In-vitro Tube Model System

Midpoint Report

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DISCLAIMER

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EXECUTIVE SUMMARY

The purpose of this report is to design and manufacture an *in vitro* model for the testing of liquid embolics as an aneurysm treatment. Dr. Tim Becker is the sponsor for this project and will use the model for his personal testing in the Bioengineering Devices Laboratory (BDL). This model will include a vasculature system that mimics high risk locations within the brain, a pump, a fluid to imitate blood, and a system to analyze the flow within the system. Current *in vitro* models on the market utilize glass or silicone as the vasculature material and DI water as their blood substitute. Because these materials do not mimic the body accurately, this project will strive to create an anatomically correct simulation of the desired vessels and aneurysm locations. The engineering requirements set forth for this project included having anatomically accurate measurements, compliance vessel material, physiologically accurate flow, physiologically accurate fluid, transparent vessels, accuracy within the data acquisition system, accuracy during the manufacturing process, a size within 36"x36"x24", and a weight greater than 75 pounds.

Through research on prior designs, the model was broken into four sub systems: the pump, fluid, model type, and heating method. Different design options were then determined for each subsystem. The final design that was chosen based on its anatomical accuracy was a roller pump, CMC fluid, 3D printed vasculature cast, and heating via a hot plate. Additionally, the vasculature was produced within the casting system with a Polyacrylamide-Alginate (PAAM-Alg) material created in the BDL. This polymer material is tunable to desired elastic properties of a blood vessel. The vasculature was originally casted via a wax outer mold of the vessel system that holds a 3D printed inner core concentric within the system. The 3D inner core has correct vessel diameters and aneurysm sizes. Additionally, there is a 2-5 mm wall thickness throughout casted vessel model. Further, a Fischer Scientific roller pump was chosen for the system. The CMC fluid was compared to blood via rheometric viscosity testing and was found to have accurate shear thinning properties. In addition, the data acquisition system was designed to analyze the flow through the model via thermocouples and pressure transducers.

However, there were difficulties within the casting method. The original method involved pouring the polymer gel into the mold while it was gelling into its solid form. This caused inconsistencies throughout the vasculature. Due to its high viscosity, air bubbles were unable to escape from the mold while the material was being poured. Additionally, the polymer material is activated to cure into a solid material with UV light or heat, neither of which were options for this system. Because of this, the vessel system did not cure entirely for numerous trials. To alleviate these issues, the outer wax mold was machined in aluminum instead of wax. This allowed the PAAM-Alg material to be heated and activated within the mold. In order to prevent air bubbles, channels were also machined in the outer mold to allow air exit the mold. Additionally, the Fischer Scientific pump did not create as accurate of a pulsatile flow as desired. Therefore, a different pump was purchased with an offset, two stage roller system to mimic the pulsatile flow of the human body.

With these improvements, the team was able to design an anatomically correct and reproducible *in vitro* model. This model successfully mimics the nature of vessels within the brain and blood flow. In addition, the flow can be successfully analyzed through a data acquisition system to ensure the physiological accuracy of the model. Further work will be done to the model to perfect the casting method and ensure the limitation of gelling inconsistencies and air bubbles. With additional funding, the project also hopes to get a programmable pump to create a pulsatile flow from biologic data.

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1 BACKGROUND

1.1 Introduction

This project's purpose is to design and construct a reusable and anatomically accurate *in vitro* model for aneurysm treatment. Unruptured brain aneurysms have various forms of treatments available. The least invasive treatment maneuvers a catheter up the femoral artery and to the location of the aneurysm. Common remedies for the aneurysm include clipping, coils and other embolization, and diversion of flow methods. Dr. Timothy A. Becker, the PI for Bioengineering Devices Lab (BDL), has focused his research on aneurysm treatment with the use of hydrogels (sodium alginate) in place of current embolization methods. Sodium alginate is bioinert and its byproduct is sodium chloride, a readily accepted compound to the body. Therefore, this treatment is safer than coils and other forms of embolization. In order to proceed in his research process, Dr. Becker needs an *in vitro* model to test the sodium alginate treatment. This project will focus on designing a model to meet to needs of such aneurysm treatment. In contrast to prior models, this model will focus on being anatomically correct. Therefore, the team will use tubing in place of glass to construct a more compliant vessel. The design will also include a pump to mimic the pulsatile flow of blood to the cerebrum. Once Dr. Becker optimizes his research, he can continue to progress in the FDA approval process to produce a regularly available treatment to patients.

1.2 Project Description

The mobile in-vitro vessel tube model system's description from our client Dr. Becker is as follows:

> "The scope of this project is to design, build, and test a replicable system for simulating vascular defects, such as aneurysms, using non-biologic materials. This system will model the vascular defect as well as allow for the testing of bioengineering devices to repair said defects. The system must be contained on a mobile platform for transportation to fluoroscopy."

1.3 Original System

This project involved the design of a completely new *in vitro* model. There was no original system when this project began. The existing *in vitro* models are all tested with the system setup in Figure 1. The "TC" is a temperature couple that heats the fluid to body temperature. "PT" is a pressure transducer and the "FM" is a flow meter. The system establishes flow using a pulsatile pump. The main element that changes is the aneurysm vessel model. The team is exploring a completely new model to use in this part of the system. Existing designs that have been previously used will be discussed in a later section of the report.

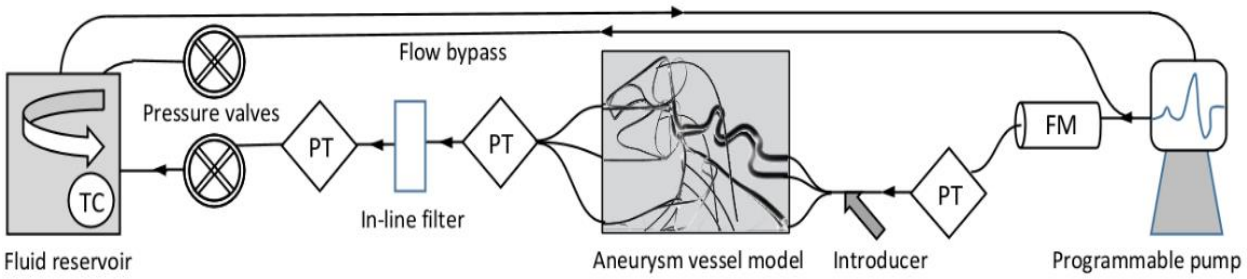


Figure 1: General *in vitro* setup [1]

2 REQUIREMENTS

2.1 Customer Requirements (CRs)

The most important requirement for the customer is anatomical accuracy. Accurately modeling vasculature and vascular defects is paramount for a successful *in vitro* model. The second most important requirement is replicable testing. In order to have confidence in data acquired from testing in this model, results must be replicable. The next most important requirement is physiological accuracy. The ISO standards for this type of *in vitro* model are not very physiologically accurate. The team plans on enhancing our model from these ISO standards to include features such as heated fluid, physiologically accurate fluid, and compliant vasculature. These enhancements, while deviating from the ISO standards, will provide us with more physiologically relevant data. Device deployment visualization, replicable manufacturing ability, and mobility are all required by the customer, but can be sacrificed if they impede any of the more important customer requirements. Device deployment visualization is required to allow for easier device deployment in the model. Mobility is important so the model can be taken to be performed under fluoroscopy. Replicable manufacturing is important in case the model breaks and needs to be rebuilt. Table 1 displays the weighted CR's.

Table 1: Weighted Customer Requirements

Requirement	Weight (out of 5)
Anatomically Accurate Model	5
Physiologically Accurate Model	3
Ability to Visualize Device Deployment	2
Replicable Testing	4
Replicable Manufacturing	2
Mobility	4

2.2 Engineering Requirements

Engineering requirements were developed as to allow for the ability to understand the specific goals that are objectives for this project. One of the requirements that were set was to make sure that anatomically that the model was accurate, as to make sure it is as close to human as possible, and therefore results could be applied to if this experiment was conducted on a human's anatomy.

The system must also not interfere with the vessel material this is important because the system must not harm the material being used for the vessel our else the experiment is a failure and results found would could not be used. The flow must also be physiologically accurate so that the flow acts exactly how it would be inside of a human blood vessel, allowing for similar stresses and forces for both scenarios. The fluid must also be physiologically accurate so the properties of the fluid are such that the viscosity and density of the fluid are similar if not exactly the same as human blood. Accuracy of the data acquisition system is important as well to make sure that what is recorded is accurate and the information gathered using this system is viable. The manufacturing process must also be accurate because this experiment must be easily repeatable, since different lab may take this design and try and repeat it, and must gain similar results no matter who is repeating the experiment. The weight must also be low since this experiment will have to be moved around the lab in which this experiment takes place allowing for easily repeatability and conducting of the experiment.

Table 2: Engineering Requirements

Engineering Requirements	Target and Tolerance
Accuracy of Anatomical Measurements	∓ .05mm between measurements
Compliance of Vessel Material	0.4∓ 0.2% change in diameter
Physiological Accuracy of Flows	2.5∓ 0.5 mL/s
Physiological Accuracy of Fluid	3.5∓ 0.5cP, 37∓ .2℃, Non-Newtonian (shear thinning)
Transparency of Vessel Material	Opacity of 15% or less
Accuracy of Data Acquisition	Pressure ∓ 0.2%, Temperature ∓ .25%
Accuracy of Manufacturing Processes	∓ 0.1mm from design
Size	36”x36”x24”(LxWxH)
Weight	75lbs≥

2.3 Testing Procedures (TPs)

1. Accuracy of Anatomical Measurements

Anatomical measurements can be measured accurately within acceptable tolerances using a micrometer and a protractor. These measurements can be compared to values acquired from literature. Measurements such as vessel diameter, branching angles, aneurysm neck, aneurysm dome, and aneurysm length will all be measured. As we measure the model, measurements should be within 0.05mm of values found in literature.

2. Compliance of Vessel Material

Compliance of vessel material can be measured in three ways: diametric compliance, cross-sectional area compliance, or volumetric compliance. Each method measures the amount of expansion (in different dimensions) per unit pressure. The materials that are being considered for this project are homogenous in nature, therefore, we can use diametric compliance. Measuring the diameter of the vessel with a micrometer before and during the application of a known pressure will provide a measurement of vessel material compliance. Compliance measurements can then be compared to data from literature. The desired compliance of our model will be 0.4 $\pm$0.2% change in diameter per mmHg

3. Physiological Accuracy of Flows

Physiologically accurate flows will be generated and monitored by the pulsatile pump system. By using data acquisition software, outputs such as pressure and temperature can be recorded in real-time and compared to data from literature. The flows in our model should be 12.5 $\pm$5 mL/s. Temperature of the fluid should be 37 $\pm$0.2 °C.

