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Suitable Image Parameters and Analytical Method for Quantitatively Measuring Cerebral Blood Flow Volume with Phase-Contrast Magnetic Resonance Imaging

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The aim of this study was to determine suitable image parameters and an analytical method for phase-contrast magnetic resonance imaging (PC-MRI) as a means of measuring cerebral blood flow volume. This was done by constructing an experimental model and applying the results to a clinical application. The experimental model was constructed from the aorta of a bull and circulating isotonic saline. The image parameters of PC-MRI (repetition time, flip angle, matrix, velocity rate encoding, and the use of square pixels) were studied with percent flow volume (the ratio of actual flow volume to measured flow volume). The most suitable image parameters for accurate blood flow measurement were as follows: repetition time, 50 msec; flip angle, 20 degrees; and a 512×256 matrix without square pixels. Furthermore, velocity rate encoding should be set ranging from the maximum flow velocity in the vessel to five times this value. The correction in measuring blood flow was done with the intensity of the region of interest established in the background. With these parameters for PC-MRI, percent flow volume was greater than 90%. Using the image parameters for PC-MRI and the analytical method described above, we evaluated cerebral blood flow volume in 12 patients with occlusive disease of the major cervical arteries. The results were compared with conventional xenon computed tomography. The values found with both methods showed good correlation. Thus, we concluded that PC-MRI was a noninvasive method for evaluating cerebral blood flow in patients with occlusive disease of the major cervical arteries.

Key words: phase-contrast imaging, image parameters, analytical method, cerebral blood flow volume measurement

Phase-contrast magnetic resonance imaging (PC-MRI) offers two advantages for the study of cerebral blood flow: the procedure is noninvasive, and anatomical information and measurement of cerebral blood flow volume can be acquired in a single procedure (1). Although it is not generally accepted as a flow study method in clinical practice, PC-MRI can help the surgeon evaluate cerebral blood flow volume in patients with occlusive disease of the major cervical arteries. Conventional imaging studies, such as angiography, xenon computed tomography (Xe-CT) and single photon emission computed tomography (SPECT) are used more widely than PC-MRI because in PC-MRI the image parameters and regions of interest are difficult to adjust when measuring actual blood flow volume. But few studies have investigated the image parameters and analytical method of PC-MRI (2-4). Furthermore, a special imager with a research package is needed to use PC-MRI in cine mode.

In this study, we created an experimental model of blood flow using the aorta of a bull. We then carried out a flow study to investigate suitable image parameters and analytical methods for PC-MRI without the cine mode. Based on the results, we measured the cerebral blood flow volume of 12 patients with occlusive disease of the

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major cervical arteries using PC-MRI. We then compared these measurements to those obtained with Xe-CT.

Materials and Methods

Experimental study. We constructed an experimental model of blood flow from the aorta of a bull and filled it with isotonic saline. The bull aorta is more similar to human vessels than a vinyl tube and has a sufficient inner diameter for studying blood flow. The isotonic saline created magnetic homogeneity around the aorta and decreased any magnetic influence on flow measurement. Each end of the aorta was joined to a reservoir by a vinyl tube (Fig. 1). To prevent turbulent flow at the connections, the inner diameter of the aorta was equal to that of the tubes. Isotonic saline was circulated in the tubes to make a parabolic flow. A mean flow velocity of 3 cm/sec was generated and maintained in the tube with a pump. The maximum flow velocity passing through the center of the tube, which was measured with Doppler imaging, was 10 cm/sec. Phase-contrast measurements were done with a Signa Advantage 1.5 T (GE, Milwaukee, WI, USA) with a research package. Phase-contrast images were obtained under a wide variety of image parameters: repetition time (TR) of 25 to 250 msec, flip angle of 10 to 90 degrees, slice thickness of 5 mm, field of view of 16 cm, matrix of 256 to 512 $\times$ 192 to 256, 16 NEX, and velocity rate encoding (VENC) of 3 to 400 cm/sec, with and without square pixels.

