In-Vitro Simulation of Acute Ischemic Stroke

Paolo Garcia

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In-Vitro Simulation of Acute Ischemic Stroke

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Submitted on 26 April 2018
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Abstract

Acute ischemic stroke (AIS) is a condition that involves the occlusion of a blood vessel within the brain, effectively preventing the passage of oxygen and nutrients. AIS is highly prevalent in the United States, where nearly 795,000 strokes happen per year and 87% of those are ischemic. From a medical standpoint, the obstructing clot can be removed with the use of a stroke retrieval device. However, a need arises for testing the aforementioned devices on a patient’s specific vascular geometries in order to increase the likelihood of a successful procedure. Outlined is a process for developing a physical simulation of patient vasculature with adjustable parameters for practical use.

This in-vitro model is created to address the following biological factors: temperature, volumetric flow rate, vessel measurements, and fluid properties of blood. Overall, the model system functions as a continuous loop that draws fluid from a heated reservoir kept at a temperature slightly above 37°C; temperature is observed through the use of a thermocouple thermometer. Similarly, volumetric flow rate is monitored through the use of a flow meter attached to a numerical display. In this case, a hollow silicone vessel was created with particular attention to the lengths and diameters of the internal carotid artery, middle cerebral artery, and basilar artery. The vessel is included as a part of the flow loop.

A clot can be introduced into the system to occlude the vessel; this can be visually observed from directly above. Once the vessel has been occluded, the retrieval device can be inserted and used. The resulting parameter changes can be observed. Overall, the factors physically represented in this simulation provide a fairly accurate depiction of cardiovascular biology in relation to AIS.
Article I. Background

Section 1.1. Overview of Acute Ischemic Stroke and Treatment Methods

One of the most prominent conditions affecting public health on the global scene is stroke, which is considered third in a lineup of the most expensive medical conditions affecting developed countries [2]. In the United States alone, this condition is very prevalent; a recent study suggested that there are near 795,000 cases of stroke in the US per year [3]. From a pathophysiological standpoint, stroke is primarily of the acute ischemic type, which is also known as AIS for short. Approximately 87% of all cases of strokes are classified as ischemic [3], where blood flow to the brain becomes obstructed by a blood clot. This occlusion can prevent the delivery of blood to the surrounding tissues, creating deficits in oxygen and nutrient supply. In this situation, the main priority of a medical professional will usually be directed towards the reestablishment of blood flow to the affected blood vessels and the removal of the clot itself. The terms for these outcomes are reperfusion and recanalization respectively.

These goals can be achieved with the use of a clot retrieval device (Figure 1) such as the Penumbra or the Solitaire mechanical thrombectomy devices for recanalization; recent studies have shown that there is a clinical advantage in using a retrieval device in comparison to standard intravenous therapy with thrombolytic...
agents such as tPA. Intra-arterial thrombolysis (IAT) has a recanalization rate of less than 50% in comparison to 85% in mechanical thrombectomy devices [2]. This statistical outcome, though encouraging, reveals the possibility of increasing the success rate of the aforementioned devices. This can be achieved through the use of a patient-specific simulation system to aid in device design and validation. Such a model could have potential applications in the fields of clinical research and education. For instance,

**Section 1.2. Device Design Criteria**

**The primary goal of this work was to develop a highly customizable system to simulate human vasculature for the purposes of thrombolytic device testing and clotting process observation.** For the purposes of evaluating the finished product, it was necessary for the completed system to be able to meet the following four criteria outlined below:

