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INVESTIGATION ON RISK FACTORS FOR CEREBRAL ANEURYSM RECANALIZATION AFTER COIL EMBOLIZATION USING CFD

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Summary. *In recent years, coil embolization has been one of the most popular methods to treat unruptured saccular cerebral aneurysms because of its minimal invasiveness. Recurrence of aneurysms after coil embolization remains as a major problem. However, the risk assessment protocol for such procedure has not been established yet, and the mechanism has not been understood clearly either. We identify 23 aneurysms, including 10 recanalized cases and 13 stable cases, with three-dimensional digital subtraction angiography. The hemodynamics of the aneurysms with coil is characterized using computational fluid dynamics (CFD). The numerical results are analyzed by a statistical method. The original parameter called FpV has significant difference between recanalized cases and stable cases. High FpV has the possibility to affect the aneurysm recanalization. ROC analysis indicates a moderate accurate discrimination for the cutoff value of 0.014 (AUC=0.82). For preventing the aneurysm recanalization, the most suitable VER for each case may be determined by counting back from the cutoff value.*

1 INTRODUCTION

Subarachnoid hemorrhage is the leading cause of death or severe disability, and cerebral aneurysm is a major cause for the disease because of its rupture [1]. Thus, the patients who have unruptured aneurysms need to be obliterated them by clipping or endovascular treatment.

Coil embolization has been one of the most popular methods to treat an unruptured saccular cerebral aneurysm because of its minimal invasiveness. In this method, thin biocompatible metal wires are inserted into an aneurysm by a catheter and the dome region is filled with this medical devices. Leading a thrombus in the aneurysm with the inserted coils, blood flowing into it is prevented and the risk of the aneurysm rupture will be decreased [2]. However, recurrence of aneurysms after coil embolization remains as a major problem [3]. This phenomenon means a re-inflow of blood into the aneurysm because of coil compaction, which means the coil is literally compacted into the aneurysm physically, or re-growth of the aneurysm [4,5,6]. Clinical reports showed that around 10% - 25% aneurysms with coil were recanalized [4,7,8] and Raftopoulos et al. reported that failed rate of coil embolization and surgical clipping are 29.3% and 5.1 % respectively [9]. These results show that coil embolization is inferior to clipping in terms of its curability, but it can be a promising method by improving the success ratio because it has great benefits like its minimal invasiveness. Unfortunately, the risk assessment protocol for such procedure has not been established yet, and the mechanism has not been understood clearly either [10,11].

In recent years, computational fluid dynamics (CFD) has widely used to analyze flow pattern in aneurysms [12,13,14]. This technic helps us to know how the blood behaves in aneurysms and physical parameters such as pressure, velocity or shear stress. There are abundant reports suggesting that hemodynamic factors may have an influence on such as aneurysmal growing or rupture [13,14]. In most of these studies, the patient-specific geometries of arteries reconstructed from the images taken before the first operation were used for CFD analysis. In contrast, there are only a few studies that analyzed the flow near the aneurysmal neck with the patient-specific geometry of the coil that gained after the coil embolization. Luo et al. reported that wall shear stress (WSS) and blood velocity near the residual aneurysmal neck were significantly higher in recanalized cases than in stable cases using CFD for total 11 cases [15]. Such result may give a useful hint to understand the occurrence mechanism and assess the recurrence risk of aneurysms. The difference between recanalized cases and stable cases is likely to be related to hemodynamic factors. However, the research on such phenomenon is still not sufficient, especially for the number of analyzed cases. Eventually, we should not only assess the risk of recanalization but also estimate its probability for each patient before the first embolization.

To reach the ideal goal, we characterize the hemodynamics of aneurysms before and after first embolization for 23 cases using CFD. In this study, the patient specific models of arteries and embolized coil from three-dimensional digital subtraction angiography (3D-DSA) data are used. We process hemodynamic and morphological parameters, and examined the difference of them between recanalized cases and stable cases statistically to investigate the occurrence mechanism of the aneurysm recanalization. The results indicate that the original parameter, which considers the morphological and hemodynamic factors simultaneously, has a significant difference between them. In addition, we propose the patient-specific indicator, volume embolization ratio (VER), to prevent the prospective recurrence of aneurysms.

