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Investigation of new flow modifying endovascular image-guided interventional (EIGI) techniques in patient-specific aneurysm phantoms (PSAPs) using optical imaging

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Abstract

Effective minimally invasive treatment of cerebral bifurcation aneurysms is challenging due to the complex and remote vessel morphology. An evaluation of endovascular treatment in a phantom involving image-guided deployment of new asymmetric stents consisting of polyurethane patches placed to modify blood flow into the aneurysm is reported. The 3D lumen-geometry of a patient-specific basilar-artery bifurcation aneurysm was derived from a segmented computed-tomography dataset. This was used in a stereolithographic rapid-prototyping process to generate a mold which was then used to create any number of exact wax models. These models in turn were used in a lost-wax technique to create transparent elastomer patient-specific aneurysm phantoms (PSAP) for evaluating the effectiveness of asymmetric-stent deployment for flow modification. Flow was studied by recording real-time digitized video images of optical dye in the PSAP and its feeding vessel. For two asymmetric stent placements: through the basilar into the right-posterior communicating artery (RPCA) and through the basilar into the left-posterior communicating artery (LPCA), the greatest deviation of flow streamlines away from the aneurysm occurred for the RPCA stent deployment. Flow was also substantially affected by variations of inflow angle into the basilar artery, resulting in alternations in washout times as derived from time-density curves. Evaluation of flow in the PSAPs with real-time optical imaging can be used to determine new EIGI effectiveness and to validate computational-fluid-dynamic calculations for EIGI-treatment planning.

Keywords

image-guided therapy; neurosurgical procedures; modeling; procedure simulation; segmentation and rendering; treatment planning

2. INTRODUCTION

2.1 Aneurysm Formation

The hemodynamic factors of the interaction between blood flow and vessel walls are believed to be among the leading causes of the formation and growth of aneurysms (Fig. 1). The vortex generated by blood flow into an aneurysm leads to high shear stress at the distal end of the aneurysm wall¹. This promotes the continued growth and increases the likelihood of vessel rupture. The formation of cerebral aneurysms can lead to hemorrhagic stroke and

thus methods have been developed to modify the flow with the intention of initiating thrombosis of the blood. This could instigate the formation of an endothelial layer across the aneurysm neck, allowing the vessel to start the healing process.

2.2 Existing/Proposed Treatment Techniques

The common endovascular method of treating neurovascular aneurysms is the use of Guglielmi Detachable Coils (GDC) or other embolic material to fill a given volume of the aneurysm and disrupt the turbulent flow within the aneurysm. There are risks in using this technique including that the coil may herniate into the vessel perforating the aneurysm or vessel wall and that incomplete filling of the aneurysm may result in its regrowth². Endovascular treatment of an intracranial aneurysm is typically accomplished using a coil or a stent or a combination of the two. Stents themselves can also be used to modify flow, but currently they are too porous to alter blood flow enough to promote remodeling of vessel lumen³ although Lieber et al⁴ has been reporting on denser stents with more struts. Therefore an asymmetric vascular stent (AVS) was introduced by Rudin et al⁵ as an alternative method of treatment. The stent consisted of a steel low porosity patch micro-welded onto a highly porous stent. The stent was deployed in an elastomer vessel aneurysm phantom and optical and radiographic analysis indicated that favorable flow modifications were produced.

The current method we are exploring here is the use of a non-porous polyurethane patch bound to an asymmetric stent. The stent is oriented such that partial coverage of the aneurysm occurs, allowing unimpeded flow to connecting major and perforating vessels. The patch will act as flow modulator by redirecting flow away from the aneurysm, minimizing the chance of rupture.

3. METHODS/MATERIALS

3.1 Previous work

In the past, our aneurysm phantom design was based on a typical rigid model. The mold was made from a translucent silicone elastomer; however the dimensions were based on an “ideal” aneurysm. The phantom was composed of a circular aneurysm located at a significant curve in the vessel (Fig. 2). This phantom met the needs of the experiment but lacked patient specificity and thus had a limited clinical application.

A more detailed commercial phantom from Elastrat (Geneva, Switzerland, Fig. 3) was then acquired. The phantom’s design consisted of patient specific vasculature suspended in a plastic box, providing the desired features of patient specificity and clinical application, absent in the rigid aneurysm model. However, the combination of pulsatile flow (to resemble arterial flow) with unconstrained vessels prevented the acquisition of reproducible quantitative data. We, therefore, combined the strongest qualities of both phantoms and fabricated a solid patient-specific aneurysm phantom that is discussed in detail in the following sections.