4. Physiological Accuracy of Fluid

By using rheological testing procedures on our client's DHR-2 Hybrid Rheometer (TA Instruments), we can accurately measure the viscosity and shear modulus of a fluid. Using a scale and a volumetric flask, we can also measure the mass and volume of the fluid and calculate its density. Using viscosity, behavior under shear, and density, we can characterize the fluid and compare it to human blood using data from literature. Viscosity should be 3.5 $\pm$5 cP. Fluid should be non-Newtonian (shear thinning) when shear is applied to the fluid.

5. Transparency of Vessel Material

The material being used in the vessel model should allow for visualization of the flow and devices within the vessel. Opacity/transparency is difficult to measure, so a more qualitative approach will be taken. A catheter will be inserted into the model and the client will be asked if they can see the advancing catheter and if the level of opacity is acceptable. A value of 15% opacity was put forth as an arbitrary goal by the client to help the team understand an acceptable level of opacity.

6. Accuracy of Data Acquisition

The data acquisition software that we are using can be calibrated using known values (i.e. pressure from a blood pressure cuff or temperature of boiling water). We can intermittently retest these known values to ensure that the data is still being collected accurately. Pressure readings should be accurate within $\pm$0.2% accuracy. Temperature readings should be within $\pm$0.25% accuracy.

7. Accuracy of Manufacturing Processes

Our manufacturing process consists of molding our material in a cast of known dimensions. By measuring the model that comes out of the cast using a micrometer, we can compare the measurements of the mold and the model to ensure that our manufacturing processes are accurate. We will also use this test to inspect for defects in the model that would affect its accuracy. Measurements of the model should be within $\pm$0.1mm from design measurements.

8. Size

The model needs to be able to fit onto a cart so it can be transported to fluoroscopy for testing. The cart that we will be using has a top surface area of 36" x 36". A maximum height of 24" has been established to help keep the center of gravity of the model as close to the cart surface as possible to prevent tipping. Our model cannot exceed this size. We can measure the size of the model using a tape measurer.

9. Weight

The model needs to be easily and quickly transported to and from fluoroscopy, so it cannot be too heavy. A maximum weight was presented to us by our client of 75lbs. This can be measured using a household scale.

2.4 Design Links (DLs)

Accuracy of Anatomical Measurements

The in vitro model that has be designed by our team will use a fluid, pump, vasculature and material that is comparable to the human body. The fluid will have viscosity and shear thinning of human blood. The pump will cycle the fluid through the model with a pulse that mimics the blood flow of the human body. The vasculature dimensions will be created at average human vessel sizes. The material that is used to create the vasculature can be any material stretchy enough to have the core removed from the vasculature. We have tested current materials to find their mechanical properties and have related those found properties to the published properties of human vessels.

Compliance of Vessel Material
The material that will be used for the model can be any material that is elastic enough to stretch around the core used for casting. The materials that we have already created in vitro models with have been tested via rheometry. A material created by two of the team members can be used to create the vasculature. This student made material can be optimized so that it best mimics human vasculature. The material optimization will be done using the rheometer in the BDL. We can also make in vitro models with clear molding material.

Physiological Accuracy of Flows
The flows will be controlled by a pulsatile pump. This pump will either be an expensive programmable pump that will be funded by a grant or a piston pump that has been designed by the team. Both pumps will have the ability to replicate blood pressures and pulsatile flows that are found in the human head. The determining factor is if a grant funds the pump by the end of the project deadline. If no grant then the piston pump will be manufactured. The flows will be monitored by a flow meter and will have pressure transducers that will measure the pressures and pressure drops.

Physiological Accuracy of Fluid
Most industry in vitro modeling is done using DI water. We have researched fluid mixtures that could be created so that the fluid mimics human blood viscosity, density and shear thinning. This fluid will be optimized by using the rheometer in the BDL.

Transparency of Vessel Material
The material used for the modeling will be transparent. It

Accuracy of Data Acquisition
The DAQ will operate using LabView. The pressure transducers, flow meter and thermocouples connected to LabView will have errors that are low enough to be negligible. Despite the accuracy we can still calculate the uncertainties so that we can prove the accuracy of the in vitro model.

Accuracy of Manufacturing Processes
The process we are using to create the in vitro model will produce a mold that holds shape. This will keep the inner diameters constant. The process is a casting method that will be used to create multiple models. All models created using our method will be the same dimensions.

2.5 House of Quality (QFD)

A house of quality was done to understand the relationship between the assigned customer's requirements what the customer has asked of this project and what they want out of it, and that of the engineering requirements of what actually is going to be developed and their associated accuracies. The QFD can be seen in Appendix A. From the QFD it can be shown that the most difficult part of this project is going to be the accuracy of the manufacturing process that is when the model and defect is being created to guarantee that the model is within a given amount of accuracy. This is very important for or experiment as to insure that this experiment can be repeated for different labs so they can have similar results, and to insure that the results found are closely related and don't have high associated error.

3 EXISTING DESIGNS

3.1 Design Research

It is first important to understand the defect that will be modeled and the current treatment techniques available. Brain aneurysms are bulges in the cranial blood vessels that form when the vessel wall is weak [2]. Most brain aneurysms are not life threatening; in fact, about 1 in 50 people in the US have an unruptured brain aneurysm [3]. However, if the aneurysm ruptures, causing bleeding in the brain, or a hemorrhagic stroke, then the fatality rates are very high (approximately 40%), and the majority of survivors will suffer permanent neurological deficit [4]. Because of this, many people with aneurysms will take surgical measures to prevent a rupture.

Current surgical techniques include aneurysm clipping, embolization, flow diversion, and parent vessel occlusion and bypass. Aneurysm clipping and an embolization technique called coiling are the most common today, but flow diversion and vessel occlusion and bypass are being seen more recently.

Aneurysm clipping requires the surgeon to perform a craniotomy so that then can insert a clip around the bulge, blocking flow from entering the aneurysm [2]. This method is more dangerous, because it requires open-skull surgery and if the patient is too ill to undergo this procedure it can lead to the death of the patient. In addition, some aneurysms can't even be reached through surgery, so it isn't always an option for some patients.

Aneurysm embolization is a less invasive technique than clipping because no craniotomy is required; the surgeon reaches the aneurysm by inserting a catheter up through the femoral artery to the aneurysm site. Then, a clotting agent is injected into the aneurysm sac, filling up the bulge so that it is strong enough to withstand the pressure of the blood, and blood will flow past the aneurysm instead of into it causing a rupture. The most common embolization technique is coiling, where shape memory coils are injected into the sac to stimulate natural blood clots [2]. A newer agent on the market is Onyx, an organic solvent that fills up the sac and quickly sets. This is the main competitor to Dr. Becker's Calcium Alginate product, which he believes will be a better alternative. The in vitro aneurysm model that our team is working to create is aiming at testing and proving Dr. Becker's embolization technique.

Flow diversion involves inserting a stent inside the defected vessel, over the opening of the aneurysm, via a catheter. This will guide most of the flow past the aneurysm and reduce pressure in the sac, so that over time, the aneurysm will start to close up [4].

Parent vessel occlusion and bypass is a more invasive technique, where the surgeon first performs an anastomosis, connecting a smaller blood vessel from another area to just past the aneurysm in the defected vessel. This is called bypass, because the blood is reaching the affected area of the brain from a new vessel. Then, the defected vessel is completely closed off (occluded), via coiling [5].

To properly understand the important aspects of creating an in-vitro defect model, key improvements from previous models must be identified. Research was conducted on models currently in use in the field. Looking into research online through accredited sources and research done through the sponsor of this project Dr. Becker, who has published numerous studies in the biomedical field showed a wide variety of models.

3.2 System Level

3.1.1 Existing Design #1: Glass Vessel [6]

This method of modeling involves using a glass tube to simulate a blood vessel in the brain. This is a relatively low cost method to produce a blood vessel since glass is very inexpensive. This allows the model to be designed at any size for various vessels. Unfortunately, this does not allow for an accurate

defect model that properly tests the treatment methods. This method can still be used to test how a catheter or other medical device will act in the endovascular system. Along with allowing for an induced flow through the system and the ability to measure the induced change in pressure on the endovascular system.

3.1.2 Existing Design #2: Animal Model [7]

Using an animal model involves taking a blood vessel out of the neck of an animal and reattaching it to another blood vessel. This is done to artificially create a defect. Once the defect is made the selected treatment method can be tested. Pigs are often used since their bodies are very similar to humans and provide a very realistic view of how the treatment will act in a human body. This method is more expensive than using other methods to test treatment for a brain aneurysm. This method is commonly used after other successful modeling has been completed, due to its high cost and the morality of testing on animals.

3.1.3 Existing Design #3: Flexible Urethane Vessel [8]

This model uses a urethane vessel that acts like a real blood vessel. This is beneficial because it gives an accurate representation of a human blood vessel. It allows for the creation of a multiple vessels just like there would be in a actual patient. This allows for testing the medical device in situations with multiple vessels near the aneurysm.

3.2 Subsystem Level

For this project the goal is to accurately model a human blood vessel. An aneurysm will be added to the vessel, which will be utilized in testing different blocking and filling medical devices. The system for the model will have fluid moving through it. The current fluid being used is usually water, which is not as viscous as blood. Other fluids are discussed later in this paper. It is important that the model is as accurate as possible so other fluids could improve the accuracy of the model. Other requirements for the model are transportability, anatomically accuracy, and a physiologically accuracy. When testing the system, the fluid will be moving through tubes and pipes while being heated to body temperature to more accurately simulate the human body. The fluid will be heated in a reservoir to ensure there will be no lack of fluid to flow through the system. A data acquisition system (DAQ) will be utilized to continuously collect data such as flow, temperature and pressure. This whole system will be transportable on a cart so that it can be easily moved to different locations around the lab. This will aid in the time it takes to set up the experiment and replicability of the experiment.

3.3.1 Subsystem #1: Accurate Defect

The defect added to the model is important so the model is physiologically correct. The defect should be as close to a human brain aneurysm in its dimensions in order to simulate a real aneurysm. This will prove the treatment methods effectiveness to treat real aneurysms. The main treatment being tested using the models is calcium alginate, which has similar material properties to that of a blood vessel.

There are many types of aneurysm that occur in the human brain. On type of defect is a large aneurysm which would commonly require an invasive procedure to remove a aneurysm. Smaller Aneurysms can be treated with medication and do not require an invasive treatment to have it removed. Another type of aneurysm has a 2-2.5 cm in diameter, these are dangerous aneurysms to have and is usually accompanied by visual failure in the patient. A wide-necked aneurysm is a aneurysm that has 4mm wide, or at least half as wide as the distance from the neck opening to the top of the aneurysm. These aneurysms usually form near major arteries in the brain making them hard to remove, due to some methods such as coiling not being able to work properly on aneurysms of this shape.

