Endovascular embolization with the use of various detachable coils has been recognized as a valid therapeutic option for cerebral aneurysms. In a recent clinical trial, researchers demonstrated that the clinical outcome in patients free of disability at 1 year after subarachnoid hemorrhage is better in those who have undergone endovascular coil insertion compared with those who have undergone another neurosurgical procedure. Nevertheless, there are numerous unanswered questions regarding the long-term anatomical durability of coil embolization of aneurysms by using existing microcoil technology. Aneurysm recanalization is the most important limitation of current coil embolization and is more noticeable in the treatment of wide-necked aneurysms.

We postulated that flow dynamics plays an important role in aneurysm recanalization as the aneurysm's anatomical characteristics. The aneurysm orifice can be divided into two definite areas: inflow and outflow zones. The inflow zone is the area of the opening where the blood flow enters into the aneurysm cavity, and the outflow zone is where the blood flow exits from the cavity. Arterial dynamic pressure induced by the impingement of pulsatile blood flow in the inflow zone, commonly called the “water hammer effect,” appears to be a significant cause of aneurysm recanalization. In some previous reports authors stressed the importance of tightly packing the aneurysm inflow zone to reduce the possibility of aneurysm recanalization.

The ICA–OphA aneurysm is the most common in our 11-year experience in Guglielmi Detachable Coil embolization of cerebral aneurysms at the University of California at Los Angeles Medical Center. The ICA–OphA aneurysm has been categorized as a side-wall aneurysm and is more noticeable in the treatment of wide-necked aneurysms.

Object. The aim of this study was to evaluate axial and secondary flow structures in a wide-necked internal carotid artery–ophthalmic artery aneurysm, one of the most common locations for endovascular coil placement.

Methods. A clear acrylic aneurysm model was manufactured from a three-dimensional computerized tomography angiogram. Intraaneurysm blood flow analysis was conducted using an acrylic aneurysm model together with laser Doppler velocimetry and particle image velocimetry. The maximal axial blood flow velocities in the inflow and outflow zones at the aneurysm orifice were noted at the peak systolic phase, measuring 46.8 and 24.9% of that in the parent artery, respectively. The mean size of the inflow zone during one cardiac cycle was 44.3 ± 9.8% (range 35.6–58.7%) the size of the axial section at the aneurysm orifice. In the lower and upper planes of the aneurysm dome, the mean size of inward and outward flow areas were 43.3 ± 6.7% and 43.8 ± 6.8% the size of the axial cross-sectional plane, respectively. The axial flow velocity structures were dynamically altered throughout the cardiac cycle, particularly at the aneurysm orifice. The fastest secondary flow at the opening was also noted at the peak systolic and early diastolic phases. Axial blood flow velocity was slower in the upper axial plane of the aneurysm dome than in the lower one. Conversely, the secondary flow component was faster in the upper plane.

Conclusions. The side-wall aneurysm in this study did not demonstrate a simple flow pattern as was previously seen in ideally shaped experimental aneurysms in vitro and in vivo. The flow patterns of inflow and outflow zones were very difficult to predict based on the limited flow information provided on standard digital subtraction angiography, even in an aneurysm with a relatively simple dome shape.

Key Words • hemodynamics • blood flow velocity • cerebral aneurysm • internal carotid artery–ophthalmic artery aneurysm

Abbreviations used in this paper: ACA = anterior cerebral artery; CT = computerized tomography; DS = digital subtraction; ICA = internal carotid artery; LDV = laser Doppler velocimetry; MCA = middle cerebral artery; OphA = ophthalmic artery; PIV = particle image velocimetry; 3D = three-dimensional.
area of the aneurysm orifice. It has yet to be shown whether side-wall aneurysms in actual patients demonstrate such a relatively simple flow pattern, however.