1. The model must be able to accurately represent vascular geometry, specifically vessel lengths, diameters, and angles.
2. The model must be able to sustain a fluid flow rate within the typical boundaries of blood flow within brain vasculature.
3. The model must be able to maintain a temperature consistent with biological temperature.
4. The model must be able to simulate the biological occurrences during AIS in some way.
To meet the first condition, particular focus was directed toward the internal carotid artery (ICA), middle cerebral artery (MCA), and basilar artery (BA), as they are integral components in brain blood flow. The ICA in particular provides blood to the MCA among other arteries. The BA receives blood from both vertebral arteries and is connected to the Circle of Willis (Figure 2), much like the MCA and ICA [1]. Even though there is not a direct connection between the BA and the ICA, the completed model will have the vessel representing the ICA bifurcate into the vessels representing the MCA and BA. The purpose of this change was due to the prevalence of bifurcations in the cardiovascular system as a whole. The angle of the model’s bifurcation will be set at an angle of 74.4°, an average of physiological parameters.

In addition, utilization of average vessel lengths and diameters will account for the highly variable differences in morphometry across individuals. For simplification purposes, the ICA portion of the model was set as 8.5 centimeters long and 5 millimeters in diameter. The model’s MCA length for this project was set at 20 millimeters and the MCA diameter was 2.5 millimeters. Lastly, the measurements of the BA were set at a length of 30 millimeters and a diameter of 3 millimeters. Through the use of rounded lengths and diameters for the ICA, MCA, and BA, the need for connection pieces was eliminated in the final model.
The normal parameters of blood flow within the human brain are highly variable between the vessels in question. Therefore, the range of flow rates in which the model should function should include all of these values. The necessary range for this model was established as 100 to 240 milliliters per minute to represent normal cerebral blood flow. All of the aforementioned chosen parameters for the vessel, from length measurements to flow rates, are detailed in Table 1 below in conjunction with their corresponding physiological values for comparison.

Table 1. Parameters for bifurcation model in comparison to physiological conditions.

<table>
<thead>
<tr>
<th></th>
<th>Physiological Conditions</th>
<th>Bifurcation Model Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICA</td>
<td>MCA</td>
</tr>
<tr>
<td>Length</td>
<td>8.9 cm [6]</td>
<td>20 mm [12]</td>
</tr>
<tr>
<td>Diameter</td>
<td>5.1 mm [11]</td>
<td>2.8 mm [15]</td>
</tr>
<tr>
<td>Bifurcation Angle</td>
<td>37° to 133° [4]</td>
<td></td>
</tr>
</tbody>
</table>

To address the third criterion, temperature in the model was set as 37°C. This temperature represents biological temperature though slight fluctuations may occur. The system must also be able to prevent major heat loss at the source of fluid flow, so sufficient insulation is required.

Lastly, the final condition details a need for simulating the events associated with AIS. To do this, the model must have a blood clot entry point and mechanism for clot insertion. Once the blood clot is inserted, it will cause fluid turbulence and the formation of circular eddies. According to previous work, flow phantoms such as the model that serves as the focus of this project can be tested by loading a blood clot into a syringe and flushing it through the system [8].
aforementioned procedure was chosen for administering the clot into this particular model. However, a guidewire will not be used as part of clot insertion.

**Section 1.3. Device Design Process**

Since the requirements of the finished model and system have been detailed, the process of developing the model itself is the next point of focus. Development of the model had to progress from the four criterion earlier in this section to a finished product. Firstly, an artificial vessel interior corresponding to the morphological measurements selected in the first criteria had to be created. From there, the vessel interior was to be surrounded by silicone rubber and removed, leaving a hollow vessel.

The process of creating the model is partially based on various flow phantom creations with changes to specific parts of the process. Similar to some previous work on simulating vasculature, the material representing the tunica intima and surrounding structures is silicone [5] [9]. Through the use of silicone, the finished product would be able to withstand the shear stress similar to that created by blood flow. A peristaltic pump was also the ideal driving mechanism behind the volumetric flow rate for simulated vasculature [8]. The most prominent difference between the aforementioned methods and the one developed is that the vessel created in this project was an original creation that was not taken from patient magnetic resonance imaging scans [8] [9].