Sagittal images were obtained to localize the spoiled gradient-recalled acquisition in the steady state (SPGR) technique, and axial images for PC-MRI were obtained from the middle of the vessel on the localized image. The slice was established perpendicular to the vessel. A region of interest was obtained in the image and the flow velocity was measured with correction. The region of interest for the vessel was 10 % larger than the size of the vessel in the image (Fig. 2A). Correction was done with an average of intensity across four regions of interest obtained from around the vessel. These regions were set as large as possible (Fig. 2B). An independent console was used

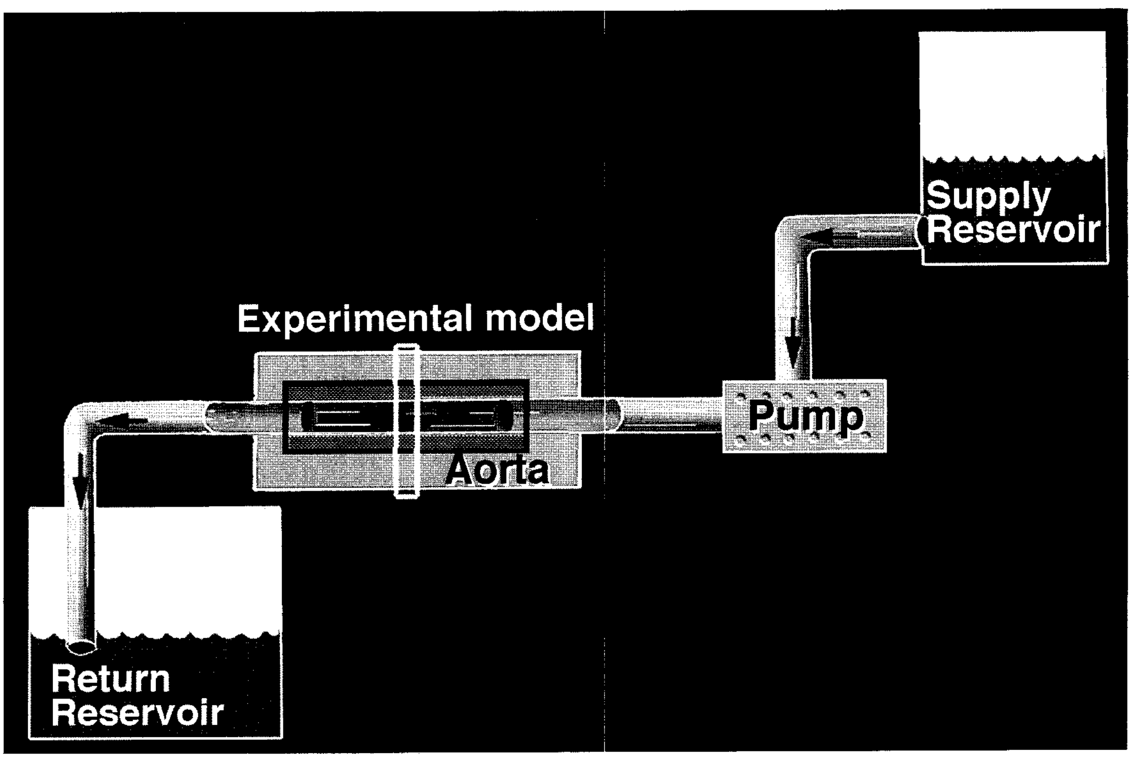
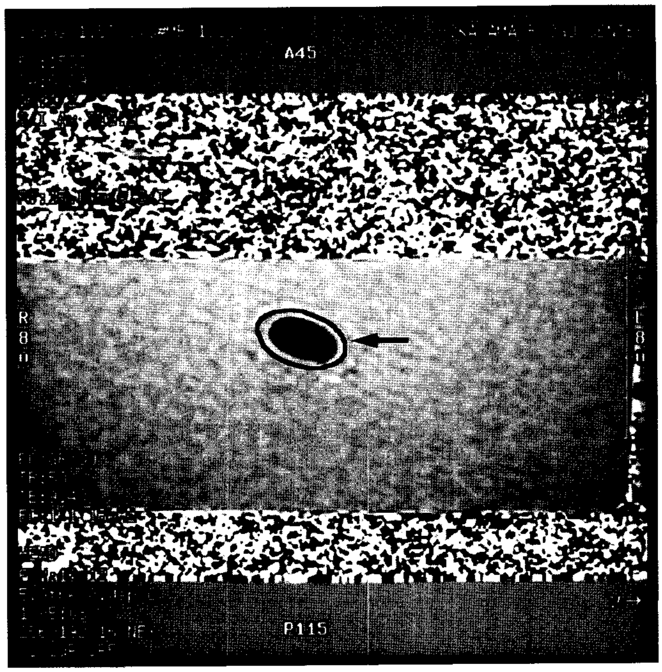
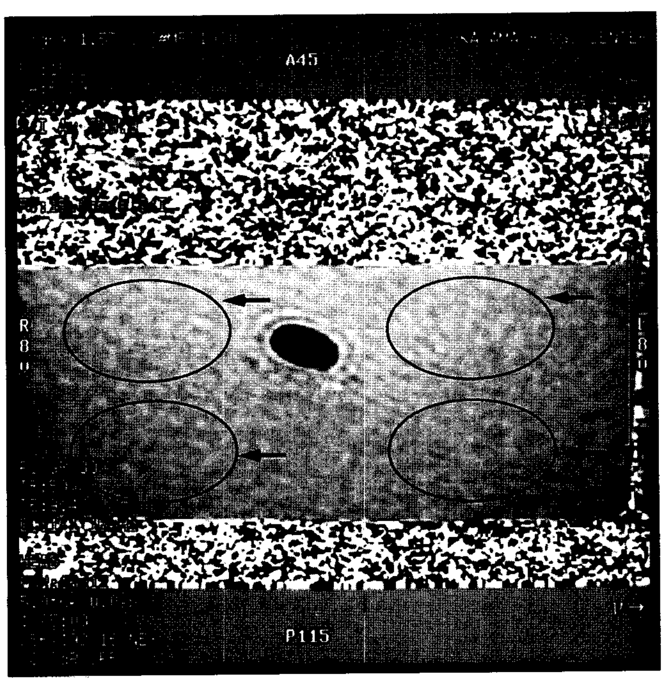