We have already reported on a method of in vitro flow simulation with a geometrically realistic clear acrylic aneurysm model manufactured from patients’ angiograms. In that study, intraaneurysm blood flow analysis in a basilar artery tip aneurysm model was performed with the use of LDV. In the present study, we conducted a detailed 3D flow analysis in a wide-necked ICA–OphA aneurysm by using LDV and also PIV. We believed that a better understanding of intraaneurysm flow patterns in this type of lesion would bring considerable benefits to the development of a therapeutic strategy to control and minimize aneurysm recanalization in wide-necked aneurysms.

Materials and Methods

Creation of an In Vitro Aneurysm Model

A 3D CT angiogram obtained in a patient with a wide-necked, unruptured ICA–OphA aneurysm was used to create an in vitro aneurysm model (Fig. 1). The 3D data were obtained using a helical CT scanner (model CT4; General Electric, Waukesha, WI). Technical parameters were 120 kVP with a tube current of 300 mA. One hundred twenty milliliters of nonionic contrast material at a concentration of 350 mg/ml (iohexol; Nycomed Amersham, Princeton, NJ) was injected at a rate of 3 ml/second, with a scan delay of 22 seconds after contrast injection. The helical pitch and slice collimation were 1.5 and 1 mm, respectively, with a 0.5-mm reconstruction interval. The field of view was 180 mm, with a matrix size of 512 × 512; spatial resolution was 0.35 × 0.35 mm. Image reconstruction used 180° linear interpolation.

The ICA–OphA aneurysm arose distal to the origin of the left OphA. The body of the aneurysm projected superiorly, with medial and anterior angulation. The diameter of the aneurysm dome measured 8.1 mm anteroposteriorly, 9.4 mm transversely, and 11.5 mm craniocaudally. The aneurysm orifice had an oval shape, measuring 5.8 mm in its anteroposterior and 6.4 mm in its transverse diameters. The cavernous and supraclinoid segments of the left ICA showed no evidence of atherosclerotic changes, measuring 3.5 mm in its largest diameter.

Three-dimensional surface data were reconstructed by interpolating the source 3D CT angiography images for the creation of a male cast of the aneurysm on a stereolithography machine (model SLA 250 RP&M system; 3D systems, Shoreview, MN). The surface data obtained from the 3D CT angiography included that from the following: the ICA–OphA aneurysm, the left ICA (from the petrous to the cervical segments), the A1 segment of the left ACA, and the M1 segment of the left MCA.

The construction method of this in vitro aneurysm model has been previously reported. In brief, stereolithography was used to create a geometrically realistic ICA–OphA aneurysm model based on the 3D surface data (Fig. 2 left). To visualize a detailed flow velocity pattern in such a small lesion, the size of the in vitro aneurysm model was scaled up to 2.7 times the size of the original (Fig. 2 center). A clear acrylic female cast of the ICA–OphA aneurysm was then constructed as an actual test section by using the geometrically realistic aneurysm model as a mold (Fig. 2 right).

Fluid Flow Condition

We applied the concept of dimensional analysis and the law of similarity to achieve the physiological flow conditions in the scaled-up aneurysm model. Non-dimensional similarity parameters such as the Womersley parameter and the Reynolds number in vitro had to be arranged to match those in vivo to achieve a similar pulsatile flow condition in the scaled-up model with a working fluid other than a blood analog. A saturated aqueous solution of sodium iodide was used as a working fluid in this study for accurate LDV and PIV measurements, because its refraction index is exactly the same as that of the acrylic resin. The kinematic viscosity of the working fluid at operating temperature was 1.64 × 10⁻⁶ m²/second. The Womersley index and the maximum Reynolds number in this experimental system were 6 and 900, respectively, when the maximal and minimal flow velocities in the parent artery were 0.11 and 0.055 m/second, respectively. The duration of one cardiac cycle was 4 seconds.