The completion of this project involves the simulation of conditions similar to AIS in a setting that does not require integration with a living organism; all clot retrieval device testing with this model can be conducted in a silicone vessel.
Article II. Materials

Section 2.1. Standard, Non-Electronic Materials

For the non-electronic and non-powered components of this in-vitro simulation of acute ischemic stroke (except for the vessel itself), the following materials were used.

- Platinum-cured Silicone MasterFlex Tubing, 8 mm I.D.
- MasterFlex Pulse Dampener
- Acrylic Tubing, 8 mm I.D.
- Polyethylene Y-connection pieces
- Polyethylene T-connection piece
- Plastic two-input stopcock with plug
- Plastic one-input stopcock
- Generic Food-Safe Silicone Tubing, 5 mm I.D.
- Generic Food-Safe Silicone Tubing, 2.5 mm I.D.
- Styrofoam Packing Peanuts
- Glass Mason Jar
- 8 mm to 5 mm Plastic connection piece
- Ring Stand and Clamp
- Plastic Tubing Clamps
- Syringe
- Electrical tape
- Silicone caulk
Section 2.2. Vessel Creation Materials

For the development of the customized vessel bifurcation, the following materials and equipment were used. Parts of the list removed for confidentiality purposes.

- MagikMold Silicone Rubber Base and Catalyst
- Plexiglass Sheets, ¼” in thickness
- Epilog Mini Laser Cutter
- Vacuum Pump & Chamber
- Electronic Balance

Section 2.3. Flow Loop Function and Regulation Equipment

In addition, the following electronic devices and equipment were used in the regulation and maintenance of flow loop conditions.

- MasterFlex Peristaltic Pump with Head Attachment
- Flow Technology Inc. FTO 3NITW Turbine Flow Meter
- Flow Technology Inc. SRI-2 Indicator
- VWR Thermal Bath with Metal Lid
- Omega HH802U Thermocouple Thermometer
Article III. Methods

Section 3.1. Pre-Vessel Flow Loop Components

Much like body circulation, the system utilized for the in-vitro simulation of acute ischemic stroke is a closed flow loop (Figure 3). The whole system is exhibited in the picture. In this case, the factors that are being monitored and directly controlled are both the temperature of the fluid in the system and the flow rate. Heated distilled water is drawn out of a container in an insulated water bath (Figure 4) at slightly above body temperature through the use of a peristaltic pump (Figure 5). The pulsatility of the fluid flowing through the pump is greatly decreased by passing through a pulse dampener. The fluid is then passed through a turbine flow meter, which displays the flow rate on an electronic

Figure 3. An overhead view of the whole system.

Figure 4. Water bath, insulated with Styrofoam and covered during operation.

Figure 5. Peristaltic pump with head attachment and pulse dampener.
indicator. A calibration curve created before flow loop assembly is used to calculate the actual flow rate. After being measured, the fluid travels past the thermocouple and toward a y-shaped polypropylene piece, where one branch provides a point for clot and device insertion. Directly after the clot insertion point is the simulated vessel bifurcation.

Section 3.2. Vessel and Construction Process

The vessel itself (Figure 6) is a bifurcation that focuses on the characteristics of three arteries near the circle of Willis: the ICA, the MCA, and the BA. These three vessels were amalgamated into a bifurcation to be used for device testing. As previously mentioned, several factors were taken into consideration; literature research provided typical vessel tortuosity/angle values of the aforementioned arteries, average diameters, and average lengths. An acrylic box was laser-cut with the Epilog Mini to accommodate the specific measurements of the vessel lumen with the tubing attached. This silicone tubing had inner diameters that matched up exactly with the outer diameters of the vessel lumen branches to prevent gaps. If a clot were to be introduced into the system, the main aim for simulation is that the clot would be stuck near the bifurcation and cause an occlusion that could be removed with a device.

