氏名（本籍地）	柳（YU） 昌昊（CHANG HO）
学位の種類	博　士（医工学）
学位記番号	医工博　第　１５　号
学位授与年月日	平成２４年　３月２７日
学位授与の要件	学位規則第４条第１項該当
研究科、専攻	東北大学大学院医工学研究科（博士課程）医工学専攻
学位論文題目	Study of Treatment Analysis from Catheterization to Stenting with in-vitro model(生体外モデルを用いたカテーテルからステント治療までの解析に関する研究)
論文審査委員	（主査）東北大学　准　教　授　太田　信 東北大学教　授　早瀬敏幸　　東北大学教　授　高橋　明 東北大学教　授　高橋昭喜　　東北大学教　授　高木敏行

論文内容の要旨

第1章

Vascular diseases, such as ischemic heart disease, infarction, aneurysms, stroke and stenosis are a leading cause of serious long-term disability and their mortality rate is as high as that of cancers in many countries. Recently, endovascular treatments have been widely accepted as minimally invasive treatment using interventional devices such as catheter, guidewire, coil and stent. The training of intervention is important, and a blood vessel biomodel with realistic geometry of blood vessel has been developed for this reason. In addition, the techniques of such treatment have gradually been improved and a catheter simulator for navigation has been developed. However, previous studies of interventional devices' (catheter, guidewire, stent and so on) performance are rare in the literature and most often are merely impressions derived from small clinical series. In vitro studies reporting the performance characteristics of catheter are even more uncommon because it is difficult to evaluate the performance and characteristics of microcatheters. To overcome this situation, the main purpose of this paper is to develop new evaluation system for interventional devices (guidewire, catheter, stent and so on) for treatment analysis from catheterization to stenting based on mechanical properties and hemodynamics using in vitro model.

第2章

Our research group developed a biomodel using poly (vinyl alcohol) hydrogel (PVA-H). PVA-H is mainly composed with poly (vinyl alcohol) (PVA) and water. It may include other organic solvent such as dimethyl sulfoxide (DMSO). The mechanical properties such as Young's modulus of PVA-H are controllable with various techniques. For example, Ohta groups not only have described ways to elucidate the mechanical properties of biomodels using various concentrations of PVA solution, degrees of polymerization, saponification values and blending techniques but also have reported that sensory evaluation of such procedures as touching, suturing or cutting of the PVA-H mucosa model yields higher scores than those of a conventional material. These results suggest that the force and balance field of an artery wall can be reconstructed by a PVA-H biomodel.

In the present study, utilizing a PVA-H model, we examined catheter movement for development of an in vitro tracking system and evaluated the system by observation of video recordings of catheter motion. The transparency of PVA-H was sufficient for observation of the catheter through the PVA-H wall shown in Fig .1. A box shaped PVA-H biomodel can provide a stable condition for this tracking system. PVA-H can be used to reconstruct the shape of an artery based on geometrical data of a patient. It also seems to be useful for medical doctors to receive training in catheter use and evaluation of catheter movement for endovascular treatment. The results in this chapter are useful not only for the experimental validation of catheter but are also expected to make a contribution in the research of developing evaluation system with *in vitro* biomodel for the mechanical property of interventional devices.

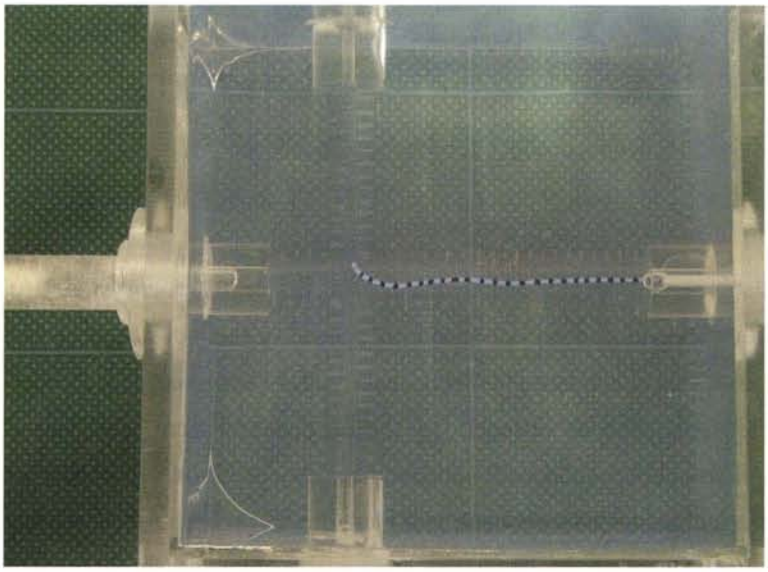

Figure 1. Micro catheter in PVA-H model with a cross geometry.

