PROGRESS IN CEREBROVASCULAR DISEASE:
Local Cerebral Blood Flow by Xenon Enhanced CT

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SUMMARY A noninvasive technique for measuring local cerebral blood flow (LCBF) by xenon enhanced x-ray transmission computed tomography (CT) has been developed and reported quite extensively in recent years. In this method, nonradioactive xenon gas is inhaled and the temporal changes in radiographic enhancement produced by the inhalation are measured by sequential computed tomography. Time dependent xenon concentration within various tissue segments in the brain are used to derive both local partition coefficient (λ) and LCBF. An assessment of this method reveals that although it provides functional mapping of blood flow with excellent anatomic specificity, there are distinct limitations. The assumptions underlying this methodology are examined and problems associated with various potential applications of this technique are discussed.

THE IMPORTANCE OF TECHNIQUES which measure cerebral blood flow (CBF) has long been recognized. A number of techniques have been developed in an attempt to find an in vivo methodology to map local or regional cerebral metabolic rates and/or CBF for normal or abnormal brain function. Most methods currently in use involve the external monitoring of the transit or clearance of inhaled or injected radio­tracer. Although these techniques have proven useful, they generally yield only gross estimates of cere­bral function within relatively large tissue volumes. This information is somewhat limited to relatively su­perficial levels of the cerebral cortex. Recent advance­ments in both single photon and positron annihilation emission computed tomography (ECT) permit improved anatomical resolution. While these tech­niques still suffer from inherent limitations of spatial resolution and require specialized imaging devices, they do allow functional measurements in deep struc­tures. The introduction of rapid, sequential trans­mission computed tomography (CT) provides a meth­od of monitoring changing tracer concentrations over time with a high degree of anatomic specificity. Although iodinated contrast media have been used to demonstrate qualitative flow patterns, methods to quantify local cerebral blood flow have had only limited success. In addition, clinically available con­trast media do not freely cross the blood-brain barrier; therefore, local tissue perfusion cannot be evaluated and quantitative information about local function cannot be inferred.

Over the past several years a number of groups have been investigating in vivo techniques in which local cerebral blood flow in extremely small tissue volumes can be derived from measurements of time dependent concentrations of nonradioactive xenon gas. These methods employ sequential CT scanning of one or more brain levels (slices) during the inhalation of xenon/oxygen mixtures in order to detect the build-up or wash-out of xenon in tissue. Since xenon is a freely diffusible tracer which readily crosses the blood-brain barrier, its time dependent concentration in tissue can serve as an indica­tor of tissue perfusion. Because of its relatively high atomic number (54), xenon yields measurable image enhancement even when it is inhaled in relatively low (subanesthetic) concentrations. The derivation of LCBF is based on the Fick principle and the underlying relationship has been described by Kety. Details of the methodology for deriving LCBF estimates from enhanced xenon CT have been described. In brief, the procedure requires the acquisition of three or more images preceeding, during and/or after a period of four to six minutes of xenon/oxygen inhalation. During this period xenon concentrations in the inspired and expired gas are monitored continuously and end­tidal xenon levels are assumed to be proportional to time dependent xenon concentrations in arterial blood. These data are then used in conjunction with time dependent xenon concentrations in tissue to derive partition coefficient (λ) and LCBF for each specific tissue of interest. This report is a review of the current status of LCBF measurements by xenon enhanced CT. Presented in it is a detailed discussion of a number of advantages and several distinct limitations of this methodology. While most of the illustrations are obtained from the authors own data files, an attempt is made to include observations and information.
which was obtained from several other investigators in this field.

**Theoretical and Computational Considerations**

a. Completeness of Diffusional Equilibrium (m factor)

Blood flow estimates which are derived from time dependent concentration measurements of diffusible indicator in tissue are based on the Fick principle, which states that tissue uptake of an indicator is equal to the amount supplied by the arterial blood less the amount drained or carried away by the venous blood. This principle was used by Kety to derive the relationship between LCBF and the concentrations of indicator in tissue and blood:19

\[ C(t) = \sum_i w_i \int_0^t C_a(u) e^{-k_i(t-u)} \, du \]  

