Intraaneurysmal flow visualization by using phase-contrast magnetic resonance imaging: feasibility study based on a geometrically realistic in vitro aneurysm model

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Object. The aim of this study was to evaluate the feasibility of complex intraaneurysmal flow visualization with the currently available phase-contrast magnetic resonance (MR) imaging modality.

Methods. A geometrically realistic in vitro aneurysm model, in which detailed flow velocity analysis had already been conducted using laser Doppler velocimetry was used for this in vitro hemodynamic simulation, so that the results of phase-contrast velocity measurements could be compared with the previous reliable results. On a 1.5-tesla unit, three orthogonal components of velocity were obtained using a standard two-dimensional fast low–angle shot flow quantification sequence. Three-dimensional (3D) intraaneurysmal flow structures recorded during one cardiac cycle were depicted in one midsagittal and three axial cross-sectional planes with the aid of gray scale phase-contrast velocity maps. Isovelocity contour maps and secondary flow vectors were also created based on the phase-contrast velocity maps by using MATLAB software. The isovelocity contours in those three axial sections could demonstrate the shapes of inward and outward flow areas and their alternation over one cardiac cycle. The secondary flow vectors demonstrated twin vortices within the outward flow area adjacent to the boundary layer of inward and outward flow in all axial planes.

Conclusions. The phase-contrast MR imaging method was able to depict the complex 3D intraaneurysmal flow structures in the in vitro aneurysm model. Detailed 3D intraaneurysmal flow information will be obtainable in vivo after improvements are made in spatial resolution, which is expected in the near future. The capability to visualize intraaneurysmal flow structures directly with the use of noninvasive MR imaging technology will have a positive impact on future clinical practice.

Key Words • cerebral aneurysm • hemodynamics • acrylic aneurysm model • cine phase-contrast magnetic resonance imaging

The current neuroradiographic technology provides molecular and physiological information on the vessel and its surrounding structures. One of the most important factors that governs the origin and natural history of vascular diseases is hemodynamics and its interaction with endothelial cells, smooth-muscle cells, and extracellular matrix in the vascular wall.1,8,13,14,18 Tissue motions, including the flow of fluids in the human body, can be qualitatively and quantitatively visualized using MR imaging by encoding the phase contrast of the magnetization.2,5–7,24 The phase-contrast MR imaging procedure has already been used in clinical settings to visualize in vivo fluid motions such as cerebrospinal fluid flow in the cisterns and ventricular systems.7,16,23 Blood flow velocity in the intracranial arteries can be measured using the phase-contrast MR imaging procedure.7,9 This technique appears to be feasible for visualizing complex 3D flow structures in large vessels with the use of phase-contrast MR imaging.11,12

It has been a challenge to visualize complex 3D flow structures in cerebral aneurysms in vivo. The careful review of conventional angiograms provides a gross idea of intraaneurysmal hemodynamics.26,30 Nevertheless, such information appears to be insufficient for an understanding of the natural history of cerebral aneurysms and its correlation with hemodynamics. The phase-contrast MR imaging procedure has been used to obtain anatomical information on cerebral vessels and aneurysms.23 This noninvasive method should be applied not only to visualize the vascular geometry, but also to analyze the intraaneurysmal hemodynamics. To our knowledge, there have been no reports that have demonstrated the feasibility of phase-contrast MR imaging procedures for 3D visualization of intraaneurysmal hemodynamics. One of the major obstacles to application of the phase-contrast MR imaging method for this particular purpose is the confirmation of results, because such a complex
in vivo intraaneurysmal flow structure is not available to compare with the results obtained using phase-contrast MR imaging.

The purpose of this study was to evaluate the feasibility of intraaneurysmal flow visualization with the currently available phase-contrast MR imaging modality. We have previously reported a new method of hemodynamics analysis in which a geometrically realistic in vitro aneurysm model based on patients' 3D angiograms is used.28,29 Detailed intraaneurysmal flow analysis could be conducted with the use of LDV in an in vitro BA tip aneurysm model, which had as complex a shape as that seen in actual patients. The LDV is one of the most reliable tools for measuring a point velocity of moving fluid. In the present study, the phase-contrast velocity measurements were conducted in the same in vitro BA tip aneurysm in which detailed flow analysis had already been conducted by using the LDV, so that the results of the phase-contrast velocity measurements could be qualitatively compared with the previously reported reliable results.