Another important factor in achieving a similar flow velocity condition in a scaled-up model is the shape of the velocity waveform. The design of the experimental flow circuit used to create a physiological waveform has been reported in the literature. Laser Doppler velocimetry was generated in the experimental flow circuit by using a velocity-controlled servomotor (model VLBS-A11012; Toei Electric, Tokyo, Japan). A steady mean flow generated by the hydraulic pressure of an elevated reservoir tank was superimposed on the pulsatile flow. The velocity waveform at the proximal parent artery successfully simulated the waveform obtained using Doppler ultrasonography. The pulsatility index of the waveform was 0.79. The flow volume rates of the ACA and the MCA were set in accordance with the cross-sectional area of each branch.

Velocity Measurements With LDV and PIV

Laser Doppler velocimetry (500-nW Ar-ion Laser; Ion Laser Technology, Frankfort, IL), and digital burst correlator model IFA 650; TSI, Minneapolis, MN) and PIV (TSI) were used for quantitative 3D velocity measurements. With LDV, one can measure point velocity by detecting the reflected laser beam from seeding particles in the working fluid, with the actual dimensions of 180 × 34.2 μm. The titanium dioxide seeding particles with a size of 0.63 μm were added to the working fluid for velocity measurements. The LDV measurement was conducted in three axial planes: one at the aneurysm orifice and two in the aneurysm dome (Figs. 3 upper and 4 upper). The axial velocity, which is perpendicular to the three axial planes, was obtained at 97 points per plane.

In the PIV measurements, silica particles with a size of 10 μm were added to the working fluid. The reflective silica particles were illuminated as they passed through a sheet of laser light, and sequential images of the illuminated particles in the sheet of laser light were acquired by PIV. From those sequential images, a computer software program calculated the direction and velocity of the particles. With the use of PIV, secondary flow was measured in the same axial planes as those selected during LDV measurements (Figs. 3 lower and 4 lower). The velocity measurement was also obtained in a mid-sagittal section by using PIV (Fig. 5).

Results

Flow Structure at the Aneurysm Orifice

The alterations in the flow pattern were demonstrated in...
six phases of one cardiac cycle. There was marked alteration of the axial flow velocity at the aneurysm orifice (Fig. 3 upper). In the late diastolic phase, a long-shaped inflow zone was noted at the center of the lesion, dividing two outflow zones located at the distal and proximal areas of the orifice. The inflow zone moved to the distal and medial aspects of the aneurysm opening and became smaller in size during the early systolic phase. There was no appreciable change in the shape of the inflow zone between the early systolic and peak systolic phases, but blood flow velocity rapidly increased. The inflow zone moved to the distal area of the orifice during the early diastolic phase. Another small inflow zone was formed at the proximal lateral aspect of the orifice. The two inflow zones became larger as the phase advanced, and the two fused to form one large inflow zone during the late diastolic phase.

The mean blood flow velocity in the inflow zone was $2.77 \pm 1.58$ cm/second (range 0.89–5.08 cm/second). The mean flow velocity in the outflow zone was $-1.64 \pm 0.68$ cm/second (range $-0.8$ to $-2.74$ cm/second). Maximal flow velocities in the inflow and outflow zones were noted during the peak systolic phase, measuring 46.8 and 24.9% of that in the parent artery, respectively. The pulsatility indices of the inflow and outflow zones were 1.4 and 1.2, respectively. The mean sizes of the inward flow areas in the lower and upper planes were $43.3 \pm 6.7\%$ and $43.8 \pm 6.8\%$ the size of the axial cross-sectional plane, respectively. The highest flow velocity was observed at the peak systolic phase, meaning that there was no significant delay in this phase in the dome when compared with the phase at the orifice.

