In vitro hydrodynamical study on aneurysmal morphology for treating intracranial aneurysms using particle imaging velocimetry

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Abstract Low-porosity stents such as flow diverters and the flow isolator, which we developed in a previous study, are expected to provide an effective and minimally invasive treatment for intracranial aneurysms (IAs). After inserting a stent, thrombus formation is promoted by the stagnation of IA blood flow. Consequently, IA embolization can occur. Therefore, IA flow intensity significantly affects IA embolization treatment. IA morphology such as aneurysm size, aspect ratio, and bottleneck factor are important parameters as general indices of IA rupture. Meanwhile, existing literature suggests that IA morphology is considerably affected by IA flow and IA embolization. Hence, this work investigates the relationship between IA flow intensity and IA morphology by using particle imaging velocimetry (PIV) and in vitro flow simulation with IA and parent vessel models. The PIV results showed that the area mean shear rate (AMSR), a hemodynamical index of thrombus formation, was higher in IA models with higher neck widths, lower aneurysm heights, and smaller dome sizes. This implies that thrombus formation is inhibited in a wide-neck and small aneurysm. Moreover, stents with effective flow-reduction properties are required for a reliable IA embolization treatment. The AMSR was well expressed by a power function using the Reynolds number and IA morphology as parameters.

Keywords aneurysm, PIV, flow diverter, covered stent, flow isolator

1. Introduction

Low-porosity stents including flow diverters (FDs) [1, 2] and a flow isolator (NCVC-CS1), which we developed in a previous study [3], have been proposed as an effective and minimally invasive treatment for intracranial aneurysms (IAs). Intracranial aneurysms treatment by stents is targeted at thrombus formation in the aneurysm, triggered by the stagnation of IA blood flow. Therefore, the flow-reduction capability of stents significantly affects the embolization treatment performance of IA. A stent with effective flow-reduction properties leads to reliable IA embolization. However, excessive flow reduction was linked to an elevated risk of intimal thickening and side-branch occlusion in the region surrounding the stent [4, 5].

Aneurysm morphology is commonly used to characterize IA ruptures. Aneurysm size is one of the most common morphologic parameters; larger aneurysms tend to rupture more easily [6]. The aspect ratio (aneurysm dome / neck width) or bottleneck factor (aneurysm height / neck width) are also frequently referred to as rupture indices [7, 8]. Aneurysm morphology is considerably affected by the IA flow and IA embolization. Consequently, the effects of IA morphology on the hemodynamics at the stent have been actively investigated [9, 10], and its relation with IA rupture has been clarified to some extent.

Computational fluid dynamics (CFD) studies have been conducted to understand IA flow and the relationships of other parameters, such as the relationship between IA flow and rupture rate [11], the influence of FDs on the IA flow rate [12], influence of FD porosity [13], prediction of thrombus formation [14], and the relationship between the IA and the parent vessel morphology [15]. Particle image velocimetry (PIV) is another common tool used to understand IA flow [16, 17]. When developing NCVC-CS1, we evaluated its IA flow-reduction properties by PIV and in vitro flow simulations using IA models. Consequently, the relationship between its pore size and flow-reduction properties was clarified [18]. Moreover, the flow-reduction
There were various studies on the hemodynamics of specific IA shapes such as ruptured IAs [20, 21]. In contrast, this study attempts to understand the relationship between the IA morphology and IA flow. Thus, IA flow was visualized using an in vitro IA flow simulator and the PIV technique. In particular, the flow velocity distribution in the central cross-section of the IA was measured for a saccular aneurysm formed on the sidewall of the straight parent vessel. Subsequently, the shear rate, which is a hemodynamical index of thrombus formation [22], was calculated. The flow pattern and area mean shear rate (AMSR) of the IA flow were measured by varying IA morphology parameters (neck width, aneurysm height, dome size).

2. Materials and methods

2.1. In vitro flow simulator

The experimental setup has already been presented in detail in previous reports [18, 19]. A schematic of the flow simulator is shown in Fig. 1. The working fluid was a mixture of glycerin (53 wt.%) and water (47 wt.%) with a density of 1130 kg/m$^3$ and kinematic viscosity of $\nu = 4.4 \times 10^{-6}$ m$^2$/s almost same as the kinematic viscosity of human blood. A steady flow was generated by a centrifugal pump. The temperature of the working fluid was kept approximately constant using a chiller to avoid changing the kinematic viscosity. The straight section of the parent vessel model was set to over 370 mm upstream and over 70 mm downstream of the IA model to obtain fully developed laminar flow and to avoid flow disturbances at the end of the parent vessel model. The definition of Reynolds number ($Re$) of the flow through the parent vessel model was

$$Re = \frac{UD_H}{\nu} = \frac{Q}{D_H \nu}$$

(1)

where $\bar{U}$ is the average flow velocity at the cross-section of the parent vessel, and $D_H$ and $Q$ denote the hydraulic diameter and volumetric flow rate at the simplified parent vessel model, respectively. $Re$ was varied in increments in the range of 160–970 ($Q$ was varied in the range of 210–1280 ml/min) by adjusting the flow rate using a flow-regulating valve.

