In Vitro Measurement of Tissue Integrity during Saccular Aneurysm Embolizations for Simulator-Based Training

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Summary

In the domain of endovascular neurosurgery, the measurement of tissue integrity is needed for simulator-based training and for the development of new intravascular instruments and treatment techniques. In vitro evaluation of tissue manipulation can be achieved using photoelastic stress analysis and vasculature modeling with photoelastic materials. In this research we constructed two types of vasculature models of saccular aneurysms for differentiation of embolization techniques according to the respect for tissue integrity measurements based on the stress within the blood vessel model wall. In an aneurysm model with 5 mm dome diameter, embolization using MicroPlex 10 (Complex 1D, with 4 mm diameter loops), a maximum area of 3.97 mm² with stress above 1 kPa was measured. This area increased to 5.50 mm² when the dome was touched deliberately with the release mechanism of the coil, and to 4.87 mm² for an embolization using Microsphere, (Spherical 18 Platinum Coil). In a similar way trans-cell stent-assisted coil embolization was also compared to human blood pressure simulation using a model of a wide-necked saccular aneurysm with 7 mm diameter. The area with stress above 1 kPa was below 1 mm² for the pressure simulation and maximized at 3.79 mm² during the trans-cell insertion of the micro-catheter and at 8.92 mm² during the embolization. The presented results show that this measurement system is useful for identifying

techniques compromising tissue integrity, comparing and studying coils and embolization techniques for a specific vasculature morphology and comparing their natural stress variations such as that produced by blood pressure.

Introduction

Vasculature representation using soft materials was proposed for *in vitro* simulation of endovascular intervention by ¹. These models are made of silicone elastomer and offer an accurate representation of patient-specific lumen of major vasculature. They enable fluid circulation to simulate blood flow and contrast media delivery, and they are compatible with most standard instruments for endovascular intervention. These models reproduce mechanical properties of human vasculature to make a realistic interaction between the instruments and the vasculature models membrane (elastic modulus: 2 MPa, friction coefficient: 0.042) ¹⁻³.

Respect for tissue is one of the criteria listed in ⁴ to evaluate how much tissue integrity is preserved during surgery. Such criteria should be measurable and considered for the development of new endovascular instruments and techniques, and simulator-based training. For endovascular intervention *Respect for tissue* should be represented by the risk of puncturing a blood vessel and stress variation within the blood vessel wall. Based on the modeling tech-

nology introduced in¹, a photoelastic effect was proposed for measuring stress within vasculature models built using urethane elastomer. The photoelastic coefficient of this material is adequate for measuring stress produced by guide-catheters, guide-wires and human blood pressure simulation, but for the measurement of smaller instruments more sensitive materials are desirable, enabling us to measure the respect for tissue integrity^{5,6}.

Microcoils are some of the smallest instruments actually used for endovascular treatment of cerebral aneurysms. The coils are initially attached to a wire that pushes them through the micro-catheter lumen. While the microcoil body leaves the micro-catheter its shape starts changing to form loops that create a wire frame within the aneurysm. The number of coils needed for an embolization depends on the aneurysm shape and size. The microcoil detachment is achieved using hydraulic or electric mechanisms placed between them and the wire. Recently stent-assisted embolizations have been used for the treatment of wide-necked saccular aneurysms. In this research we present epoxy resin as a photoelastic material for vasculature modeling, we measured its photoelastic characteristics, and we constructed models of saccular aneurysms. With them we measured the respect of tissue integrity during embolizations with different coil sizes, stent-assisted coil embolization and human blood pressure simulation.

Materials and Methods

Photoelastic Properties of Epoxy Resin

For a transmission polariscope, photoelastic stress analysis is based on the relation between the stress within a photoelastic material and the intensity of the light beam passing through it (Figure 1). To achieve stress measurement the photoelastic coefficient C must be known, the thickness of the material (optical path length) D must be measured beforehand. Then the retardation must be measured based on the light beam intensity⁷. The equation describing the relation of retardation with stress in this case is given by:

$$\sigma_1 - \sigma_2 = \frac{Re}{CD} \quad (1)$$

where σ_1 , σ_2 are the principal stresses on each side of a biaxial stress field⁵. In previous stud-

ies, we presented a method for calibration of photoelastic stress analysis in vasculature models, including the characterization of urethane elastomer as a photoelastic material⁵. For this study we characterize epoxy resin PL-3 of the Vishay Precision Group using the previously mentioned method. The mixture ratio between resin and hardener changes the stiffness and color of the material. A mixture ratio of 10:17.5 (resin: hardener) was used.