Figure 6. The silicone vessel.
Section 3.3. Post-Vessel Flow Loop Components

Once the fluid passes through the vessel, it returns to the container in the water bath. From there, the water is reheated and returned through the flow loop once again. The bypass system, however, is not included in the pathway of the flow loop during normal function. Designed for pressure relief, it is attached with a polyethylene T-connector piece and is present before the thermocouple insertion point. Throughout the process of preliminary testing, this bypass has been shut with a clamp. It would only be opened should the turbulence in the system be noticeably damaging to the vessel upon visual observation.

An insertion point for the thermocouple thermometer is positioned after the bypass point but before the clot insertion point. This was achieved with the use of a polyethylene T-connector piece attached to a one-input plastic stopcock. A plastic male luer piece with a lock ring and a small hose barb was attached to the input. The thermocouple was then administered into the connector piece and securely sealed in place with electrical tape and silicone caulk to prevent leakage. Any temperature readings could be seen on the thermocouple console’s display screen (Figure 7). Similarly, the second thermocouple was placed in the reservoir and monitored on the display with the insertion point. Thus, the system is completely assembled (Figure 8).
Section 3.4. Measurement Validation

In order to test the flow loop’s functionality, water was initially used as the circulating fluid. The accuracy of volumetric flow rate readings was ensured for the particular pump used through the creation of a calibration curve. Readings for mass of water displaced, indicator value, and time elapsed were taken over a range of pump RPM values from 20 to 70; this process was repeated three times to ensure accuracy. First, the pump was attached in series with a pulse dampener and the turbine flow meter, the latter of which was connected to the indicator (Figure 9). Unlike the flow loop, the assembled complex was an open system as it started and ended in different points. The pump itself drew room temperature distilled water from a reservoir and passed it through the pulse dampener and flow meter, where it exited the system into a cup on a tared balance.
The pump was allowed to run for approximately one minute for each reading; the exact times at which the pump was halted were measured with a stopwatch. From this, the volumetric flow rate in mL/min (Q) for a particular reading could be calculated (Equations 1 and 2) given the mass in grams (m), the time elapsed in minutes (t), and the density of water (ρ), which was assumed to be 1 g/ml.

\[
\frac{m_{\text{water}}}{\rho_{\text{water}}} = V_{\text{water}} \quad (1)
\]

\[
Q = \frac{V_{\text{water}}}{t} \quad (2)
\]

Equations 1 and 2. Volume and flow.

These readings were then used to create the graph for the calibration curve (Figure 10); doing so allowed for the prediction of a volumetric flow rate based on an indicator value. The indicator value was chosen as the dependent variable on this curve as it was a more consistent measure of flow in comparison to RPM.

This curve can then be used to estimate the indicator values that correspond to the average lower and upper limits of blood flow rate in humans, which were defined in the background section as 100 mL/min and 240 ml/min respectively. Calculations with the calibration equation in Microsoft Excel revealed that the indicator unit (variable depicted as \( U_{\text{Indicator}} \) and unit depicted as...
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\[ U_{\text{Indicator}}(Q) = 0.0009Q - 0.0222 \quad (3) \]

\[ U_{\text{Indicator}}(100 \text{ mL/min}) = 0.0009 \times 100 - 0.0222 = 0.0678 \text{ IU} \]

\[ U_{\text{Indicator}}(240 \text{ mL/min}) = 0.0009 \times 240 - 0.0222 = 0.1938 \text{ IU} \]

*Equation 3. Use of calibration equation to calculate upper and lower bounds of \( Q \).*

Therefore, flow within the flow loop must be constantly regulated so that the indicator value reads between 0.0678 and 0.1978 to maintain biological accuracy.

To verify the accuracy of the calculations, the peristaltic pump was adjusted until the lower and upper boundary rates were achieved. Once this was done, the flow rates were verified through the previously mentioned process involving a mass balance, stopwatch, and Equations 1 and 2.

\[ \% \text{error} = \frac{|Q_{\text{actual}} - Q_{\text{theoretical}}|}{Q_{\text{theoretical}}} \]

*Equation 4. Percent Error*

The testing was also repeated three times for both boundary values. Afterwards, the percent error of each flow rate data point in comparison to those calculated from the calibration curve was taken using a formula (Equation 4).