Fig. 1 The experimental model was constructed from the aorta of a bull and filled with isotonic saline. A pump produced a flow of 3 cm/sec. Phase-contrast images were obtained from the middle of the vessel, which was not influenced by turbulent flow.



A



B

Fig. 2 The regions of interest in phase-contrast images of the experimental model
A: The region of interest used to calculate flow was 10% larger than that of the vessel (arrow).
B: Four regions of interest on all sides of the vessel were used for correction.
These regions were set as large as possible (arrows).

to measure and analyze the flow volume. Image parameters were studied using percent flow volume, which was defined as the ratio of the flow volume from the graduated cylinder to the flow volume measured from the phase-contrast image.

Clinical application. Twelve patients with stenosis of 60% or more in major cervical arteries on conventional angiographical images participated in this study. They comprised 10 men and 2 women with a mean age of 61.6 years (range, 41 to 72 years). In six patients, the internal carotid artery was affected by stenosis; in the other six patients, the stenosis was in the vertebral arteries. PC-MRI was done with a Signa Advantage 1.5T (GE) with a research package. Based on our findings in the experimental model, we used the following image parameters: a TR of 50 msec, a flip angle of 30 degrees, a slice thickness of 5mm, a field of view of 16 cm, a matrix of 256 × 192, 16 NEX, and VENC of 120 cm/sec. To avoid any influence by turbulent flow, axial phase-contrast images perpendicular to the straight position and 2cm distal to the location of the stenosis in the cervical artery were obtained in all 12 patients. Xe-CT was done with a Hispeed Advantage (GE). Six slices of Xe-CT images at equal distances from the brain stem to the parietal lobe were obtained and cerebral blood flow volume was measured from whole brain tissue without the ventricle with an AZ-7000 (Anzai Medical Co., Ltd., Tokyo, Japan). The values measured with these two techniques were compared. In addition, this study investigated the correlation between the variability of cerebral blood flow volume measured with the two techniques described and the stenotic changes of arteries shown by conventional angiography in five patients.

Results

Experimental study. When the high-resolution mode (512 × 256) and a TR of 50 msec were used, the percent flow volume was more than 95% and stable with a flip angle ranging from 10 to 30 degrees. The percent flow volume was highest with the high-resolution mode combined with a TR of 50 msec and a flip angle of 20 degrees. When the 256 × 192 mode was used with a TR of 50 msec, the percent flow volume was more than 85% and was stable within the same range. The percent flow volume was highest with the 256 × 192 mode, a TR of 50 msec and a 30-degree flip angle (Fig. 3A).

