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# Characterization of pressure reduction in coil-filled aneurysm under flow of human blood with and without anti-coagulant

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***Abstract*—Filling aneurysms with embolization coils is a widely used part of the treatment to stop intracranial aneurysm from rupturing. However, the effect of coiling on aneurysmal pressure has not been established. In this study, the effect of intra-aneurysmal coiling on pressure reduction was characterized. Coil deployment in the aneurysm will disturb flow and may induce aneurysmal coagulation. These effects were experimentally examined in this study using silicone rubber saccular aneurysm models. Changes in aneurysmal blood pressure under pulsatile flow were characterized. With coils in the aneurysm, results showed that flow reduction of anti-coagulated blood in the aneurysm did not reduce aneurysmal pressure. Significant pressure reduction was observed only when the blood's coagulation ability is restored to normal. These results suggest that blood coagulation is pivotal to pressure reduction and concomitant with rupture risk reduction in treatments of aneurysm with coils.**

## I. Introduction

Aneurysm growth and rupture is attributable to the high stress within the aneurysmal wall associated with pressure inside aneurysm [1, 2]. The wall itself may be weakened by wall remodeling induced by abnormal wall shear stress (WSS) on endothelial cells [2-4]. Both embolization coils with stent treatment, and flow diverter insertion have been used to treat aneurysms. While aneurysms filled with metallic coils cannot shrink significantly, aneurysms treated with flow diverters have been observed to shrink and disappear. Various theories for the shrinkage of aneurysm have been proposed [5, 6], where aneurysm shrinkage is triggered by reduction of WSS induced by flow diversion. However, it is unclear if lowering of WSS results in pressure lowering. If aneurysmal pressure remains high, the tensional wall stress inside the aneurysmal wall will remain high and the aneurysm cannot shrink even when WSS is lower.

Recent studies showed that the state of the blood may be an important factor in pressure reduction [7, 8]. The effect of the state of blood on pressure reduction was investigated in a companion study with flow diverting mesh device. The study used anti-coagulated blood and showed that pressure reduction is not observed in aneurysm with flow diversion alone [7]. In hospitals, patients are often treated with anti-coagulants to prevent unwanted clotting during surgery. This means that the aneurysmal pressure is not lowered in these patients despite the regulation of WSS by coils or flow diverters.

In a parallel study on the effect of aneurysmal pressure change as a function of flow diverting device deployment, we showed for the first time that aneurysmal pressure (AP) can be significantly reduced when the blood inside aneurysm is coagulated after deployment of flow diverting device [8]. This confirmed that aneurysmal pressure reduction and shrinkage observed in clinical treatment [9-11] occurs *only* after intra-aneurysmal coagulation has taken place.

In treatments for intracranial aneurysms using embolization coils, the coils are packed into the aneurysm lumen and the aneurysmal flow velocity and vorticity are reduced. Like the earlier case with flow diverting devices, it is also conjectured that the WSS is reduced with flow reduction by coil deployment and further wall weakening is prevented. Since anti-coagulants such as heparin and aspirin are injected to or taken by the patient before and during endovascular coiling procedure, the blood is in anti-coagulated state and the aneurysmal pressure may remain high despite lowering of WSS by the deployment of coils. In this study, the effects on aneurysmal blood pressure in elastomer saccular aneurysm models filled with coils are examined.

## II. Methods

A closed flow circulation system modeled in an earlier study (Fig. 1) was set up to generate and circulate pulsatile flow of human whole blood. The pressure pattern under pulsatile flow at range of human blood pressure is monitored (Fig. 2). The set-up was placed on the same horizontal plane to minimize hydrostatic pressure effect.

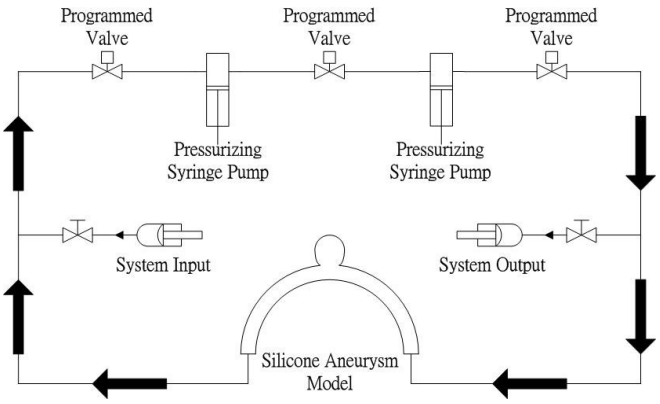


Figure 1. Schematic diagram of in-vitro experimental setup for pressure profile study in silicone aneurysm model