(1)

where \( i \) symbolizes the various compartments to be considered (fast, slow) and \( w_i \) is the fraction of tissue in each of these compartments. If instantaneous equilibrium between arterial blood and the surrounding tissue exists the flow (1) is given by: \( f_i = \lambda k_i \). When such equilibrium cannot be assumed \( f_i = \lambda k_i / m \) where \( m \) is a number between 0 and 1 which measures the effectiveness of achieving equilibrium (at equilibrium \( m = 1 \)).24 Most measurements based on diffusible indicator techniques have assumed equilibrium, although a recent article challenges the validity of this assumption in tissue with fast flow.25 If this contention holds, the ratio (\( f_i / f_w \)) between LCBF in tissue with fast flow (i.e. gray matter) and slow flow (i.e. white matter) should be lower for diffusible indicator measurements as compared to other more direct methods (i.e. microsphere techniques). Data presented in a recent review of CBF measurements by many investigators indicate that the ratios between fast and slow flows when measured by diffusible indicators are not lower than the comparable ratios which are based on direct measurements.26 Hence, the published data does not support this contention. On the other hand, at extremely high flow states (\( \text{PaCO}_2 > 52 \text{ torr} \)) there are indications that diffusible indicator techniques yield lower results than obtained with microsphere techniques.44 If \( m \) does indeed decrease in high flow states, the implication exists that the lowered equilibrium may extend to other substances such as metabolism so that the "effective" flow is, in a sense, more meaningfully presented when the \( m \) correction is not made. Obviously, much is to be learned and deduced in this line of reasoning. An assumption that \( m \) is strongly dependent on gas concentration cannot be easily justified based on simple physical principles, therefore, \( m \) should not differ in Xe-133 measurements (low concentrations) and nonradioactive xenon enhanced CT studies (high concentrations). Therefore, unless there is more definitive evidence that \( m \) is significantly less than one for freely diffusible indicators, we believe that the assumption of "instantaneous equilibrium" may be used. In cases where \( m \) significantly deviates from one it can be speculated that diffusible indicators are more likely to better represent effective tissue perfusion than direct methods (i.e. microsphere techniques) while the latter is more likely to better represent actual blood flow.

b. Xenon Concentrations in Arterial Blood

A number of direct and indirect methods have been employed to monitor time dependent xenon concentrations in arterial blood. Two methods for direct measurements have been reported. The first uses the difference method whereby sealed arterial blood samples drawn at known time intervals, are monitored for \( \text{PaCO}_2 \) and \( \text{PaO}_2 \) and based on the assumption that nitrogen had been washed out prior to initiation of xenon inhalation (denitrogenation), \( \text{PaXe} \) can be estimated by subtraction of the above partial pressures and water vapor tension from the atmospheric pressure.27 If arterial-venous equilibrium can be assumed (heated palm or fingers), "Arterialized" venous blood could theoretically be used for this purpose as well. The second method involves CT scanning of blood filled syringes and directly measuring the enhancement to determine the xenon concentrations in the blood.21 Unfortunately, both methods are somewhat invasive, and significantly complicate the procedure.

In the indirect methods, end-tidal gas is monitored for time dependent xenon concentrations which are assumed to be in equilibrium with arterial blood. This assumption has been validated in several studies and it should also apply here.6 An exception is the case of severely impaired gas exchange in the lung. The methods utilizing this approach include the mixing and monitoring of minute quantities of radioactive xenon gas with the nonradioactive gas; the monitoring of thermal conductivity changes; or the direct mass spectrometric measurement of xenon concentration in expired gas (fig. 1).22 28 29 50 All indirect methods require that the estimated concentration in arterial blood be converted into equivalent enhancement in CT units \( [\Delta C(t)] \). This can be easily done if blood hematocrit is known and a technique dependent (kVp, mA) conversion factor is established for CT enhancement as a function of the amount of xenon dissolved in blood.17 22 It is interesting to note that the build-up or washout of xenon in arterial blood can be assumed to be monoexponential in most cases, a phenomenon that can significantly reduce the computational complexity of solving the convolution integral.20 21 51

c. Derivation of LCBF in a Single Region of Interest (ROI)

There are several indications that in many cases, tissue with slow flow exhibits monocompartmental behavior while tissue with fast flow appears to be multicompartamental.20 21 It is unclear at this point whether this phenomenon is attributable to the limitation of anatomic specificity (partial volume effects) or if there is indeed multicompartmental diffusion in tissue volumes consisting predominantly of gray matter.

Two methodologies for determination of LCBF and partition coefficients in a single region of interest (ROI) have been utilized. One methodology is based on an independent determination of partition coefficients in each ROI from a late scan, followed by the
derivation of flow rate constants from a single enhanced scan during build-up or washout phases ("in vivo autoradiography").