**Materials and Methods**

**In Vitro Aneurysm Model**

An in vitro aneurysm model manufactured from a 3D CT angiogram of a patient’s BA tip aneurysm was used for a hemodynamics study of phase-contrast MR imaging (Fig. 1 left). The aneurysm measured 10.1 mm in the craniocaudal and 9.1 mm in the transverse diameters with a neck diameter of 8.4 mm. The aneurysm neck incorporated the origins of the bilateral posterior cerebral arteries; the neck also incorporated the distal BA above the origins of the superior cerebellar arteries. The largest diameter of the BA measured 3.7 mm.

**Fig. 1.**  *Left:* A 3D CT angiogram demonstrating a BA tip aneurysm, posteroanterior view. *Right:* Photograph showing a geometrically realistic in vitro aneurysm model made of clear acrylic plastic, posteroanterior view.

**Fig. 2.**  *Left:* Photograph showing the in vitro aneurysm model inside a customized container (arrow), which was placed on an MR imaging table. *Right:* Photograph showing the in vitro aneurysm model submerged in the customized container with tubes connected to the parent arteries; the apparatus could be placed in the regular MR head coil.
The creation method and details of this in vitro aneurysm model have been published previously. In brief, 3D surface data obtained in a wide-necked BA tip aneurysm were reconstructed by interpolating source axial images of the CT angiogram, followed by creation of an aneurysm male cast with the use of rapid prototyping technology. This male cast had been scaled 2.6 times as previously reported. A clear acrylic female cast of the BA tip aneurysm was then constructed for the actual test section by using the geometrically realistic male cast of the aneurysm as a mold (Fig. 1 right).

**Experimental System**

The pulsatile flow in the experimental circuit was created by a computer-controlled pump system (Cardioflow 100 MR; Shelley Medical Imaging Technologies, London, ON, Canada), which can be placed near a magnetic bore. Blood-mimicking fluid (Shelley Medical Imaging Technologies) was used as a working fluid in the experimental circuit. This fluid had a density of 1.03 g/cm³ and a coefficient of viscosity of 2.5 × 10⁻³ kg/m/sec. The T1 and T2 relaxation times of the fluid at 1.5 teslas were 650 and 350 msec, respectively.

According to the concept of dimensional analysis and the law of similarity, not all flow parameters, such as coefficient of viscosity, fluid flow velocity, and duration of pulsatile waveform need to be arranged to achieve the similar flow condition in scaled models as long as dimensionless similarity parameters and the waveform shape in the parent artery are matched. Because in this study we measured fluid flow velocity in the pulsatile condition, two dimensionless similarity parameters, the Reynolds number and the Womersley PI, had to be arranged to match those values in vivo to achieve a similar flow condition. The maximum and minimum velocities in the BA of this scaled-up model were set at 15.4 and 5.1 cm/second, respectively, with the duration of one pulsatile waveform at 2.19 seconds. In this condition, the peak, mean, and minimal Reynolds numbers were 700, 365, and 230, respectively, and the Womersley PI was 5.

The shape of pulsatile waveform programmed by the computer-controlled pump system could faithfully simulate that in the human BA. The PI of the waveform was 0.9 at the BA of this in vitro model. The flow rates in each arterial branch were set in accordance with the cross-sectional area of each branch.

The values of the Reynolds number and Womersley PI, and the relative shape of the pulsatile waveform used in this study were exactly the same as those described in the previous LDV measurement. Thus, the pulsatile flow velocity condition in the present study was similar not only to that measured in vivo, but also to that created in the previous LDV measurement. Therefore, the results obtained using phase-contrast MR imaging could be compared with the result obtained using the LDV measurement.

**Data Acquisition With MR Imaging**

The in vitro aneurysm model was submerged in a customized acrylic container with fitted connecting tubes (Fig. 2). The computer-controlled pump system was placed inside the room containing the MR unit and caused no appreciable imaging artifacts. Three-dimensional time-of-flight MR angiograms of the in vitro aneurysm model were obtained while fluid was running in the experimental circuit to select the planes of subsequent phase-contrast flow measurements (Fig. 3).

By using the standard 2D fast low–angle shot flow quantification sequence, all images were acquired on a 1.5-tesla MAGNETOM Sonata unit (Siemens AG, Munich, Germany) with 40-mtesla/m gradients. The pulse sequence parameters were as follows: 99/9.8 msec (TR/TE); 20° flip angle; 22 cm/second encoding velocity; 110 Hz/pixel bandwidth; 210 × 118 mm field of view; 2-mm axial slice thickness; 256 × 144 imaging matrix, interpolated to 512 × 288; prospectively gated by the external trigger of the computer-controlled pump system to 21 cine frames; four averages; imaging time 3 minutes and 4 seconds. The three orthogonal components of velocity were obtained over three separate images to allow a larger number of cine frames. Although it is more efficient to acquire images of all three components at once, the data acquisition time was not a major concern for us in this in vitro study. Images were taken offline and isovelocity contours, secondary flow vectors, and cines were created using scripts written in MATLAB (The MathWorks, Inc., Natick, MA).
Results