2 METHOD

2.1 Patients

Patient-specific 3D-DSA data were obtained from the data base of The Jikei University Hospital for the analysis. We identified 23 aneurysms, including 10 recanalized cases and 13 stable cases. The specific information about the analyzed cases is shown in Table.1. The all cases were treated with coil only; a combined method like stent assist was not included. Each case was followed up for 12 months. The recanalized cases were defined as ones which were not occluded completely as a result of coil compaction, aneurysm regrowth or both of them and have had reoperation at the same site. While, the stable cases were defined as ones which have had no reoperation at the same site. We analyzed a flow pattern of each patient's aneurysm at the state before and after coil embolization.

Table 1: Patients Population

N		Volume [mm^3]	Site	VER
Recanalized	Case1	992.5	rt ICA-pthalamic	17.0%
	Case2	268.6	rt ICA-opthalamic	17.0%
	Case3	1863.7	rt ICA-Pcom	21.5%
	Case4	1209.7	rt ICA-Pcom	18.9%
	Case5	419.4	VABA-top	19.1%
	Case6	178.8	rt MCA	18.0%
	Case7	1925.0	rt MCA	26.0%
	Case8	2040.8	rt ICA-Sup.hypophyeol	19.0%
	Case9	182.8	lt MCA	17.0%
	Case10	3240.8	rt ICA-Sup.hypophyeol	18.0%
Stable	Case1	73.6	lt ACA-Acom	31.1%
	Case2	211.0	ACA-Acom	21.4%
	Case3	408.4	rt ICA-cavenous	20.9%
	Case4	239.0	rt ICA-Sup.hypophyeol	24.3%
	Case5	13.9	ACA-Acom	26.0%
	Case6	170.3	ACA-Acom	24.3%
	Case7	78.3	lt ICA-SAH	30.3%
	Case8	40.1	lt ICA-Pcom	23.7%
	Case9	109.9	lt ICA-paraclinoid	26.8%
	Case10	187.5	lt ICA-ant.choro	27.0%
	Case11	57.7	rt ICA-Pcom	18.2%
	Case12	79.1	lt ICA-opthalamic	24.6%
	Case13	96.6	lt MCA	29.7%

2.2 Modeling

Using 3D visualization software, Amira 5.6 (FEI/VSF-division, Bordeaux, France), the shape of the arteries and the embolized coil were modeled from Digital Imaging and Communication in Medicine data (DICOM data) obtained from DSA by trimming and smoothing, shown in Fig.1. STL (Standard Triangulated Language) was generated as a data of the 3D model.

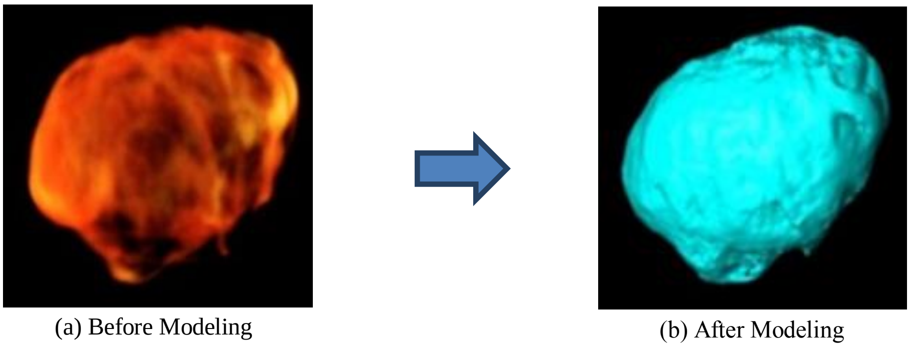


Figure 1: Modeling of Coil

2.3 Mesh generation

Computational grid was generated based on the STL data using ANSYS ICEM CFD 15.0 (ANSYS, Inc., Canonsburg, PA, USA). The unstructured grid was created. Prism mesh and tetra mesh were arranged at the vicinity of the vessel wall and the lumen of the vessel respectively. 75mm extension tubes were connected to inlet and outlet boundary.

2.4 Numerical analysis

The blood flow was analyzed using ANSYS CFX 15.0 (ANSYS, Inc., Canonsburg, PA, USA). The flow field was assumed as a laminar since the Reynolds number based on the blood artery diameter was around 500. The blood model was defined as a Newtonian fluid with density and viscosity of 1,100 kg/m^3 and 0.0036 Pa･s respectively. The embolized coil surface and the vascular wall were defined as rigid and non-slip boundary. The pressure was fixed to 0 Pa at the outlet boundary of the vessels. Considering pulsation, unsteady flow analysis was executed over two heartbeats (1.8 sec.) with a time step of 5×10^{-4} sec. The pulsation of the average mass flow rate measured from healthy adults at the Internal Carotid Artery (ICA) and the Vertebral Artery (VA) were referred from [16] and imposed at the inlet boundary.