Each enhancement value [ACT(t)] can be used to derive a flow estimate which is then averaged (weighted or non-weighted) or several enhancement values can be used for curve fitting. The derivation of LCBF from a single enhanced scan during build-up or washout assumes by necessity that the tissue within the ROI is homogeneous and monocompartmental. On the other hand, the use of several enhancement scans during build-up and/or washout can be used in multivariable analyses for mono or multicompartmental solution of the convolution integral (Equation 1). Theoretical simulations indicate that fast flows in multicompartamental regions are systematically underestimated somewhat when a single compartment is assumed. In particular this is true in extremely high flow states. A recent attempt to assess the errors in estimated blood flow values when heterogeneous tissue is assumed homogeneous has yielded "unacceptable errors." Unfortunately, the authors used the fast flow component (f) as the reference flow rather than the total flow within the ROI f_total = w_f + (1-w_f)f_e. If one corrects for this mistake the errors are significantly lower than reported. A comprehensive theoretical comparison of the various approaches indicates that the multi-compartmental approach should yield better results and such an approach is currently being investigated. Nonetheless, the limited signal-to-noise ratio provided by xenon enhanced CT on one hand and the desire to reduce the radiation dose by limiting the number of scans on the other hand, reduce the feasibility of using a multi-compartmental model. This is especially true when human studies are considered. Because of these limitations, most of the reported results are based on single compartmental approach. Because pathological changes in diseased tissue may significantly alter the partition coefficient, the determination of tissue specific partition coefficient has been considered an important advantage of the xenon methodology. The validity of using the xenon methodology in ischemic and/or infarcted tissue has been challenged because relatively low partition coefficients had been reported in infarcted tissue 15–25 days post infarction. Although major changes in tissue composition and therefore in partition coefficients may not occur within several days post infarction as the authors indicate, significant changes do occur after this period with a partial replacement of infarcted tissue. These changes may explain the lower partition coefficients which have been reported 15 to 25 days post infarction. Further examinations of λ during the infarction process are required to fully validate these arguments. The model of an infarct consisting of tissue with and without circulation is of interest and further investigations are required to validate it. Nonetheless, it has been shown that errors in the estimation of partition coefficients tend to be compensated by the estimation of the flow rate constant in tissue with extremely slow flow. Therefore, for a given time dependent enhancement pattern, the derivation of blood flow is relatively insensitive to errors in assumed or measured partition coefficient. A mixture of perfused and nonperfused tissue in a single tissue segment will most likely yield errors in the derived partition coefficient if either computational methodology is used (autoradiographic or multivariable analysis). This is but a special case of a general concept that when any inhomogeneous tissue volume is assumed homogeneous.

d. Recirculation Corrections

One of the major early concerns associated with this methodology was the required recirculation correction. This concern is valid if xenon concentration in arterial blood is assumed to behave as a step function. However, if xenon concentration in arterial blood C_i(t) is a true representation of the input function in the convolution integral (Equation 1), any derivation of LCBF which is based on iterative or exact solution of this integral automatically accounts for the effects of recirculation. Therefore, the use of either end-tidal or direct measurements for the input function C_i(t) in the computations, accounts for the effect of recirculation on the derived LCBF values. The errors associated with overestimation of build-up rate of xenon concentration in arterial blood have been shown to be significant if scanning is performed early after initiation or termination of xenon inhalation (t < 1.5 min). These errors decrease when time of scanning increases.
e. Generation of Flow Maps

Once the methodology for derivation of LCBF in a single ROI is developed, it can be expanded to the derivation of LCBF in a single slice (functional mapping). Such LCBF maps can be generated with any preselected ROI size. Unfortunately, the pixel-to-pixel variation in CT images is limited by the use of unsmoothed images for such purposes. Various methods of image smoothing have been described in the literature.

In most cases a weighted average of either 3 x 3 or 4 x 4 pixels “Bell” shape filters have been recommended. Recently, this technique has been used to generate LCBF maps in lightly anesthetized primates and awake humans.

A “sliding window” filter, used to reduce system noise by smoothing out pixel-to-pixel variations, precedes the derivation of blood flow estimates for each pixel. The resultant blood flow maps can be displayed adjacent to the standard morphologic CT images (fig. 2).

Current Status

Most of the reported results to date have been based on a single compartmental approach. Multilevel LCBF maps (typically four) in lightly anesthetized and awake normal and infarcted baboons have been generated from data accumulated during studies when xenon was inhaled for four to six minutes. Xenon concentrations from 20–80% have been used in these studies and the results indicate that while signal-to-noise improves with increased concentration, time dependent patterns when xenon concentrations below 40% are employed are similar to those observed with higher xenon concentrations (fig. 3).