By using phase-contrast velocity maps, alternations of 3D intraaneurysmal flow structures during one cardiac cycle could be visualized in one midsagittal cross-sectional plane (Fig. 4) and also in three axial cross-sectional planes in the aneurysm dome perpendicular to the natural axis of the BA (Fig. 5). The gray level in the phase-contrast velocity maps corresponds to velocity in the encoded direction. For example, the whiter a pixel becomes on a velocity map encoded in the anterior-to-posterior direction, the faster the flow velocity becomes, the faster the flow velocity is in the posterior-to-anterior direction.

Midsagittal Plane

The gray scale phase-contrast velocity maps in the midsagittal plane are shown in Fig. 4. The velocity map encoded in the caudocranial direction demonstrates a fast parabolic flow in the BA entering into the aneurysm dome in the anterior aspect of the aneurysm orifice and a slow outward flow in the posterior aneurysm dome. The fast inward flow component was noted along the anterior wall of the aneurysm dome throughout one cardiac cycle. The gray scale phase-contrast velocity mapping images of the midsagittal section could clearly depict an intraaneurysmal circulation pattern. The phase-contrast velocity map encoded in a right-to-left direction shows that a slow left-to-right flow component is also seen at the top of the aneurysm dome. The flow velocity was altered in the inward flow area during one cardiac cycle. On the other hand, it was relatively stable in the outward and anterior-to-posterior flow areas.

Axial Planes

The gray scale phase-contrast velocity maps encoded in all three directions were obtained in three axial cross-sectional planes in the aneurysm (Fig. 5). The flow velocities in the axial cross-sectional planes were documented with two velocity components: axial and secondary flow velocities. The axial flow velocity is a flow velocity component that is parallel to the natural axis of the BA and perpendicular to the axial cross-sectional planes. The secondary flow velocity represents flow velocity vector components parallel to the axial cross-sectional planes. Based on the gray scale phase-contrast velocity maps, isovelocity contour maps and secondary flow vectors were created using MATLAB (Fig. 6).

The isovelocity contour maps and the secondary flow vectors could clearly depict the complex flow velocity structure of the geometrically realistic in vitro BA tip aneurysm model. There was an inward flow area in the anterior aspect of the aneurysm throughout one cardiac cycle. The inward flow area changed slightly in its appearance and location in one cardiac cycle of the lower and mid axial planes (Fig. 6A and B). The size of the inflow zone (inward flow area at the aneurysm orifice) was the smallest during the late systolic phase. A new inward flow area was formed in the left side of the aneurysm orifice during the diastolic and early systolic phases in the low and mid axial planes. There was a relatively high outward flow component noted in the aneurysm bleb (Fig. 6C). Otherwise, the maximal flow velocity and the PI were much slower in the outward flow area than in the inward one. The outward flow area was much larger compared with the inward one throughout a cardiac cycle in all three axial planes.

The secondary flow vectors show twin vortices within the outward flow area adjacent to the boundary layer of inward and outward flow in all axial planes (Fig. 6). The velocity of the vortices was likely to be higher in the middle and bottom planes compared with the lower plane. The secondary flow vectors in the upper axial plane demonstrate another small vortex within the aneurysm bleb (Fig. 6C).

Discussion

Modern biofluid mechanics describes not only simple hemodynamics or flow dynamics of body fluids, but also its interaction with pathophysiological conditions in the blood vessels, lymphatic system, and microcirculation.\textsuperscript{14} Numerous biofluid mechanics investigations have been conducted during the past two decades that have correlated hemodynamic factors with the development of atherosclerotic plaques in relatively large vessels.\textsuperscript{4,13,20} Those studies successfully emphasized the idea that not only the vascular geometry and atherosclerotic risk factors, but also the fluid-induced wall shear stress and flow velocity pattern played a role in the development of atherosclerosis. The accumulation of knowledge from those investigations of atherogenesis has identified a new risk factor: the oscillatory shear...
index.\cite{15} In contrast, the role of biofluid mechanics in cerebrovascular diseases, particularly in cerebral aneurysms, is poorly understood despite the fact that intraaneurysmal hemodynamics seems to play a major role in its generation, growth, and rupture (natural history). The difficulty of in-depth evaluation of flow structure in such a small lesion confined in the skull has been the major challenge.