The mean flow velocities in the inward and outward flow areas of the lower axial plane of the aneurysm dome were $2.29 \pm 0.61$ cm/second (range 1.27–3.12 cm/second) and $-0.84 \pm 0.35$ cm/second (range $-0.51$ to $-1.52$ cm/second), respectively. The mean flow velocities in the upper axial plane of the aneurysm dome were $1.84 \pm 0.57$ cm/second (range 1.07–2.9 cm/second) in the inward flow area and $-0.99 \pm 0.3$ cm/second (range $-0.63$ to $-1.36$ cm/second) in the outward flow area. Pulsatility indices of inward flow areas in the lower and upper planes were 0.85 and 0.91, respectively. Overall, axial flow velocity was slower in the upper plane than in the lower one. Conversely, the secondary flow component was faster in the upper plane. The faster secondary flow was located in the distal lateral aspect of the planes (Fig. 4 lower). These findings were likely owing to the transition between the inward and outward flow areas in the upper plane. The direction of the

Flow Structure in the Aneurysm Dome

The axial and secondary flow patterns in the lower and upper axial planes were very similar. In these planes in the aneurysm dome, the inward and outward flow areas altered their appearance during one cardiac cycle, but their locations did not change throughout the cycle (Fig. 4 upper). The inward flow areas were located in the distal and lateral aspects of the axial planes. The size of the inward flow area became smaller toward the peak systolic phase, but recovered its original size at the diastolic phase. The mean sizes of the inward flow areas in the lower and upper planes were $43.3 \pm 6.7\%$ and $43.8 \pm 6.8\%$ the size of the axial cross-sectional plane, respectively. The highest flow velocity was observed at the peak systolic phase, meaning that there was no significant delay in this phase in the dome when compared with the phase at the orifice.

The mean flow velocities in the inward and outward flow areas of the lower axial plane of the aneurysm dome were $2.29 \pm 0.61$ cm/second (range 1.27–3.12 cm/second) and $-0.84 \pm 0.35$ cm/second (range $-0.51$ to $-1.52$ cm/second), respectively. The mean flow velocities in the upper axial plane of the aneurysm dome were $1.84 \pm 0.57$ cm/second (range 1.07–2.9 cm/second) in the inward flow area and $-0.99 \pm 0.3$ cm/second (range $-0.63$ to $-1.36$ cm/second) in the outward flow area. Pulsatility indices of inward flow areas in the lower and upper planes were 0.85 and 0.91, respectively. Overall, axial flow velocity was slower in the upper plane than in the lower one. Conversely, the secondary flow component was faster in the upper plane. The faster secondary flow was located in the distal lateral aspect of the planes (Fig. 4 lower). These findings were likely owing to the transition between the inward and outward flow areas in the upper plane. The direction of the
secondary flow did not change very much throughout one cardiac cycle in either—upper or lower—plane.

Flow Structure in the Midsagittal Plane

The flow velocity pattern in the midsagittal plane was obtained using PIV (Fig. 5). In this plane, the inflow zone at the aneurysm orifice could not be clearly visualized, especially during the diastolic phase. At the peak systolic phase, a relatively fast inward flow was noted at the center of the aneurysm orifice, which disappeared in the next phase (Fig. 5, t = 1.77). There was also a relatively fast outward flow posterior to the relatively fast inward flow at the peak systolic phase. There was a slow inward flow along the distal...
portion of the aneurysm dome during the late systolic to late diastolic phases. The midsagittal plane alone appeared to be insufficient to visualize the alteration in the detailed flow pattern during one cardiac cycle in this particular aneurysm, because the inflow area changes its location and shape within the axial plane throughout one cardiac cycle.

