Functional Imaging of Cerebral Blood Volume using Simultaneous Measurements of Dynamic and Xenon Computerized Tomography (CT)

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This report describes a method for measuring regional cerebral blood volume (r-CBV), by simultaneously using dynamic computerized tomography (DCT) and stable Xenon-enhanced CT (Xe CT). Local cerebral blood flow (CBF) was measured using a Xe CT blood sampling method, and mean transit time (MTT) was calculated using DCT after a rapid injection of iodinated contrast material. A functional image of r-CBV was obtained from multiplication of CBF and MTT on each pixel using the formula:

\[ \text{CBF} \times \text{MTT} = \text{CBV} \]

This calculated value is not suitable to indicate a r-CBV which directly reflects cerebral microcirculation. Accordingly, only a comparative estimation of relative r-CBV images is applicable. However, laterality of image and comparison of serial studies are useful in hemodynamic evaluations, especially in ischemic cerebrovascular diseases, because they indicate hemodynamic reserve within the hypoperfused region.

(Key Words: cerebral blood volume, dynamic CT, xenon enhanced CT)

INTRODUCTION

A number of studies on cerebral hemodynamics in cerebral vascular diseases, using dynamic computed tomography (DCT) or Xenon enhanced tomography (Xe CT), have recently been reported. However, the studies were mere measurements of cerebral circulation time or regional cerebral blood flow (CBF). The present paper describes a method for the measurement of regional cerebral blood volume (CBV) by the simultaneous use of DCT and Xe CT. The determination of CBV by these procedures may be useful in diagnosing and studying the pathophysiology of cerebrovascular diseases.

MATERIALS AND METHODS

Pre- and post-operative simultaneous measurements of DCT and Xe CT were performed in 2 patients with cerebroischemic disease who underwent a superficial temporal artery—middle cerebral artery anastomosis (STA-MCA anastomosis).

A Hitachi CT-W600 (Hitachi Medical Co., Tokyo) was used for the DCT and Xe CT studies. Closed circuit anesthesia (Xetron II: Anzai Sogyo Co., LTD., Tokyo) was used for the Xenon gas inhalation. The patients received diazepam (10 mg) and atropine sulfate (0.5 mg) as pre-medication. Anesthesia was induced with a minimum dose of flunitrazepam and/or diazepam. For the Xe CT study, 40% cold Xenon was inhaled for 15 minutes. Arterial Xenon concentrations were evaluated by sequential scanning of syringes inserted into the phantom placed over the patient's vertex (Fig. 1). The syringes contained blood samples drawn, at 2-minute intervals, from the canulated radial
artery. For the calculation of CBF, the arterial blood accumulation rate constant (K) and arterial blood saturation value were first calculated from the following equation, using the method of least squares:

\[ \text{Ca}(t) = A \left[ 1 - \exp(-Kt) \right] \]

where \( \text{Ca}(t) \) is the Xenon concentration in arterial blood at time \( t \). The brain tissue accumulation rate constant \( (k) \) and partition coefficient \( (\lambda) \) were calculated using the following integration of Fick's formula:

\[ \text{Cb}(T) - \text{Cb}(0) = k \int_0^T \text{Ca}(t) \, dt - \int_0^T \text{Cb}(t) \, dt \]

where \( \text{Cb}(t) \) is the xenon concentration in brain tissue at time \( t \). The CBF value was calculated from the equation:

\[ \text{CBF} = k \cdot \lambda \times 100, \]

and a functional image was created using each CBF value on a \( 5 \times 5 \) pixel matrix.

DCT was performed at the same level of the brain not less than 20 minutes after the completion of the Xe CT study. Upon the initiation of the second scanning, 40 ml of 60% urografin was injected at a rate of 5 ml/sec through a needle placed in the antecubital vein.

Eight serial scans were obtained at one second intervals with a scan time of 3 seconds. The time density curve was fitted to the following gamma variate except for recircuit data (Fig. 2 solid line):

\[ F(t) = k(t - T_0)^a \times \exp\left(-\frac{(t - t_0)}{b}\right) \]

where \( k \) is a constant scale factor, \( t \) is the time after injection, \( T_0 \) is the time fitting started, and \( a \) and \( b \) are arbitrary parameters. The mean transit time (MTT) was obtained for the duration from \( t_0 \) to the time of the center of gravity on the fitting curve using the following formula:

\[ \text{MTT} = t \int \text{ACT}(t) \, dt / \int \text{ACT}(t) \, dt \]

A functional image of the MTT was created using each MTT value on each \( 5 \times 5 \) pixel as a matrix. A higher density on the image indicated a prolonged MTT.

