Letters to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1,000 words (typed double space) in length, and may be subject to editing or abridgement.

Local Cerebral Blood Flow by Xenon Enhanced CT

To the Editor:

We take exception to the remarks of Gur et al in their recent Progress in Cerebrovascular Disease article (*Stroke* 13: 750–758, 1982), which may mislead your readership as to the magnitude of the errors associated with xenon CT measurements of rCBF. In discussing our error analysis of the single-scan "autoradiographic" approach to xenon CT rCBF measurements[1] (an approach originally championed by Gur and his colleagues[2]), Gur et al fault us for using the fast-flow component, f_g, rather than "total flow" as the reference flow in our definition of percent error. They go on to conclude that "if one corrects for this mistake the errors are significantly lower than reported."

As is apparent from figures 1 and 2, which depict the effect of tissue (gray matter-white matter) heterogeneity *in the absence of CT noise*, the magnitude of measurement error depends upon (i) whether gray matter (GM) flow, f_g, or "total flow," $f_t = w_g f_g + w_w f_w$ [where w are proportional weights, and the subscripts g and w refer to gray and white matter (WM), respectively], is used as the reference flow and (ii) whether λ_g or λ_t [$= w_g\lambda_g + w_w\lambda_w$] is used as the blood-brain partition coefficient for xenon in Kety's blood flow equation. Three definitions of percent error (E_1, E_2, E_3) are illustrated: $E_1 \equiv (f_g - \hat{k}_g\lambda_g)/f_g$, $E_2 \equiv (f_t - \hat{k}_t\lambda_t)/f_t$ and $E_3 \equiv (f_t - \hat{k}_g\lambda_g)/f_t$, where $\hat{k}_g$ and $\hat{k}_t$ are the solutions to Kety's equation when λ_g and λ_t, respectively, are substituted for the partition coefficient. We originally proposed E_1 to emphasize that, in a one-compartmental model, an anatomic region of interest (ROI) is presumed to be homogeneous[1]; the quantity $\hat{k}_g\lambda_g \equiv \hat{f}_g$ was therefore interpreted as estimated GM flow, and the "true" GM flow, f_g, was taken as the reference flow in Equation E_1. If, however, one measures (or extrapolates) the regional partition coefficient, this "measured λ" is, in a heterogeneous ROI, the weighted average of GM and WM partition coefficients, and the quantity $\hat{k}_t\lambda_t \equiv \hat{f}_t$ could be interpreted as estimated "total flow," though the physical meaning of $\hat{f}_t$ is problematical. If f_t is taken as the reference flow, then E_2 is probably an appropriate definition of percent error. In contrast, the use of E_3, proposed by Gur et al[3] as the most favorable definition of percent error, cannot be justified; $\hat{k}_g\lambda_g$ *should not be taken as an approximation of total flow, and the use of* f_t *as the reference flow is inappropriate.* Using the parameter values in the legend to figure 1, errors predicted by E_3 are significantly lower than those predicted by E_1 or E_2. However, as f_g and λ_g decrease (as, for example, in stroke[4]), the magnitude of E_3 may exceed that of E_1 or E_2. This is especially apt to occur with the longer inhalation/scanning times required to achieve adequate enhancement under low-flow conditions (fig. 2). Parameter-specific values do not justify the use of E_3 as an estimate of the accuracy of autoradiographic xenon CT rCBF measurements.

While we applaud the enthusiasm of Gur et al, we must insist that enthusiasm is not an adequate substitute for critical judgement.

D. A. Rottenberg
H. C. Lu
Department of Neurology
Memorial Sloan-Kettering Cancer Center
1275 York Avenue
New York, NY 10021

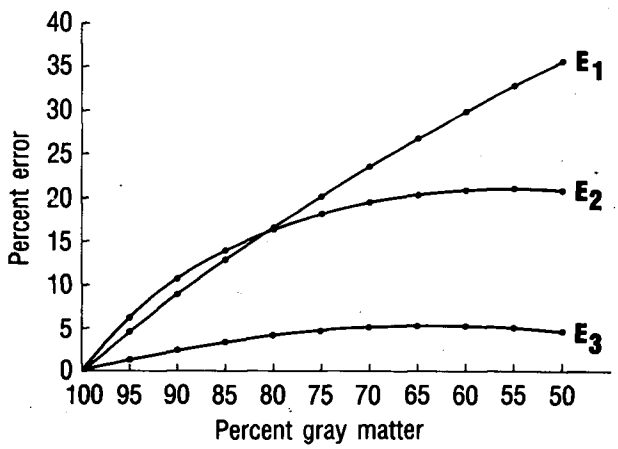

FIGURE 1. *Parameter values used to generate error curves: f_g = 0.64 ml/min/g, f_w = 0.225 ml/min/g, λ_g = 0.8, λ_w = 1.5, T [scan time] = 2.5 min; the arterial input was simulated as 1 − exp(−mt), where m = 1.4 min^{-1}.*