**Discussion**

**Hemodynamic Factors and Aneurysm Recanalization**

Flow velocity, pressure, and fluid-induced wall shear stress have been identified as three important hemodynamic factors related to aneurysms. Flow velocity, pressure, and fluid-induced wall shear stress have been identified as three important hemodynamic factors related to aneurysms. The pressure can be divid-
ed into two components: hydrostatic pressure and dynamic pressure. Hydrostatic pressure is best known as blood pressure. Dynamic pressure is a force produced when the circulating blood flow impinges on the arterial wall and is superimposed on the hydrostatic pressure. This is the reason why specific points of arteries such as branching points are exposed to higher pressure. The fluid-induced wall shear stress has also been discussed in previous hemodynamic studies. The wall shear stress is a very small frictional force produced by a viscous fluid moving across the inner surface of a vessel, and it appears to be related to the initiation and development of cerebral aneurysms. The normal range of wall shear stress on the arterial inner surface is approximately 1 to 7 Pa (1 mm Hg = 1.33322 × 10^{-2} Pa); it is much smaller than dynamic and hydrostatic pressures. Furthermore, the direction of wall shear stress is theoretically parallel to the direction of blood flow, whereas the direction of hydrostatic and dynamic pressures is perpendicular to vessel walls. Therefore, fluid-induced wall shear stress cannot be the cause of the coil compaction.

The dynamic pressure induced by the impingement of the bloodstream onto the coil mesh appears to be closely related to aneurysm recanalization after embolization with Guglielmi Detachable Coils. We believe that an appropriate analysis and understanding of hemodynamics in aneurysms are key factors to achieving successful long-term anatomical results. This is particularly true in large aneurysms with wide necks. Postembolization aneurysm recanalization is more frequently noted in patients with wide-necked aneurysms than in those with small-necked lesions. Aneurysm recanalization mostly occurs because of coil compaction at the level of the aneurysm neck inflow zone. This phenomenon can be interpreted as a failure to control aneurysm hemodynamics. Given that the dynamic pressure induced by the impingement of blood flow on the coil mesh appears to be the direct cause of coil compaction, the axial flow velocity at the aneurysm orifice is a more significant factor than the secondary flow component.

In the present study, the inflow zone of the aneurysm was exposed to fast and highly pulsatile axial flow. Data from a previous hemodynamic study have indicated that the location of the inflow zone is altered more by flow characteristics from the parent artery than the shape of the aneurysm itself. Coils placed near the aneurysm neck inflow zone are exposed to significant dynamic pressure even after an alteration in the intraaneurysm flow pattern has been achieved using coil embolization. The flow pattern in the parent artery near the aneurysm orifice should be similar before and after aneurysm embolization, because the geometrical features of the parent artery are essentially unchanged. These facts support the importance of tightly packing the aneurysm inflow zone.

Flow Information Based on Catheter Angiography

The attraction of standard DS angiography resides in the fact that it can demonstrate not only anatomical information of small cortical branches or perforating arteries, but also valuable physiological information such as blood flow, capillary stain, and capillary or venous phase transit time. Previous researchers also have shown that intraaneurysm flow rates can be determined based on time-density curves with the use of DS angiography. A careful review of the motion of contrast material provides an approximate idea of the location of the aneurysm inflow zone prior to coil embolization. Interventional neuroradiologists analyze postembolization flow changes in aneurysms by depicting contrast stagnation in the coil mesh; however, it is impossible to depict an accurate location for the aneurysm inflow zone based on standard DS angiography.
First, even side-wall aneurysms in actual patients demonstrated complicated movement in the inflow and outflow zones throughout one cardiac cycle. The inflow zone of a side-wall aneurysm in a patient may not necessarily be located in the distal area of the lesion opening, as observed in the current study. The flow characteristics noted at the aneurysm orifice in the present study were complicated, which seemed to be difficult to appreciate with catheter angiography. Conversely, flow characteristics in the aneurysm dome were relatively simpler when compared with those at the aneurysm orifice. The flow analysis in this study shows that the locations of inward and outward flow areas in the dome of this ICA–OphA aneurysm were nearly constant throughout one cardiac cycle. With conventional catheter angiography, we might have called this easily detectable, nearly constant inward flow area in the lower plane of the aneurysm dome “an inflow zone in the aneurysm orifice.”