D is measured using blue light attenuation through the material. The equation used for this purpose is obtained from corresponding measurements of thickness and blue light intensity at different location of a variable thickness membrane. In this research a membrane with linearly increasing thickness between 246 μm and 1991 μm and with a length of 60 mm was constructed. The thickness of the membrane was measured with a UV laser microscope in the border every 5 mm for 13 locations (Figure 2). Blue light intensity was obtained from an image of the membrane while submerged in glycerin over a blue light source. The corresponding measurements are shown in Figure 3, and their relation is described by:

$$I_{NB} = -6.10^{-8} D^2 - 6.10^{-6} D + 0.993 \quad (2)$$

where I_{NB} is the normalized blue light intensity and D is the optical path length given in micrometers. For the polariscope shown in Figure 1, the equation describing the relation between green light intensity and retardation is approximated with⁸:

$$I_{GN} = \sin^2 \frac{\pi Re}{\lambda_G} \quad (3)$$

where I_{GN} is the normalized green light intensity, λ_G is the wave-lengths of the perceived green light. Re is the retardation that the light beam undergoes while passing through the photoelastic material. The photoelastic stress coefficient was measured in a similar way than⁵ but using the polariscope in Figure 1 by using (3) and by measuring the variation of green light intensity and width L while the membrane with homogeneous thickness is under tensile force F the photoelastic coefficient can be deduced from:

$$C = \frac{L Re}{F} \quad (4)$$

Thirty-one samples of L and I_{GN} were measured for a tension range of 0.255–1.797 N. The mean photoelastic coefficient obtained from

Figure 1 A) Example of modeling of carotid artery with the epoxy resin as photoelastic material. A 5F catheter and its guide wire are in contact with the model membrane. Stress within the membrane is visualized by the light intensity variation that is called birefringence. B) Polariscope used in this study for stress visualization and measurement.

Figure 3 Blue light transmittance equation calibration shows the parabolic relation between the normalized blue light intensity with the thickness of the membrane measured with the UV laser microscope for the epoxy resin.

these samples is 3.25×10^{-9} Pa-1 (standard deviation= 8.16×10^{-10}). This coefficient is about twice as large as that of urethane elastomer (Figure 4).

We used equations (1-3) for calculating the stress in the blood vessel models. For the following experiments, the stress contribution of the studied tools and pressure simulation was separated from other stress sources by sub-

Figure 2 Thickness measurements obtained with the UV laser microscope. The distribution of the measurement locations along the membrane is shown in the bottom with the variable thickness membrane.

Figure 4 Photoelastic coefficient measurement for the epoxy resin while a tension 0.255 and 1.797N was applied. The average value is 3.25×10^{-9} Pa-1.

tracting the initial stress conditions using the following equation:

$$(\sigma_c)_{t(k)} = (\sigma_1 - \sigma_2)_{t(k)} - (\sigma_1 - \sigma_2)_{t(0)} \quad (5)$$

where $(\sigma_c)_{t(k)}$ is the stress contribution of the studied tool of phenomena at discrete time k , $(\sigma_1 - \sigma_2)_{t(k)}$ is the observed stress field at that time and $(\sigma_1 - \sigma_2)_{t(0)}$ are the initial stress conditions.

Figure 5 Designs for the saccular aneurysm models: A) with bleb, B) wide neck.

Figure 6 Morphology changes in the bleb area while pressure rises from P₁ (-130 mmHg) to P₄ (130 mmHg) shows the membrane configuration of the model.

Figure 7 Blue light transmittance in aneurysm models built using the studied epoxy resin in a membranous configuration: A) Saccular aneurysm with bleb. B) Wide-necked saccular aneurysm, and their corresponding optical path length measurements C) and D).

Preparation of the Vasculature Model

A model of a saccular aneurysm with bleb was designed with an aspect ratio of 1.6 and with dome diameter of 5 mm. The aneurysm is attached to a cylinder (cross-section diameter:

4 mm). The bleb has a diameter of 1 mm. Using rapid prototyping and lost-wax method¹ and the studied epoxy resin; a single layer model of saccular aneurysm with bleb was constructed (Figure 5A). The membranous configuration in the bleb area was confirmed by observation of

Figure 8 Coils used for respect for tissue measurement in saccular aneurysm with bleb.

Figure 9 Enterprise stent installed within the model for trans-cell embolization study. Inserted: Model placed within the polariscope, before and during the trans-cell embolization.

Figure 10 Pump for human blood pressure simulation and flow temperature control (Left). Human pressure waveform at 50 bpm simulated using magnetic drive pump with feedback control of pressure limits and pre-programmed wave profile (Right).

the morphology changes with negative and positive pressure. While filled with glycerin, the saccular aneurysm model was connected in a closed loop to a syringe and manometer. The blood vessel model is submerged into glycerin tank. Using the syringe, pressure was raised from -130 mmHg to 130 mmHg. Figure 6 shows the morphology changes during this experiment confirming the membranous configuration in the bleb area. Another membranous vasculature model was fabricated for the study

of trans-cell stent-assisted coil and human blood pressure simulation. This model has the shape of a curved pipe with 3mm diameter and has a saccular aneurysm with a dome diameter of 7 mm and a neck size of 6 mm (Figure 5B). Figure 7 shows the vasculature models under blue light and the optical path length measurements using equation (2). This figure shows for the bleb area an optical path length of $100\text{ }\mu\text{m}$, corresponding to a membrane thickness of about $50\text{ }\mu\text{m}$.

