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D Gur and L Shabason

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to the total surface area of the scan slice that any averaging phenomenon would not be of any magnitude.

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Lesley A. Cala
Gary W. Thickbroom
John L. Black
David W.K. Collins
Frank L. Mastaglia
Queen Elizabeth II Medical Centre
Nedlands, Western Australia, 6009

Local Cerebral Blood Flow Measurements

We read with interest the paper, "Local cerebral blood flow measured by CT after stable xenon inhalation" [1] which appeared in the August 1980 *AJR* and the May/June 1980 issue of *AJNR*. We disagree with a number of statements made in this article and question others.

The authors state in the abstract that "local cerebral blood flow measurements are possible with a single 1 min scan." We believe this statement should be qualified. An estimate of blood flow may be based on one datum point requiring at least two scans (a baseline and an enhanced image) only if blood:brain partition coefficients (λ) are assumed known. However, this approach ignores an important advantage of the "xenon methodology". Partition coefficients can be derived when additional enhanced images are acquired when equilibrium is generally reached within 4 min in tissue with fast flow but it may require 30 min or more in tissue with slow flow (normal or diseased) [2]. We emphasize that all "direct" and "indirect" methods require estimates (measured or approximated) of xenon concentration in both arterial blood and tissue at equilibrium. There are other methodologies which do not require scanning at equilibrium, however, they do require multiscanning during buildup and multivariable analysis to obtain estimates for both flow rate (k) and partition coefficient (λ). These techniques are not possible with a single scan and the derived estimates improve significantly with additional scans [3].

The authors emphasize their preference of using "slow" scans (about 60 sec) for blood flow studies. We believe slow machines can be used but special consideration should be given to the effect of relatively poor temporal resolution. The use of midscan as the effective scan time results in systematic errors that depend on scan time (t) and flow rate constants (k) (Spital R, personal communication). These errors may be significant during the rapid buildup phase (first minute) in tissue with rapid flow. We believe that the in vivo autoradiographic technique is not the best or the most precise. Its major advantage lies in its simplicity since it requires few computations. It has been shown that other techniques yield better estimates (small errors) of flow [3].

We fail to understand how enhancements of about 18 CT units in gray matter as shown in figure 2 and an error of ± 1 CT unit on both baseline and enhanced scans, yield errors of under 5% of blood flow (table 3). In addition, we cannot comprehend how errors of derived flow based on estimates of both blood:brain partition coefficient (λ_i) and flow rate constant (k_i), $F_i = \lambda_i k_i$, can be less than the error of partition coefficient alone (table 3).

We also question a number of statements made in the article concerning the results shown in figure 7. The low blood flow estimates based on a scan performed within the first minute of xenon inhalation may be due to a number of factors:

A. If the expired gas is monitored but true end-tidal values are not used for iteration of the convolution integral (equation 6), the

xenon buildup rate in arterial blood is overestimated and flow may be significantly underestimated.

B. The error in using midscan as effective scan time is more pronounced in the first minute during rapid buildup.

We agree with the authors that scanning during the first minute of xenon inhalation should not be recommended due to the limited enhancement and the significant increase in the errors of estimated blood flow. This is particularly true when the in vivo autoradiographic technique is used.

We concur with the authors that cerebral blood flow decreases under anesthesia. Table 5 indicates a decrease of about 40% in fast flow and a somewhat lesser decrease in slow flow. On the other hand, figure 7 shows a dramatic decrease of about a factor of three in flow. When the in vivo autoradiography method is used, tissue volumes intermixed with small quantities (10%–20%) of tissue with slow flow (white matter or other), will demonstrate a similar flow pattern, namely, a decrease in estimated flow with time. We think this effect should be seriously considered before attributing the dramatic decrease in estimated flow solely to anesthesia.