3.2 Patient Specific Aneurysm Phantom Fabrication

Cerebral basilar bifurcation aneurysms are very challenging to effectively treat and therefore were an ideal candidate to evaluate new endovascular image guided intervention (EIGI) treatment techniques. Images of the aneurysm were acquired via computed tomographic angiography (CTA) and reconstructed eliminating bone and small vessels (ie superior communicating artery). The resulting 3D rendered structure included the basilar artery, the right-posterior communicating artery (RPCA) and the left-posterior communicating artery (LPCA); the bifurcating aneurysm with diameters of 2.2mm, 1.95mm, 2.1mm and 2.9mm respectively (Fig. 4).

The images were converted into a solid model stereolithographic (STL) file where the 3D lumen geometry was represented. Figure 4 shows the bifurcation aneurysm that our phantom model was based on. The STL image was used to make a mold by means of a rapid prototyping process (Realize Inc, IN) known as stereolithography apparatus (SLA). This process utilizes a vat-filled photo-reactive liquid resin and an ultraviolet laser to selectively cure liquid plastic (Accura 25) to the specifications of the aneurysm. The mold is created layer by layer (0.004") resulting in a highly accurate and very detailed solid SLA part. A separate silicone mold is then made from the SLA part (Fig. 5) which can then be used to create multiple casts of the aneurysm vessel. This is done by injecting wax with a low melting point into the mold and allowing it to cure. The two-halves are separated and the wax mold is delicately removed from the cavity resulting in a patient-specific wax aneurysm vessel (Fig. 6).

A custom designed water-tight Plexiglas box was constructed in order to fabricate numerous aneurysm phantoms for experimentation. The wax aneurysm vessel was suspended in the box and a predetermined volume of Elastomer 184 silicone (Dow Corning, Midland MI) mixed with a curing agent (10% by volume) was poured into the box, fully submerging the wax mold. The elastomer filled box was then placed into a vacuum (VWR Scientific Products, West Chester PA) in order to remove any air bubbles that would create artifacts and distort the acquired images. The silicone required 24 hours to cure at room temperature in air, after which the hardened elastomer mold was removed from the box and placed into an autoclave machine. When warmed to 100 degrees Fahrenheit for 5 minutes the wax melts and drains from the phantom providing a patient specific aneurysm cavity for the evaluation of EIGI treatment techniques. Flow modulation within the phantom was then visually assessed at 30 frames per second (fps) by the injection of optical dye (Fig. 7) into a closed loop flow system described below.

3.3 Partially Covered Polyurethane Stent (PPCS)

A PPCS (Fig. 8) is created by using a commercially available asymmetric stent and partially submerging it in a polycarbonate-based polyurethane solvent solution. The excellent physical and mechanical properties of polyurethane along with its good biocompatibility⁶ made it a strong candidate for this biomedical application. Medicalgrade polyurethane from Cardiotech International (Woburn, MA) was chosen based on its significant flexure endurance and superior corrosion resistance.

3.5 Phantom treatment techniques

The final product is a clear elastomer model of an aneurysm cavity with patient specificity. Multiple identical elastomer phantoms were created and treated using various stent placement orientations. We have focused our attention not only on the details of fabricating a patient specific aneurysm phantom (PSAP) but also on the evaluation of PPCSs as treatment devices in these phantoms. The PPCSs were oriented in 2 treatment configurations: along the RPCA (acute) and along the LPCA (obtuse) as illustrated below in Figure 9. The stent was placed so that the polyurethane patch partially covered the neck of the aneurysm with the intention of diverting the initial aneurysm-creating flow. Thrombus formation can be triggered by stasis or creating slow recirculation⁷ in a vessel. In addition, with the stent only partially covered, there is no occlusion of perforating vessels.