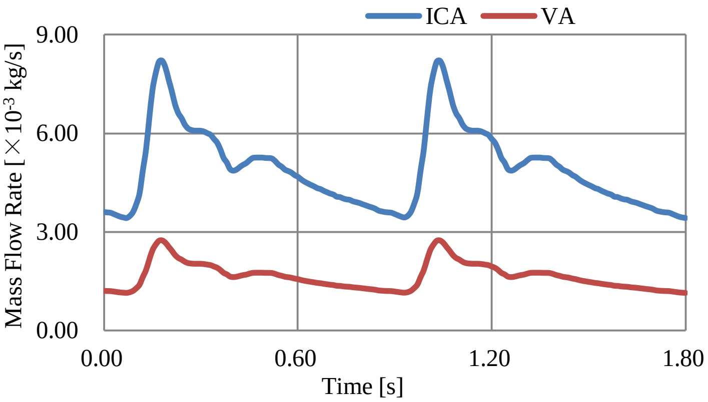


Figure 2: Mass Flow Rate of the ICA and the VA [16]

3 PARAMETERS

3.1 VER (Volume Embolization Ratio)

Volume Embolization Ratio (VER) is a parameter which indicates the ratio of a physical volume of inserted coils to aneurysm volume. VER is described as follows:

$$VER = \frac{Coil\,Volume}{Aneurysm\,Volume} \tag{1}$$

where *Coil Volume* and *Aneurysm Volume* are the volume of the coil inserted into the aneurysm and of the aneurysm itself respectively. VER is available one by one during the embolization.

3.2 MCP (Maximum Coil Pressure)

Maximum Coil Pressure (MCP) is defined as a parameter which represents the maximum pressure on the coil surface. MCP is defined as follows:

$$MCP = \frac{\int_0^T (P_{Max} - P_{ave})dt}{T} \tag{2}$$

where P_{Max} and P_{ave} are the maximum pressure and the area-averaged pressure on coil surface, T is the time for one pulsation.

3.3 FpV (Force per VER)

The original parameter called Force per VER (FpV) is defined as follows:

$$FpV = \frac{MCP_{Coil} \cdot Area_{Neck}}{VER} \tag{3}$$

where $Area_{Neck}$ is area of the aneurysm neck. The FpV is considered the morphological factors (the area of the aneurysm neck and the volume embolization ratio (VER)) and the hemodynamic one (the maximum pressure at the coil surface) simultaneously. In other words, this parameter represents the force per unit VER if the maximum pressure at the coil applies force on the coil surface which blood is in contact with.

4 STATISTICAL METHODS

We examined statistically significant difference for each parameter between the analysis result of recanalized cases and stable cases. The Mann-Whitney test (U test) was used if either result groups had non normality. On the other hand, if both the result groups had normality, the Student's t-test and the Welch's t-test were used when both the result groups had equal variance and did not respectively. There were significant differences if the P value was under 0.05.

5 RESULTS AND DISCUSSION

5.1 Streamline visualizations and pressure distributions (Qualitative comparison)

As describe in “1. Introduction”, hemodynamic factors may affect recanalization after first embolization. In general, blood flow in the sidewall type aneurysms is along the wall of the aneurysm and that in the bifurcation type aneurysms forms like a jet flow into the aneurysm directly. In this study, for the each type of aneurysms, the recanarized cases and the stable cases were compared; the internal carotid artery (ICA) and the middle cerebral artery (MCA) aneurysms were classified into the sidewall type and the bifurcation type respectively. The streamline visualizations before and after first operation, and pressure distributions on the coil surface after the operation in a recanalized and a stable MCA case are shown in Fig.3 and Fig.4 respectively. The models of coil after first operation and after one year follow-up from DSA are also shown in them.

It is confirmed that the high pressure point is near the inflow zone both the recanalized case and the stable case from the pressure visualization of the coil surface. It is thought that this result is brought since the coil prevents blood from flowing into the aneurysm. This is a common characteristic between both the cases. However, coil compaction occurred at the high pressure point in the recanalized case.