Using this methodology, flow can be consistently characterized in tissue with fast, slow, and extremely slow flows (i.e. infarcted tissue). With 3 x 3 or 4 x 4 pixel weighted smoothing routines spatial resolution of 4 mm or less (FWHM < 4 mm) can be achieved (fig. 4, tables 1–3). The correlation to LCBF with anatomic structures and the morphologic CT images is good (figs. 2, 4). Using this approach tissue specific response to alteration of PaCO₂ can be demonstrated and LCBF patterns in normal and infarcted tissue can be differentiated. Although almost all reported studies to date have been carried out with either 4 or 5 mm slice thicknesses, anatomic specificity could probably be improved upon with thinner slices. However, the reduction in signal-to-noise when imaging narrower slices appears to eliminate the advantages of increased anatomic specificity.

Tolerance studies in awake human volunteers suggest the existence of minimal side effects in most subjects when concentrations of 35% xenon are breathed for not more than five minutes. More prolonged studies at this or higher concentrations are not frequently associated with clinical sedation which may be preceded or followed by agitation. Despite the limited enhancement in such studies, LCBF maps in awake volunteers and patients have been generated with functional and spatial resolution similar to that obtained in baboons (fig. 5). Successful studies in awake patients have been reported by several groups of investigators. Yet, many of these reports indicate reservations about the limited signal-to-noise associated with such studies.

Despite minor partial volume effects, the differentiation between tissue with high and low partition coefficients can be easily demonstrated in figure 6 where the subtracted images after short (2 min) and long (25 min) periods of xenon inhalation clearly reverse anatomically with respect to relative level of enhancement. It is interesting to note that LCBF response to systemic stimuli such as PaCO₂ is tissue specific and while LCBF increases generally in all regions with slow and fast flow tissue, selective areas with fast flow increase significantly more than others. Typical reported averages for tissue with slow flow (white matter) range between 16–28 ml/100g/min at normal PaCO₂. Yet, in each study we consistently measure slow flows in the range of 8–15 ml/100g/min which are significantly below the expected values for white matter flow. One could hypothesize that these findings are caused by the effects of xenon but our results do not support this contention (see section on xenon effects).

Errors Associated with Xenon Enhanced LCBF Determinations

Analysis of propagation errors through the computational process indicate that in most cases the poor signal-to-noise ratio (SNR) associated with the limited CT enhancement is the limiting factor for accuracy in the determinations of absolute values of derived LCBF. These errors depend on the computational method used, xenon enhancement (SNR) in a single...
image, the number of images used in each derivation etc. It has also been demonstrated that the times of scanning after the initiation of xenon inhalation is an important factor for the determination of fast flow.\textsuperscript{29,31} Optimization of each of these parameters is, for the most part, both procedure and flow specific.\textsuperscript{29} With the noise levels associated with currently available scanners and limiting xenon concentrations to below 50%, several studies have indicated that overall errors in the range of ±15% are probably as low as we can hope to consistently achieve within reasonable ROI sizes.\textsuperscript{29,31} It should be noted that improvement in CT technology continues and reduction in system noise may enable the use of lower concentrations and/or reduction of these errors.

A number of other techniques such as selection of large tissue volumes for analyses, acquisition of several baseline (pre-enhancement) images or multicompartamental analyses of several enhanced images, may be applied to further reduce uncertainties in blood flow determinations. However, all of these techniques have associated shortcomings such as loss of anatomic specificity or increased radiation dose. One should also remember that similar systematic and random errors are associated with other methods for estimating CBF values. For example, in most cases the two com-

\textbf{FIGURE 3.} Time dependent xenon enhancement in tissue with fast (A) and slow (B) flows of a 9.8 kg baboon’s brain. Similar time dependent patterns are observed during 64% (a) and 38% (b) xenon inhalation.
and should be verified by preliminary studies of phantoms and by careful scrutiny of the baseline image or images prior to the initiation of xenon inhalation. In addition, the quality of the data can be evaluated from the distribution of the enhancement values since they