A functional image of the CBV (ml/100g) was obtained by multiplication of the CBF (ml/min/100g) and MTT (sec) from each matrix using the formula:

\[ \text{CBF} \times \text{MTT} / 60 \]
RESULTS

Case 1: A 41-year-old female was admitted to the hospital because of left hemiparesis of one week duration. A diagnosis of moyamoya disease was made after cerebral angiography. Three weeks after the onset, functional imaging showed a low CBF, prolonged MTT and increased CBV in the right cerebral hemisphere, especially in the gray matter. The CBF in this area increased following a right STA-MCA anastomosis and neither MTT nor CBV showed differences between the two hemispheres (Fig. 3). Her hemiparesis improved post-operatively and she was able to walk alone without difficulty.

Case 2: A 45-year-old female suffered a sudden onset of left lower extremity monoparesis and was admitted to our hospital. The CT scan depicted a low density area in the territory of the right anterior cerebral artery (ACA). Cerebral angiography demonstrated a stenosis of the right ACA with faint collateral flow from the middle cerebral artery (MCA). She eventually underwent ACA side-to-side anastomosis about two months after the onset. Pre-operative functional imaging showed low CBF and prolonged MTT without differences between the two hemispheres in CBV in the territory of the bilateral ACA. However, following surgery, the CBF in this area decreased and the values of MTT and CBV are undetectable due to severe hypoperfusion. In the other area, the images showed a prolongation of MTT and a high CBV when compared to the pre-operative images (Fig. 4). Although there was no significant neurological alteration, the post-operative angiography demonstrated a stenotic change at the site of anastomosis, and left common carotid angiography did not illustrate right distal ACA branches.

DISCUSSION

For CBV evaluation, previous reports described various methods using radioisotopes (\(^{131}\)I-albumin (12), \(^{99m}\)Tc-RBC(5)), CT, positron emission tomography (PET)(8), X-ray fluorescence (3), and a photoelectric method (14). Using CT, there were two procedures. One adapted the subtraction images obtained before and after iodinated contrast material injection (1, 6, 7), and the other calculated the CBV from both the CBF and MTT (4). With either method, absolute values were not obtained, and only a relative estimation of CBV was feasible. The former is quite difficult because: 1) it requires measurement of the hematocrit and intravascular iodinated material concentration, 2) the measurement is subject to effects from intravascular contrast material leakage, and 3) technically, it is difficult to get and maintain a saturated state of intravascular contrast material. A more convenient and reliable image can be obtained using the method described in this communication, because the image is created by a calculation of the CBF and MTT values in the pixels. This method is also advantageous in evaluating CBF and MTT images against the CBV image.

A controversial point in this method is the
Fig. 3 (case 1) Preoperative functional images with low CBF, prolonged MTT and increased CBV in the right cerebral cortex. Following STA-MCA anastomosis, CBF in this area increased and neither the MTT nor CBV showed differences between the two hemispheres.

Fig. 4 (case 2) Preoperative functional images with low CBF, and prolonged MTT without laterality of CBV in the territory of the bilateral ACA. Following surgery, the CBF in this area decreased, and the values of MTT and CBV were undectable. In the other area, the images showed a prolonged MTT and higher CBV than the preoperative images.
visualization of the CBV image from a calculation of both the CBF and MTT values and therefore is not a direct measurement which reflects microcirculation. Accordingly, CBV changes are always attributed to individual changes in CBF and MTT. In particular, the MTT should be carefully evaluated. It is difficult to quantitate the MTT value or to establish a normal baseline value because of differences in bolus inputs from the venous system due to disparities in systemic hemodynamics among individual cases. Furthermore, in cases with leptomeningeal anastomosis as a collateral circulation, comparison between the MTT and normal flow MTT is difficult because the bolus of contrast agent is modified twice; during its passage through the pulmonary circulation, and retrograde collateral circulation (13). Measurement of CBV using this method in these cases is useless.

As cerebral perfusion pressure (CPP) falls, CBF is maintained through a compensatory dilation of precapillary resistant vessels and, consequently, increases in CBV. Increases in cerebral oxygen extraction maintain cerebral oxygen metabolism. When the capacity for compensatory vasodilation has been exceeded, cerebral autoregulation fails and the CBF begins to fall. CBV may decrease as vessels collapse with disruption of normal cellular metabolism and function (11). This suggests that CBV is an important factor as an index of cerebral circulatory reserve (2). In cases in which STA-MCA anastomosis were carried out, Powers et al. (9, 10) reported that CBV did not change following surgery suggesting that CPP was still low and compensatory vasodilation was still occurring. Similarly, in case 2, it is suggested that the CPP increase following surgery did not satisfy the demands of the ischemic brain tissue.

As an indicator for cerebral perfusion reserve, image differences between the two hemispheres and a comparison of serial studies in individual cases are useful in evaluating hemodynamics ischemic cerebral disease.

REFERENCES