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Stable Xenon CT CBF: Effects of Blood Flow Alterations on CBF Calculations During Inhalation of 33% Stable Xenon

Jens-Peter Witt, Kurt Holl, Hans Egmont Heissler, and Hermann Dietz

Recent studies in humans on the effect of inhaling 25–35% stable xenon reported an average increase of cerebral blood flow from 13% to 38% [1–3]. While Giller et al. [3] found a marked delay of about 2 min between the onset of xenon inhalation and the rapid increase of blood flow velocity, results obtained by Ueltzen (Ueltzen J, personal communication) and our own findings (Holl K, unpublished data) indicated that the start of xenon inhalation is followed immediately by an almost linear rise of flow velocity in the middle cerebral artery. On the other hand, Giller et al. [3] reported a marked decrease of flow velocity during xenon inhalation in two of his 13 volunteers, but he did not correct the transcranial Doppler (TCD) values for end-tidal pCO₂.

In our own study, 68 continuous and simultaneous TCD recordings (TC 2-64 B, EME, Überlingen, FRG) were performed in 58 patients with different diagnoses during stable xenon CT CBF measurements. We found an average middle cerebral artery velocity increase of 18% (Fig. 1). The rise is almost linear, and correlates with the corresponding tissue xenon enhancement as represented in Hounsfield units (r = .44, p < .001).

Giller et al. [3] argued that flow alterations might influence CBF calculations in an "unpredictable fashion." Recently, computer simulations have considered the effects of different ways of calculating wash-in and wash-out scanning protocols. The results indicated that in the worst-case scenario of a wash-out scanning protocol and a flow activation of +45%, which remains during the wash-out, the errors in derived flow values are +41% and +27% for gray and white matter, respectively. Flow values derived only from the wash-in scanning protocol were elevated by 3% and 4.5% for gray and white matter, respectively, during a flow activation of +45% (Good W, personal communication).

Materials and Methods

We simulated the influence of linear blood flow alterations induced by the inhalation of 33% stable xenon on the calculation of cerebral blood flow, taking into account that the flow map is derived from a 4-min xenon wash-in calculation protocol. The mathematical model is based on the Kety equation formulated for the behavior of free diffusible inert tracer in the human multicompartiment model [4]:

\[ C(T) = \lambda_k \int_0^T C_i(t) e^{-\lambda_k (t-t)} dt \]  

where \( C(T) \) = xenon concentration in brain tissue, \( C_i(t) \) = xenon concentration in arterial blood, \( \lambda_i \) = brain tissue-blood partition coefficient, and \( \lambda_k \) = flow constant of xenon enhancement in brain tissue.

![Graph showing linear alteration of mean flow velocity](image)

Fig. 1.—Almost linear alteration of mean flow velocity in middle cerebral artery during a 4-min inhalation period of a 33% xenon/67% oxygen mixture. Data were obtained during 68 stable xenon CT CBF studies in 58 patients with different diagnoses. Flow velocity (FV) values are given as percentage differences from baseline before xenon inhalation. (Measure of dispersion: standard error of mean.)

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Typical xenon enhancement in brain tissue, and $k_a = \text{arterial rate constant}$. Then we took a closer look at two exemplary theoretical brain regions: a purely gray matter region with a given partition coefficient $A_g$ and an arterial rate constant $k_a$, and a purely white matter region with a given partition coefficient $A_w$ and an arterial rate constant $k_a$. Substitution of solution (2) in (1) yields the analytical form of the time course of xenon enhancement in brain tissue in Hounsfield units (HU) [5]:

$$A(t) = A_g \lambda' \left(1 - e^{-\lambda' t}\right) - \frac{k_w}{k_w - k_i} \left(e^{-k_i t} - e^{-\lambda' t}\right)$$

where $A(t) = \text{brain tissue enhancement}$, $A_g = \text{arterial enhancement}$, $\lambda' = \text{brain tissue-blood partition coefficient}$, $k_w = \text{flow rate constant of xenon enhancement in brain tissue}$, and $k_i = \text{arterial rate constant}$. With regard to our clinical experience we assumed an arterial enhancement $A_g$ of 8 HU and an arterial rate constant $k_a$ of 2.5 min$^{-1}$. Then we took a closer look at two exemplary theoretical brain regions: a purely gray matter region with a given partition coefficient $\lambda = 0.8$ and a prestudy flow of 0.8 ml/g/min, and a purely white matter region with a given partition coefficient $\lambda = 1.6$ and a prestudy flow of 0.2 ml/g/min. The corresponding prestudy flow rate constants $k_i$ were assumed to be 1.0 min$^{-1}$ for gray matter and 0.125 min$^{-1}$ for white matter. Linear blood flow alterations were simulated beginning at the start of xenon inhalation and reaching $+18\%$, $+30\%$, $+50\%$, and $-20\%$ at the end of the inhalation period.

The flow rate constant $k_i$, which characterizes the flow alterations for a defined brain region was assigned a range of values during CT scanning. For each particular enhanced scan out of a series of six a new $k_i$ was calculated, and in the overlaid enhancement curves a slight distortion effect could be seen (Fig. 2).

**Results**

The new xenon enhancement values (Fig. 3) for brain tissue in Hounsfield units $C(t)$ were recalculated by (3) using Marquardt's nonlinear approximation algorithm. Both $\lambda_i$ and $k_i$ were reestimated and the tissue-specific blood flow recalculated. Results are displayed in Table 1. The table shows the stability of the $k_i$ values but also notable distortion of the $\lambda_i$ values.

**Discussion**

In summing up the results we were able to demonstrate the stability and robustness of flow calculations based on Kety's equation [4]. Even if the individual flow activation reaches $+50\%$ at the end of inhalation the estimated flow value ranges in the worst case only between $+6.7\%$ for gray matter and $+10.3\%$ for white matter from the prestudy flow. Taking into account the case of a $20\%$ decrease in cerebral blood flow during inhalation of 33% stable xenon, the derived flow values are lowered by 3.0% and 0.9% for gray and white.
TABLE 1: Recalculation of $F$, $k_1$, and $\lambda$ Values After Simulation of Linear Alterations of Blood Flow During Xenon Inhalation

<table>
<thead>
<tr>
<th>Prestudy Values</th>
<th>Recalculated Values</th>
<th>Percentage Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda$</td>
<td>$k_1$</td>
<td>$F_1$</td>
</tr>
<tr>
<td>G</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>W</td>
<td>1.6</td>
<td>0.125</td>
</tr>
<tr>
<td>G</td>
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<td>1.6</td>
<td>0.125</td>
</tr>
</tbody>
</table>

Note.—G = gray matter, W = white matter. $F$ (%) = flow alteration after 4 min inhalation of 33% xenon, $k_1$ (min$^{-1}$) = flow rate constant, $\lambda$ = brain tissue-blood partition coefficient for xenon, $F_1$ (ml/g/min) = cerebral blood flow. Values corrected for flow alterations are marked with index r.

matter, respectively. These reported effects are valid for the CT scanning protocol described above, which consists of two baseline scans and six enhanced images during xenon inhalation lasting for 4 min. Another result is that the robustness in computed flow values of white matter is purchased by an extreme distortion of the partition coefficient $\lambda$. This should warn us against using pure $\lambda$ maps.

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REFERENCES