

Comparison of flow patterns around stenotic area in elastic PVA-H model and in rigid-like silicone model

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INTRODUCTION

Vascular stenosis reduces the volume of blood flow, resulting in embolism, or rupture of blood vessels [1]. Plaques exhibit a wide range of stiffness [2], and stiffness is an important factor in plaque behavior [3]. Moreover, plaque is a sign of high-risk plaque vulnerability, leading rupture of the fibrous cap associated with the release of thrombogenic factors into the arterial lumen, and resulting in repeated ischemic stroke during a short interval after diagnosis [4]. The changes in the blood flow conditions associated with types of soft plaque are often in contrast to the changes associated with calcified plaque, which is a type of hard plaque and is immobile.

Blood flow conditions are attractive features for the advancement of diagnostic techniques for detecting stenoses or plaques. Many studies have been performed focusing on stenotic flow conditions using rigid tubes to represent blood vessels [5, 6]. These studies report that the geometry of the stenosis is an important factor influencing blood flow conditions. However, few studies have investigated the effect of the soft plaques on the blood flow behavior.

In this study, the effect of the plaque and blood vessel deformation on blood flow conditions has been evaluated using *in vitro* studies. Stenosis severity (SS) is an important factor for diagnosis. Hence, we measured SS under various pressure levels. Flow velocity measurement is also important because a peak systole velocity greater than 200 cm/s in internal carotid artery (ICA) is one of the most reliable predictors of an ICA SS of greater than 70% [7]. Wall shear stress (WSS) is one of the risk factors for vessel diseases [8, 9], and the WSS is strongly affected by eddies in the recirculation area [10]. Reattachment point (RAP) can be one index for determining the size of the eddies. Thus, we located the RAP instead of WSS because the former can be more easily identified in the images of flow distributions using PIV measurement in this *in vitro* study.

A biomodel with varying plaque stiffness is useful for measuring SS, WSS, and RAP. To represent an *in vivo* condition, a poly (vinyl alcohol) hydrogel (PVA-H) biomodel imitating the mechanical properties in the human body has been introduced instead of a silicone biomodel [11]. Owing to its transparency [12], PVA-H is beneficial for observing flow using PIV method [13].

A PVA-H stenosis model has been developed. Shimizu et al. developed the model with varying stiffness [14]. Ji et al. developed another PVA-H stenosis model to demonstrate plaque deformation with pulsatile flow [15]. They reported that variation in the flow rate caused the deformation. They proposed that plaque stiffness is an important parameter associated with deformation of blood vessels and plaques themselves. Thus, it is considered that flow pattern in blood vessels can be changed by vessel and plaque deformations. Furthermore, observations of flow conditions using a PVA-H stenosis model may provide better understanding of vessel diseases because flow pattern and deformation of the model can be simultaneously observed with the PIV method.

The purpose of this study is to determine differences in flow conditions between the silicone and PVA-H models in order to discuss experimental materials for arterial wall and flow observations. In particularly, the relationship between the deformation of the vessel after the stenosis and RAP change was observed in this paper. In combination with our previous paper [16], such information helps to establish a relationship between blood flow conditions and disease progression.

MATERIALS AND METHODS

The PVA-H stenosis model was prepared with 4 mm in diameter and 160 mm in length were used as the mold for the PVA-H stenosis model with 70% blockage, as defined by NASCET method (Eq. (1));

$$SS = \left(1 - \frac{D_s}{D}\right) \times 100 \quad (1)$$

In Eq. (1), D_s is the diameter of stenosis and D is the diameter of the parent artery, as shown in Fig. 1. The PVA solution (JF-17, Japan Vam & Poval Co., Ltd., Japan) was dissolved in a mixed solvent of distilled water and dimethyl sulfoxide (DMSO) (Toray Fine Chemicals Co., Ltd., Japan) (20/80, w/w). The solution was stirred for 2 hours at 100°C. Then, the solution was poured into a mold and the PVA solution in the mold was cooled at -30°C for 24 hours to promote gelation of the PVA solution. Afterward, the mold was removed. The silicone rigid model was prepared based on the PVA-H model dimensions.