3.6 Experimental Set-up

The experimental set-up illustrated in Figure 10 starts with a pulsatile pump (Cole Parmer, Vernon Hills, IL) generating a sinusoidal wave in a closed flow loop system of a 25% glycerin & 75% water solution with a viscosity of 2.45 cP and a density of 1059 kg/m³ similar to that of the blood. The average flow velocity was regulated by a flow meter (TS410, Transonic Systems Inc, Ithaca, NY) at 30 cm/sec to simulate flow in the cerebral arteries. The AC and DC components of the pulsatile flow were altered by using a flow dampener (Cole-Parmer, Vernon Hills, IL). By controlling these data from a connected oscilloscope, we were able to generate a desired average Reynolds number of 2608. An auto-injector (PHD 4400, Harvard Apparatus, Holliston, MA) located 20 cm from the aneurysm was used to inject 1 mL of optical dye in 600 milliseconds.

3.7 Imaging/Measurements

Single injections for each treatment technique with both a zero and 60 degree input vessel angle were assessed. The degree of the input vessel (basilar vessel in phantom) refers to its orientation with respect to the inflow. When the basilar vessel is parallel to the inflow, it is said to have a zero input angle and subsequently the 60 degree input angle is the basilar vessel rotated 60 degrees in relation to the inflow. Two input vessel angles were evaluated in order to determine the effect vessel geometry has on the flow into and out of the aneurysm. The differences in flow should be taken into consideration when applying different EIGI treatment techniques. The flow into and out of the aneurysm was visually captured using a charge coupled device (CCD) camera at 30 fps. The images were separated into individual frames using QuickTime (Apple, Cupertino CA) and the background noise was subtracted out with image processing and analysis in java (ImageJ). From these images we observed the effects of each treatment technique in modifying the initial flow of optical dye into the PSAP. ImageJ's ROI manager was used to generate time density curves (TDCs) of flow into the basilar artery, the RPCA, the LPCA and the aneurysm to further quantify flow diversion^{9,10}. The inflow ROIs for each phantom were chosen based on where the streamline was first visible and was kept at the same relative position throughout. The RPCA and LPCA ROIs were located after the bend in each artery, distal to the aneurysm and the entire aneurysm was selected for the aneurysm ROI.

4. RESULTS/DISCUSSION

The following images will illustrate the effects various treatment orientations have on the flow dynamics within a bifurcation aneurysm. We will initially show the flow into and filling of an untreated aneurysm using optical dye. This provided us with a comparison for our PPCS-treated phantoms. We observe the effective deflection of streamline flow away from the aneurysm. The effects of the angle that the input vessel makes with the phantom basilar artery on streamline characteristics and resulting flow modification are also presented and discussed, first for a straight vessel input at 0 degrees followed by the results for 60 degrees.

4.1 Analysis of treatment techniques with straight vessel input

Figure 11 demonstrates the flow characteristics into an untreated basilar bifurcation aneurysm. These images were acquired at 30fps providing an image every 33.3 milliseconds. Initially a streamline is created (Fig. 11a) and collides with the wall of the aneurysm (Fig. 11b). The collision initiates the dispersion of flow into the RPCA and LPCA (Fig. 11c). The dye continues to fill the vessels until the input concentration of optical dye appears to equal the output concentration of the 2 vessels (Fig. 11d). It is however important to note that the streamlines observed in Figures 11(a) and 11(b) continue to generate turbulent flow at the site of the aneurysm throughout the injection. The graph in Figure 12 highlights the similarity in filling rates of the aneurysm, RPCA and LPCA. The streamline flowing directly into the aneurysm is an expected feature since the high shear stresses produced are most likely a contributing cause of the formation of the aneurysm¹¹.

In Figure 13 below, we see a PPCS placed along the RPCA (“acute”) with a polyurethane patch partially covering the neck of the aneurysm. Here, a similar streamline (Fig. 13a) as the aforementioned untreated case is observed, however here flow strikes the polyurethane patch (Fig. 13b) causing the flow of optical dye to be diverted along the RPCA (Fig. 13c). The diversion of flow continues even with the complete filling of the basilar artery (Fig. 13d). With the patch only partially covering the neck of the aneurysm, the optical dye eventually trickles into the aneurysm (Fig. 13e), but with what appears to be less force on the aneurysm wall. These flow characteristics are desired in order to promote the initiation of thrombosis and vessel healing. Flow then slowly propagates from the aneurysm along the LPCA (Fig. 13f and Fig. 13g). The significant flow diversion along the RPCA can also be seen graphically in Figure 14, where approximately 50 milliseconds after the initial inflow into the basilar artery the patch diverts all of the flow along the RPCA. It is not until 150ms that the aneurysm fills initiating flow into the LPCA. This treatment technique shows significant deflection of initial flow while permitting necessary flow to the LPCA.