After the verification of the volumetric flow rate parameters to be used in the simulation, it was necessary to ascertain the exact value that the thermal bath needed to be set to. As the fluid in question is pumped through the system, it inevitably loses heat to the surrounding environment. Therefore, the temperature at the clot insertion point should be closest to normal body temperature. To discern the correct setting, a one-way flow system was used; the liquid in question would be drawn from a heated reservoir by the pump and transferred throughout the entire flow loop system. However, instead of returning the fluid to the reservoir, the temperature of the output was measured...
immediately in a separate container and recorded. The value obtained from the tubing output was then compared to the temperature of the thermal bath to determine how close the value was to 36°C and how much heat was lost. Heat loss along the tubing after the vessel model was also taken into account as the temperature exiting the system should be slightly less than 37°C; doing so would satisfy the assumption that the fluid within direct proximity to the vessel would be closest to biological temperature conditions. By monitoring the area temperature with the thermocouple thermometer, the necessary adjustments to the water bath setting could be made in order to maintain the correct temperature within the vessel.

Section 3.5. Clot Insertion Mechanism Validation

The clot insertion point was kept shut during measurement and only opened when testing the insertion mechanism. This was achieved by creating three “clots” of sponge that were cut into small cylindrical portions of a set diameter of 2.5 millimeters and varying lengths. The first piece of sponge had a length of 2.5 millimeters, forming a small and nearly spherical clot analog. The second pieces and third pieces had lengths of 1 centimeter and 2 centimeters respectively, forming more cylindrical shapes. These sponges were briefly hydrated and loaded into the insertion point, which has a female luer piece for attaching a syringe. Using the same circulatory fluid in the loop, the two-input stopcock was adjusted to allow flow from the syringe, which in turn would push the clot into the system. Once complete, the insertion point could be shut off and reopened again to insert a device guidewire for testing purposes.
Article IV. Results

The following data points (Table 2) are a representation of the averages for each value obtained over three trials. These values were obtained through testing flow through the system without the vessel and without taking the temperature into account.

Table 2. Values for open system without vessel and temperature measurement

<table>
<thead>
<tr>
<th>RPM</th>
<th>Volumetric Flow, mL/min</th>
<th>Indicator (T)</th>
<th>Indicator (A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>70.8</td>
<td>0.066</td>
<td>0.043</td>
</tr>
<tr>
<td>30</td>
<td>105.7</td>
<td>0.098</td>
<td>0.310</td>
</tr>
<tr>
<td>40</td>
<td>142.1</td>
<td>0.131</td>
<td>0.110</td>
</tr>
<tr>
<td>50</td>
<td>175.2</td>
<td>0.160</td>
<td>0.141</td>
</tr>
<tr>
<td>60</td>
<td>211.6</td>
<td>0.193</td>
<td>0.173</td>
</tr>
<tr>
<td>70</td>
<td>247.8</td>
<td>0.226</td>
<td>0.206</td>
</tr>
</tbody>
</table>

The following data points (Table 3) are a representation of the averages for each value obtained over three trials. These values were obtained through testing flow through the closed flow loop depicted in Figure 3.