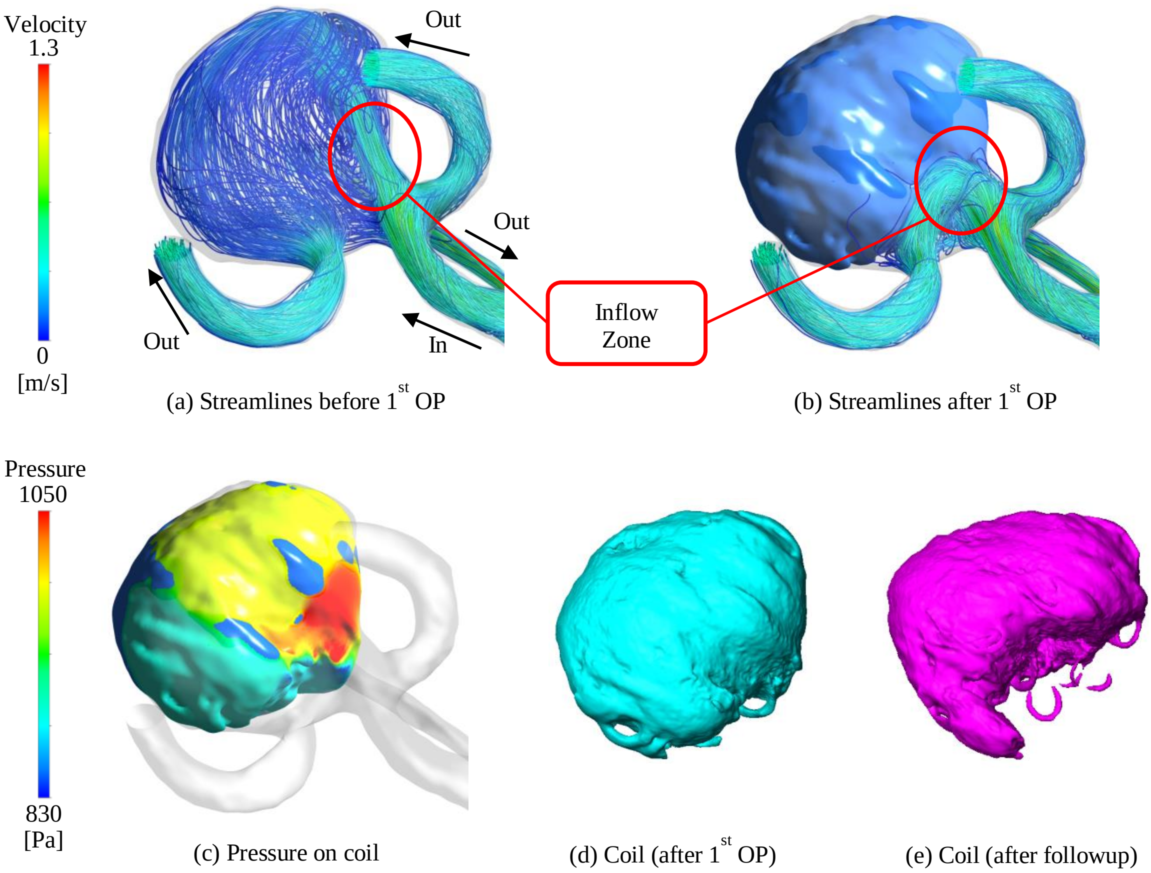
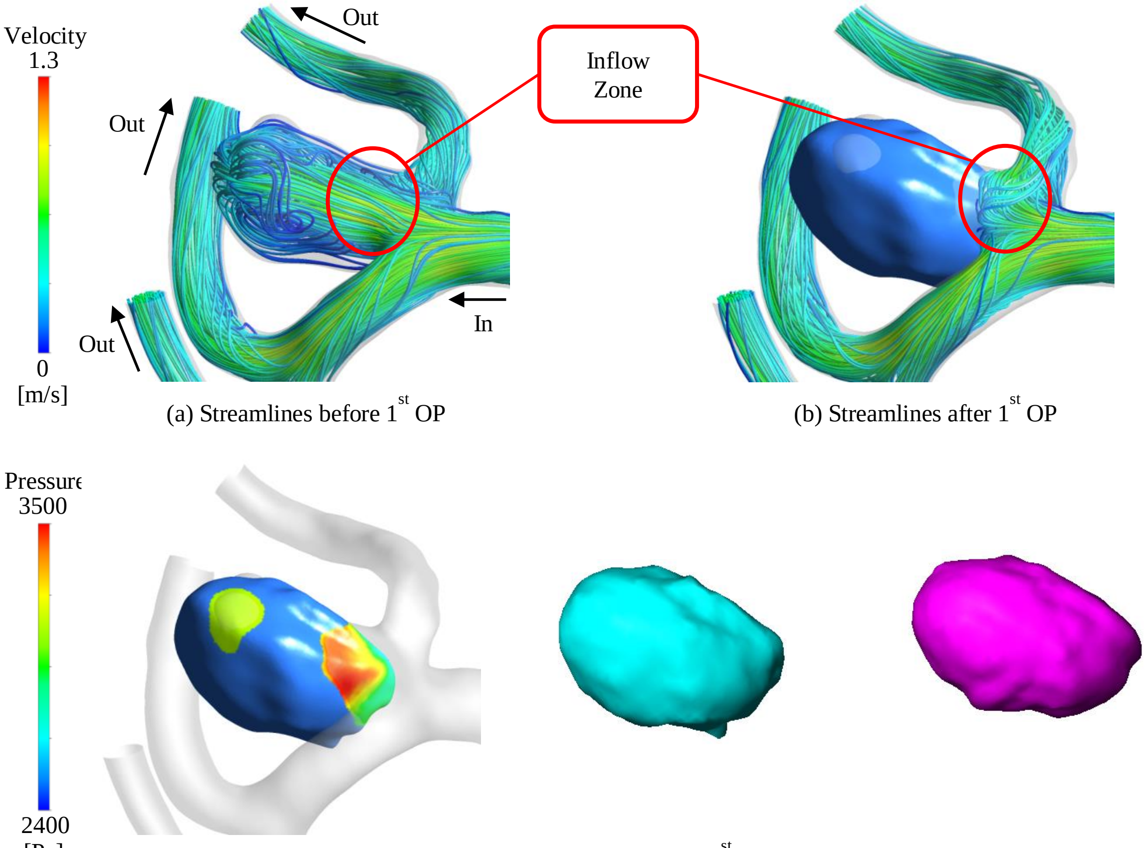