David Gur
Leonard Shabason
University of Pittsburgh
Pittsburgh, PA 15261

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Reply

The comments of Gur and Shabason have been noted and we thank them for their interest in our paper. We agree that at least one (and preferably two or three) steady state (noncontrast) brain scans measured in Hounsfield units (H) must be obtained before local cerebral blood flow measurements can be calculated from ΔH changes from single 1 min scans during stable xenon inhalation by the in vivo autoradiographic or any other method. Local cerebral blood flow values can only be calculated with accuracy if the λ has been measured at saturation. These questions are discussed on pages 216–220 of our paper. For example, on page 218 we state: "The ΔH units for each region of interest during saturation for each of two brain sections, recorded concurrently 4 mm apart, were measured by examining volumes as small as 0.04 cm^3 (4 voxels). At 1 min intervals, the Hounsfield units were reproducible with low standard deviations and computed blood flow values showed statistically significant reproducibility. Thus, minute-to-minute flow values were obtained." The article also explained how λ is measured after 10 min inhalation, that regions of low flow need extrapolation of λ to infinity or to tissue equilibrium, and stressed the importance of this measurement. We also discussed and gave results of other measuring methods from serial scans during buildup or washout phases based on modifications of the Fick principle. In later publications we have confirmed that λ undergoes changes in

pathologic tissue, and this may be of value in evaluating infarction and edema [1-6].

The xenon CT cerebral blood flow method has now been successfully applied to 53 human subjects. Detailed descriptions of these methods with reports of local cerebral blood flow and $L\lambda$ values in health and disease are currently in press in *Stroke* [5] and a review [6]. In this paper [5], in collaboration with Walter Obrist, we report a newly developed computer program that calculates $L\lambda$ (extrapolated to infinity) and cerebral blood flow values derived from double integration of the end-tidal xenon curves and tissue ΔH changes. This is a similar approach to Kanno and Lassen's [7] theoretical model which was mentioned in our AJNR paper and is similar to Wong's theoretical model. At least two slices (and preferably more) ΔH values are required during saturation or desaturation in addition to the steady state (noncontrast) values. This method gives highly reproducible values for cerebral blood flow and $L\lambda$ measured in human subjects provided scans are not made in the first minute because of problems with signal-to-noise ratio and delays between the rapidly changing rise time of arterial (end-tidal) xenon and tissue ΔH . We agree that this method gives smaller errors in computing flow than the in vivo autoradiographic method.

In the *Stroke* article, we also measured the signal-to-noise ratio for the EMI 1010, 1 min scanner and showed it to be better than the GE 8800 fast scanner. I have discussed with Dr. Gur the question of temporal resolution with the "slow scans" when EMI Medical Inc. was asked to make special studies of this question. John Wholahan, then working for EMI Medical Inc. reported to us in January, 1980 that he had simulated the effects of changing attenuation coefficients during the course of a 1 min scan and he was "pleased to report that virtually no error will be introduced by the assumption that the Hounsfield values represent the true attenuation coefficients at the midpoint of the scan. This is certainly true if the rate of increase in attenuation coefficients is constant throughout the scan, and even in the case where the rate of increase is changing, as when you approach saturation, no appreciable error will be introduced."

As we stated in the *AJNR* paper, we agree with Gur and Shabason that cerebral blood flow calculations should not be based on data obtained in the first minute. In their critique, they appear to have confused tables 3 and 4 and misread our measurement errors for local cerebral blood flow and $L\lambda$. The mean error for blood flow was $10\% \pm 4.1\%$ as shown in table 4 (not table 3) and mean error was $5.2\% \pm 1.9\%$ for $L\lambda$ (not, local cerebral blood flow).

We agree with their listed explanations A and B, for errors introduced when xenon scans are made during the first minute, and we agree that problems of tissue overlap or partial volume effect must be considered when interpreting data. This is less of a problem

in the human brain when volumes of gray and white matter are about 15 times larger than those cursored in the baboon.

We thank the authors for their comments and share with them our concern for defining the reliability, reproducibility, limits, and advantages of a scientific method that may have considerable application in future clinical research.

John S. Meyer

Takahiro Amano

Terry Shaw

Veterans Administration Medical Center
Houston, TX 77211

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