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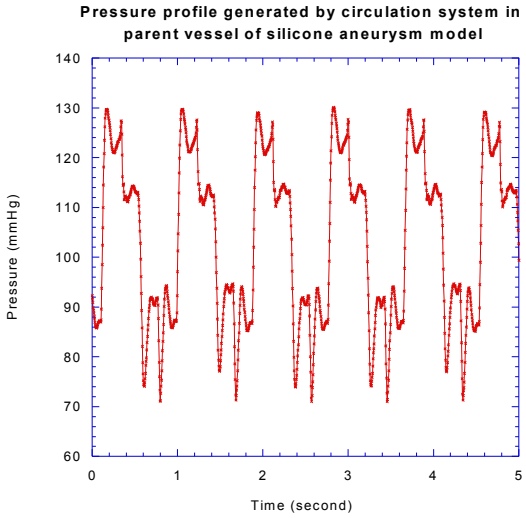


Figure 2. Pressure profile generated by circulation system in parent vessel at aneurysm model section

Internal carotid arteries (ICA) are major locations with intracranial aneurysms [12]. The ICA diameter is reported to be 4.66±0.78mm in female and 5.11±0.87mm in male [13]. On the basis of these data, parent artery with 5 mm diameter is used for the aneurysm model in this study. The aneurysm model section is wax formed and casted using medical grade silicone elastomer (NuSil Technology LLC, California, US). The inner lumen of the model with parent vessel and aneurysm is firstly modeled using a wax pattern. The pattern is then coated with three layers of silicone and cured. The remaining wax inside is then melt-drained to produce a silicone saccular aneurysm model. The resulting radius of curvature of parent vessels of silicone replicas is 75mm.

Pulsatile flow experiments were conducted using this system with both anti-coagulated human whole blood and blood with normal coagulability. After the flow system is filled with citrated human whole blood from blood bag, calcium gluconate (0.23mmol $Ca^{2+}$ in 1ml) is injected into the blood stream at 0.1ml/s to restore the blood coagulation ability to normal. The dosage of calcium gluconate required is determined according to the amount of blood flowing in the system. The setup is placed inside an acrylic chamber and is maintained at human body temperature of 38 ˚C. Other flow parameters are listed in Table 1.

Pressure profiles at 2 different positions (Fig. 3) in the aneurysm model section were measured using fiber optic pressure sensors (OPP-M Fiber optic miniature physiological pressure sensor, opSens Ltd., Canada). Pressure sensors are placed at the tip of a needle and are inserted to center of aneurysm and center of parent vessel respectively. Data were collected using SoftSens acquisition software from opSens.

TABLE I. FLOW PARAMETER USED IN PULSATILE FLOW EXPERIMENTS

| | |
|---|---|
| Flow Pressure [14] | Systolic: 125-135 mmHg |
| | Diastolic: 65-75mmHg |
| Blood Flow Rate | 200-300 mL/min<br>(The ICA volume flow in subjects with a complete configuration of the Circle of Willis was 245 mL/min ± 65(standard deviation) [15]) |
| Pulse Period | 0.8-0.9 second |

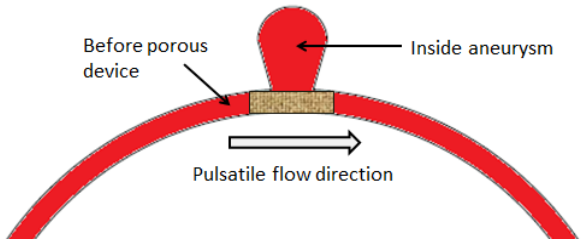


Figure 3. Positions in aneurysm model section to be measured to obtain pressure profile

Figure 4. Aneurysm model with stainless steel coils at maxiumum achievable packing density (PD=15%)

For a closed flow system, the pressure inside the parent artery would increase when pressure inside aneurysm is reduced. To simulate the pressure auto-regulation inside the human vascular system, the pressure pattern generated by the flow system was regulated reproducibly using a customized pump-controlling program. 1-hour long experiments were conducted for each setting, and 7 data sets were collected in each experiment in 10-minute intervals, giving 1250 data in each set.