Table 3. Values for closed system with vessel and temperature measurement

<table>
<thead>
<tr>
<th>RPM</th>
<th>T(Reservoir), C</th>
<th>T(Insertion), C</th>
<th>T(Diff), C</th>
<th>Indicator Units</th>
<th>Volumetric Flow, mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>43.6</td>
<td>35.1</td>
<td>8.47</td>
<td>0.048</td>
<td>77.6</td>
</tr>
<tr>
<td>35</td>
<td>43.4</td>
<td>35.2</td>
<td>8.23</td>
<td>0.060</td>
<td>91.0</td>
</tr>
<tr>
<td>40</td>
<td>43.4</td>
<td>35.2</td>
<td>8.13</td>
<td>0.071</td>
<td>103.2</td>
</tr>
<tr>
<td>45</td>
<td>43.2</td>
<td>35.5</td>
<td>7.67</td>
<td>0.084</td>
<td>117.6</td>
</tr>
<tr>
<td>50</td>
<td>42.9</td>
<td>35.7</td>
<td>7.23</td>
<td>0.095</td>
<td>130.6</td>
</tr>
<tr>
<td>55</td>
<td>42.6</td>
<td>36.0</td>
<td>6.60</td>
<td>0.106</td>
<td>142.8</td>
</tr>
<tr>
<td>60</td>
<td>42.4</td>
<td>36.5</td>
<td>5.97</td>
<td>0.118</td>
<td>155.2</td>
</tr>
<tr>
<td>65</td>
<td>42.2</td>
<td>36.5</td>
<td>5.70</td>
<td>0.129</td>
<td>167.8</td>
</tr>
<tr>
<td>70</td>
<td>41.9</td>
<td>36.4</td>
<td>5.53</td>
<td>0.137</td>
<td>176.9</td>
</tr>
<tr>
<td>75</td>
<td>40.4</td>
<td>36.3</td>
<td>4.07</td>
<td>0.148</td>
<td>188.7</td>
</tr>
<tr>
<td>80</td>
<td>39.2</td>
<td>36.3</td>
<td>2.83</td>
<td>0.159</td>
<td>201.3</td>
</tr>
<tr>
<td>85</td>
<td>39.2</td>
<td>36.4</td>
<td>2.73</td>
<td>0.172</td>
<td>216.1</td>
</tr>
<tr>
<td>90</td>
<td>40.2</td>
<td>36.5</td>
<td>3.67</td>
<td>0.186</td>
<td>231.5</td>
</tr>
<tr>
<td>95</td>
<td>40.5</td>
<td>36.7</td>
<td>3.77</td>
<td>0.197</td>
<td>243.9</td>
</tr>
<tr>
<td>100</td>
<td>40.5</td>
<td>36.7</td>
<td>3.83</td>
<td>0.209</td>
<td>256.5</td>
</tr>
</tbody>
</table>

According to many trials with the vessel, percent error between the theoretical and actual indicator values was variable upon a first glance. But upon closer inspection, a slightly negative
correlation (Figure 11) could be found between indicator value percent error and volumetric flow rate. As the flow rate gradually increased, the percent error of the turbine flow readings was generally lessened.

![Volumetric Flow vs. Percent Error](image)

*Figure 11. Negative correlation between flow and percent error.*

All three sizes of sponge “clots” were successfully administered into the tubing through the clot insertion point upon testing. In addition, there were no leaks at the various connection points in the most recent iteration of the system. Therefore, the risk of continued circulatory fluid loss was greatly decreased.
Article V. Discussion

Section 5.1. Project Accomplishments

The system as a whole is a fairly accurate representation of AIS in that nearly all of the physiological parameters were represented by components in the flow loop. For instance, the peristaltic pump provides consistent movement of fluid in the system, much like the human heart. The water bath functions as a parallel to the homeostatic mechanisms that regulate temperature in the body. All of the tubing and the vessel itself serve as a representation of arteries and veins. Each component was carefully configured to work together to form an accurate simulation.

In the process of constructing and designing the system, all of the criteria detailed in Section 1.2 was also successfully met to create a fully functional product. Physiological accuracy in factors such as flow rate, temperature, and shape gives the model a unique advantage over other models; some only account for one or two of the aforementioned factors. In addition, no other stroke simulation devices on the market sell all of the model’s components together as a completed flow loop. Lastly, the high degree of system customizability offers the user more control; certain components can be removed or altered to suit the needs of the user. This is best observed in the creation of the vessel, as the dimensions of the lumen can be adjusted in size through the use of computer-assisted design software or even based on patient vascular geometry.