The PIV circuit is shown in Fig. 3. For PIV measurements, a Nd:YAG solid laser system (532NM-X-300MW, B&W TEK INC., Newark, DE) was used to provide a 1 mm thick continuous laser sheet through the center plane of the tube with a power of 100 mW and a wavelength of 532 nm. Images of the internal process were captured using a high speed camera (Fastcam SA3, Photron Limited Co. Ltd., Japan) equipped with a telescopic micro-lens having a focal length of 105 mm and an F ratio of 2.8 (Micro-Nikkor, Nikon Co. Ltd., Japan). The frame rate and shutter speed during photo acquisition were 3800 fps and 7500 sec⁻¹, respectively, for all measurements. The flow rate was maintained at 150 mL/min of steady flow using a screw pump (NBL30PU, R'Tech Co. Ltd., Japan) and was measured using a Coriolis flow meter (FD-SS2, Keyence Co. Ltd., Japan). The upstream and downstream pressures of the stenosis were measured using pressure meters (PW-100KPA, Tokyo Sokki Kenkyujo Co. Ltd., Japan). The pressure sensors converted the strain voltage into pressure that was in turn amplified by strain amplifiers (NPM-600, Kyowa Electronic Instruments, Co. Ltd., Japan). The pressures and flow rates were collected by data acquisition (DAQ) devices (NI cDAQ-9172 and NI 9215, National Instruments Japan Co. Ltd., Japan). The height of the fluid column in the reservoir was adjusted to load hydrostatic pressures in the circuit. The pressure of the water column was used for calibration. A bifurcation flow channel and a valve were used to adjust the flow rate into the stenosis model and the pressure drop. The images were analyzed using a PIV software (DaVis 8.1, LaVision), and Reynolds number (Re) was calculated as below;

$$Re = \frac{U_{max} D}{\nu} \quad (2)$$

In Eq. (2), ν is the kinematic viscosity, U_{max} is the velocity at the center of the parent artery, and D is diameter of the parent artery.

Working fluid in a previous study consisted of a mixture of solvent of glycerol/water solution and an aqueous sodium iodide solution, and included tracer particles [13]. In the PVA-H model pertaining to the present study, the working fluid consisted of a mixture of solvent of 35.0 wt% glycerol/water solution and 65.0 wt% aqueous sodium iodide solution and included acrylic particles covered with gold and nickel (Bright 6GNR30-MX, Nippon Chemical Industry Co. Ltd., Japan). The glycerol/water solution consisted of 89.0 wt% glycerin and 11.0 wt% distilled water, while the aqueous sodium iodide solution consisted of 53.4 wt% sodium iodide and 46.6 wt% distilled water. In the silicone model, the working fluid consisted of a mixed solvent of 75.0 wt% glycerol/water solution and 25.0 wt% aqueous sodium iodide solution and included polystyrene particles (Techpolymer MBX-20, Sekisui Plastics Co. Ltd., Japan). The glycerol/water solution consisted of 57.0 wt% glycerin and 43.0 wt% distilled water, and the aqueous sodium iodide solution consisted of 38.5 wt% sodium iodide and 61.5 wt% distilled water. The final working fluids were developed in order to reduce the optical refraction of the models and to match the mechanical properties of human blood. The viscosity of the fluid was measured by a viscosity meter (SV-10, A&D Co. Ltd., Japan) and the refractive index by a critical angle refractometer (R-5000, Atago Co. Ltd., Japan). The refractive index, density, and kinematic viscosity of the final working fluids were 1.455, 1.476 g/mL, and 4.03 mm²s⁻¹ (at 21.0 °C, PVA-H model), respectively, and those of the silicone model were 1.411, 1.194 g/mL, and 4.58 mm²s⁻¹ (at 21.6 °C, silicone model), respectively.

RESULTS AND DISCUSSION

Figure 4 shows the relationship between the vessel diameter at the downstream section and the inlet pressure for both elastic and rigid models. As seen, for the PVA-H model, the diameter expands 0.2 mm in accordance with the increase in the inlet pressure from 0 to 50 mmHg, while the diameter is almost constant for the silicone model. It was also observed that as the inlet pressure increases the flow velocities in the PVA-H model decreases due to the expansion of the PVA-H model in the y direction (data not shown). As depicted in Figure 5, the reattachment length (RAL) in the PVA-H model extends about 3 mm based on 0.2 mm in diameter expansion. It means that there is a positive correlation between the reattachment length (RAL) and the vessel diameter in the PVA-H model while the RAL in the silicone model remains constant. These results agree with our previous study [16, 17] showing that the vessel diameter at the pre stenotic section increases as the inlet pressure increases.

Using a rigid model, the changes in Re and RAL resulting from the change in inlet pressure are similar to the report by Banerjee et al. [18], who measured that RAL increases with increasing SS when Re is constant or with decreasing Re when SS is constant using a computational simulation. In our study, the result demonstrating that RAL