References

1. Rottenberg DA, Lu HC, Kearfott KJ: The *in vivo* autoradiographic measurement of regional cerebral blood flow using stable xenon and computerized tomography: the effect of tissue heterogeneity and computerized tomographic noise. J Cereb Blood Flow Metabol **2:** 173–178, 1982
2. Drayer BP, Gur D, Wolfson SK Jr, Cook EE: Experimental xenon enhancement with CT imaging: Cerebral applications. Am J Radiol **134:** 39–44, 1980
3. Gur D, Shabason L, Wolfson SK, Yonas H, Good WF: LCBF by xenon enhanced CT imaging. J Cereb Blood Flow and Metabol, in press
4. Drayer BP, Gur D, Yonas H, Wolfson SK Jr, Cook EE: Abnormality of the xenon brain-blood partition coefficient and blood flow in cerebral infaction: an *in vivo* assessment using transmission computed tomography. Radiology **135:** 349–354, 1980

The authors reply:

In their letter Drs. Rottenberg and Lu persist in their criticism of the "autoradiographic technique" for measurements of Local Cerebral Blood Flow (LCBF) by Xenon enhanced CT, and they remind the reader that it was "originally championed by Gur and his colleagues." We

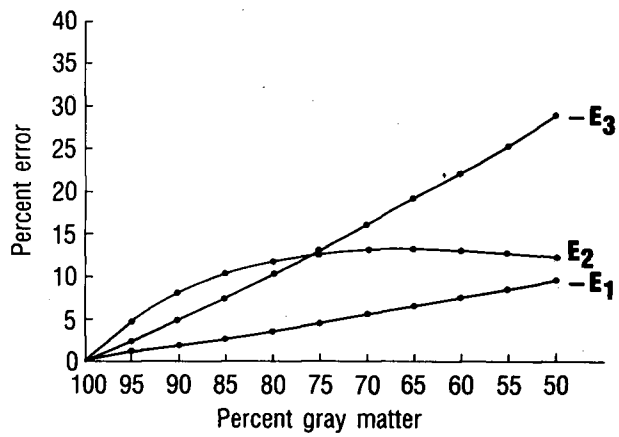

FIGURE 2. *Parameter values used to generate error curves: f_g = 0.32 ml/min/g, f_w = 0.225 ml/min/g, λ_g = 0.64, λ_w = 1.5, T = 3.5 min; the arterial input was simulated as 1 − exp(−mt), where m = 1.4 min^{-1}. [At T = 3.5 min, gray matter enhancement, $C_g(T)$, has attained 73% of its asymptotic value vs 57% at T = 2.5 min.]*

must admit that we are proud to have "originally championed the autoradiographic approach to Xenon/CT LCBF measurements" at a time when most CT scanners were slow (≥ 20 seconds scan time) and interscan delays were much longer (≥ 30 sec) than those currently available on many machines. There is no doubt that this method is now outdated. Since 1979–80 we, along with other groups, have been developing and using more sophisticated multivariable methods of analysis such as the weighted mono- or bi-compartmental least square fits. We believe that the true flow through a tissue volume should be used as a reference flow in error analyses and therefore, we do agree with Rottenberg, et al that what they define as E_2 is the error due to heterogeneity if the mono-compartmental model is used. Rottenberg's data show that E_2 is significantly smaller than E_1 in tissue with a significant mixture (percent gray ≤ 75%). Therefore, the statement we made in our recent review in STROKE is fully supported by their own data. The rest of the story has already been published and rebattled in the Journal of Cerebral Blood Flow and Metabolism and we see no reason to repeat it here.

David Gur
Sidney K. Wolfson, Jr.
Howard Yonas
Walter F. Good
Leonard Shabason
Department of Radiation Health
University of Pittsburgh
Pittsburgh, Pennsylvania 15261

Atriopathic Arrhythmias — Sick Sinus Syndrome

To the Editor:

I would like to comment on the paper of Abdon et al in: Stroke 13 (6), 832–837, 1982, by the following letter-to-the-Editor:

The study of Abdon et al[1] demonstrates that the incidence of finding the heart as the source of a focal cerebral infarction is related to the intensity of investigating the heart as such. In their study on long-term electrocardiographic recording they found a significant higher prevalence of "atriopathic arrhythmias" in a population of stroke patients than in a reference group. Sick sinus syndrome was one of these arrhythmias and it was present in 19 of 88 stroke patients and in only 9 of 103 patients of the control group. I wonder what strategy the authors apply when sick sinus syndrome is a fortuitous finding, and when it appears to be present in a stroke patient. Is anticoagulant therapy indicated? The authors use the temporal pattern at stroke onset as the only criterium to distinguish embolic from thrombotic infarction and found approximately the same percentage of atriopathic arrhythmias in both groups. Does this imply that these arrhythmias occur in patients with thrombotic stroke while the cardiac arrhythmia is not causally related to the occurrence of the stroke, or was the prior clinical diagnosis incorrect and suffered the 15 patients in the supposed thrombotic group in fact a cerebral embolus? This point could be relevant regarding anticoagulant treatment.

Sincerely Yours,

Jan Lodder
Dept. of Neurology.
Rijksuniversiteit Limburg,
P.O. Box 616
6200 MD Maastricht
the Netherlands

References

1. Abdon NJ, Zettervall O, Carlson J, Berglund S, Sterner G, Tejler L, Turesson J: Is occult atrial disorder a frequent cause of non-hemorrhagic stroke? Long-term ECG in 86 patients. Stroke **13:** 832–837, 1982

The authors reply:

We are pleased to answer the questions raised by Dr. Lodder. In our report the sick sinus syndrome (SSS) was present in 21 of 86 stroke patients. It has been shown that persons with stroke and SSS, even where the etiological connection is uncertain, have a future risk for cerebral emboli of 7% per individual and year.[1] We therefore find preventive measures advisable where possible and subscribe to the following general policies:

1) If other aggravating drugs are present, i.e. beta blockers or digitalis in the case of sinus bradyarrhythmia, they should be withdrawn and arrhythmia re-evaluated.

2) Where possible, anticoagulants should be given.

Due to the high frequency of concomitant disease in this patient group anticoagulants are often inadvisable and individual judgement must be made.

We have followed tradition in classifying stroke which occurs during sleep or with unclear onset as "thrombotic". Some of these strokes may well have been embolic in origin. Only one patient with a "thrombotic" stroke and atriopathic arrhythmia demonstrated progessive neurological deficit after admission. We are more inclined to regard the classification of stroke as embolic or thrombotic using only anamnestic data as insufficient than to consider the presence of atriopathic arrhythmia in the "thrombotic" group as purely coincidental.

Yours sincerely,

Nils-Johan Abdon, M.D.
Gunnar Sterner, M.D.
Joyce Carlson, M.D.
Ingemar Turesson, M.D.
Olle Zettervall, M.D.
Stig Berglund, M.D.
Lars Tejler, M.D.
Department of Medicine
University of Lund
Malmö General Hospital
S-214 01 Malmö, Sweden

References

1. Abdon NJ, Jönsson BM: High risk of systemic embolization in episodic sick sinus syndrome. *In:* Meere C, ed. Proceedings of the VIth world symposium on cardiac pacing. Montreal Pacesymposium: Chapter 17-11, 1979 (PACE **2:** A50, 1979).

Hypertensive Encephalopathy

To the Editor:

Dinsdale,[1] in his recent review of hypertensive encephalopathy (HTE) in this journal; mentions sodium nitroprusside (SNP) as often being the initial drug of choice in the treatment of HTE. While this choice is supported by a large segment of the available neurology and internal medicine literature, we feel that a significant amount of theory and objective information exists that make this drug appear less than optimal. The danger in use of SNP is the same mechanisms as for other direct acting vasodilators: cerebral arteriolar dilation allows delivery of more pressure to the microvascular bed, hence increased edema, and increase in cerebral blood volume (CBV), both of which increase intracranial pressure (ICP) when intracranial compliance is low.[2, 3]

There would not be a problem in using SNP in HTE if there was not a problem with either intracranial compliance or ICP. However, this is not the case. In a study reported in 1954, elevated lumbar pressures were found in 39% of patients with HTE.[4] More recently, Griswold[5] measured ICP with a subdural bolt in three children with stage III coma from HTE. ICP was found to be elevated in two of these patients with a range of 32–70 mm Hg.

Studies[2, 6, 7] have already demonstrated a significant increase in ICP and decrease in CPP while using SNP. One study[7] looked at ten patients with intracranial masses and demonstrated marked increases in ICP with a diminished CPP while using SNP, leading them to conclude that SNP should not be used in patients with increased ICP unless measures to improve intracranial compliance are instituted prior to its use. In a comparison of 45 patients in which deliberate hypotension was used for neurosurgery, in normocapnic patients SNP caused a significant rise in