Based on these findings, we used the high-resolution mode with a 20-degree flip angle and varying TRs and the 256 × 192 mode with a 30-degree flip angle and varying TRs. When we used the high-resolution mode with a 20-degree flip angle, the percent flow volume was more than 90% with a TR above 50 msec. The percent flow volume was more than 85% with a TR above 30 msec when we used the 256 × 192 mode with a 30-degree flip angle (Fig. 3B). The higher flow volumes were obtained using the high-resolution mode with a TR above 50 msec and the 256 × 129 mode with a TR above 30 msec with a flip angle ranging from 10 to 30 degrees. A TR of 50 msec with either the 256 × 192 mode or the high-resolution mode was considered more appropriate because the scanning time was shorter than 10min. The percent flow volume with the high-resolution mode was higher than that using the 256 × 192 mode because of the high spatial resolution and lower partial volume effect. The percent flow volume rose above 100% when phase-contrast images were obtained using square pixels in the 256 × 192 mode. The number of phase-encoding steps affected the measurement of flow velocity when we used square pixels. The percent flow volume was more than 90 % using the high-resolution mode either with or without square pixels (Fig. 3C).

In addition, a percent flow volume of almost 85% was obtained when VENC was set between the maximum flow velocity in the vessel and five times the maximum flow velocity in the 256 × 192 mode. The more VENC approached the maximum flow velocity, the higher the resultant percent flow volume (Fig. 3D). The best VENC was the maximum flow velocity in the vessel.

According to these results, the following imaging parameters were judged to be suitable for accurate measurement of blood flow with PC-MRI: TR of 50 msec, flip angle of 20 degrees, and a 512 × 256 matrix without square pixels. Furthermore, VENC should be set ranging from the maximum flow velocity in the vessel to five times this value.

Clinical application. The total blood flow volume of the bilateral internal carotid arteries and vertebral arteries is the same as the cerebral blood flow volume. The relationship between the values obtained for blood flow volume of the internal carotid artery and the vertebral artery (cervical flow volume) by phase-contrast imaging (PC) and cerebral blood flow volume (cerebral flow volume) by xenon imaging (Xe) were compared by regression analysis and t testing. The coefficient of determination between the values obtained for cervical flow volume by PC and cerebral flow volume by Xe was 91 % in the right hemisphere and 83 % in the left hemisphere ($P <$ 0.01) (Fig. 4A). The coefficient of determination between the values obtained for total cervical flow volume by PC and whole cerebral flow volume by Xe was 99 % ($P <$ 0.01), and there was a good correlation between these