We have reported LDV flow measurements in geometrically realistic in vitro aneurysm models based on patients’ angiograms, which have provided us with the capability to evaluate detailed flow structure in a cerebral aneurysm with a complicated geometry.\cite{28,29} The accumulation of knowledge from retrospective and/or prospective in vitro intraaneurysmal flow analysis based on patients’ angiograms can reveal its correlation with the natural history of cerebral aneurysms and also with the risk of aneurysm recanalization after embolization with currently available microcoils.\cite{6,7,31} Nevertheless, such knowledge cannot be applied to the clinical setting without the capability to evaluate actual intraaneurysmal flow structure in vivo. The development of a minimally invasive or noninvasive modality of qualitative and quantitative in vivo intraaneurysmal hemodynamic evaluation concomitant with such in vitro hemodynamic analyses is mandatory for the future clinical application.

Since the introduction of MR imaging, this modality, because of its noninvasive nature, has gained increasing interest in clinical settings and also in the research field for the assessment of anatomical as well as physiological information in vivo. In particular, the currently available MR imaging provides a reasonable capacity for in vivo flow velocity qualification and quantification.\cite{6,7,31} Phase-contrast velocity mapping is one of the most accurate in vivo noninvasive methods to quantify flow in the large vessels.\cite{4} Velocity-encoded cine MR imaging provides sequential phase-contrast images at multiple phases during one cardiac cycle. The technique has already been used in the clinical setting to visualize the motion of the aneurysm dome and also to evaluate the hemodynamics of intracranial circulation.\cite{9,17} On the phase-contrast MR images, fluid flow velocity can be measured at specific points. It appears to be feasible to measure a 3D time-dependent flow velocity field anywhere in the human body.\cite{11,12} All of the features of this noninvasive procedure are favorable to evaluate 3D flow structures in the cerebral aneurysms.

### Intraaneurysmal Flow Structures Identified Using LDV and Phase-Contrast MR Imaging

The intraaneurysmal flow velocity structure in the geometrically realistic in vitro BA tip aneurysm model has been evaluated using LDV, and the result has been published previously.\cite{28} In the present study, the same BA tip
Aneurysm model was used for the phase-contrast intraaneurysmal flow evaluation. The saturated sodium iodine solution was used as a working fluid in the previous LDV measurement to eliminate optical distortion of the laser beam. Therefore, the maximum and minimum flow velocities and duration of one cardiac cycle had to be rearranged in this study to achieve a similar flow condition with the blood-mimicking fluid as a working fluid instead of the sodium.

Fig. 6. Alterations of intraaneurysmal flow structures in three axial sections during one cardiac cycle are shown by means of isovelocity contours and secondary flow vectors. Isovelocity contours at the levels of the upper dome (C), lower dome (B), and aneurysm neck (A) were created based on the gray level phase-contrast velocity maps encoded in the caudo-cranial direction at the corresponding levels. Secondary flow vectors in all three axial sections were created based on the gray level phase-contrast velocity maps encoded in the anterior-to-posterior and right-to-left directions at the corresponding levels.
iodine solution. Because the Reynolds number and Womersley index were matched between the previous LDV measurement and the present phase-contrast velocity measurement, it is possible to compare the results obtained from both experiments based on the concept of dimensional analysis and the law of similarity.3,28,32

The results of previously conducted LDV measurements showed that a fast flow entered into the aneurysm dome along the anterior wall, and a relatively slow flow exited from the aneurysm dome along the posterior wall.28 The same intraaneurysmal flow pattern could be visualized in the present study with the use of phase-contrast velocity mapping. The shapes of the inward and outward flow areas were similar in axial sections. Moreover, this study demonstrated that another inward flow area appeared on the left side of the aneurysm orifice during the late systolic and dias-tolic phases (Fig. 6A). This unique alteration in the shapes of the inward flow areas was also documented in the previ-ous report.28

In the present study, the wall shear stress was not calculated based on the flow velocity information, because the spatial resolution of currently available phase-contrast MR imaging measurements was insufficient for an accurate wall shear stress calculation.15 There was, however, a relatively high outward flow noted near the aneurysm bleb (Fig. 6C), which might be indicative of focally increased wall shear stress, because the value of wall shear stress is proportional to the flow velocity near the arterial wall. Indeed, the LDV measurement in the previous study showed increased wall shear stress in the corresponding area.28

Overall, the 3D intraaneurysmal flow structure identified using phase-contrast MR imaging appears to be similar to that depicted by state-of-the-art technology, that is, LDV measurement. The study of a single in vitro aneurysm model may not have complete relevance to other aneurysms with different morphological features. Nevertheless, the time-consuming nature of data acquisition in this experimental design limits our ability to study a large number of cases. Given that in the current study we used a geometri-cally realistic aneurysm model that had a relatively com-plicated shape (BA tip aneurysm with a bleb), the results of this feasibility study indicate that the phase-contrast MR imaging modality has the potential to provide useful intraaneurysmal hemodynamics information in future clinical practice. There is no doubt that further investigations have to be conducted to validate the results as well as to sharpen the technique.