3.3.2 Subsystem #2: Pump

This subsystem will move the flow through the system with the correct velocity that would normally be present in a blood vessel and aneurysms. Some higher precision pumps have the ability to instantly control the flow rate and pulsate the fluid, just like heart pumps blood through the body.

3.3.2.1 Existing Design #1: Faucet

This technique involves connecting a tube from a faucet to the system directly. It is not very accurate and does not allow for pulsating flow. This is a very simple example of what could be done to move fluid through the system. Models are commonly tested for leaks using faucet flow water.

3.3.2.2 Existing Design #2: Roller Pump

This pump pushes water through the system using a sinusoidal wave with gradual increases and decreases in flow. This gives a better model of how a heart pushes blood, since an actual heart does not pump fluid at a constant rate. Using this will give a change in pressure which is beneficial in making the model more accurate for testing.

3.3.2.3 Existing Design #3: Programmable Pump

This pump can be programmed to any specification required for the flow rate. It has built in settings that allow the pump to mimic how a heart beats. It also has functions which change the flow rate depending on which part of the body you want to mimic fluid flow. This would be helpful for testing since it can perform for aneurysms in any location in the brain so that the medical treatment method being used is under accurate conditions.

3.3.3 Subsystem #3: Flow Meter

The flow meter measures how much fluid is moving through the system and the corresponding pressure on the vessel walls that result from using the pump. Also if there an issue within the system it can be noticed with this device by finding a corresponding pressure drop reading of the flow.

3.3.3.1 Existing Design #1: Measure Volume over Time

This method involves letting the water drain into a reservoir and using a stopwatch to take the time it took to displace the fluid. This is not the most accurate way to measure the flow of water, but it is the least expensive way. Repeating trials is difficult with this method because measuring the flow rate can become time consuming.

3.3.3.2 Existing Design #2: Pressure Transducer Differentials

A pressure transducer uses an elastic material which as it contacts the water it reads electrical signal to find the amount of fluid going through the pipe at any time.

3.3.3.3 Existing Design #3: Electromagnetic Low Flow Meter

An electrical field is induced in the fluid and using Faraday's law of electromagnetics the fluids magnetic fluid associated with it is measured. Using another sensor, the moving flow is measured at that location in the system. This is a highly accurate tool to measure the amount of fluid and can be quite expensive.

3.3.4 Subsystem #4: Fluid Properties

The fluid properties are important for the testing of the model, due to the fluid applying pressure to the walls of the vessel and the defect. The fluid must be an accurate representation of blood and have similar viscosities and densities, along with the ability to go through the corresponding pump and flow meters

without interfering operation.

3.3.4.1 Existing Design #1: ISO Di Water

Water has very close density to that of blood, but the viscosity of blood is higher than water. Blood is a non-Newtonian fluid and has different shear stresses when there is a velocity gradient. The pressure gauges and pumps are setup to work with water, which allows it to be easily tested within the system.

3.3.4.2 Existing Design #2: Glycerin

With a mixture of about 20-25% glycerin in water, it becomes more viscous with properties closer to blood. This method does not take into account the change in shear stress that blood undergoes due to its non-Newtonian properties, the viscous forces will act more closely to that of water.

3.3.4.3 Existing Design #3: Carboxymethyl Cellulose [9]

Since blood is a shear-thinning non-Newtonian fluid, it would be ideal to use a similarly acting fluid. Carboxymethyl cellulose (CMC) is a highly water-soluble substance with a shear-thinning behavior with increasing viscosity at higher concentrations, which is similar to the behavior of blood. Using a rheometer, an optimal concentration could be tested for to match blood as closely as possible. CMC solutions are also mostly transparent, which is ideal for opacity.

3.3.5 Subsystem #5: Heater

To make sure the experiment is setup under correct circumstances the temperature of the fluid must be at the correct temperature of 37 degrees Celsius which is body temperature. This is important because the method being tested by the model might depending greatly on the temperature of the fluid and the model so altering either could interfere with the results obtained.

3.3.5.1 Existing Design #1: Hot Plate

A hot plate will be used to bring the fluid to body temperature, this will be done by placing a flask on the hotplate and heating up the hot plate to body temperature. Than tubes will be placed in the container and the fluid will be pulled into the system by the pump.

3.3.5.2 Existing Design #2: Solar powered water heater

For this method tubes will be placed outside in direct sunlight and the fluid will be warmed up by the radiation from the sun and the convection from the air on the tubes. The temperature achieved using this method is up to the temperatures of the outside as there will be no way to alter the temperature the fluid reaches.

3.3.5.3 Existing Design #3: Body heat

To warm up the fluid tubes will be attached to the system and from those tubes they will be wrapped around a person who is wearing a coat. In doing this the fluid will circulate around the person and warm up to their body temperature, although the temperature is not exactly the 37 degrees Celsius it will be close to the desired temperature.

3.3.5.4 Existing Design #4: In-line heaters

An In-line heater will be used to bring the temperature of the fluid up to the prescribed temperature, with this method there is no need to keep the fluid in a separate storage area since the In-line heater will be able to heat up the fluid as it moves through the pipe.

4 DESIGNS CONSIDERED

For sketches of the sub systems that are described in section 4 refer to Appendix B.

4.1 Design #1: Design 1.0

This design is ideal because it allows for the most anatomical and physiological accuracy. Using a hand-pump is not ideal for reproducibility and accuracy, but it is very inexpensive. The 3D printed cast allows for more control over the anatomical details which increases accuracy and reproducibility. Since blood flow is what the design is trying to imitate, blood is a logical choice for our system. However, blood may not be compatible with certain aspects of the system and could potentially pose health risks if human blood is used. Having the fluid heated with an in-line heater is beneficial because you can place the heater after the pump and ensure that the fluid entering the vessel model is at a physiologically accurate temperature.

Pros:

- Physiologically accurate
- Anatomically accurate
- Versatile, robust system
- Reproducible conditions

Cons:

- High cost
- Using blood poses risks and challenges for the system

4.2 Design #2: Design 2.0

This design is ideal because it allows for the most anatomical and physiological accuracy. A sink was chosen for use due to its ease of access since most labs that would be performing this experiment would have access to a faucet which could supply water to the system. Wax casting was chosen for the method of molding defect, since this method has already been done with members of team 23 it would be easy to repeat. Water would be used for the experiment to represent blood's characteristics in the body, and since a sink is being used as the pump it is the only option. Then to warm up the fluid to body temperature the sun will be used as a source of heat, the temperature achieved will be highly dependent on the temperature of the ambient air and the amount of radiation from the sun, so this method is not ideal.

Pros:

- Physiologically accurate
- Anatomically accurate
- Easily setup

Cons:

- Low accuracy
- Hard to achieve correct temperature of fluid

4.4 Design #3: The Body Milk

This design is feasible and allows the model to have the most control for pulsatile flow and anatomically correct dimensions. The programmable pump would control the flows of the water and allow for the most accurate representation of the fluid within the system to represent human blood. 3D printed vasculature would give the model correct dimensions but we would not be able to control the material compliance as well as poured mold. The powdered milk would replicate the density of blood and similar viscosity but it is still a Newtonian fluid and would not have shear thinning properties that blood has. Using body heat is a feasible idea but would be very difficult to regulate the correct temperature of the fluid.

Pros:

- Anatomically accurate
- Versatile, robust system
- Reproducible conditions

Cons:

- High cost
- Temperature would be hard to regulate

4.5 Design #4: HPVM (Human-Powered Vessel Model)

The pump used to create a flow in this case will be a hand pump which will supply pressure through the system and mimic the heart; this is an easy solution for a pump although the pressure at the defect is going to vary greatly depending on individual that is doing the pumping at any time and may vary greatly experiment to experiment if the different people are pumping the fluid. Wax casting will be done for the molding of the vasculature, it has already been done with members of team 23 and provides a simple solution to molding the defect. Water was chosen to be pumped through the system since it is readily available, and is used in many of situations in industry to model similar experiments. To heat up the fluid body heat was chosen due to its simplicity, a person would wrap tubes around themselves to warm up the fluid to body temperature and insure and was kept at the appropriate temperature. Although the outside of the body is not necessary exactly the same temperature as a blood vessel in the brain it is close, but there is some error in using this method that must be accounted for.

Pros:

- Physiologically accurate
- Anatomically accurate
- Simple solutions
- Low cost
- Reproducible conditions

Cons:

- Fluid used will not have the same properties as human blood does
- There will be error associated with the heating method

4.6 Design #5: Becker's Big Baller System

This design is ideal because it allows for the most anatomical and physiological accuracy. By using a programmable pump, the design can achieve physiologically accurate pulsatile pressures as well as many different pressure waves which may be useful for future studies. The 3D printed vasculature allows for

more control over the anatomical details which increases accuracy and reproducibility. Since blood flow is what the design is trying to imitate, blood is a logical choice for our system. However, blood may not be compatible with certain aspects of the system and could potentially pose health risks if human blood is used. Having the fluid heated with an in-line heater is beneficial because you can place the heater after the pump and ensure that the fluid entering the vessel model is at a physiologically accurate temperature.

Pros:

- Physiologically accurate
- Anatomically accurate
- Versatile, robust system
- Reproducible conditions

Cons:

- High cost
- Using blood poses risks and challenges for the system

4.7 Design #6: CMC 1.0

This design is considered because of its high feasibility. The roller pump provides a pulsatile-like flow because it pumps the fluid due to a pressure differential. While a programmable pump would be ideal, if the team's budget prohibits it from purchasing such a pump the roller pump will be sufficient for the project. Additionally, using a 3D printed vasculature cast would allow for precise anatomical measurements and be easily reproducible. However, there may be inconsistencies during the reproduction because of the need to cast the mold each time the team wishes to reproduce the model. While it is opaque, the use of powdered milk provides the opportunity to tune the viscosity to desired values. Finally, this model will regulate the temperature with a hot plate which is readily available in the research lab and would provide sufficient heating and prevent the team from spending more money on a heating system. Additionally, the hot plate probe provides the team with the ability to accurately measure the fluid temperature.