As the stent model, a microporous sheet was placed between the IA and the parent vessel model to simulate the flow-reduction properties of NCVC-CS1 (Fig. 2). The pore diameter and porosity of the microporous sheet were approximately 0.1 mm and 30%, respectively. The microporous sheet was fabricated by laser processing (Femtosecond laser micro-nanomachining system, Tokyo Instrument Inc., wavelength: 800 nm, repetition rate: 1 kHz, pulse energy: 1 mJ, pulse duration: 90 fs).

2.2. IA model

An actual aneurysm has a complicated 3D shape. However, to clarify the physical phenomena with high generality and reproducibility, the IA and parent vessel model had a 2D projection shape with an elliptical sphere IA and a circular vessel with constant thickness. The thickness of the IA and parent vessel model was 5 mm to adjust the hydraulic diameter $D_H$. The parent vessel height $H_{PV}$ was 5 mm. Figure 3 shows the reference shape of the IA model. The neck width $W$, aneurysm height $H$, and dome size $D$ of the reference shape were 7.9, 9.1, and 10.0 mm, respectively. The neck width $W$ was varied in the range of 2.0–19.9 mm.

Figure 1 Schematic of the in vitro flow simulator with the IA model. The microporous sheet of the stent model was inserted between the IA and parent vessel models. Particle image velocimetry measurements were performed at the symmetry plane of the IA model.
The neck width $W$ was set by using a slit sheet to determine the width or by including fillets at the base of the IA model. The aneurysm height $H$ and dome size $D$ varied in the ranges of 3.6–20.0 mm and 7.1–20.0 mm, respectively, by scaling the reference shape vertically and horizontally. The IA and parent vessel model were manufactured by machine processing acrylic resin. The IA and parent vessel parts were prepared separately and assembled later to enable the accurate placement of the stent model’s mesh sheet.

2.3. PIV measurement

The flow fields of the symmetry plane in the IA model were measured via PIV technique. Fluorescent tracer particles (FLUOSTAR, EBM Co., excitation: 550 nm, emission: 580 nm) were seeded in the working fluid. The particles were illuminated using a 1-mm-thick laser sheet generated by an Nd:YAG Laser (DPIV-S50, LaVision GmbH, 532 nm). The fluorescent particle images were acquired by a high sensitive CCD camera (Pixel fly QE-S Double shutter, PCO GmbH, 12 bit, 1392 × 1024 pixels) placed on the side of the IA model. A long-pass filter (cut-off wavelength: 570 nm) was installed on the camera lens. The distributions of the flow velocity were measured using cross-correlation PIV (VidPIV 4.0, Intelligent Laser Applications GmbH) based on images taken at 100 temporal points. The shear rate $\dot{\gamma}$ and area mean shear rate (AMSR) $\bar{\dot{\gamma}}$ were defined as

$$\dot{\gamma} = \frac{\partial v}{\partial x} + \frac{\partial u}{\partial y}$$

$$\bar{\dot{\gamma}} = \frac{\int_{A_{IA}} \dot{\gamma} dA}{\int_{A_{IA}} dA}$$

where $v$ and $u$ are the flow speed in the $x$ and $y$-direction, respectively, and $A_{IA}$ is the area of the center plane of projection shape of the IA model.

3. Results

3.1. Velocity and shear rate maps of the IA flow

The distributions of the flow velocity and shear rate for $Re \approx 600$ ($Q \approx 790$ ml/min) are shown in Fig. 4. In the measurements without the stent model, counterclockwise
flows were observed in all IA models. High-shear rate region was often observed in the IA neck and downstream region. The flow velocity and shear rate of IA neck were higher for wider-neck IA models. In the IA models with high values of $H$ or $D$, relatively low shear rate regions were observed.

In the measurements with the stent model, clockwise flows were observed in all IA models. The velocity and shear rate of IA flow were considerably lower than those without the stent model. The flow velocity and shear rate of IA neck were higher for wider-neck IA models. In the IA models with high values of $H$ or $D$ and low value of $W$, relatively low shear rate regions were observed.