Advantages and Limitations of Flow Visualization by Phase-Contrast MR Imaging

Phase-contrast velocity mapping has some advantages over the other flow measurement modalities. The first ad-advantage is that theoretically the phase-contrast velocity measurement is not affected by the presence of bone structures. This feature is favorable for flow analysis in the parent arteries and aneurysms near the skull base, whereas other flow measurement modalities such as transcra-nial Doppler ultrasonography are affected by the bone structures.10 The capability of visualizing the full 3D flow structure seems to be another advantage, because 2D flow analysis may not be helpful for visualizing complex intraaneurysmal flow structure.22,26,29 Conventional catheter an-giography and intravascular ultrasonography likely provide overall intraaneurysmal flow structure. An intrinsic limi-tation of these technologies, however, is that the flow condi-tions in the parent artery may be significantly altered by the rate of contrast injection or by the intravascular place-ment of a catheter or probe.

The present disadvantages associated with phase-con-trast flow evaluation for in vivo cerebral aneurysms include imaging time and spatial and temporal resolution as well as quantification errors. In this study, we obtained a pixel size of 0.82 × 0.82 mm (1.22 pixels/mm) interpolated to 0.41 × 0.41 mm (2.44 pixels/mm) with a 2-mm slice thickness. The currently available resolution of phase-contrast velocity mapping was adequate for the evaluation of detailed 3D flow structure in the in vitro aneurysm model scaled up by 2.6, but it may be insufficient for small aneurysms in vivo, leading to partial volume errors. Intravoxel phase dispersion from turbulent flow on the order of the size of the pixel can cause loss of signal as well. Reducing the pixel size causes a loss in the signal-to-noise ratio proportional to the voxel volume, which requires increases in averaging. A more significant limitation is the slice thickness, which we already had set at the minimum for our standard 2D fast low–angle shot sequence (2 mm). Three-dimensional se-quences allow thinner slices, but scan times can be much longer, and may be more prone to failures regarding in vivo measurement because of a patient’s motion. These limi-tations will be soon resolved, however, as technology pro-gresses. Utilization of a higher-magnetic field MR imager may be an answer to shorten imaging times and to optimize the signal-to-noise ratio.27 The temporal resolution in our study was on the order of 100 msec per frame, which would be adequate for flow evaluation in cerebral aneurysms in vi-vo, although shorter times are possible with the use of the current technology.

Phase-Contrast Velocity Mapping and CFD

The application of CFD to evaluate intraaneurysmal flow structure is another option. Particularly, current CFD simu-lation technology based on clinical images can be readily incorporated into neurovascular imaging tools of 3D digi-tal subtraction angiography and CT angiography.19,22 More-over, the beauty of the CFD simulation is that it can provide not only flow velocity structure, but also the other important hemodynamic information on intraaneurysmal pressure or fluid-induced wall shear stress.33 Nevertheless, the major in-trinsic limitation of this technology is that the CFD is a sim-ulation, and not a measurement. Therefore, the results of CFD simulation could be completely altered if inappropri-ate boundary conditions were applied. On the other hand, phase-contrast velocity mapping is a direct measurement of fluid flow, and obtaining boundary conditions is not an issue. The phase-contrast MR method presented here can provide fairly accurate flow velocity information in the neck and intracranial arteries.46,7,34 Concomitant use of both CFD simulation and direct intraaneurysmal flow measure-ment with the phase-contrast technique may be of benefit in its future clinical application.

Conclusions

Three-dimensional intraaneurysmal flow structure could
be visualized in a geometrically realistic in vitro aneurysm model with the use of the phase-contrast MR imaging modality. The results of phase-contrast MR imaging measurement were similar to those previously obtained using LDV. Although the current study featured a scaled-up in vitro model, phase-contrast MR imaging was able to depict the complex 3D intraneurysmal flow structure in the aneurysm model, which had the complex geometry seen in actual patients. The same high-quality detailed intraneurysmal flow information will be obtainable in vivo with the improvement of spatial resolution in the near future. The capacity to visualize the intraneurysmal flow structure directly with the use of noninvasive MR imaging technology will have a positive impact on the future clinical management of cerebral aneurysms.

References


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