Pros:

- Anatomically accurate vasculature
- Sufficient temperature regulation
- Translucent solution
- Accurate fluid viscosity behavior
- Versatile, robust system
- Easily reproducible
- Budget friendly

Cons:

- Imprecise pulsatile flow

4.7 Design #7: CMC 2.0

This design is ideal because it allows for the most anatomical and physiological accuracy without using bovine or human blood. The programmable pump creates physiologically accurate pulsatile pressures (and potentially, temperature control, depending on how expensive the pump is). 3D printed vasculature provides an anatomically accurate vessel model. CMC acts very similar to water having the fluid heated

with an in-line heater is beneficial because you can place the heater after the pump and ensure that the fluid entering the vessel model is at a physiologically accurate temperature.

Pros:

- Physiologically accurate flow
- Anatomically accurate vasculature
- Accurate fluid viscosity behavior
- Easy and accurate temperature regulation
- Versatile system
- Easily reproducible

Cons:

- High cost

4.8 Design #8: R3GH

This is a reasonable design to choose from since it is relatively low in cost and provides a accurate representation of the vascular system. The roller pump is the closest pump to use to represent an actual heart beat and the pressure and flow induced in the vascular system, although a programmable pump would give better accuracy it is very expensive and if it was bought would require most of the budget. For the modeling process the best method to use is the 3D printed vasculature, due to its ability to repeat the process for multiple experiments, unfortunately this will take some time to develop a way to 3D print which could be difficult. Mixing glycerin with water will provide closer properties to that of actual blood then water would, although it is still not the exact specifications of actual blood, so there will be some associated error in using glycerin. But since glycerin and water are being used it will allow for the ability to visualize the device deploying which is important for the customer. Lastly to heat up the fluid to body temperature a hot plate can be used this will provide a close temperature to the human body.

Pros:

- Easily repeatable
- Relatively cheap design to implement
- Low cost for materials
- Are able to visually see device deployment

Cons:

- Fluid used provides some error
- Pump's supplied pressure to defect may be off

4.9 Design #9: Pump That Pump

This design is going to have a higher budget compared to the other designs and provide the model with high accuracies in some subsystems and low accuracies in others. The programmable pump is going to cost a large amount of money that would basically be the entirety of the budget, but would give the most accurate pressure and fluid flow at the defect where it is needed. To negate this cost for the pump simpler low cost solutions were chosen for the other systems of the design. Wax casting can be used to develop the model and defect, this is a tried and true method for molding the model and can be done easily for any type of defect. Unfortunately, this method for casting does not provide easy replicable testing which is a customer requirement for our design. Powdered milk was chosen for the fluid being used, which has the closest properties to that of human blood without being a biological material (human blood or animal blood), which allows for easy use without contamination of the system, which might require sterilization.

To heat up the fluid a solar powered water heater will be used, this is an inexpensive way to match the fluid temperature with body temperature. This method does have its drawbacks since the sunlight will be heating up the fluid, it will be nearly impossible to have any way to control and what rate the fluid is heated up by, and if the temperatures outside are not optimal it will not be able to heat up the fluid to the correct temperature.

Pros:

- Simple design to implement
- No need for sterilization

Cons:

- Fluid used provides some error
- Cannot visualize the device deployment
- Expensive
- Slightly harder to do replicable testing
- Will need a grant for the pump

4.10 Design #10: Simplification Model

This design is feasible and allows the model to have control for pulsatile flow and anatomically correct dimensions. The programmable pump would control the flows of the water as well as heat the water. 3D printed vasculature would give the model correct dimensions but we would not be able to control the material compliance as well as poured mold would. The powdered milk would replicate the density of blood but would not be shear thinning which is necessary for mimicking blood's properties. The use of body heat is a feasible idea but would be very difficult to regulate due to issues dealing with the individual that is using their body heat to heat up the fluid.

Pros:

- anatomically accurate
- versatile, robust system
- reproducible conditions
- temperature control
- no need for temperature regulator

Cons:

- high cost

5 DESIGN SELECTED

5.1 Rationale for Design Selection

This project involves four main components; pump, model type, fluid, and heating. The decision matrix in Table X below shows each category and the different elements compared. Since this is an original design to start with and the elements can be substituted in for each other, the decision matrix was the only comparing method needed. The matrix allowed the team to compare each component separately to see which would complete the job the best. Then once the elements are selected they will be assembled together.

Table 3: Decision Matrix

	Cost	**Anatomical Correctness**	**Physiological Correctness**	**Visibility**	**Replicable Testing**	**Replicable Manufacturing**	**Mobility**	**Result**
Weights	0.13	0.22	0.13	0.09	0.17	0.09	0.17	
Pump								
Sink	5	1	1	3	1	3	1	1.88
Programmable	1	5	5	3	5	3	5	4.12
Roller	3	4	4	3	5	3	5	4.03
Fluid								
Water	5	1	1	5	3	5	3	2.92
Glycerin	4	3	3	4	3	3	3	3.22
Powdered Milk	4	3	3	3	3	3	3	3.13
Blood	1	5	5	1	3	4	3	3.35
CMC	4	4	4	4	3	3	3	3.57
Model Type								
2-Part Cast	5	2	2	5	2	1	3	2.74
3D Printed Vasculature Cast	2	4	4	4	4	4	3	3.57
3D Printed Vasculature	3	4	4	4	3	4	3	3.53
Heating Method								
Hot Plate and Flask	5	4	4	3	5	5	5	4.47
Solar Water Heater	1	3	3	3	3	3	2	2.57
Body Heat	3	3	3	3	2	2	3	2.74

The selected design includes a roller pump, which are less expensive than programmable pumps, therefore the team is opting for the roller pump unless grant money can be used as funding.

The model type is still dependent on the feasibility of each model. The current two-part wax casting method works but is not as accurate as 3D printing the vasculature. 3D printing the vasculature or the cast is the preferred modeling method. Since this project is focused on utilizing 3D printing, one of these methods will be used.

This design utilizes CMC and water mixture as the selected fluid. This is a less expensive option other than DI water. Blood would be the most accurate but it adds extra cost, health concern, and opacity issues. The glycerin mixture is clear and has a higher viscosity than water with a shear thinning behavior, which is the closest option to blood.

The heating method for this design is the hot plate and flask method. A flask will be placed on a hot plate and heated up. A thermometer will indicate the temperature of the water being used as the hot plate temperature is adjusted. These already exist in the lab so they will not add to the cost and are the best option for heating the fluid.

5.2 Design Description

5.2.1 Fluids

To further understand the forces that are involved within our model an analysis of the fluid properties of blood was done, and compared with a wide variety of other fluids to see if similar properties of blood could be reflected in another fluid. The two properties that were important to understand as to identify the correct fluid to use for this model is the density and viscosity of the fluid. Two fluids were narrowed down, Carboxymethyl Cellulose (CMC) (1% Wt.) which was the closest approximation to the same viscosity of blood with a viscosity of 3.8025*10^-3 (Pa*s) [1] to blood which has a viscosity of 3.5375*10^-3 (Pa*s) [2], both of the viscosities of these fluids are non-Newtonian, exhibiting shear thinning. The other fluid that was chosen as an option is powdered milk due to it having a similar density and viscosity to blood with a viscosity of 2*10^-3 (Pa*s) [3] and a density of 1029 (kg/m^3) [4], with blood having a density of 1060 (Kg/m^3) [5].

Table 4: Fluid properties

Types of Fluid	Density (Kg/m^3)	Dynamic Viscosity (Pa*s)	Relative error of density against human blood	Relative error of viscosity against human blood
Water	998 [7]	.001002 [8]	5.84906%	71.6749%
Bovine Blood (Cow)	1045.9 [9]	.003 [9]	1.33019%	15.1943%
Glycerol Mixture (22% Wt.)	1052.9 [10]	.001240 [10]	0.669811%	64.947%
Homogenized Milk @ 20 C	1033.0 [4]	.002 [3]	2.54717%	43.4629%
CMC (1% Wt.)	1000.4 [6]	.003002 [1]	5.28113%	15.1378%
Human Blood at Circle of Willis	1060 [5]	.0035375 [2]	None	None

Due to the fluid properties of blood it was important to understand the shear rate going on in the circle of Willis since the majority aneurysms occur in this area of the brain.

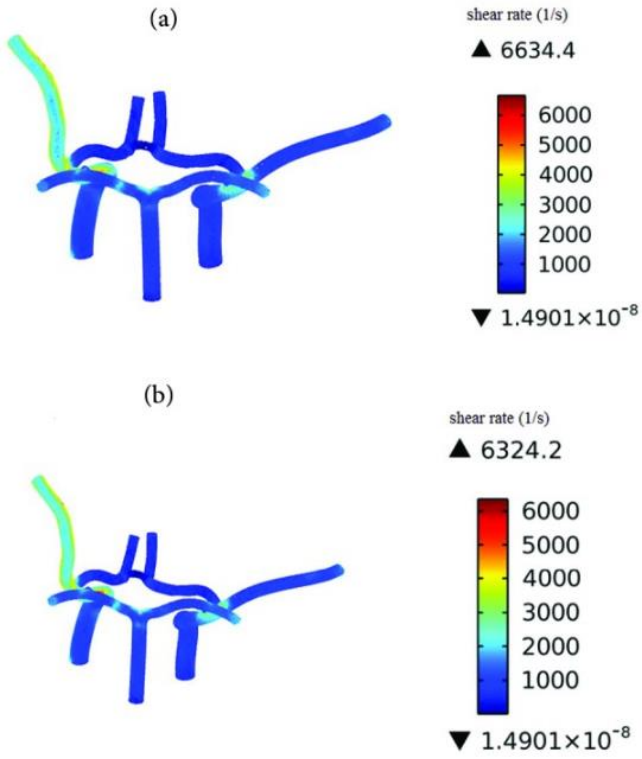


Figure 2: Shear rate in Circle of Willis [11]

From (Fig. 2) it can be shown that the minimum shear rate that occurs are 1.4901*10^-8 (s^{-1}) in the Circle of Willis, which with bloods properties of shear thinning for this low shear rate would give the highest viscosity and provide the highest shear forces on the walls of the blood vessel. Along with that in (Fig. 2) through sources that were found, the fluid was treated as a Newtonian and non-Newtonian fluid and in steady state in two separate cases, it stated that treating the fluid as Newtonian or non-Newtonian the shear rate was close enough that the blood flow through the Circle of Willis could be treated as a Newtonian fluid for steady state conditions. Using this data, it can be concluded that it is a safe assumption to use Newtonian fluid to represent bloods non-Newtonian properties within the model if steady state conditions are met within the system.

Although it is still undetermined if steady state conditions will be met when conducting this experiment due to issues involving which pump will be used for testing the model. If a programmable pump is used this assumption will not be valid due to steady state conditions not being met, but if a simple pump is used, that provides steady state conditions, then this assumption can be used and Newtonian fluid can be used to represent blood within the system.