3.2. Area mean shear rate

The AMSR of the whole mapping area in the IA model was used for comparison of the IA flow intensity of various IA models. Figure 5 shows the relationship between the AMSR and $Re$ obtained by the PIV experiments. The AMSR exhibited a high correlation with $Re$. By including the stent model, the AMSR was reduced by more than an order of magnitude, compared with no sheet. Figure 6 shows the relationship between the AMSR and the IA morphology parameter. The AMSR was higher for IA models with higher $W$, lower $H$, and smaller $D$. The relationships between AMSR and $Re$ or IA morphology parameters were well described by a power function. Table 1 lists the average exponent values of the fitted power functions.
4. Discussion

The relationship between the IA morphology and IA flow was investigated to obtain an index for IA treatment using low-porosity stents. According to the obtained results, the AMSR of IA flow was higher in IA models with higher $W$, lower $H$, and lower $D$. This was because the fast flow inside the parent vessel is easily transmitted into the IA at wide-neck IA, and a smaller amount of fluid being swirled in the smaller IA. This means that thrombus formation is less likely in wider-neck and smaller aneurysms. Moreover, stents with effective flow-reduction properties are required for a reliable IA embolization treatment.

The relationship between the ASMR and $Re$ or IA

Figure 5 Area mean shear rate in various IA models as a function of $Re$ in double logarithmic charts. The parameters are neck width (A), aneurysm height (B), and dome size (C). The lines represent fitted exponential curves.
The ASMR trend is well expressed by Eq. (4). Thus, the IA flow intensity can be determined from the blood flow rate and IA morphology; thus, a stent that can sufficiently promote thrombus formation and IA embolization is required.

The observed transition of the swirl flow direction depends on placing of the stent model, as shown in Fig. 4. This phenomenon was observed in previous studies [16, 17].

Figure 6 Area mean shear rate of various IA models as a function of the IA morphology parameters in double logarithmic charts: neck width (A), aneurysm height (B), and dome size (C). The lines represent fitted exponential curves. The data are the same as in Fig. 5.
According to these works, the main factor determining the swirl flow in the absence of a stent is the shear stress between the parent vessel flow and the fluid at the IA neck. In contrast, in the presence of a stent, the main factor is the pressure gradient at the IA neck. The exponent values of the fitted power functions depended on placing of the stent model, suggesting the influence of the flow-type. It is considered that the absolute exponent value of $W$ increased and that of $H$ and $D$ decreased by placing of the stent model, because the IA flow without the stent model is swirling in the whole aneurysm and that with the stent model swirls at the IA neck in a semicircular-shape.

The three factors determining the intensity of the IA flow from the parent vessel to the IA, flow-reduction capabilities of the stent, and IA morphology are considered to be the most important factors in predicting the intensity of the IA flow. The flow-reduction capabilities of stents were investigated in various previous studies [16, 18], and was found to be strongly dependent on the porosity and the pore size of the stent. The effects of the IA morphology are shown in this study. The intensity of the IA flow from the parent vessel to the IA was influenced not only by the intensity of the parent vessel flow, but also by the parent vessel morphology. In IAs that occur outside the curved vessels, the IA flow intensity is considerably higher than that of those that occur in straight vessels because of the direct inflow and secondary flow effects. Thus, it is necessary to use a stent with high flow-reduction capabilities, such as a flow isolator, for treating IAs exposed to fast flow [19]. It is a remaining task to explain the relationships between AMSR and IA morphology by hemodynamic theory. Furthermore, by clarifying the relationship between the IA flow intensity and the outcome of IA embolization treatments, more accurate objective indicators for IA treatment are expected to be obtained.

### 5. Conclusions

A hemodynamic study was conducted using *in vitro* flow simulations using a saccular IA model formed on the side-wall of a straight parent vessel model to clarify the relationship between the IA flow intensity and IA morphology. The AMSR of IA flow was higher in wider-neck and smaller IA models. The AMSR was well expressed by an exponential model including the $Re$ and IA morphology parameters.

#### LIMITATIONS

PIV measurements were performed at the symmetry plane of the IA model, which had a 2D projection shape with a suitable thickness. However, the AMSR may differ

### Table 1

| Stent model | Varied IA morphology parameter | The average exponent value of fitted power function $Re$ | IA morphology parameter |
|-------------|--------------------------------|----------------------------------------|------------------------|
| No sheet    | $W$                            | 0.67                                   |                        |
|             | $H$                            | 0.66                                   | −1.12                  |
|             | $D$                            | −0.96                                  |                        |
| With sheet  | $W$                            | 1.24                                   |                        |
|             | $H$                            | 0.85                                   | −0.62                  |
|             | $D$                            | −0.64                                  |                        |

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**Figure 7** Area mean shear rate of various IA models organized according to the obtained experimental formula in a double logarithmic chart. Data are the same as in Fig. 5 and 6.
in other planes, and so might the average characteristic of the whole 3D model. Furthermore, the flow reduction in an in vitro experiment and the IA embolization effect in clinical and in vivo studies may not necessarily coincide.

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