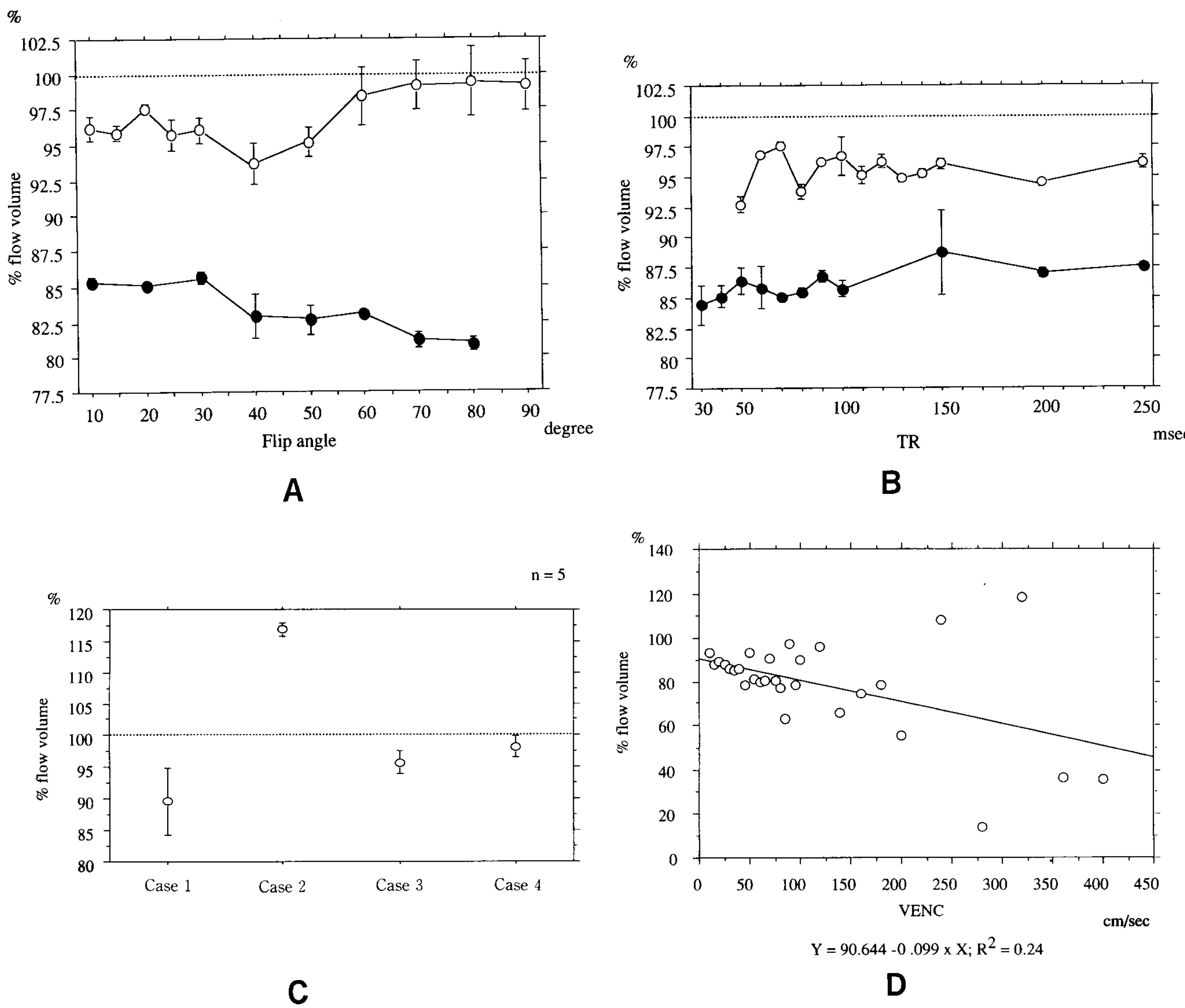


Fig. 3 The correlation between percent flow volume and varying image parameters of phase-contrast magnetic resonance imaging

A: When the flip angle (FA) was changed with a repetition time (TR) of 50 msec, the flow volume of the two modes was more than 85% and was stable with a flip angle ranging from 10 degrees to 30 degrees. ○: matrix 512 × 256 n = 5. ●: matrix 256 × 192 n = 3.

B: When a high-resolution mode with a 20-degree flip angle and a 256 × 192 mode with a 30-degree flip angle were used, flow volume was more than 85% with a TR above 30 msec. ○: matrix 512 × 256 n = 5. ●: matrix 256 × 192 n = 3.

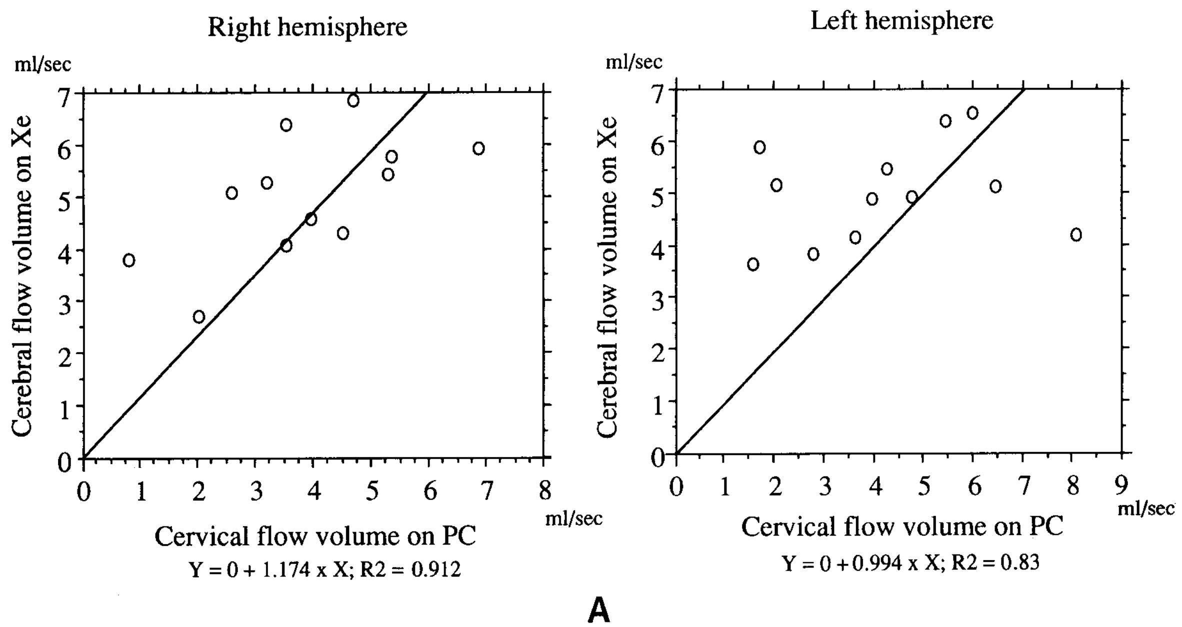
C: With square pixels in the 256 × 192 mode (Case 2), the flow volume was above 100%.