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>LCBF Values in a Selected Region (9.6 × 9.6 mm²) of Interest (ROI #1 in figure 4a)</th>
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<tbody>
<tr>
<td></td>
<td>26 34 42 49 62 71 63 56 51 49 58 65</td>
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<td>24 36 48 60 76 80 67 54 42 38 46 53</td>
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<td></td>
<td>22 36 55 74 84 77 62 50 38 37 47 51</td>
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<td>22 38 62 84 84 65 50 42 37 44 55 58</td>
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<td>22 36 59 78 74 53 39 33 34 47 60 67</td>
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<td>20 33 50 64 61 45 35 32 38 55 70 77</td>
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<td>19 29 45 55 41 35 33 44 64 80 90 90</td>
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<td>16 26 38 46 44 38 36 35 46 65 83 98</td>
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<td>14 24 34 39 37 34 36 45 61 78 98 98</td>
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<td>16 27 38 41 38 35 35 43 58 75 97 97</td>
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<td></td>
<td>19 31 44 48 46 44 42 40 44 56 72 94</td>
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<tr>
<td></td>
<td>22 33 46 54 56 54 49 44 46 55 67 90</td>
</tr>
</tbody>
</table>

Each value represents a voxel of 0.8 × 0.8 × 5 mm³. LCBF values are given in cc/min/100g.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>LCBF Values in a Selected Region (9.6 × 9.6 mm²) of Interest (ROI #2 in figure 4a)</th>
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<tr>
<td></td>
<td>41 40 37 36 38 43 46 48 56 76 97 97</td>
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<tr>
<td></td>
<td>37 38 40 47 60 71 75 71 68 79 93 90</td>
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<td>74 84 86 83 79 74 65 55 50 50 51 50</td>
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<td>85 89 78 66 59 56 53 52 58 62 60 58</td>
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<td>67 67 57 48 47 51 56 63 76 83 79 72</td>
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<td>40 39 37 39 47 60 71 81 95 100 89 76</td>
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<td>52 55 67 82 98 102 86 67 55 52 45 45</td>
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<tr>
<td></td>
<td>67 72 84 92 96 90 70 30 38 34 33 30</td>
</tr>
</tbody>
</table>

Each value represents a voxel of 0.8 × 0.8 × 5 mm³. LCBF values are given in cc/min/100g.

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>LCBF Values in a Selected Region (9.6 × 9.6 mm²) of Interest (ROI #3 in figure 4a)</th>
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<td></td>
<td>78 80 74 53 32 24 28 38 55 65 60 47</td>
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<td>91 97 91 66 39 27 29 39 59 75 72 57</td>
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<td>93 97 93 74 49 33 30 40 62 81 81 67</td>
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<td>84 88 87 76 58 38 31 41 64 84 89 77</td>
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<td>70 86 96 85 62 40 32 40 58 74 79 73</td>
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<tr>
<td></td>
<td>64 62 60 63 81 93 86 79 78 72 82 81</td>
</tr>
</tbody>
</table>

Each value represents a voxel of 0.8 × 0.8 × 5 mm³. LCBF values are given in cc/min/100g.

Figure 4a. A color display of LCBF in a 5 mm thick brain slice of a baboon (PaCO² = 50 mm Hg). The scale is given in cc/min/100g. Three selected regions 9.6 × 9.6 × 5 mm² each are magnified (×3) and displayed. The discrete LCBF values of these regions are given in tables 1–3. Note, a CT image of the same slice is given in figure 2 (third level).

Figure 4b. A photograph of a 3 mm thick brain section comparable with the brain level in figure 4a. Note the correlation between the blood flow maps and the anatomic structures.

partimental models for estimating rCBF from Xe-133 measurements is proportional to a theoretically derived partition coefficient. An error in this estimated parameter will yield a systematic error in derived rCBF values.

One problem that can be easily overcome in these studies is the possible systematic shift in CT numbers due to heat loading and/or minor output variations during the various scans. A water bag (cushion like) or any other material with density close to that of brain tissue can be placed in the field and serve as reference for monitoring the constancy of numerical values. The absence of image artifacts is of extreme importance.
should fall within an expected range of values. This procedure can serve as an easy qualitative measure of the reliability of the data (fig. 7).