Today, interventional neuroradiologists try to achieve a tight packing of coils near the aneurysm orifice where the coil mesh is exposed to maximal flow impingement. Nevertheless, in our study the inflow zone became the smallest in size when the maximal axial flow velocity was noted. This small area in the aneurysm orifice may be difficult to locate on two-dimensional images, even with the use of current state-of-the-art biplane technology. Accordingly, there is a limitation in obtaining accurate aneurysm flow patterns by using conventional DS angiography.

Intraaneurysm Flow Structure

The blood flow analysis in this ICA–OphA aneurysm showed a complex flow pattern despite its relatively simple round shape. This might be due to the tortuous course of the carotid siphon. Results of a recent flow simulation in the ICA indicated that the curvature of the carotid siphon determines flow characteristics in the suprachiasmatic ICA. Thus, there may be complex blood flow patterns in ICA–OphA aneurysms as well as other suprachiasmatic ICA lesions such as superior hypophysial, posterior communicating, and anterior choroidal aneurysms.

Previously, we investigated the flow pattern of a basilar artery tip aneurysm by using LDV. Although the secondary flow component was not discussed in that study, the flow structure in the basilar artery tip aneurysm orifice was also complex (as seen in the present study with the use of both LDV and PIV). We have demonstrated flow velocity structure by using axial and midsagittal planes. In previous flow dynamics studies, a midsagittal plane was frequently selected to visualize intraaneurysm flow. This was not sufficient in the present study, however, because of the complex 3D characteristics. Therefore, the flow pattern in a realistic aneurysm model should be presented in multiple sagittal planes when needed. The axial plane appeared to be favorable for visualizing complex flow characteristics at the aneurysm orifice, particularly the location of the inflow zone.

In Vitro Flow Simulation

The geometrically realistic acrylic aneurysm models based on 3D CT angiograms allowed us to use LDV and PIV for quantitative flow analysis. The time-consuming nature of LDV measurements was a limitation in the previous study. With the combined use of LDV and PIV, the data acquisition process to assess the entire flow field was dramatically shortened. Another merit of the PIV measurement was that it provided readily comprehensible visualization of complex flow patterns, and it was particularly advantageous to demonstrate the secondary flow on axial planes.

The use of nonelastic material is a limitation in this hemodynamic study. It is very difficult to reproduce the elasticity of the heterogeneous tissue of cerebral aneurysms in living patients. Data from a past report have indicated that a rigid aneurysm model could provide a reasonable result, however.

The computational flow simulation seems to provide well for flow investigations. It may be incorporated as part of a software package of 3D vascular imaging reconstruction. In the absence of a corresponding experimental flow study, however, it cannot be validated; that is, the combined in vitro and computational flow simulation are mandatory for the development of a valid system. The development of appropriate pretherapeutic systems of computational qualitative and quantitative flow simulations based on dedicated 3D anatomical information will bring considerable benefits to the research for aneurysm treatments, especially given that detailed intraaneurysm flow patterns appear to be very difficult to visualize with the use of current diagnostic techniques.

Conclusions

An in vitro study of intraaneurysm flow dynamics was conducted using a clear acrylic model based on 3D CT angiograms of an ICA–OphA aneurysm. In our model we found that the side-wall aneurysm did not demonstrate a simple flow pattern, as was previously seen in ideally shaped experimental aneurysms in vitro and in vivo. The inflow zone of the aneurysm was exposed to fast and highly pulsatile axial flow. Despite the fact that blood flow control is one of the key factors to improving the long-term anatomical outcome of aneurysm embolization, the results of the present study indicate that current neurodiagnostic technologies such as DS angiography do not have the capability to provide sufficient hemodynamic information, including the location of the inflow zone. The endovascular treatment of aneurysms may benefit from an accurate pretherapeutic evaluation of flow patterns in the aneurysm neck and dome, which can be achieved using validated computational fluid flow simulation software or other modalities to visualize the complex intraaneurysm flow pattern.

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