Case 1: Matrix 256 × 192, TR 50 msec, FA 30 degrees, square pixel (−).
Case 2: Matrix 256 × 192, TR 50 msec, FA 30 degrees, square pixel (+).
Case 3: Matrix 512 × 256, TR 50 msec, FA 20 degrees, square pixel (−).
Case 4: Matrix 512 × 256, TR 50 msec, FA 20 degrees, square pixel (+).

D: The most effective velocity rate encoding (VENC) was maximum flow velocity, and the highest percent flow volume was almost 95%.

values. This correlation was stronger than that between the values obtained for cerebral blood flow volume in each hemisphere due to collateral circulation. The values obtained by Xe for whole cerebral flow volume were 24 % higher than those obtained by PC for total cervical flow volume (Fig. 4B).

The variability of cervical flow volume measured with PC was compared to the stenotic change of arteries depicted by conventional angiography. The decrement ratio of cervical flow volume by PC was correlated with the angiographical stenotic ratio; this coefficient of determination was 43 % ($P < 0.01$). But no correlation could be found between the angiographical stenotic ratio and the decrement ratio of cerebral flow volume by Xe (Fig. 5A). In addition, with PC we were able to show variations in blood flow volume caused by surgery to correct carotid-endarterectomy (Fig. 5B). Therefore, PC was judged to be useful for evaluating cerebral blood flow volume in



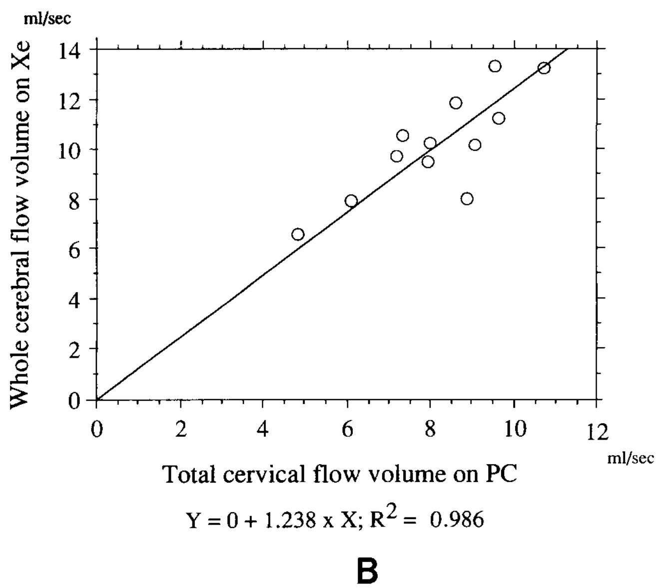
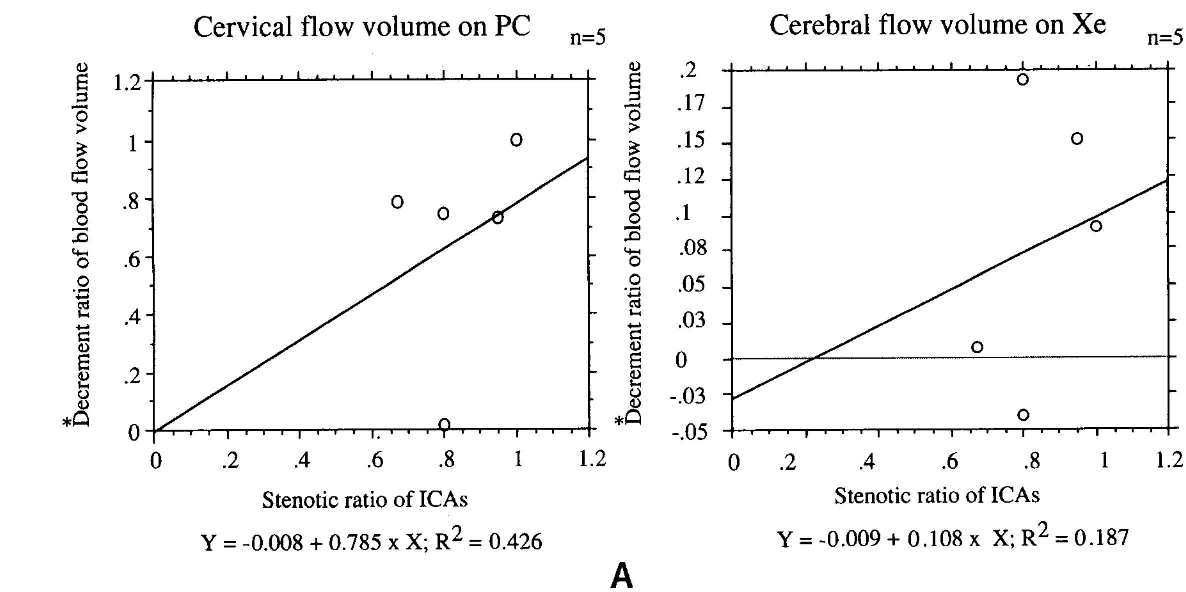