Figure 3: Visualization of Results (Recanalized MCA aneurysm)



(a) Streamlines before 1st OP (b) Streamlines after 1st OP

(c) Pressure on coil (d) Coil (after 1st OP) (e) Coil (after followup)

Figure 4: Visualization of Results (Stable MCA aneurysm)

5.2 Statistical results (Quantitative comparison)

Some reports have suggested morphological and hemodynamic factors of aneurysms as cause of recanalization [15,17,18]. To find out the factor related to them, the statistical analysis was performed between recanalized cases and stable cases. In this study, the original parameter called FpV was defined to consider morphological and hemodynamic factors simultaneously. The statistical result of FpV is shown in Fig.5. The significant difference was identified (P=0.01); the FpV in recanalized cases tends to be higher than that in stable cases (see Table.2). This result indicates that the force working on the coil surface in recanalized cases is significantly higher than that in stable cases. Aneurysm recanalization can be assumed to be caused by the FpV. In addition, ROC analysis was applied to the FpV to identify the most suitable boundary value between the recanalized cases and stable cases. Fig.6 and Table.3 show the ROC curve and the result value of ROC analysis respectively where the FPR is the false positive rate and the TPR is the true positive rate. In this study, the TPR and FPR mean the probability of assessing stable cases as recanalized cases falsely and recanalized cases as recanalized cases truly before the first embolization respectively. The analysis indicate the possibility of moderate accurate discrimination for the cutoff value of 0.014 (TPR = 1.00, FPR = 0.38, area under the curve (AUC) = 0.82).

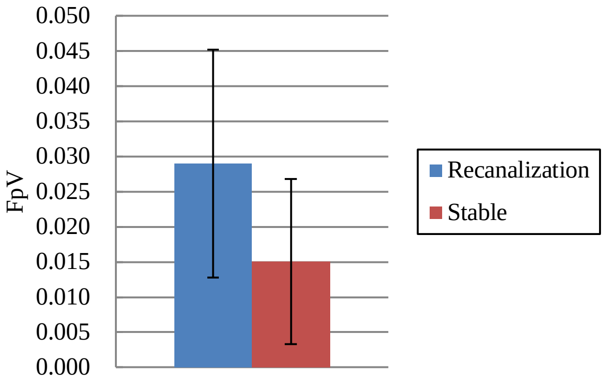


Figure 5: Result of FpV

Table 2: Result of Statistical Test (FpV)