Respect for Tissue Quantification with Photoelastic Stress Analysis

For endovascular intervention *Respect for tissue* relates to the risk of puncturing the blood vessel membrane and producing unnecessary stress on the vasculature wall. This risk assessment can be done by comparing the studied embolization with well-known situations where tissue integrity is compromised or by comparing it with normal stress variations such as that produced by human blood pressure. In this research we present an example for each of the assessment approaches.

Approach 1

While treating cerebral aneurysms by embolization with microcoils, special care has to be taken to keep the release mechanism within the catheter⁹. During a treatment the deployment of this system into the aneurysm is unacceptable, as it compromises tissue integrity. We use this as a reference point for our quantification of *Respect for tissue* using photoelastic stress analysis. In this experiment we compared the stress in the aneurysm area during the embolization of the aneurysm shown in Figure 5 while using microcoils with different sizes. The first embolization was done with a *Micrusphere (Spherical 18 Platinum Coil)* coil whose sphere has a diameter of 6 mm. A second embolization was done using a *Microplex 10 (Complex 1D)* whose loops have a diameter of 4 mm (Figure 8). Using the *Microplex 10*, we measured the stress produced by the deployment of its release mechanism. The coils were delivered using a 2.3F microcatheter that remained still during the process. Pressure remained below 40 mmHg during the different embolization procedures.

Approach 2

An Enterprise stent for blood vessels with a diameter in the range of 3-4 mm and with a length of 28 mm was placed covering the neck of the aneurysm model shown in Figure 9. While the stent was placed in the model a fluid was circulated within the model using a pump for human blood pressure simulation¹⁰. A sample of the pressure waveform produced by this simulator is shown in Figure 10. For this experiment the maximum pressure was set to 130 mmHg and the minimum to 75 mmHg. The stress changes produced during this blood pressure simulation were measured. A trans-cell embolization was simulated in this model too.

The measurement started after a microguide wire was passed through the cell of the *Enterprise* stent and before a 2.4F microcatheter was passed through the cell. The measurement continued after the microcatheter entered the aneurysm dome, the guide wire was removed and during the embolization using a *Guglielmi detachable coil (GDC)* with a helical coil diameter of 5 mm.

Results

Comparison of Embolization Using Micrusphere and Microplex 10

Birefringence images are shown above the stress calculations during the embolization using *Micrusphere*, *Microplex 10* and during the deployment of the release mechanism of *Microplex 10* in Figure 11. For *Micrusphere*, in t_1 the coil had its first contact with the aneurysm wall, birefringence was seen at the tip of the coil and in the dome area near the microcatheter tip. Birefringence also increased from t_3 to t_4 in the bleb neck and at contact points between the aneurysm dome and the sphere formed by the coil. During the embolization using *Microplex 10* the birefringence variation was less visible. In t_1 the birefringence variation was almost imperceptible when the coil tip touched the aneurysm dome, however from t_1 to t_2 variations are seen near the microcatheter tip while the loops of the microcoil started forming within the aneurysm. Birefringence changes were not visible with the bleb area during the process. This is supported by the stress calculations where we saw the local maxima of stress near 4kPa appearing near the catheter tip area as an effect of the catheter kick-back (Pointed out with arrow heads in t_5 for the three cases). During the deployment of the release mechanism this local maximum area exceeded that of the embolizations made with *Micrusphere* and *Microplex 10*. At t_5 for the last case a second local maximum appeared near the dome top as a consequence of deformation in the aneurysm model, but the stress near the bleb area was almost invariant. Figure 12 summarizes the stress analysis for the aneurysm dome in terms of area with stress above 1 kPa for the embolization using *Micrusphere*, *Microplex 10* and when the release mechanism was deployed out of the catheter. For the data in this figure the average area with stress above

Figure 11 Top: Embolization of saccular aneurysm with bleb using a *Micrusphere* coil. Birefringence rises when the coil tip touches the dome in t_2 , during the sphere formation process in t_3 and t_4 , and rises in the bleb area at the end of the embolization in t_5 and t_6 . Center: Embolization of saccular aneurysm with bleb using *Microplex 10*. Birefringence levels are lower than with *Micrusphere* as the size of *Microplex 10* is smaller. Birefringence changes due to motion of the micro-catheter within the aneurysm model (arrowheads in t_1 , t_2). Bottom: Birefringence changes in aneurysm dome are visible when the release mechanism of the microcoil is deployed and touches the membrane. The release mechanism is visible in t_4 and t_5 and pointed with an arrow.