第3章

The requirements of the neurointerventional community and competition in the marketplace are the driving forces behind the development of new and innovative products. However, there have been few previous reports of catheter performance and they are often merely impressions derived from small clinical study series. *In vitro* studies reporting the performance characteristics of microcatheters are even more uncommon because it is difficult to evaluate the performance and characteristics of microcatheters.

Previous researchers reported the performance characteristics of a microcatheter system using a tortuous pathway based on compressive force. They used only one velocity and distance of catheters. However, parameters such as the distance of catheters have an effect on the compressive force. Thus, in order to develop an evaluation system, these parameters should be defined.

In this study, we enumerated several parameters and investigated the effects of these parameters on the compressive force. We then determined the parameters that had greater effects and those with little effect. Several performances could be observed and defined using our system, such as passing through a curve, slippage, and stopping. The balance of the bending force and the pushing force can lead to specific tip behaviors such as slippage and stopping. The maximum stress (or force) required to destroy an artery is unknown. However, the maximum force can be predicted using a tubular model. We produced a realistic simulation of the actual geometry for our measurements, but this geometry is not representative of all geometries. The use of a guidewire required a more sensitive load cell. This system can be used to analyze slippage and stopping behaviors, which may facilitate three-dimensional computational simulations. In this chapter, the ability of the catheter and guidewire tip to bend will depend on both their geometry and material. It would seem that pushability and bending stiffness, should be related. A lower bending stiffness means that the interventional device is more deformable.