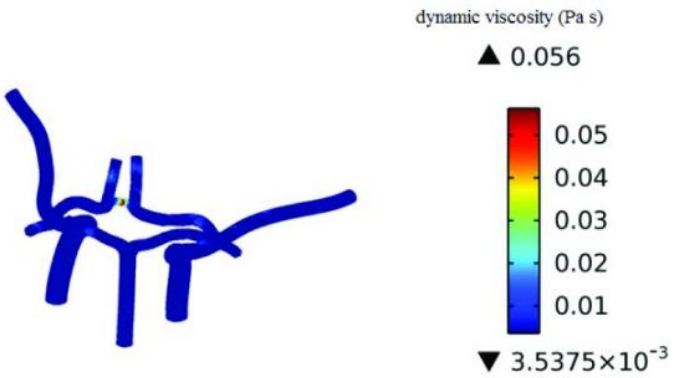


Figure 3: Dynamic Viscosity in Circle of Willis [11]

The dynamic viscosities that are present within the Circle of Willis range from a value of 3.5375*10^-3 (Pa*s) to .056 (Pa*s) as seen in (Fig. 3). Since the majority of the dynamic viscosities are at the lower end of the range, 3.5375*10^-3 (Pa*s) was used as the goal for the dynamic viscosities within the system.

Unlike the other fluids that were found CMC is a non-Newtonian fluid that exhibits thixotropic behavior and has a different shear stress depending on the shear rate of the fluid. So the following table's properties were used and plugged into (Eq.1) to get the dynamic viscosity. The shear rate that was used for this calculation was the lowest shear rate found on the Circle of Willis (Fig. 3), because that would yield the highest shear stress that would be possible in an actual human brain vessel. The values were randomly plugged in to achieve closest properties to that of blood, the results of this can be seen in (Table 3).

Table 5: CMC properties [1]

CMC (%)	λ_c (s)	n (−)	μ_0 (Pa s)	μ_∞ (Pa s)
0.2	0.010	0.67	0.019	0.001
0.4	0.016	0.65	0.045	0.001
0.8	0.060	0.60	0.230	0.002
1.0	0.088	0.61	0.530	0.003
1.5	0.172	0.64	1.970	0.020
2.0	0.287	0.66	6.355	0.024
2.5	0.530	0.69	21	0.038
3.0	0.865	0.69	48	0.040
4.0	1.026	0.68	70	0.040
5.0	1.804	0.67	200	0.045
6.0	3.459	0.67	700	0.060

$$\frac{\mu - \mu_\infty}{\mu_0 - \mu_\infty} = \frac{1}{1 + \left(\lambda_c \cdot \dot{\gamma}\right)^n} \quad [1]$$

- Dynamic viscosity (Pa*s)

$_0$-Zero shear rate (Pa*s)

$_\infty$-Infinite shear rate (Pa*s)

$\dot{}$-Critical shear rate ($^{-1}$)

$_c$ – Time constant (s)

-Degree of dependency

Powdered milk was chosen as a Newtonian fluid that could best represent blood, since its density and viscosity are very close to that of blood and its non-biological and would allow for repeatability. If a steady state pump is used this type of fluid would be able to approximate the stresses within the Circle of Willis since in steady state systems a Newtonian fluid can be used, from the reasons shown above.

The other option is to use the CMC fluid since it will allow for repeatability as it is non-biological, and its properties are the closest to that of blood compared to any of the other non-biological fluid, and it is non-Newtonian, which is the same as blood. If a transient state pump is used than the CMC fluid should be used since it will be able to change its viscosity similarly to that of blood when the shear rate is changed, since it is thixotropic.

5.2.2 Casting

Assumptions and Analysis:
The different casting methods for the *in vitro* model include a wax vasculature with a rubber cast, a 3D printed cast, and a CNC machined cast with a 3D printed vasculature and a hydrogel or silicone vessel. These models will be analyzed based on their lifespan based on manufacturing time and usage and their manufacturing tolerances.

Lifespan and Manufacturing Analysis
The lifespan of each casting method will be evaluated by observing the time it takes to fabricate each model and the maintenance, based number of usages it can withstand. The manufacturing times will be analyzed with the following equation:

$$T = (100/N)*t$$

Where:

T: Total time for manufacturing and life span
t: Time for manufacturing
N: Number of uses before need for new cast
100 was assumed as the total number of cycle

For the wax model with rubber cast, Team 23 has created previous prototypes in Dr. Becker's Bioengineering Devices Lab (BDL). The fabrication process includes making the wax mold by hand and creating the two-part rubber mold. The wax mold takes approximately 45 minutes to create. The two-part mold requires a total of 48 hours to fully cure, 24 hours for the first half and another 24 hours for the second. After ample testing, Team 23 believes this model could withstand 50 trials. Therefore, the equation listed above would provide a total time of 5,850 minutes.

The 3D printed cast would only require 3d printing for its manufacturing processes. Due to the complexity in the vessel curves, the 3D printing could take up to four hours. Additionally, Team 23 assumes that this cast, due to its rigidity, will withstand all 100 trials. As a result, the total time is 240 minutes.

The final option requires 3 stages to the manufacturing process. First, the mold material would be cut to the correct vasculature measurements, based on the outside diameter of the vessel walls) with a Control Numerical Control machine (CNC). Due to Team 23's experience in Northern Arizona University's (NAU) Machine Shop, it can be assumed that the CNC process will take 120 minutes. This includes the time to write the code and to run the machine. The second stage involves creating a 3D printed (solid) vasculature, which can take up to 240 minutes. Finally, the cast would be created from silicone, which would take up to 24 hours to create and cure [1]. Team 23 believes the silicone vasculature will withstand 100 trials. Thus, the total time for this process would be 1,800 minutes.

In contrast to the silicone, Team 23 could use their Polyacrylamide-Alginate hydrogel composite as the casting material. The total time it takes to make this material is approximately 240 minutes. Team 23 believes this model could last 20 trials. However, only the hydrogel composite would have to be fabricated again. As a result, the total time for this process is 1,560 minutes. The equations stated above becomes:

$$T=(100/N)*h + (t-h)$$

Where:

T: Total time for manufacturing and life span
t: Time for manufacturing
N: Number of uses before need for new cast
h: Time for hydrogel manufacturing
100 was assumed as the total number of cycle

Manufacturing Tolerances

In addition to the time required for manufacturing and maintenance, the casting methods are also analyzed by their manufacturing tolerances.

The handmade wax cast and rubber mold are made directly by Team 23, not machines, causing a large discretion in vasculature lengths, diameters, and curvature. Due to this human error, Team 23 estimated the tolerance to be +/- 1.0mm. The next casting method, 3D casting, would be completed with NAU's Fortus 400mc 3D printer. With the specifications of this printer, the tolerance for this casting method is +/- 0.127 [2]. Finally, the CNC machined mold, with 3D printed vasculature, and a hydrogel/silicone cast will have multiple tolerances. The CNC machined mold would be manufactured with Tormac 700 that has a tolerance of 0.0156 mm [3]. While the 3D printed vasculature would have a similar tolerance as the 3D printed cast, Team 23 plans to utilize an acid bath in NAU's art department to smooth the printer layers. However, the acid bath may increase the tolerance because the bath may remove material off of the printed dimensions. Therefore, this tolerance is estimated to increase to 0.15.

Results

The *in vitro* model casting methods do not require extensive calculations, only a comparison of required times and tolerances. Among the different calculations for maintenance and manufacturing times, the 3D printed cast required the least amount of time, followed by both CNC machined molds-3D printed vasculature-hydrogel/silicone casts, and the wax cast with two-part rubber mold. For tolerances, the casting methods were ranked in the same order. However, Team 23 will not proceed with the 3D printed cast due to its inaccuracy in other anatomical aspects as analyzed by other members of the team.

Therefore, Team 23 plans to proceed to optimize the CNC machined-3D printed vasculature-hydrogel/silicone cast model. This model will also provide further optimization in other analytical analysis.

5.2.3 Pumps

Introduction

The In-Vitro Tube model will need to have fluid flowing through the model. The solution for this problem will be a pump. This report will analyze two types of pumps: programmable and student designed piston pump (SDPP). Three programmable pumps have been assessed and the best pump has been selected. If our PI qualifies for a grant, then the programmable pump will be purchased. If there is no grant then the SDPP will be fully designed.

We are choosing to analyze programmable pumps because these pumps are designed specifically for replicated the flows of the human body.

The SDPP is the second pump we are analyzing because this type of pump is relatively simple to design. It is simple because it is just one piston pushing fluid, then sucking fluid in from the reservoir, then pushing the fluid back out again. After research we found that the piston pump would be the best student designed pulsatile pump.

Assumptions

The pump that is selected for the in-vitro model must have an anatomically correct flowrate and pressure. To solve for the pressures and flow rates, we will assume the fluid to be Newtonian as well as the density and viscosity to be constant.

For the programmable pumps we assume that the most important quality is accuracy.

Equations

All equations use variables defined in the left column. All the equations in the right column and variables in the left column correlate to Figure 1 below the columns.

The flow rate (Q) of the pump and the frequency for the pump (f_p) determine the volume per stroke (V_s). The V_s can then be used to find the bore (D) and the stroke length (L_s).

$$\frac{Q}{f_p} = V_s$$

$$\frac{\pi D^2}{4} * L_s = V_s \quad \text{where} \quad D \cong L_s$$

The pressure delivered from the pump (P) is determined by the diameter of the in-vitro model (D), the force of the pump (F_p) and the resistance force from the model (F_r). The F_r is dependent on the D and the pressure drop from the entrance and the exit of the in-vitro model (ΔP).

$$P = \frac{4[F_p + F_r]}{\pi^2 D}; \quad F_r = \Delta P \frac{\pi}{4} D^2;$$

$$F_r = \frac{\pi D^2}{4}(P - \Delta P)$$

The power needed for the pump (H) is determined by the P and Q. H can also be descried using voltage

(E) and current (I).

$$\square = \square\square; \square = \square\square$$

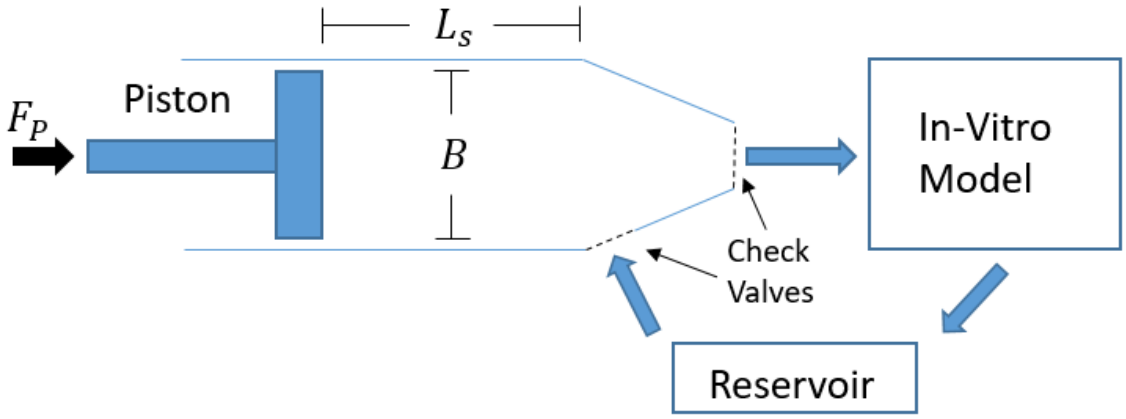


Figure 4: SDPP Sketch.