Parameter	Group	Average	SD	P
FpV[N]	Recanalized	0.0290	0.0162	P<0.05
	Stable	0.0150	0.0117	

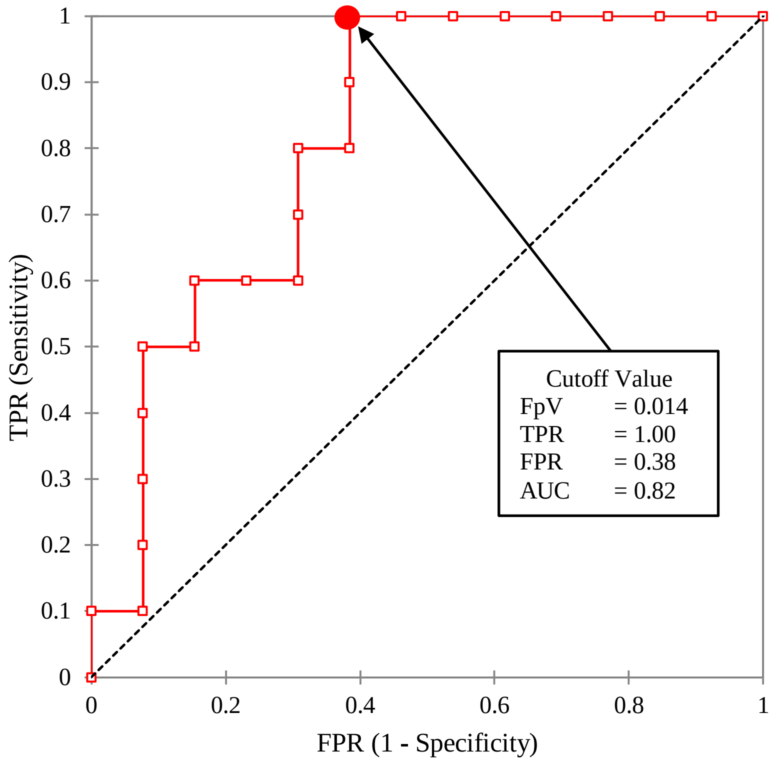


Figure 6: ROC Curve of FpV

Table 3: FPR, TPR and Specificity for each FpV

FpV[N]	FPR	TPR	Specificity
0.001	1.000	1.000	0.000
0.005	0.923	1.000	0.077
0.007	0.846	1.000	0.154
0.008	0.769	1.000	0.231
0.011	0.692	1.000	0.308
0.012	0.615	1.000	0.385
0.012	0.538	1.000	0.462
0.013	0.462	1.000	0.538
0.014	**0.385**	**1.000**	**0.615**
0.014	0.385	0.900	0.615
0.015	0.385	0.800	0.615
0.016	0.308	0.800	0.692
0.017	0.308	0.700	0.692
0.020	0.308	0.600	0.692
0.021	0.231	0.600	0.769
0.022	0.154	0.600	0.846
0.024	0.154	0.500	0.846
0.028	0.077	0.500	0.923
0.037	0.077	0.400	0.923
0.038	0.077	0.300	0.923
0.039	0.077	0.200	0.923
0.047	0.077	0.100	0.923
0.065	0.000	0.100	1.000

As mentioned above, the FpV considers morphological factors, especially the volume embolization ratio (VER). Although it is difficult to gain the value of FpV by analyzing the flow one by one during operations, VER is available. The most suitable VER value will be very useful to determine the plan of embolization because unreasonable packing density may cause a rupture of aneurysm during the operation. For preventing the rupture during operations and recanalized aneurysms after coil embolization, the most suitable VER value for each case may be determined by counting back from cutoff value of the FpV, the area of aneurysm neck and the pressure on coil obtained from the computation using an artificial coil model and an artery model from angiography before the first operation.

6 CONCLUSIONS

We analyzed the blood flow for the recanalized cases and the stable cases using patient-specific vessel models. By comparing parameters between them with the statistical method, the results from this investigation are summarized as follows:

- The FpV, which is the parameter including factors of morphology as well as hemodynamics, is significantly higher in the recanalized cases than the stable ones.
- From the statistical result, pressure load may affect the aneurysm recanalization.
- For preventing the aneurysm recanalization after the coil embolization, the most suitable VER value for each case may be determined by counting back from the cutoff value of the FpV, the area of the aneurysm neck and the pressure on the coil obtained from the computation using an artificial coil model and an artery model from angiography before the first operation.

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