Figure 15 illustrates flow into a phantom with a PPCS placed along the LPCA (“obtuse”) and partially covering the neck of the aneurysm. Initially, the streamline of optical dye that is created in the center of the basilar artery (Fig. 15a) collides with the polyurethane patch and is fully deflected along the LPCA (Fig. 15b). The basilar artery then becomes filled with optical dye and with the aneurysm only partially covered; leakage into the aneurysm occurs (Fig. 15c). The RPCA then begins to fill (Fig. 15d) until the phantom becomes completely saturated with optical dye (Fig. 15e). The significant flow modulation can also be seen in

Figure 16 where a complete deflection of flow occurs along the desired LPCA. With this diversion of flow, optical dye slowly enters the aneurysm with the potential of initiating vessel healing.

4.2 Analysis of treatment techniques with a 60 degree input vessel

The effects of the angle that the input vessel makes with the basilar artery phantom segment and of gravity on the flow dynamics within the phantom is addressed here. Vessel geometry plays a significant role in determining streamline characteristics which in turn alters the flow. The input basilar vessel angle with respect to the inflow vessel was changed to 60 degrees by rotating the phantom and in doing so we altered the streamlines of the inflow (Fig 17). In this orientation (Fig. 18), the streamlines are along the right side of the basilar artery (Fig. 18a) as opposed to the center of the vessels as observed (Fig. 11b) when the input vessel angle was zero degrees (inflow is parallel to basilar vessel). In the untreated case below, the streamline characteristics show flow of optical dye into the right portion of the aneurysm (Fig. 18b) which then propagates into the RPCA (Fig. 18c). Flow into the LPCA (Fig. 18d) is initiated by the continued filling of the basilar artery; however even in the final stage (Fig. 18e) an inflow streamline is still visible as noted by the arrows in Figure 18f indicating a space between the vessel wall and the boundary of the streamline. This can also be seen graphically in Figure 19 where the mean gray value of the RPCA surpasses that of the basilar artery at 100ms as illustrated in Figure 18d where the RPCA is completely filled and the basilar artery is not.

The PPCS placed along the RPCA of the bifurcation aneurysm in Figure 20 notably modifies flow of the initial streamline of optical dye (Fig. 20a). With the streamline traveling along the right side of the basilar artery, it will strike more of the patch and ultimately deflect more of the flow (Fig. 20b). The flow is diverted into the RPCA. Once the basilar artery is filled, some optical dye bypasses the patch, entering the aneurysm and ultimately flowing into the LPCA (Fig. 20c). The mean gray values collected from Figure 20d and graphically represented for times > 100 ms in Figure 21, show significantly less flow into the RPCA than for the untreated case, indicating the vessel may not be fully saturated. Whether this is caused by the change in the detailed streamlines will require further study. The treatment technique did however successfully deflect the flow of optical dye away from the aneurysm while permitting essential flow to the LPCA.

The placement of a PPCS along the LPCA is shown in Figure 22. The previously discussed streamline characteristics of flow along the right side of the basilar artery can be seen here (Fig. 22a) as well. With the patch oriented to deflect streamlines occurring in the center of the basilar vessel, no initial deflection of flow to the LPCA is observed. It appears as if the flow may be diverted by the polyurethane patch (Fig. 22b), but the streamline bypasses the patch and strikes the aneurysm first (Fig. 22c), resembling the flow of the aforementioned untreated aneurysm. Flow then travels along the RPCA and struggles to enter the LPCA due to the boundary created by the patch. With the filling of the basilar artery, flow is subsequently deflected into the LPCA (Fig. 22d) until no visible change can be seen (Fig. 22e). The treatment technique was incapable of deflecting the initial inflow of optical dye away from the aneurysm given that the streamlines were flowing in a manner that avoided

directly striking the patch and, as seen in Figure 23, the optical dye entered the aneurysm before entering the RPCA and LPCA.