If we use Q=750cc/min, $\square\square_{\square}$=60 bpm, $\Delta\square$=40 mmHg, D=5mm, blood pressure of 120/60 mmHg, a static pressure of 60 mmHg and an E=10V then by using the equations above we find that $\square_{\square}$=12.5cc, B=2.50 cm , $\square_{\square}$= 2.50 cm, $\square_{\square}$=0.523 N, H=.1 W and I=.02 ohm's. With an Arduino connected to a servo motor, the SDPP designed can be finished to these specifications to allow for pulsatile flowrates.

Programmable Pump

Out of the three pumps we looked at, pump 2 (PD-1100, BDC Laboratories) has the lowest error, pump 3 (CardioFlow 5000, Shelley Medical) has the second lowest error and pump 1 (Pulsatile Blood Pump 55-3305, Harvard Apparatus) does not have an error published. Because pump 1 has no error published we will consider that the least desirable pump.

Results

Until we find out if we will be receiving the grant, we will wait to decide on the pump for the in-vitro model. If we receive the grant then we will purchase pump 2 because it has the lowest error. If the grant is not received, then we will finish our designs for the SDPP.

5.2.4 3D Model

Design Set-up

Design Variables

For the vasculature model, the following design variables were considered.

- Vasculature size (male/female, age, etc)
- Relevant vessels and their geometries
- Locations and orientations of aneurysms
- Type of aneurysms
- Dimensions of aneurysms

Assumptions

Relevant vessels and aneurysm types were obtained from Dr. Becker, leading to the following assumptions:

- Average adult cerebral vasculature system.
- The vascular scope will include the Internal Carotid Artery (ICA) and Middle Cerebral Artery (MCA) within the vicinity of the Circle of Willis.
  - Smaller branches can be neglected.
- Saccular side-wall and bifurcation aneurysms.
  - All wide-neck aneurysms (dome to neck ratio less than 2:1).
  - Small, medium, and large aneurysms.
  - 2-3 aneurysms per model.

Dimensions and Schematics

Vasculature

To describe the geometry of the vasculature, including diameters and bifurcation angles, references shown in Figure 5 will be used. All diameters will refer to the lumen, or inside diameter, of the vessel at an intermediate point between vessel branches for an average adult.

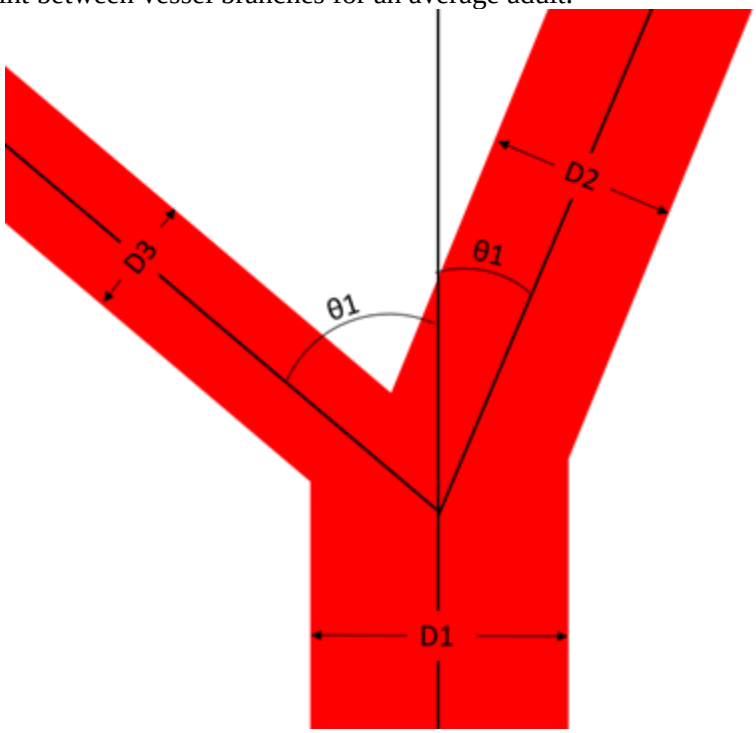


Figure 5: Vessel Diagram

The geometry of the ICA and MCA and the major branches have significant variation in all three dimensions; however, for the sake casting, the model will need to accurate in two dimensions, therefore, multiple views will be utilized and projected onto a single plane.

The lateral view of the ICA at the point of bifurcation from the common carotid artery (CCA) up to the carotid siphon, shows the most variation, with negligible angling in other planes. Several points were chosen along the ICA from an angiogram in this plane, and were used to create the first spline of the ICA, and entry point of the model [1]. A list of these points is provided in Table 6. The diameter of the ICA is about 5mm throughout this section [2].

Table 6: ICA Spline Points

X (mm)	Y (mm)
0	0
2.469136	13.75661
-0.35273	26.10229
-4.58554	38.44797
-5.64374	47.26631
-3.88007	61.37566
-4.58554	73.72134
-9.87654	79.01235
-16.9312	82.53968
-21.5168	85.71429
-23.6332	92.06349
-25.3968	97.70723
-31.0406	99.11817
-38.448	99.11817
-41.2698	101.2346
-40.9171	103.351
-38.8007	106.1728
-35.2734	110.4056

The carotid siphon is an important part of the ICA because it marks the entry point of the vessel into the skull, through the foramen lacerum and cavernous sinus of the sphenoid bone and then through the dura, the brain's protective epithelium [1]. From this point, the ICA only extends about 13mm until it branches into the ACA and MCA [3]. The angle of the carotid siphon also makes it an important landmark because it is so sharp, 35°, on average [4].

After the carotid siphon, the ICA branches into the ophthalmic artery, which will not be included in this model because of its small size and negligible influence on the flow [2]. The ICA also changes direction around this point, going "into the page" from the lateral view perspective, and therefore, the frontal view of the ICA will be used for a small segment, with this second spline generated similarly as the first, but projected onto the x-y, or lateral, plane [1].

As the ICA approaches the MCA-ACA bifurcation, it branches into the posterior and anterior communicating arteries (PCoA and ACoA). The ACoA is relatively small and will be neglected, but the PCoA will be included in the model, as it is a common bifurcation aneurysm location, and will need to be present to divert flow because the ICA diameter reduces at this point to about 3.6mm on average [5]. The diameter and bifurcation angle of the PCoA are 1.4mm and about 45°, respectively [2]. Since only the length of the PCoA proximal to the ICA bifurcation is relevant for this model (no aneurysms will be modeled along the PCoA), the modeled PCoA will divert upwards towards the top of the model where the flow will exit.

Closely after the PCoA bifurcation, the ICA ends, sharply branching into the ACA and MCA. The MCA is the major branch, with a diameter of 2.6mm and bifurcation angle of 59°. The ACA has a diameter and bifurcation angle of 2mm and 90°, respectively [5]. Because of these sharply diverting flows, relatively large aneurysms can be seen at this bifurcation. Both the ACA and MCA will eventually divert upwards for the flow to exit the model.

Aneurysms

Aneurysms will be modeled as revolved ellipses with dimensions referenced as shown in Figure 6 below.

