). All blood samples had been collected in silicon-coated vacutainer tubes and the serum stored frozen in the silicon-coated tubes. All tests were performed in duplicate on the same day.

The results of the serum FT_4 measured by the five methods in 20 euthyroid subjects are shown in Fig. 1. All values were in the normal range when assayed by the Immo Phase, Liquisol, and Amerlex methods. In contrast, serum FT_4 values were above the normal range in nine of the 20 normal subjects when measured by the GammaCoat, one-step kit and in 12 subjects measured by the GammaCoat, two-step kit. The tests were repeated using other GammaCoat kits, and similar results were obtained. Therefore, these observations could not be explained on the basis of defective reagents or experimental error.

One explanation for the elevated values obtained by the GammaCoat methods could be that the silicon used to coat the vacutainer tubes might interfere with the assays. To test this hypothesis, blood samples were collected from ten more euthyroid subjects in vacutainer tubes both with and without silicon coating, and serum was stored frozen for 3 days in the respective tubes. Serum FT_4 was measured in duplicate by both GammaCoat kits in the sera

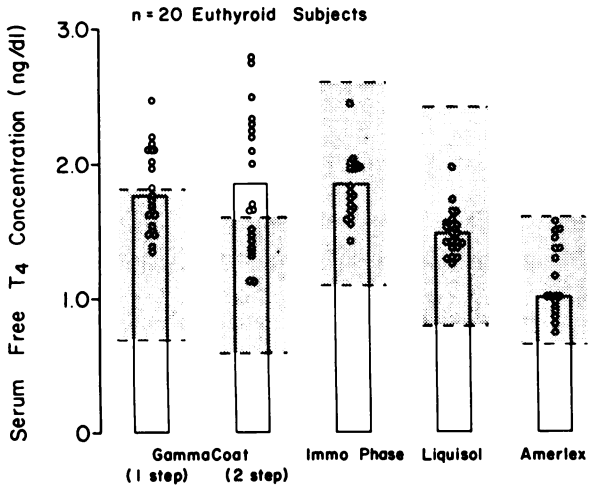

FIG. 1. Serum FT_4 (RIA) in 20 normal subjects measured by five commercial kits. Shaded areas indicate normal range for each test, and bars show mean values for each test.

collected and stored in both kinds of tubes. All samples were evaluated in one assay. The results are shown in Fig. 2. Values for FT_4 in serum samples collected in tubes without silicon coating were in the normal range in both kits. The FT_4 was always higher in both GammaCoat methods in serum collected and stored in silicon-coated tubes, as compared with values in serum collected and stored in tubes without silicon coating ($p < 0.001$, paired t-test). In the GammaCoat one-step assay, two of ten samples were above the normal range, and in the GammaCoat two-step assay, six of ten samples were.

These findings suggest that blood collected in at least some batches of silicon-coated vacutainer tubes result in spuriously elevated FT_4 values when measured by either the one-step or two-step GammaCoat methods. The explanation for these observations remains unknown. Since silicon-coated tubes do not appear to affect other methods for measuring FT_4 by RIA, it seems likely that silicon must specifically interfere with the assay involving the antibody-coated RIA tubes. It is suggested, therefore, that until further studies are carried out, tubes should not be silicon coated if used in collecting blood and storing serum for measurement of FT_4 with the GammaCoat kits.

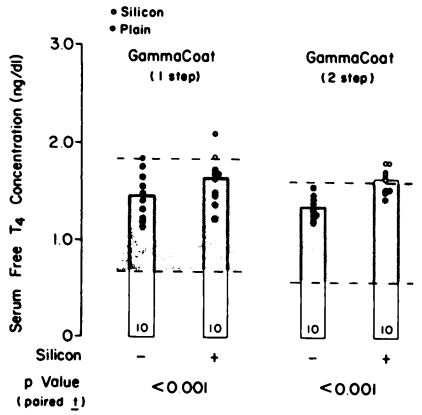

FIG. 2. Serum FT_4 (RIA) in ten normal subjects measured by GammaCoat one-step and GammaCoat two-step kits. Black dots represent blood samples collected in tubes not silicon coated; open dots represent blood samples collected in silicon-coated vacutainer tubes. Shaded areas indicate normal range of each test; bars show mean values for each test; numbers in the bars show numbers of subjects evaluated. Statistical analyses are performed by paired t-test.

RAJATA RAJATANAVIAN
LAWRENCE FOURNIER
CYNTHIA M. ABREAU
LEWIS E. BRAVERMAN
University of
Massachusetts
Medical School
Worcester, Massachusetts

FOOTNOTES

* Clinical Assays, Division of Travenol Laboratories, Cambridge, MA.
† Corning Medical, Medfield, MA.
‡ Damon Diagnostic, Needham Heights, MA.
§ Radiochemical Center, Amersham, U.K.

ACKNOWLEDGMENT

Supported in part by Grant AM 18919 from the NIAMDD, Bethesda, MD.

REFERENCES

1. HENNEMANN G, DOCTER R, KRENNING EP, et al: Raised total thyroxine and free thyroxine index but normal free thyroxin. A serum abnormality due to inherited increased affinity of iodothyronines for serum binding protein. *Lancet* 1:639-42, 1979
2. LEE WNP, GOLDEN MP, VAN HERLE AJ, et al: Inherited abnormal thyroid hormone-binding protein causing selective increase of total serum thyroxine. *J Clin Endocrinol Metab* 49:292-9, 1979
3. RUIZ M, RAJATANAVIN R, YOUNG RA, et al: Familial Dysalbuminemic Hyperthyroxinemia. A syndrome that can be confused with thyrotoxicosis. *N Eng J Med* 306:635-9, 1982

Automatic Edge Detection of Scintigraphic Images

It may be appropriate now to reflect on the great efforts that are being made in automatic edge detection of scintigraphic images, especially in relationship to cardiac left ventricular wall motion studies. The academic exercise is noble, but we should consider what the thrust of the effort is. If the thrust is to automate the study so that minimal intervention of a trained physician is required, the experimental studies should include an indication of the time saved compared with manual methods for defining the left ventricular wall. They should be done in an average clinical setting that includes patients with tortuosity of the aorta, with abnormal contours of underlying left atria, and with activity of radiopharmaceuticals in other organs that may be included in the frame.

If the thrust is toward a more uniform computer treatment of the studies, the experiment must show us variance statistics demonstrating uniformity or nonuniformity of the technique in comparison with the manual method. Alternatively, if we are attempting to show greater accuracy in the technique, comparison of the edge detection algorithm, the manual technique, and a ventriculography gold standard should be made.

Unfortunately, in the effort to make progress in automated