Fig. 4 Correlation between the values obtained for cervical flow volume by phase-contrast imaging (PC) and cerebral flow volume by xenon imaging (Xe)

A: The coefficient of determination between the values obtained for cervical flow volume by PC and cerebral flow volume by Xe was 91% in the right hemisphere and 83% in the left hemisphere.

B: The correlation between the values obtained for total cervical flow volume by PC and whole cerebral flow volume by Xe was better than the correlation between the values obtained by each method in the separate hemisphere. The ratio of the value for total cervical flow volume obtained by PC to the value for whole cerebral flow volume obtained by Xe was 0.76.



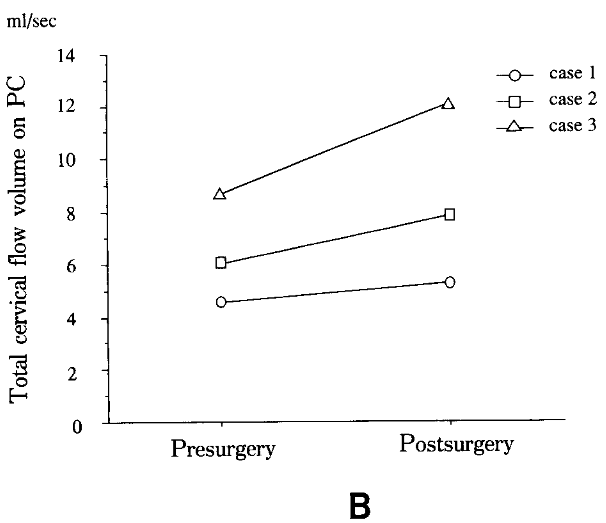


Fig. 5 The correlation between the values obtained for cervical flow volume change by phase-contrast imaging (PC) and angiography

A: The coefficient of determination between the decrement ratio of cervical flow volume by PC and the angiographical stenotic ratio was 43%. No correlation could be found between the angiographical stenotic ratio and the decrement ratio of cerebral flow volume by xenon imaging (Xe). ICA: Internal carotid artery.

B: Two of the five patients refused to undergo carotid-endarterectomy. In the three patients who underwent the surgery, PC showed increases in total cervical flow volume.

*Decrement ratio of cerebral blood flow =

$$\frac{\text{blood flow of normal side-blood flow of stenotic side}}{\text{blood flow normal side}}$$

these patients.

Discussion

Many studies have found the cine mode of PC-MRI to be useful for measuring blood flow volume of vessels (5–11). The cine mode of PC-MRI, however, is not generally accepted for flow study in patients with cervical vascular disturbance because a special imager and a long time are needed for measurement. Consequently, the cine mode of PC-MRI is not considered useful for studying blood flow in patients.

Currently, actual blood flow volume can be measured using PC-MRI without the cine mode (12–14) and investigators have proposed calculating blood flow volume using PC-MRI without the cine mode. Unfortunately, none of these studies investigated the image parameters and analytical method necessary for accurately measuring blood flow volume using PC-MRI without the cine mode. This study proposes suitable image parameters and an analytical method for measuring flow volume with 16 NEX in both an experimental model and clinical application.