5. CONCLUSION

We have successfully demonstrated an effective method of fabricating patient specific aneurysm phantoms. The process of converting 3-D rendered CTA scans of a patient's aneurysm into an STL file and ultimately into an exact wax replica were discussed. With phantoms such as these, the effectiveness of new and old endovascular image-guided intervention treatment techniques can be tested and evaluated. We proposed and tested our own new treatment techniques by partially blocking flow into the aneurysm while maintaining flow to parent vessels and perforators. A polyurethane partially covered stent to treat vascular aneurysms via flow modification was introduced as a new EIGI device. The treatment can be evaluated using real-time optical imaging or x-ray imaging techniques such as region-of-interest cone-beam-computed-tomography (ROI-CBCT)^{12,13}. The ROI-CBCT can provide high-resolution 3D images of the stent assuring accurate placement of the polyurethane patch. Real-time optical imaging was utilized to accurately place treatment devices as well as evaluate the resulting flow modification. Qualitative data of the effects of the treatment techniques on streamline characteristics are demonstrated. An important result to note is that vessel geometry plays a significant role in determining streamline characteristics which then alters the effectiveness of a particular PPCS orientation. This is apparent in the above experiments for the obtuse PPCS placement; where a straight input vessel with a streamline traveling along the center of the vessel was deflected as planned along the LPCA whereas the altered streamline from a 60 degree input was unsuccessful in diverting the flow away from the aneurysm.

Further research quantifying the modifications in flow dynamics created within the aneurysm by the PPCS will be addressed in future experiments. In addition, more PSAPs will be fabricated, treated with a PPCS and flow modification will be evaluated. ROI-CBCT and TDCs based on high resolution micro-angiography will also be needed for evaluating EIGI treatment devices in animals and subsequently in humans where optical techniques are not possible.

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Fig. 1.
Fluoroscopic image of iodine contrast flowing through vessels

Fig. 2.
Rigid Aneurysm Phantom

Fig. 3.
Non-Rigid Aneurysm Phantom

Fig. 4.
STL image file of a bifurcation aneurysm

Fig. 5.
Two halves of a silicone mold with wax injected and hardened

Fig. 6.
Wax aneurysm vessel

Fig. 7.
PSAP filled with Optical Dye

Fig. 8.
Polyurethane film applied onto a commercial stent

Fig. 9.
PPCS Treatment Configurations

Fig. 10.
Experimental Set-up

Fig. 11.
 CCD images (@30 fps) of the initial inflow of optical dye into an untreated aneurysm phantom with a straight input vessel (each picture is taken 33.3 milliseconds from the previous)

Fig. 12.
TDC of flow into the basilar artery, RPCA, LPCA and aneurysm of an untreated PSAP

Fig. 13.
 CCD images (@30 fps) of the initial inflow of optical dye into an aneurysm phantom treated with a PPCS stent placed along the RPCA (“acute treatment”) and a straight input vessel

Fig. 14.
TDC of flow into the basilar artery, RPCA, LPCA and aneurysm of a PSAP with an acutely treated aneurysm

Fig. 15.
 CCD images (@30 fps) of the initial inflow of optical dye into an aneurysm phantom treated with a PPCS stent placed along the LPCA (“obtuse treatment”) and a straight input vessel

Fig. 16.
TDC of flow into the basilar artery, RPCA, LPCA and aneurysm of a PSAP with an obtusely treated aneurysm

Fig. 17.
Orientation of 60 degree basilar input angle phantom

Fig. 18.

CCD images (@30 fps) of the initial inflow of optical dye into an untreated aneurysm phantom with a 60 degree input vessel where this bend is at the top outside the area of the image (see flow indication at top of Fig. 17). Small arrows in Fig. 18f indicate location of streamline as described in the text. Each picture is taken 33.3 milliseconds from the previous

Fig. 19. TDC of flow into the basilar artery, RPCA, LPCA and aneurysm of an untreated PSAP with a 60 degree input vessel angle

Fig. 20.
 CCD images (@30 fps) of the initial inflow of optical dye into an aneurysm phantom treated with a PPCS stent placed along the RPCA (“acute treatment”) and a 60 degree input vessel

Fig. 21. TDC of flow into the basilar artery, RPCA, LPCA and aneurysm of a PSAP acutely treated and with a 60 degree input vessel angle

Fig. 22. CCD images (@30 fps) of the initial inflow of optical dye into an aneurysm phantom treated with a PPCS stent placed along the LPCA (“obtuse treatment”) and a 60 degree input vessel

Fig. 23.
TDC of flow into the basilar artery, RPCA, LPCA and aneurysm of a PSAP obtusely treated and with a 60 degree input vessel angle