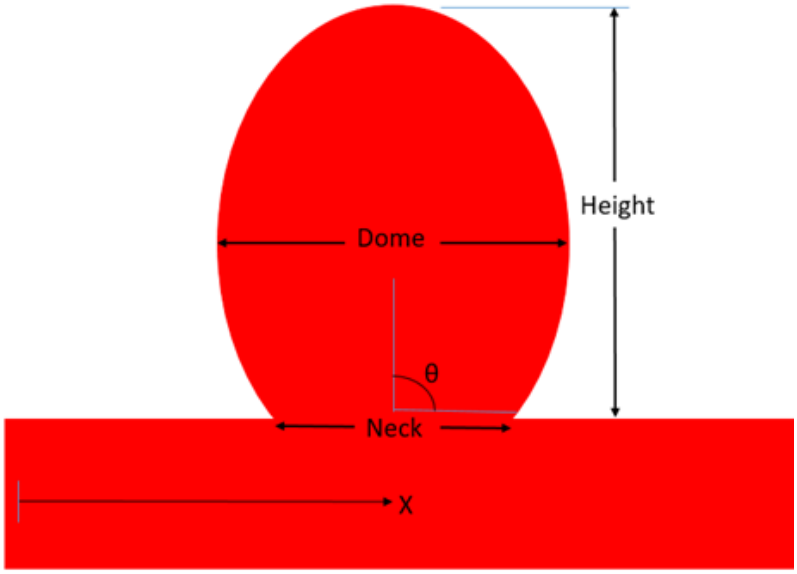


Figure 6: Aneurysm Diagram

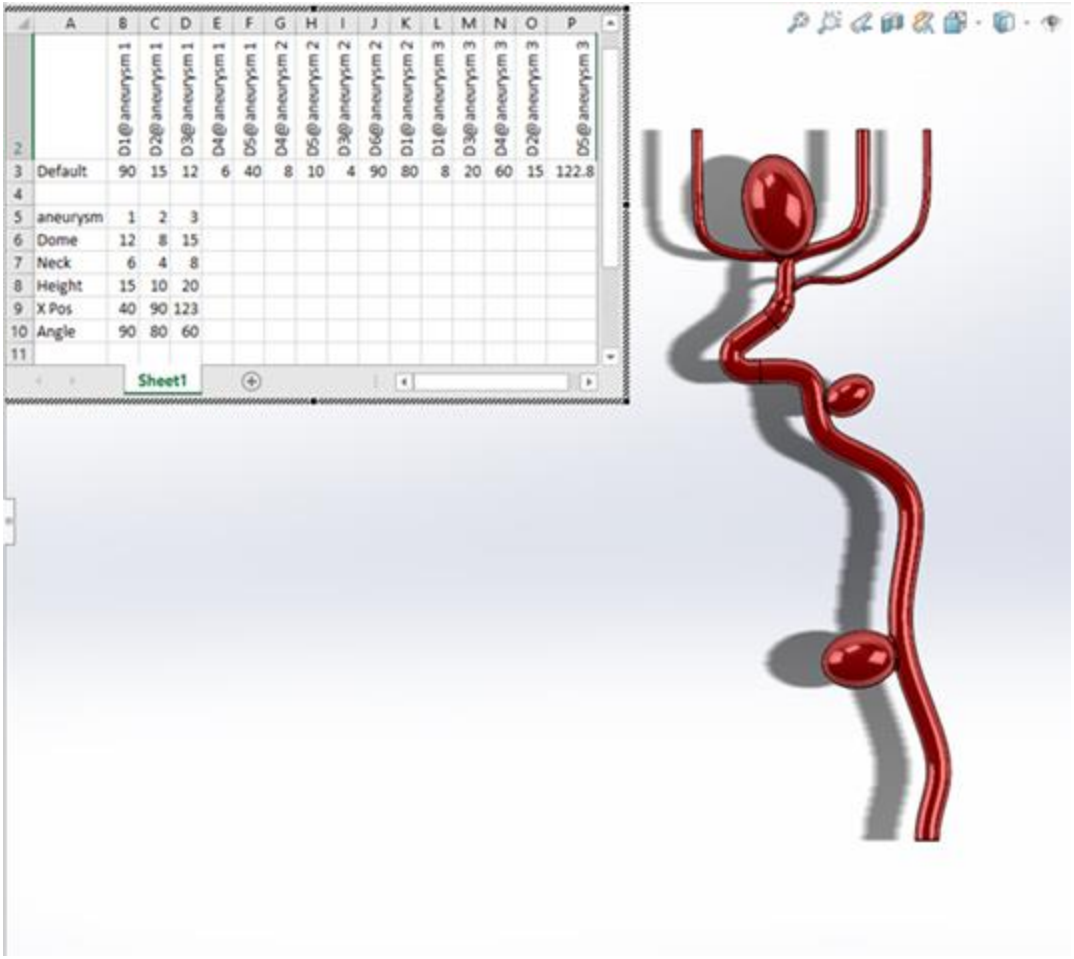
The x-position refers to the lateral distance from the entry point of the model (ICA bifurcation from the CCA) and the angle theta refers to the orientation of the aneurysm measured from the main artery, which is especially important for bifurcations. The scope of size-related dimensions, as given by Dr. Becker will be:

- Dome width: 8-15mm
- Neck width: 4-8mm
- Height: 10-20mm

Aneurysms will be parametrically designed per these dimensions along the main ICA-MCA spline using a design table in SolidWorks, so that inputs can be easily changed and a new model quickly created.

CAD Model

Figure 7 below depicts the anatomically accurate vasculature with three parametrically designed aneurysms along the main ICA-MCA spline; one small, one medium, and one large. The design tree is included for dimension references.



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
2		D1@ aneurysm 1	D2@ aneurysm 1	D3@ aneurysm 1	D4@ aneurysm 1	D5@ aneurysm 1	D4@ aneurysm 2	D5@ aneurysm 2	D3@ aneurysm 2	D6@ aneurysm 2	D1@ aneurysm 2	D1@ aneurysm 3	D3@ aneurysm 3	D4@ aneurysm 3	D2@ aneurysm 3	D5@ aneurysm 3
3	Default	90	15	12	6	40	8	10	4	90	80	8	20	60	15	122.8
4																
5	aneurysm	1	2	3												
6	Dome	12	8	15												
7	Neck	6	4	8												
8	Height	15	10	20												
9	X Pos	40	90	123												
10	Angle	90	80	60												
11																

Sheet1

Figure 7: Cerebral Vasculature and Parametric Design of Aneurysms

The above CAD model will be 3D printed and used to cast the lumen, or "core", of the tube model for this project with anatomically correct geometries. The volume of this part is 7,450mm^3, as given by SolidWorks, which will help determine the cost of the 3D printing job once a material is known.

This vessel core design is the basis of the tube model, and will reflect the design of the top and bottom pieces of the mold, with swept cuts following the exact same splines, and aneurysms in the same positions (also parametrically designed), only larger. The bottom piece of the mold is shown in Figure 8, which will be mirrored for the top piece.

Figure 8: Bottom Piece of Mold

Figures 7 and 8 depict the first revisions of the mold components. Newer revisions are ongoing, but the most up to date versions of the design with assembly views of the model and the casted tube are included in Section 6, Proposed Designs.

5.2.5 Materials

Introduction

As in vitro models progress, along with endovascular devices and biomaterials, understanding the model material properties is critical in creating an accurate simulation of the neurovasculature. NAU's Bioengineering Devices Lab (BDL) developed various models that test stability and function of artificial blot clots, capture devices, catheters, and new aneurysm filling devices and materials. To test how closely the model represents real vessels, the use of a high-precision Hybrid Rheometer tested the selected material. This poster focuses on the properties of the in-vitro vessel model such as elastic modulus and shear modulus. The material used for this capstone project is the focus of this analysis.

Initial qualitative evaluation

The materials used to form these neurovascular models must accurately replicate vessel properties to help simulate medical device delivery and endovascular surgical techniques. The in vitro model material properties depend on the type of polymer used and the curing process. Further testing was performed on two potential polymer candidates seen in Figure 9. Clear Flex 50 by Smooth-On, left, and Mold Max 15T

by Smooth-On, left.

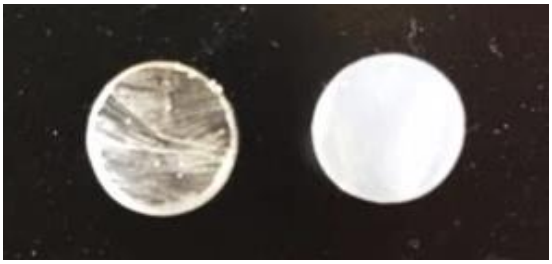


Figure 9: 20mm Material Test Samples

Mold Max 15T proved unworkable as a mold making material. Because of its soft nature, it was difficult to prepare, too opaque to visualize in an *in vitro* model, and did not respond to the mold release such that it became one piece instead of the intended two piece mold. Clear Flex 50 produced the most reliable models.

2-Part Model Casting Procedure

Below are the steps detailing the current method the BDL is utilizing to create *in-vitro* models. Though the capstone project focuses on 3D printed aspects, the creation and materials used in the 2-part model are applicable.

1. Vessel geometries are made by rolling flex wax to the correct geometries and sizes.
2. Nozzles (for subsequent hose attachment for flow model) are inserted onto the ends of the wax vessels.
3. The first layer of casting is poured into the mold and allowed to set long enough for the substance to have enough strength to support the wax vessels
4. The wax vessels are pressed (halfway) into the mold material along with latex rings for proper model alignment. The mold is allowed to set per manufacturer's directions.
5. A layer of mold release is applied to the cured model. A second layer of mold material is poured into the container and allowed to set per the manufacturer's directions shown in Figure 10.

Figure 10: ICA/MCA model-making in progress

Selected Model Material Testing

Rheological measurements (shear modulus and elastic modulus) of Clear Flex 50 and comparisons to

blood vessel properties were conducted using a Discovery HR-2 rheometer. [5] For the shear modulus testing, the head applies a constant compressive force and rotates the sample surfaces at various rates. For the elastic modulus testing, the head moves vertically (dynamic oscillation) at various rates. For both tests, a 20mm flat plate head and a Peltier plate bottom (allowing for body temperature (37°C) testing) are used seen in Figure 11.

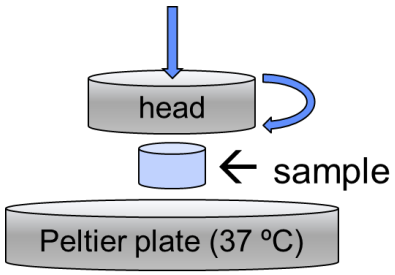


Figure 11: Sample Testing Setup

Samples are created using an 8mm hole-punch. Because the bottom and top of the samples must be parallel for most accurate results, swatches of model material were inspected for the flattest, most consistent areas. Samples need to be loaded concentric to the top plate for best results and surrounded by water. Surrounding the sample with water allows the sample to further be tested closer to human body conditions and in most cases water is flowing through the models.

Each test duration is 60 seconds with an axial strain of 1 % at a frequency of 1 Hz. Applied compressive axial force is 0.1 N and each sample was tested at least five times. The data points are taken at intervals of radians per second, meaning how much the sample gives with the force and turning of the head. The main difference is how the force is applied based on what the test is finding.

Mechanical properties as compared to vessels

Because Clear Flex 50 became the front running candidate for a model material, only its material properties were explored with the rheometer. The material does have some post-processing tunability; it could be room temperature cured only (>16 hours), post-cured once in a ~60°C oven for 8 hours, or post-cured twice in a ~60°C oven for 8 hours each time. All three sample types were explored.

The shear modulus curves (Figure 12) and elastic modulus curves (Figure 13) of each sample were compiled. As seen in the graphs below, the air cured and once cure models have very similar values. The model that underwent two cures had a significantly higher value that is roughly twice as stiff as the other samples.