Suitable image parameters must be selected for exact measurement of blood flow volume. These parameters must take into account factors such as decreasing saturation effects, the acquisition of adequate signals, and high spatial resolution. Actually, a long TR, a small flip angle, and a small pixel size have been reported to be good imaging parameters (4), and our results substantiate these findings. In addition, when VENC was less than the maximum flow velocity, flow-rate aliasing occurred in the center of the vessel because the flow was not equal and the maximum flow velocity was in the center of the vessel (12, 15-17). If VENC was five times the maximum flow velocity, the peripheral flow in the vessel could not be detected because it was slow and the difference between the peripheral flow velocity and VENC was large (15, 17).

When PC-MRI is used in clinical practice, however, there are limitations in selecting the imaging parameters. For example, a TR of approximately 30 msec is generally used to shorten the examination time (4). In addition, the high-resolution mode is not useful for measuring the flow volume in cervical arteries because it is difficult to obtain a good signal-to-noise ratio for the complicated structures of the human neck. Thus, the use of the high-resolution mode to measure the exact flow volume limits the range of image parameters. The imaging parameters must be simple, and the measurement of blood flow volume using these parameters must also be useful in clinical practice. With suitable image parameters, PC-MRI can be used to measure blood flow volume accurately.

Previous reports have not given special consideration to the analytical method used in PC-MRI imaging, although the exact measurement of blood flow volume is influenced by the analytical method used. Several problems prohibit more precise measurement of flow volume with PC-MRI. The first is the method used to determine the region of interest by measuring the size of the artery. When the region of interest is set on the magnetude image of PC-MRI, detecting the peripheral blood flow volume of the artery is difficult because the artery pulsates and the blood flow close to the arterial wall is slow. In this study, the region of interest was 10 % larger than the arterial size on the magnetude image so that we could detect the peripheral blood flow volume. This is due to the fact that the arterial size on the phase image of PC-MRI is 10 % bigger than that on the magnetude image of PC-MRI.

The second problem is that correction, based on background intensity, is essential in measuring blood flow. A stationary background cannot produce a phase shift; thus, the background velocity is 0 cm/sec (18-21). We suggest that the intensity of the background be identical to the background velocity. This is useful for the correction as it eliminates any magnetic heterogeneity. Magnetic homogeneity differs slightly along the slice-selection and frequency-encoding directions. We also decided that the correction should be done with an average of the intensity of four regions of interest established in the background around the artery. The intensity of the background varies because the difference between the background velocity and VENC is large. There are also many tissues surrounding arteries *in vivo*. The larger the size of the region of interest established in the background, the smaller the effects of the intensity of variance in the region of interest (22). The sizes of the four regions of interest on the background were set as large as possible.

Our experimental study proposes suitable image parameters and improves several analysis problems. In the clinical study, we compared the PC-MRI study to conventional Xe-CT in evaluating cerebral blood flow volume for patients with occlusive disease of the major cervical arteries. In this study, we determined that the value obtained for whole cerebral flow volume by Xe was 24 % higher than the value obtained for total cervical flow volume by PC due to the inherent characteristics of these two measuring techniques. PC-MRI cannot accurately detect peripheral blood flow volume around an artery and cerebral flow volume by Xe is corrected with cerebral weight for the comparison with cervical flow volume by PC. Nonetheless, there was a good correlation between the values obtained for cervical flow volume by PC and for cerebral flow volume by Xe in these patients. In previous reports, the value of blood flow volume measured with PC-MRI was about 25 % higher than the value of blood flow volume measured with Doppler imaging. There was a good correlation between the values of blood flow volume with these two techniques (11, 23). The cervical blood flow volume using PC-MRI showed the difference in blood flow volume between the healthy side and the diseased side without the influence of collateral circulation. We also evaluated the change in cervical flow volume associated with the appropriate treatment using PC-MRI. The PC-MRI proved useful for measuring cerebral blood flow volume and evaluating the changes in blood flow volume brought about by surgery to correct blood flow disturbances.

In this paper, we have introduced a method whereby PC-MRI can be used to measure blood flow volume without the cine mode. Our results show that PC-MRI is noninvasive and has good potential for evaluating the cerebral blood flow volume of patients with cerebral vascular disturbance (23). As a result, PC-MRI may be more widely accepted as one of the techniques for measuring cerebral blood flow volume in clinical practice. Furthermore, if problems such as the general use of the ECG-gating cine mode and the development of variable VENC are addressed, blood flow volume can be measured more exactly with PC-MRI. If PC-MRI is combined with perfusion imaging, partial changes in cerebral blood flow volume and changes in cerebral blood flow volume associated with multiple arterial stenosis can also be measured and visualized with MRI.

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