The effect of the flow reduction by embolization coils on the aneurysmal pressure was examined by comparing aneurysmal peak pressure change with and without embolization coils deployed inside the aneurysm in model A1 and A2 respectively. Both tests (A1 and A2) were conducted under pulsatile flow of citrated blood, and with flow diverting device placed across the neck of aneurysm. A maximum of 15v% of embolization coils, which are stainless steel in this study, were packed into the cavity (Fig. 4). The coils were caged into place by a flow diverting 30% porous device made from parylene-coated rolled stainless steel mesh. In addition with the case with anti-coagulated blood, the effect of coagulation by embolization coils was examined by using blood with coagulability restored. Anti-coagulated blood with citrate was used in model B1, and normal blood with citrate's anti-coagulating function reversed was used in model B2. Both models (B1 and B2) have stainless steel coils placed inside the aneurysm but without flow diverting mesh device.

## III. RESULTS

### *A. Effect of flow reduction by embolization coils on aneurysmal pressure with anti-coagulated blood*

Fig. 5 shows the peak pressure profiles measured inside the aneurysm and parent vessel under pulsatile flow of anti-coagulated human whole blood.

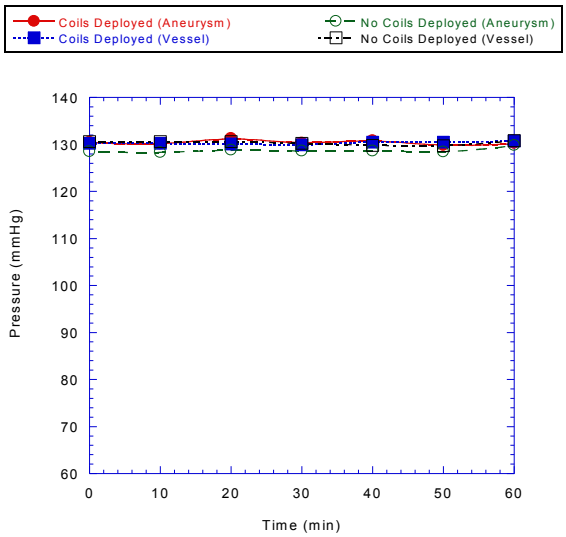


Figure 5. Effect of flow reduction by embolization coils on aneurysmal peak pressure for anti-coagulated blood.
(Locations of pressure measurements are shown in Fig. 3.)

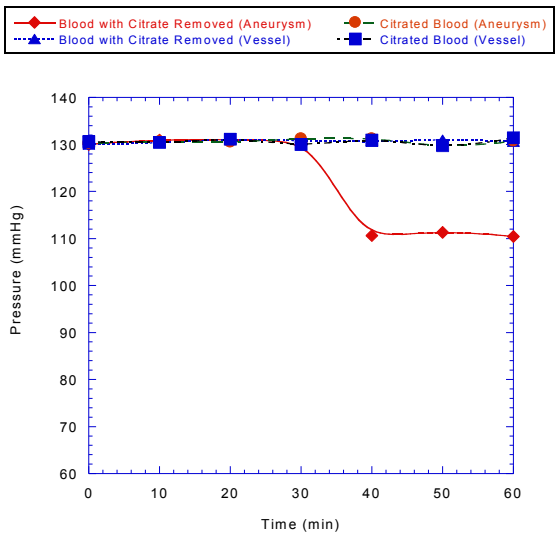


Figure 6. Effect of coagulation on aneurysmal peak pressure with embolization coils deployed (PD=15%).
(Locations of pressure measurements are shown in Fig. 3.)

The peak profiles showed that the pressure did not change with location in model A1. The peak pressure profiles measured at the aneurysm and at the parent vessels were identical (filled circles and filled squares). The results also showed that the peak pressure profiles were unaffected by coil deployment inside the aneurysm (filled circles and open circles). For the case where no coils were deployed in model A2, the aneurysm remained bounded by the flow diverting mesh device at aneurysm neck so flow was still diverted and WSS was reduced. Despite reduction of WSS, aneurysmal pressures remain identical to pressure in the parent vessel (open circles and open squares). These results suggest that aneurysmal pressure reduction does not directly follow from reduction in WSS or flow diversion, whether the reduction and diversion are from deployment of embolization coils, flow diverters or both.