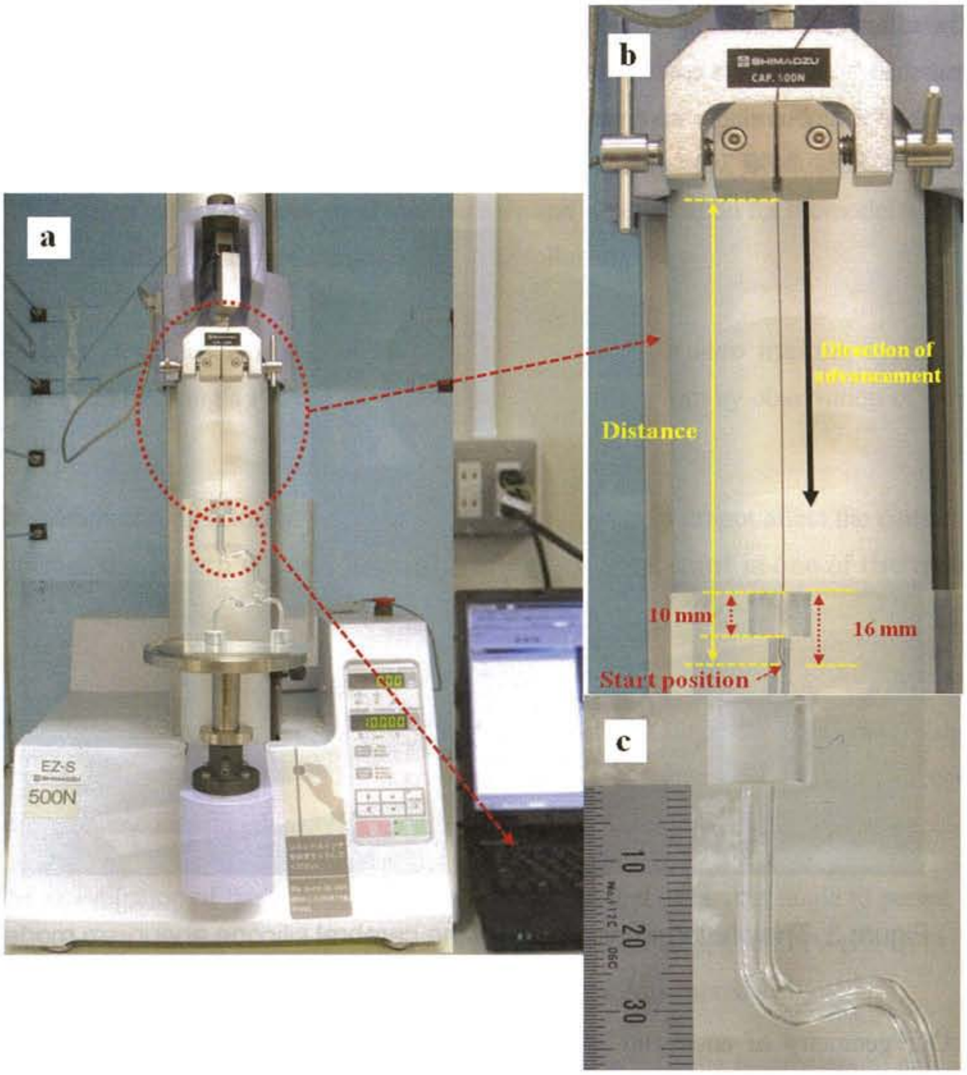

Figure 2. (a) Experimental setup used to measure the compressive force between interventional devices and the walls of PVA-H or silicone biomodels. (b) Definition of the distance. (c) Experimental section.

Since stent implantation treatments in cerebral aneurisms are a recent treatment, involving complex hemodynamic mechanisms, understanding the relation among the flow characteristics over obstacles will be important. However, none of these studies attempted to clarify mesh stent design issues, i.e., evaluating the changes in hemodynamics based on stent design parameters. The current study in this chapter attempts to make a step in this direction.

The purpose of Chapter 4 is to develop the estimation system for stent by evaluating the changes in hemodynamics based on stent design parameters such as porosity, poredensity, strands and stent strut shape on the hemodynamic properties of the flow inside an aneurysm using a Particle Image Velocimetry (PIV). PIV is a non-intrusive technique which allows reconstructing the velocity vector fields in a flowing fluid seeded with particle. The treatment of cerebral aneurysms with a porous stent has recently been proposed as a minimally invasive way to prevent rupture and favor coagulation mechanism inside the aneurism. The efficiency of stent is related to several parameters, including porosity, poredensity, strands and stent strut shape. We use the concept of flow reduction to characterize the stent efficiency. A 20 mm long mesh-work of rhombus shape stent was developed and tested in this investigation in Fig. 3. Five stent porosities of 100%, 80%, 74%, 71%, and 64 % were examined.

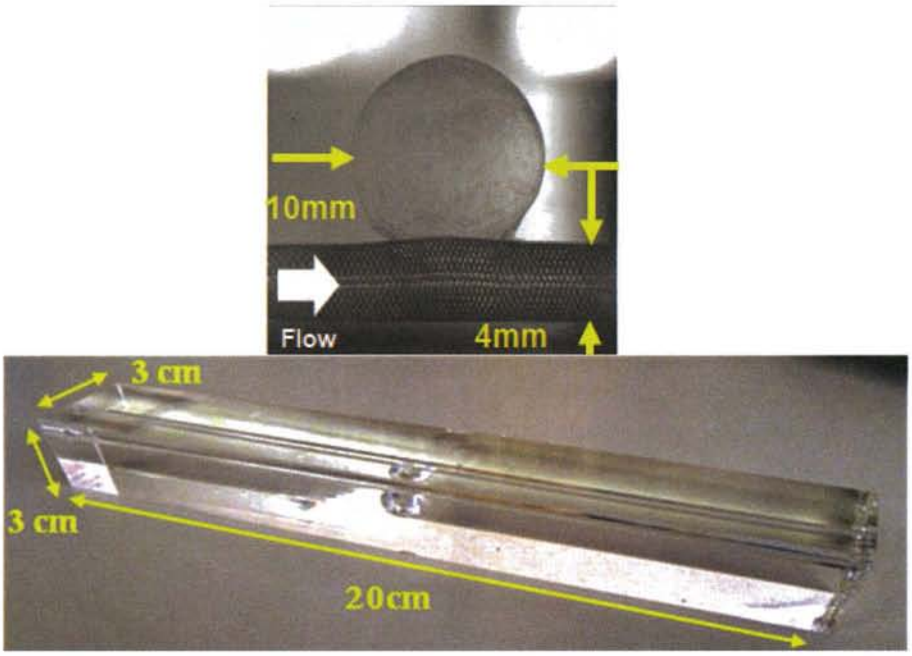

Figure 3. The photographic image of the cerebral silicone aneurysm model.