When considering the values in Table 3, it is important to take into consideration that the system was open ended and water was flowing out of the tubing to be measured and recorded. While this occurred, the flow meter display screen exhibited a value other than zero. Thus, it can be said that volumetric flow is present whenever the monitor displays a positive, nonzero value. Since each reading for indicator units in Tables 2 and 3 meet these conditions, then the fluid is
traveling in the tubing whenever the pump is enabled. Flow within the system conclusively functions.

**Section 5.2. Project Limitations and Solutions**

There were only a few challenging aspects in the maintenance of basic flow loop function. However, each of these challenges were resolved. For instance, the volumetric flow rates displayed on the indicator would fluctuate rapidly on certain occasions. This fluctuation would make the recording of data points less accurate, considering that the fluctuations were over a wide range. However, this issue was resolved with the incorporation of the pulse dampener, which would reduce the fluctuations to a smaller difference of around 0.003 indicator units between the higher and lower measurements at a particular RPM.

The second most challenging issue facing the system’s development was the maintenance of system temperature at 37°C. Since the water bath device functioned through cyclic heating, fluctuations in temperature would occur near the vessel. The fluctuations occurred from between roughly 35°C to 38°C. This problem was addressed with the addition of added insulation and constant monitoring of the temperature indicated on both the water bath heating device and the thermocouple thermometer’s display.

The main limitation of this device is the lack of a system that controls pressure within the vessel. Since most components of the model are at roughly the same height off of the ground (except for the area of tubing close to the vertically oriented flow meter), the pressure at these points can be presumed to be equal. This situation, however, is not a realistic depiction of pressure in the human body. A proposal to address this limitation is detailed later, in Article VII of this document.
Article VI. Conclusion

The finished model and flow loop system as a whole successfully fulfill all of the criteria detailed in the background section of this document. Through the use of SolidWorks to design the vessel, the model accurately represented average diameters and lengths of the ICA, MCA, and BA. Physiological temperature of 37°C was achieved through the use of an insulated reservoir, a water bath, and constant monitoring. Flow rates close to those recorded in the aforementioned arteries were repeatedly achieved in the system and recorded for future use. Lastly, a mechanism for administering clots into the vessel was developed and successfully functioned in directing clot-like entities towards the correct sections of the system. With these things in mind, this system for the in-vitro simulation of AIS is a fairly accurate model that can be used to test new thrombolysis devices. The completion of this model also opens up a wide variety of potential projects and changes (detailed in the next section) that can be conducted in the future.
Article VII. Future Work

The development and completion of this project has created a wealth of opportunities for system customization. Combined with the use of a device and clot, an interventional cardiologist has the opportunity to rehearse the procedure before it takes place.

Visibility of the vessels in question can also be adjusted through the use of a more opaque material in conjunction with an imaging modality such as ultrasound to reflect the possible conditions of a true AIS treatment procedure. The material used can also be chosen to more accurately depict the stress-strain properties of endothelial cell tissues.

In order to make the model even more accurate, pressure drop across the vessel can be simulated with the use of elevated reservoirs on adjustable scissor lifts. The height differential can be adjusted to increase or decrease the hydrostatic pressure, which can be quantified by pressure transducers.

The rheological and dynamic properties of blood can also be simulated with the use of a blood analogue. In this case, a 40% by weight mixture of glycerin and water can be used with the system [10]. Red dye can also be added to simulate the color of blood.

Lastly, the flow loop regulatory devices can be connected to both a data acquisition device and a computer in order to simplify continuous observation and handling of data points. This process can even be taken a step further with the implementation of an automated pressure valve attached to the bypass tubing; the valve can release to relieve pressure buildup should the system pressure exceed a maximum threshold.
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