grows with decreasing Re is observed in a PVA-H biomodel and is confirmed by its comparison to a silicone model. The PVA-H has mechanical properties similar to those of the arterial wall [19], and in the PVA-H model, the wall expands with increasing inlet pressure. In combine with our previous paper [16], the expansions between proximal and distal vessels of the plaque are same range. The flow velocities simultaneously decrease with increasing inlet pressure. As a result, in the PVA-H model, Re decreases while it remains constant in the silicone model. Thus, Re is affected to a greater extent by the velocity reduction than by the decrease in SS in the PVA-H model. As a result, the decrease in Re causes the RAL to increase and its reduction can be observed in the PVA-H model having an expanding wall. This result seems to be similar to the result in numerical simulations showing that the RAL in larger parent artery and in slower velocity is long [17]. Conversely, in the silicone model, Re remains constant as the upstream pressure increases, which causes RAL to be maintained at a constant level. The change in RAL may be an important factor contributing to disease progression because at the RAP, $WSS = 0$ [10, 20]. Soulis et al. [9] suggested that low density lipoproteins clump in an area of low WSS , and Kudo et al. [21] suggested that the shape of endothelial cells in an area of low WSS (especially around a RAP) is round, and the cells are randomly aligned. Thus, the observation of the increase in RAL with the expansion of the model in the current study may contribute to an understanding of the mechanism of development of intravascular diseases.

CONCLUSION

In conclusion, an elastic PVA-H model makes it possible to observe both model deformation and flow distribution simultaneously. In addition, the flow pattern especially flow velocity and RAL of the PVA-H model are markedly different than those of the rigid-like silicone model.

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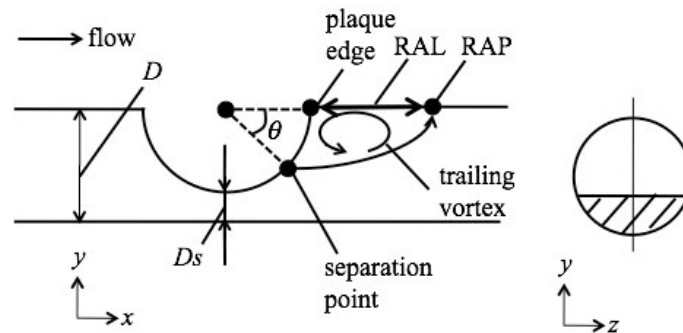


Figure 1 Flow and geometry at the stenotic region

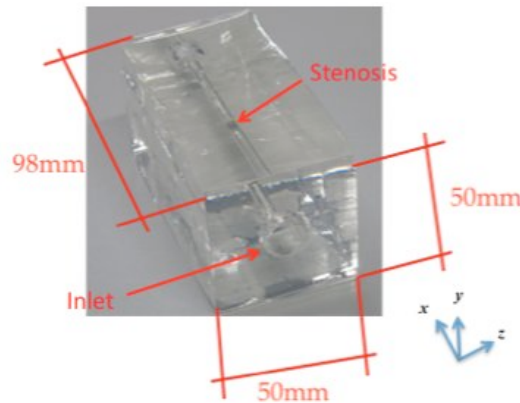


Figure 2 PVA-H stenosis model.

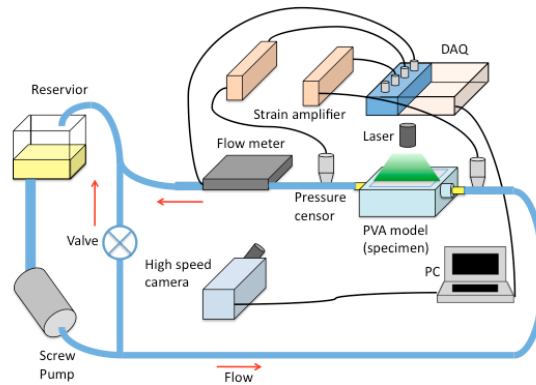


Figure 3 PIV circuit

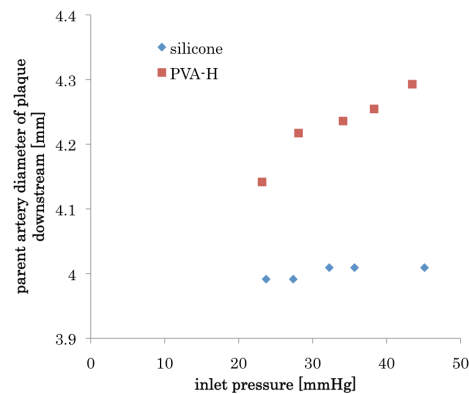


Figure 4 The relationship between the parent artery diameter at downstream section and inlet pressure.

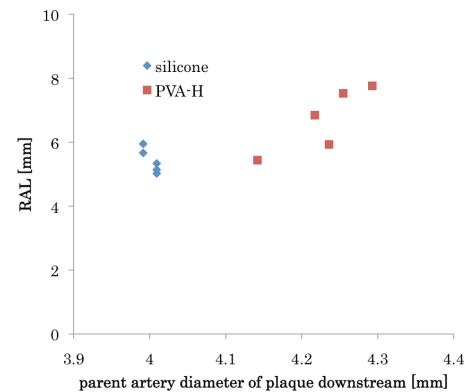


Figure 5 The relationship between RAL and parent artery diameter at downstream section.

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