### *B. Effect of coagulation by embolization coils on aneurysmal pressure with normal blood*

The cases with normal blood are shown in Fig. 6. When blood with coagulability restored to normal was used, the blood coagulated after flow slowed or stopped. When flow was slowed by embolization coils, observation showed that the normal blood coagulated and formed clots (Fig. 7) within 1 hour. Fig. 6 showed that significant pressure reduction (>10%) was observed in the aneurysm, when the flow was slowed by the embolization coils in model B2. With blood flow not affected in the parent vessel, coagulation did not occur with normal blood and pressure in the parent vessel was not reduced. Thus, while normal blood can coagulate, flow must be slowed in order for blood to coagulate (solid diamond in Fig. 6). The results also showed that the peak pressure profiles were unaffected in model B1 with anti-coagulated blood. This consolidates that when flow is slowed, pressure can only be reduced when coagulability of blood is restored.

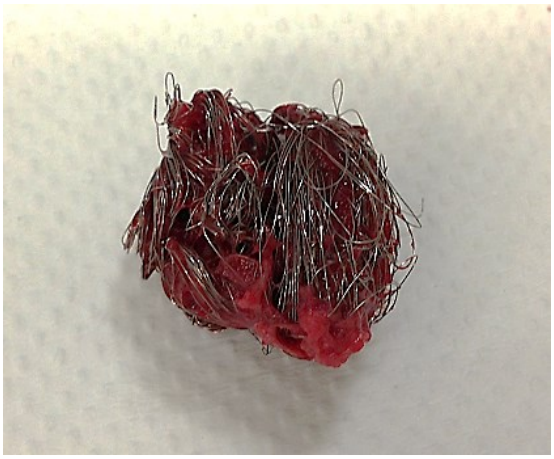

Figure 7. Coagulated thrombus formed on stainless steel coils in aneurysm under pulsatile flow of human normal (citrate removed) blood.

## IV. DISCUSSION

Embolization coils are used to prevent aneurysmal rupture in endovascular treatment for intracranial aneurysm. When deployed, they will slow blood flow in the aneurysmal cavity, and is assumed to reduce rupture risk. Experiments to measure aneurysmal pressure change with the deployment of endovascular coils under pulsatile flow were conducted previously [16, 17], but none of them used human blood or other blood with coagulability as the flow medium. Wakhloo et al. packed 93v% of hydrogel-coated coils into aneurysm, and no aneurysmal pressure reduction was observed [17]. When aneurysmal flow is slowed by flow diverting device or flow reducing embolization coils, aneurysmal WSS is also reduced [18].

The results from this investigation with human blood showed that rupture risk can be lowered if the blood's coagulating function is restored. However, if the blood is filled with anti-coagulants, the aneurysmal pressure is unaffected by

the deployment of embolization coils or flow diverters until the coagulability is restored.

In clinical practice, anti-coagulants are used during and after surgery to control blood clotting. Angiograms are often used during and after surgery to examine the blood flow, and they may show flow stasis inside aneurysm [19, 20]. It is tempting to assume that rupture risk is controlled when flow stasis is established. However, the experimental results from this investigation suggested that aneurysmal pressure may not have been reduced when high concentration of anti-coagulants is present in the blood. In addition, computational studies with flow diverter deployed across intracranial aneurysm showed that aneurysmal pressure [21] can sometimes increase with deployment. The heightened aneurysmal pressure together with suppression of clot formation inside the aneurysm maybe the mechanism underlying reported cases of delayed rupture of aneurysm after flow diverter deployment [21, 22].

Anti-coagulating medication is indispensable to prevent in-stent stenosis, but steps should be taken to reduce rupture risk. Insertion of coils into aneurysm in flow diverter treatment had been suggested to prevent formation of unstable thrombus which exhibits autolytic characteristics and leads to delayed rupture [22]. From our observations, the risk can also be lowered if thrombogenic coils are inserted into the aneurysm to enhance intra-aneurysmal coagulation to counter-balance the increase in aneurysmal pressure caused by flow diverter deployment.

In treatment of intracranial aneurysm at bifurcation, deployment of embolization coils only without diverter is commonly used [23, 24]. On the basis of our observations and hypothesis, lower anti-coagulant medication should be considered after coiling procedures. This would enable coagulation and prompt pressure reduction inside aneurysm.

## V. Conclusions

The rupture risk of intracranial aneurysm can be reduced by reducing the pressure inside aneurysm. This can be achieved by deployment of embolization coils. Together with our previous findings, the study series showed that both flow diversion by flow diverting porous device in parent vessel and flow reduction by embolization coils inside aneurysm do not affect the aneurysmal pressure significantly and cannot reduce the rupture risk of aneurysm alone. To lower rupture risk, aneurysmal pressure reduction can be achieved by slowing aneurysmal blood flow to induce intra-aneurysmal coagulation in systems where the blood has certain coagulability and without high doses of anti-coagulants.

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