1 kPa during the embolization with *Microplex 10* is 2.26 mm² (maximum: 3.97 mm²), and 3.19 mm² (maximum: 4.87 mm²), when the *Micrusphere* is used. This high stress area increased to 3.24 mm² (maximum: 5.50 mm²) when the de-

tachment mechanism of *Microplex 10* touched the aneurysm dome. This datum corresponds to the specifications of each coil and the known risk of the deployment of the release mechanism.

Figure 12 High-stress area variation in aneurysm dome for the studied embolization types.

Figure 13 Left: Stress measurement for blood pressure simulation. Right: Stress measurements along different stages of the trans-cell embolization treatment simulation. Stress produced by the kick-back of the catheter is pointed with arrow heads.

Figure 14 High-stress area variation in aneurysm dome for the human blood pressure variation.

Figure 15 High-stress area variation in aneurysm dome for the human blood pressure variation during the trans-cell embolization simulation.

Trans-Cell Embolization Using Enterprise and GDC Coil

Figure 13 shows the stress calculations during the blood pressure simulation experiment and during the trans-cell embolization. Variations of area with stress above 1 kPa are shown in Figures 14 and 15 for each of the experiments. For the stress calculations in the blood pressure simulation the area with red color representing stress above 4 kPa is almost non-existent, the red color is clearly visible for the catheter kick-back area while passing through the cell of the stent, when the coil is being inserted into the catheter, and during the embolization at the local maxima 1 and 2. The area with stress above 1 kPa is about nine times larger during the treatment simulation than under normal stress conditions. During the trans-cell embolization stress increased in the vasculature model since the catheter enters the aneurysm. The stress during the trans-cell condition was worsening by the insertion of instruments within the catheter as it increased the stiffness of the catheter.

Discussion

From experimental results we can see that the presented epoxy resin can be used for modeling minute tissue structures with a membranous configuration such as a 1 mm lumen bleb in a saccular aneurysm (Figures 6, 7, 11). The epoxy

resin proved to have a superior photoelastic coefficient compared with urethane elastomer^{5,6}, and has additional advantages in that the color and stiffness of the material can be changed according to the tissue properties to modeled. For this case the mixture of hardener and resin was chosen to have an elastic modulus between 1-3 MPa, the same as human blood vessels. The epoxy resin combined with the proposed stress analysis system was also suitable for measuring stress produced by standard instruments for endovascular intervention such as a micro-guide wire with 400 μm diameter, microcatheter of 760 μm diameter, stents for cerebral aneurysm treatment, and coils for aneurysm embolization. For the analysis in the aneurysm dome, touching the aneurysm with the release mechanism corresponds to an increase of 5.50 mm^2 the initial area with stress above 1 kPa. This points out a situation that compromises tissue integrity. For an ideal treatment the area with stress above 1 kPa would never surpass the initial conditions. From this we can say that embolization with the smaller size coil (*Microplex 10*) was superior in terms of respect for tissue integrity as it showed a maximum area with stress above 1 kPa of 3.97 mm^2 . On the other hand, during the embolization with the larger coil (*Microsphere*) the initial area with stress above 1 kPa increased 4.87 mm^2 . An advantage of this sensing technology is that during the study the evaluated instruments did not require any modifications to be analyzed. This characteristic is desirable during the devel-

opment process of micromechanisms and micro-robotics, as well as for simulator-based-training. Catheter kick-back effects were observable for all the embolizations in both experiments. This area that reaches stresses above 4kPa was larger for the release mechanism experiment than for *Micrusphere* and *Microplex 10*. Embolization with *Micrusphere* raised the levels of stress near the aneurysm bleb due to its large size compared to the dome diameter. This did not happen with the smaller coil even if the release mechanism was deployed. For the trans-cell embolization the kick-back was visible while the catheter passed through the cell of the stent, while the coil was traveling along the catheter and during the embolization. This condition was caused in part by trapping the catheter within the cell of the stent.

Conclusion

Human tissue modeling with photoelastic materials has applications for studying strain in ligaments¹¹, surface strains in femurs for pros-

thesis design¹², catheter trajectory analysis during robotic manipulation⁶.

The presented photoelastic material proved to have enough sensitivity to measure stress variations produced during the interaction of microscale mechanisms and instruments with human vasculature models.

This provides an *in vitro* evaluation environment for these and larger scale mechanisms, enabling us to develop them considering tissue integrity.

It also enabled us to identify which tissue areas have the higher risk of being damaged during an embolization, according to the selected coil size and embolization technique.

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