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Accuracy of Xenon CT Measurement of Cerebral Blood Flow

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In recent years, quantitative determination of cerebral blood flow (CBF) by xenon-enhanced CT has become an increasingly important research and clinical tool. Concurrently, the possibility that inhalation of stable xenon in the concentrations required for this procedure might itself alter CBF also has received increasing attention. Several studies [1–6] have examined this problem by using various concentrations of xenon in both humans and research animals. These generally have shown an increase in CBF during xenon inhalation, although in some cases the opposite effect has been observed. The magnitude of the changes ranged from −25% to +100% in animals and from −20% to +56% in humans. Measurements of CBF in these studies were obtained by using microsphere or in vivo radionuclide techniques. As these methods cannot be repeated at intervals of less than a few minutes, the time course of the changes has been difficult to determine.

In the January 1990 issue of the AJNR, Giller et al. [7] described a study in which continuous transcranial Doppler sonography (TCD) was used to measure changes in blood velocity in the middle cerebral artery (MCA) during inhalation of stable xenon. Xenon concentrations and inhalation times were similar to those used in most commercially available xenon CT systems. They found an average increase in MCA blood velocity of 38% in 85% of their patients and an unspecified decrease in velocity in the other 15%. The changes in blood velocity began 1–2 min after inhalation started and continued to rise for several minutes thereafter. They appeared to be attenuated by hyperventilation during the inhalation of xenon, although this was not examined specifically.

Along with blood velocity, measurement of vessel diameter is also necessary to calculate actual blood flow through the vessel [8]. If the diameter of the vessel is assumed to be constant, a change in blood velocity will proportionally reflect increased flow through the vessel and at equilibrium will be accompanied by increased flow in the distal territory supplied by that vessel. During distal vasodilatation or vasoconstriction, distal blood flow transiently may be greater or less than flow in the parent artery [8], but at equilibrium, total flow in the parent vessel and its distal circulation must be the same. Giller et al. did not measure the diameter of the MCA, which is difficult to obtain with TCD technique, or blood pressure. However, increased MCA blood velocity was accompanied by, and slightly preceded by, a decrease in the Gosling pulsatility index. This suggests that the increase in velocity was due to decreased distal vascular resistance rather than to changes in the diameter of the MCA or in blood pressure, and implies that CBF ultimately was increased at the tissue level.

Results similar to those of Giller et al. were noted in two TCD studies of xenon flow activation in humans presented at the recent International Conference on Stable Xenon/CT CBF, held in February 1990 in Orlando, FL. In one study, Marks found that the blood velocity in volunteer subjects increased an average of 40% during inhalation of 33% xenon. The change in velocity was only 11% during the first 3 min; the remainder of the increase occurred during the next 4 min. In the other study, Broich et al., using 28% xenon, showed an average increase in MCA blood velocity of 38–42%, with a decrease in pulsatility of 12%. Changes in velocity were detected first at 1 min, were maximal at 5–10 min, and returned to baseline 1–2 min after xenon inhalation was finished.

The time course and magnitude of the changes described

This article is a commentary on the preceding article by Good and Gur.

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by Giller et al. and in the other TCD studies have important implications for the accuracy of xenon CT scanning and have led to efforts to examine the effects of these changes quantitatively. The results of one such study are reported by Good and Gur [9] in this issue of the AJNR. They used a computer simulation to study the effects of a 15%, 30%, or 45% linear increase in CBF occurring between 1.5 and 2 min after the start of xenon inhalation. The effects of the increase in flow on the calculated CBF were simulated by using washin, washout, and combined washin and washout protocols. The simulations were carried out over a range of baseline blood-flow and $\lambda$ values, including those characteristic of normal gray and white matter.

Flow activation effects were minimal when a washin protocol was used with a 5-min inhalation and scans every minute. This protocol is similar to those most often used with commercially available equipment. It gave maximal errors in the calculated flow values, relative to the actual initial values used to program the simulation (before the flow increase), of 2.9% for normal gray matter and 4.5% for normal white matter. Errors were higher for the washout and the combination washin and washout protocols, reaching a maximum of 40.8% for a washout protocol and 45% flow activation. Errors for other combinations of initial blood-flow and $\lambda$ values, perhaps including those characteristic of injured or ischemic gray and white matter, were not reported but would be of interest.

These findings are similar to those reported by Lindstrom at the International Conference on stable Xenon/CT CBF. He examined the effects on the flow calculation of a 40% linear "ramp-up" increase in CBF between 1.5 and 2.5 min in a computer simulation of a 7-min xenon inhalation and scans obtained at 1.5, 3, 5, and 7 min. Calculated flow values were, at most, 5% high for gray matter and 12% high for white matter. These data confirm that with the commonly used washin scanning protocols and short inhalation times of less than 7 min, the errors induced by xenon flow activation are relatively small and fall within the 15% to 20% limit of the overall accuracy of this technique [10].

Previous studies have examined other aspects of the quantitative accuracy of xenon CT measurements of CBF. Several of these [11–13] have found good correlation between CBF values determined by using xenon CT vs radiolabeled microspheres in baboons. These were done by using prototypes of commercially available systems. Similar findings were reported recently from a study [14] that compared xenon CT vs $^{14}$C-iodoantipyrine for measurement of CBF. Computer simulation studies of the errors introduced into xenon CT scanning by estimation of the arterial xenon uptake from end-tidal data [15], and by CT noise and tissue heterogeneity [16], showed that the errors were relatively small. The changes in xenon CT-derived flow measurements that occur after physiological challenges are similar to those found by other methods [13, 17]. Clinically, flow values less than 10 ml/100 g/min are associated with clinical and follow-up conventional CT evidence of cerebral infarction, whereas lesser degrees of ischemia may be associated with recovery of neurologic function and absence of a permanent anatomic lesion [18]. These findings, which are similar to our own observations (unpublished data), are also similar to threshold values for infarction and reversible ischemia found experimentally [19].

The results presented by Good and Gur [9], and those described by Lindstrom at the Florida meeting, provide further evidence of the reliability of xenon CT measurement of CBF with the short inhalations commonly used. With longer inhalation times, the effects of flow activation are magnified, and it would be prudent for those investigators who use longer inhalations or more unusual study protocols (washout or washin and washout) to examine the effects of flow activation on their own measurements. Additional studies also may be needed to define more precisely the effects of flow activation on measurements of CBF in injured tissue. Nevertheless, more widespread acceptance and application of xenon CT technology should not be delayed by excessive concern about xenon-induced flow activation. The weight of evidence indicates that with commonly used techniques, flow activation does not significantly affect the clinical accuracy or usefulness of xenon CT-determination of CBF.

REFERENCES