Stability and Sensitivity of CBF Indices in the Noninvasive $^{133}$Xe Method

W. D. OBRIST$^1$ and W. E. WILKINSON$^2$

Although the two-compartment model for $^{133}$Xe inhalation/IV injection studies (Obrist et al. 1975) has proven useful in a variety of applications, under certain pathologic conditions the computed CBF parameters become quite unstable due to shifts in compartment size (Risberg et al. 1975). This phenomenon, referred to as “slippage,” applies not only to the noninvasive method, but also to compartmental variables of the intracarotid $^{133}$Xe technique (Waltz et al. 1972; Iliff et al. 1974; Heiss et al. 1975; Enevoldsen and Jensen 1977).

Adequate compartmentalization requires distinctly separate blood flow components that are within the resolving power of multiexponential analysis, a situation that prevails in healthy subjects where gray and white matter have two different distributions of flows (Reivich et al. 1969). Unfortunately, pathologic tissue (or extreme physiologic conditions) may not provide such a clear separation of tissue components, so that some gray matter may “slip” into the slow CBF compartment, or vice versa. When this happens, compartmental flows vary inversely with the relative weight of the fast compartment. This not only presents difficulties in the anatomic designation of flow as gray or white and in the assignment of proper partition coefficients, but the computed blood flow values become unstable, showing large interregional and intertest variability. Although such instability can be reduced by obtaining higher count rates and/or extending the length of curve analyzed (Obrist et al. 1975), even these procedures may not solve the basic problem when tissue components are overlapping.

One solution to this problem is the use of a noncompartmental index similar to the height-over-area analysis of the intracarotid technique (Hoedt-Rasmussen et al. 1966). Indeed, Bruce and co-workers (1975) found that CBF$_{15}$ (height-over-area to 15 min) was relatively immune to shifts in compartment size.

Another approach is the use of slope measurements such as the “initial slope index” (ISI), introduced by Risberg and co-workers (1975) for the $^{133}$Xe inhalation method. Although considerably more stable than compartmental variables, this index lacks the sensitivity to high flows obtained by the initial slope of the intracarotid technique (Olesen et al. 1971).

The present study was designed to assess the effect of slippage on both compartmental and noncompartmental CBF indices, and to compare the sensitivity

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1 University of Pennsylvania, Philadelphia, PA, USA
2 Duke University, Durham, NC, USA
of the several indices with respect to changes in fast compartment flow. Relevant information was also obtained on the length of clearance curve analysis.

**Methods**

Three sets of computer simulated head curves were constructed, each based on 1 min of $^{133}$Xe inhalation and containing 100 random patterns of Poisson-distributed noise. The three curves represented: (1) a normal resting CBF, (2) an elevated flow typical of cortical activation, and (3) a pathologically reduced flow with overlapping tissue components. Except for noise, count rates for the three curves were equivalent (peak = 1000/s). A three-compartment model was used to generate the curves, consisting of gray matter, white matter, and extracerebral (scalp) contamination, which had relative tissue weights of 0.4, 0.4, and 0.2, respectively. The individual compartments were constructed from a Gaussian distribution of rate constants, as described previously (Obrist et al. 1975). Air passage artifact (6% at 1 min) was added to each curve. True cerebral values for the several CBF variables (independent of noise and extracerebral contamination) are given in Tables 1 and 2.

A two-compartment analysis was performed on the three different head curves using the 20% point of the end-tidal air curve as a start-fit time (Obrist et al. 1975). Curve fitting ended at 11.0 min, except in the case of pathologically reduced flow, where the analysis time was extended to 14.0 min for comparison. The traditional compartmental variables, $f_1$ (fast flow), $f_2$ (slow flow), $w_1$ (relative tissue weight), and FF$_1$ (fast compartment fractional flow) were compared with two noncompartmental estimates proposed by the authors (Obrist and Wilkinson 1980). The latter, designated CBF$_{ex}$ and CBF$_{15}$, are mathematically equivalent to the height-over-area index employed in the intracarotid technique, where the upper limit of integration is infinity and 15 min, respectively. Each of these variables was also compared with the initial slope (IS), defined as the tangent at time zero of an equivalent bolus injection (Obrist and Wilkinson 1980), and with the initial slope index (ISI) of Risberg and co-workers (1975).

In terms of the four unknown parameters $(k_1, k_2, P_1, P_2)$ determinend by least squares fit:

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FF_1 = P_1/(P_1 + P_2) \quad \text{and} \quad FF_2 = 1.0 - FF_1,
\]

\[
\text{CBF}_{ex} = \frac{\tilde{\lambda}}{(FF_1/k_1 + FF_2/k_2)},
\]

\[
\text{IS} = FF_1 \cdot k_1 + FF_2 \cdot k_2,
\]

where $\tilde{\lambda}$ is the assumed mean tissue–blood partition coefficient. CBF$_{15}$ is the same as CBF$_{ex}$, except for correction factors that adjust the integration time.

**Results**

Table 1 presents the findings for normal resting and activated flows, while Table 2 shows the findings for reduced flow with overlapping tissue com-