Our geometry of aneurysm applied to the system is the sidewall aneurysm because this geometry is one of the simplest one but it is better to realize flow condition of the poiseuille in the parent artery as a base of flow condition. This is very important because the other geometry of aneurysm model is difficult to perform comparison and evaluation of the stent may not efficiency. Reduced velocity, smaller average vorticity magnitude and different flow patterns inside aneurysm are observed when the 5 different proposed stents are used. We found that the lower porosity stent (Porosity : 64%) decrease the magnitude of the velocity by 98%, higher poredensity stent has a tendency to decrease the mean and maximum velocity, and also strands and stent strut shape affect the velocity reductions changing the flow pattern in the aneurysm. Our results show that not only the role of the porosity, poredensity and strands but also the stent strut shape affects the flow. Moreover, we hope that it help us understand the characteristic of stent designs.

第5章

Endovascular intervention is a minimally invasive procedure with various interventional devices and improves quality of life of patients with various merits such as quick recovery, short hospital stay, and small economical charge and so on. Therefore, the procedure has increasingly been employed for the treatment of cardiovascular disease. However, previous studies of interventional devices' (catheter, guidewire, stent and so on) performance are rare in the literature and in vitro studies reporting the performance characteristics of catheter are even more uncommon.

To overcome this situation, the main purpose of this paper is to develop new evaluation system for interventional devices (guidewire, catheter, stent and so on) for treatment analysis from catheterization to stenting based on mechanical properties and hmodynamics using in vitro model. To do this challenge successfully, PVA-H biomodel has been applied to our experimental study. Because PVA-H has realized a biomodel with low surface friction and good transparency and its application for biomodel was suggested. All findings obtained in this study are summarized as the followings.

1. We have described a study on the development of an *in vitro* tracking system for catheter movement by using a PVA-H model and evaluated the system by observation of filmed catheter motion.

2. The parameters of velocity, position of device in the system do not affect the compressive force, whereas the length of catheter from the tip to fixed point is one of the most effective parameters for the force. In this experimental study, the limitation of length is relatively long, and the geometry of artery should be considered.

3. The investigation of the evaluation system confirmed that high reproducibility with short error bar is indicated. The observation with movie record is also advantage of our system because the high transparency of materials with silicone and PVA-H can check the inside of artery.

4. The investigation of the evaluation system confirmed that stent strut angle to parent artery has a tendency that higher strut angle stent has the lower mean velocity in PIV and CFD. However, it is relatively smaller effect when compared with porosity and poredensity.

5. Our evaluation system suggested the best combinations between parameters to develop the ideal stent which is with lower porosity, higher poredensity, and higher strut angle.

論文審査結果の要旨

血管内治療は低侵襲治療として注目されている。さらに近年、脳動脈瘤治療にステント治療が新しい有効な治療法として認識され、盛んに研究が行われている。この治療を遂行するには、ステントの持つ血流減少効果だけではなく、ステントを患部まで到達しうるディリバリー能力も必要とされる。これらの治療法の力学的評価を生体外循環路で可能にすることは、今後のステント治療開発のために重要である。本論文は，これらの研究成果をまとめたものであり，全編５章からなる。

第１章は序論であり、本研究の背景、目的及び構成を述べている。

第２章では、生体の力学的特性と摩擦係数によく似た透明ゲルを用いて、カテーテルの挙動やディリバリー能力を調べるための生体外循環路トラッキングシステムを開発している。この成果により、カテーテルの挙動を視認で観察することが可能になり、カテーテルを統一的に比較し、評価することができる。これは、斬新なアイデアであり重要な成果である。

第３章では、第２章で開発したシステムのパラメータスタディを行い、各パラメータの結果に対する影響を調べている。さらに垂直荷重を測定し、カテーテルの挙動と相関があることを示している。これは、システムの特性を調べ、各カテーテルの挙動の改良に対する指針を示す重要な成果である。

第４章では、血流測定用生体外瘤モデルを開発し、ステントの脳動脈瘤内の血流に対する血流減少と、ステント加工を決定する各形状変数との関係を調べている。これは、ステント加工の可能性および制限と、血流減少効果に対する新たな主眼の可能性を示した重要な成果である。

第５章は結論である。

以上要するに本論文は，ステント治療に対してカテーテル挿入からステント留置までについての力学的評価の方法を開発し、ステント開発を含む治療行為開発法に指針を示したものであり、医工学及び機械工学の発展に寄与するところが少なくない。

よって、本論文は博士（医工学）の学位論文として合格と認める。