Problems Associated with Xenon Enhanced CT Studies

a. Radiation Dose

The classic signal-to-dose dilemma is of great importance when CT studies are performed using stable xenon. Although the collimated beam limits the radiated field, repeated scans at the same level result in a significant dose (particularly if repeat studies are to be performed). Many of the limitations described above are reduced when the “in vivo autoradiographic” method is used. However, a major shortcoming then becomes the dependence of flow estimates on the accuracy of a single datum point. A typical multilevel study would require as a minimum one baseline and two enhanced scans which, depending on the machine and technique used, will result in approximately 15 to 20 rads to the tissue investigated and much lower doses to target organs outside the radiation field. This “whole body” dose which results mostly from scattered radiation is comparable to typical doses received during Xenon-133 blood flow studies but the thyroid dose is likely to be higher with the CT method.35

b. Patient Motion

At this stage there is no doubt that patient motion is a most difficult problem associated with human studies or voluntarily breathing awake patients. Misregistration of images is noticeable on 5 mm thick slices when motion of 1–2 mm had accrued during the study and it is extremely difficult for an awake patient to remain perfectly still during a 6–10 minute study. One could correct for head rotation and/or translation in the image plane but corrections for motion which changes the slice plane require three dimensional coordinates of each tissue voxel investigated. This can be done if adjacent tissue slices are investigated but it significantly complicates the computational aspects of a study. Another approach to reduce this problem in patients is to use somewhat thicker CT slices (≥ 10 mm).

In order to reduce motion as much as possible, a heat sensitive moldable, reusable material which can be fitted for each patient and used as a head holder (Hexaplast) has been tested. This material has been used successfully in ECT studies where the requirements on motion are somewhat less stringent due to the limited spatial resolution.36 As applied to our own work, it has
permitted good registration and flow map generation even in an advanced Alzheimer’s disease patient who was awake but uncooperative and subject to random voluntary and involuntary movements. This work is to be described in a future report.

c. Xenon Side Effects

Several investigators have concluded that prolonged inhalations (> 5 min) of xenon concentrations above 40% may be anesthetic.\(^{37-39, 52}\) No significant ill effects of xenon inhalation were reported in the 1950’s when this gas was used as an anesthetic agent at high concentrations.\(^{40-42}\) It has to be noted that in one patient intracranial pressure (ICP) increased moderately during xenon inhalation. While this was an uncontrolled observation, further study will be needed to determine whether special precautions have to be exercised when some patients are studied (i.e. acute head injury). Recent observations have indicated that EEG alterations do occur during xenon inhalation.\(^{37}\) Our preliminary data on changes in LCBF during prolonged inhalations indicate that there is a gradual but slow decrease in blood flow of approximately 25% at 8 minutes. A significant reduction (×2 to 3) in LCBF during the first few minutes of inhalation of high xenon concentrations (~80%) has been reported\(^{22}\) but these results have been criticized in that mixed flows may have contributed to these observations.\(^{43}\)

Preliminary data from microsphere studies confirm our observations of a gradual but slow decrease in LCBF after several minutes of xenon inhalation. However, no significant changes in LCBF have been observed during the first two minutes of inhalation. On the contrary, a marginal increase (~5–10%) was measured.\(^{44}\) These observations will be the subject of a separate report. Similar preliminary observations on increase in LCBF were reported elsewhere.\(^{29}\)

Summary and Conclusion

Xenon enhanced CT offers a non-invasive method for deriving functional maps of local cerebral diffusion or perfusion with spatial resolution which has not been surpassed by other available non-invasive in vivo methods. This may prove to be a major advantage in studies of small heads in general (i.e. pediatric) and, in particular, in research applications where animal brain function is investigated. If flow is to be related to deep seated anatomical structure smaller than 0.7 cm\(^2\) in any subject, the method offers a distinct advantage. At this stage we have concluded that washin studies are preferable to clearance, particularly if applications to humans are considered. However, the use of both washin and washout data may prove advantageous if the multi-compartmental approach is utilized. Depending on the computational method used scanning should be carried out between 1.2 and five minutes after initiation of xenon inhalation. However, if only characterization of fast flow components is of interest, scanning beyond 3 minutes of xenon inhalation provides little additional useful information. On the other hand, it may provide valuable information concerning tissue heterogeneity within the ROI. These conclusions are in agreement with other feasibility studies on this matter. While the potential for obtaining clinically useful information is real, there is no doubt that further investigations are required before a procedure can be offered as optimal for these purposes. This is especially true if awake humans are to be studied. Even at this early stage it is clear that xenon enhanced CT is a unique research tool for animal studies which may yield valuable functional information within specific tissue volumes of interest such as the boundary of a developing brain infarct (evolving stroke) or specific nuclei or functional centers and may be used with relatively minor difficulties in intubated humans. Its potential as a routine clinical tool in many institutions depends on our ability to resolve at least some of the many problems which have been discussed here.

Acknowledgments

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References


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