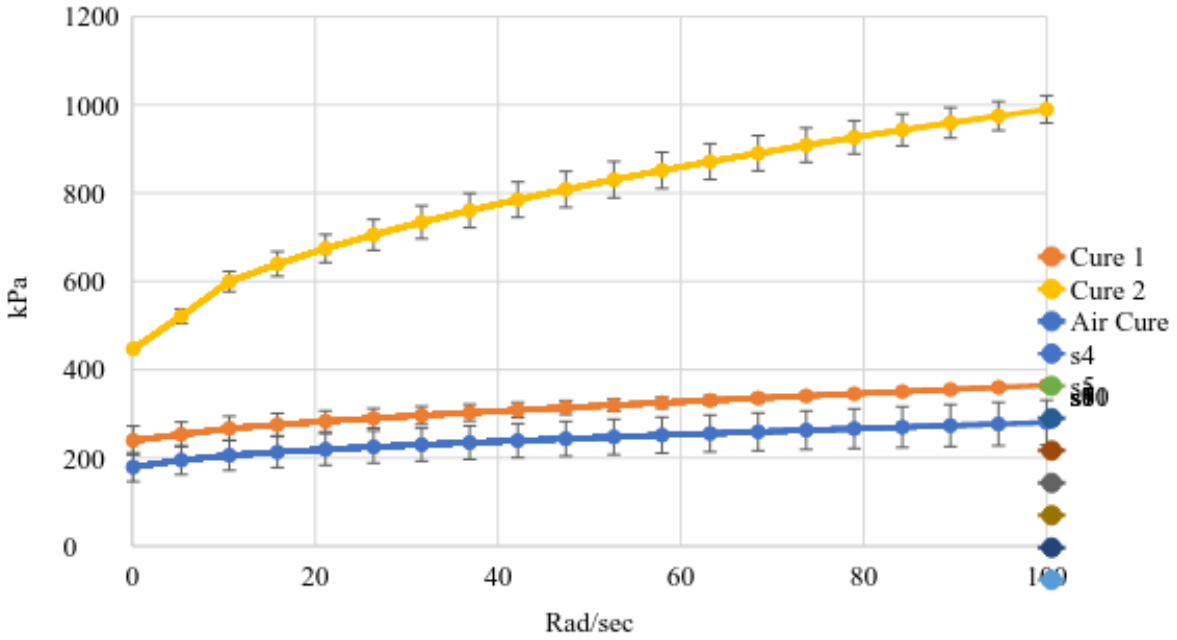


Figure 12**:** Shear Modulus

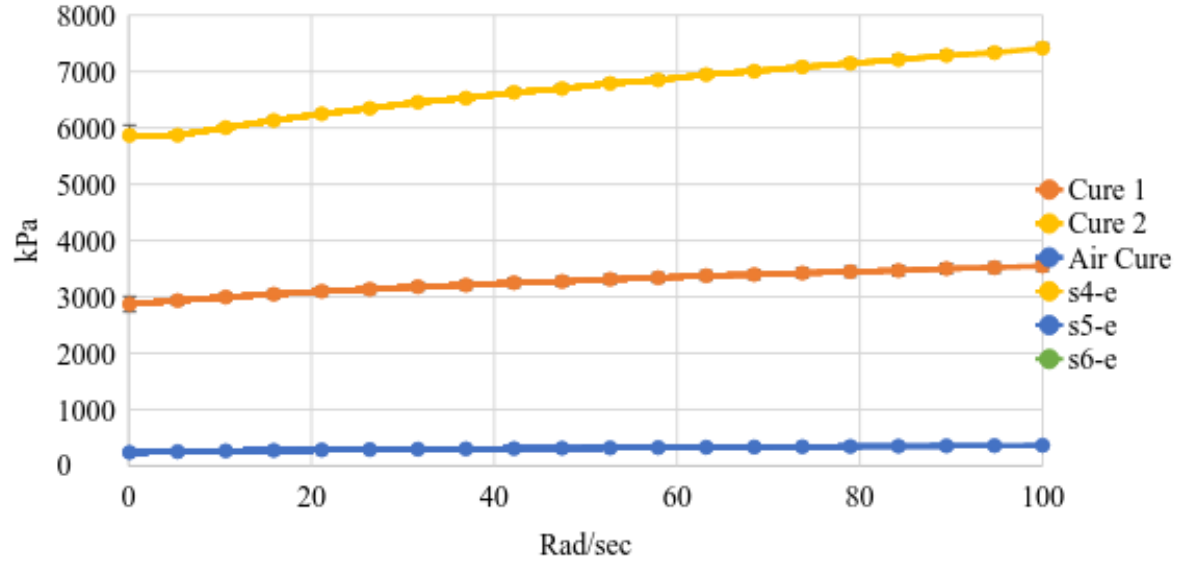


Figure 13**:** Elastic Modulus

The lower strain rate results (1 to 30 rad/s) were in phase and 30 to 100 rad/s shifted out of phase. Therefore the low strain rates maintained contact between the testing head and the sample, whereas higher strain rates may have begun to slip around 30 rad/s. However, the phase change did not affect the data trend. Error caused by concentricity and surface defects. All materials were compared at a physiologic strain rate of approximately 1 Hz (6.3 rad/s, see Fig. 14 & 15).

Rheometer data compared to Bank's values [6] for vessel wall stress and elastic modulus. Vessel wall stresses are compared to shear modulus (Figure 14). Laplace's Law is used to convert shear modulus to wall stress. Wall stress is calculated using pressure, radius, and vessel wall thickness. Using the

approximate dimensions of the in vitro model (Radius = 2mm and Thickness =0.5mm).

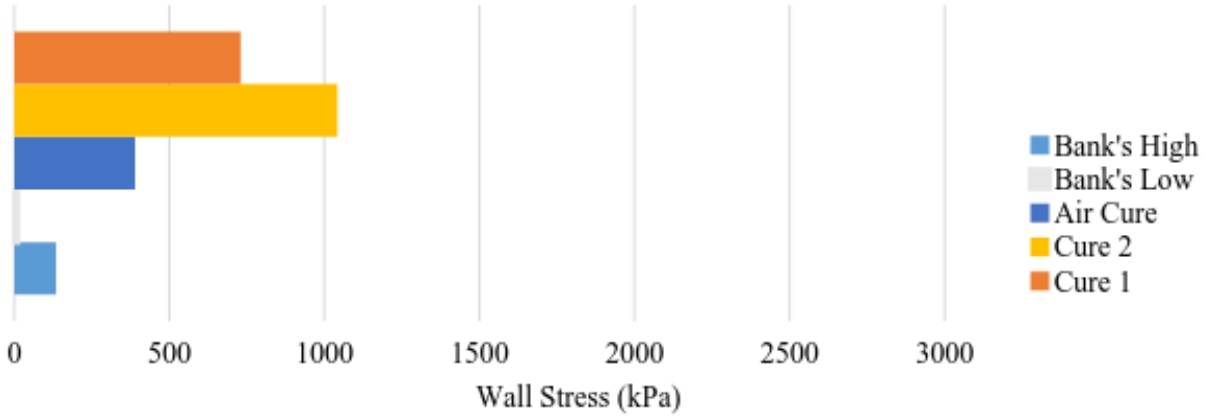


Figure 14: Wall Stress Comparison

It is important to note that Bank's data is from bronchial vessels. The vessels inside the brain are more delicate than the bronchial artery since they have thinner walls and smaller diameters. "Bank's Low" represents thinner, relaxed vessels, whereas "Bank's High" represents stiff vasoconstricted vessels. For neurovasculature, a lower stiffness, between the Banks High and Low range, is desired.

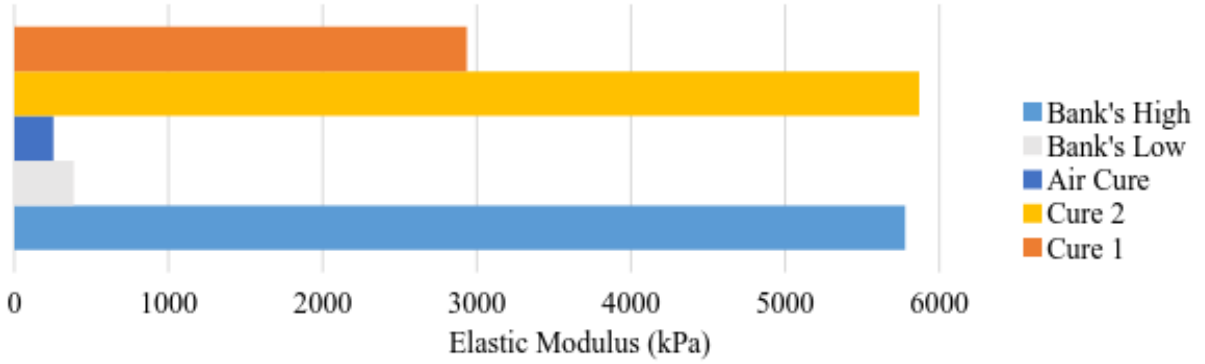


Figure 15: Elastic Comparison

BAM Material Comparison

A potential material that can be used in the model is in development in the lab. It is a polyacrylamide-alginate (PAAM-Alg) with some binding agents. This material has been named BAM, standing for Bill and Anne Marie, who are the two students who have continually worked with the material. BAM is highly elastic and could be a useful for the model. Its elasticity would potentially make it easier to remove the core of the *in-vitro* model which is a desirable aspect. Below in Figure 16 is the BAM material elastic properties added to the elastic graph above. The extremely low bar on the graph for high and low BAM values show how much more elastic this material is compared to the other material. Though it is more elastic than human vessels, this will not affect the overall purpose of the model.

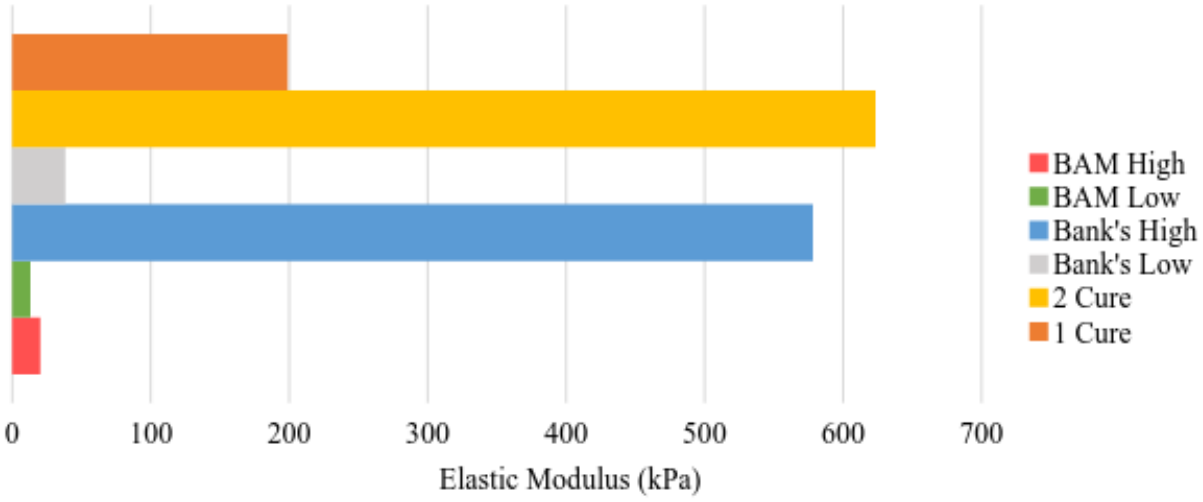


Figure 16**:** BAM Elastic Comparison

Conclusion
Overall, the Cure 1 materials have properties closer to human vessels (Figure 14 & 15), and are half as stiff as a Cure 2 material. The in-vitro model created using Air Cure has smaller, less stiff, and more elastic vessels to better simulate the neurovasculature. Cure 2 material is not desirable due to its increased stiffness. Utilizing the BAM material is currently the best material for the 3D printed model but the Clear Flex will be an alternative material.

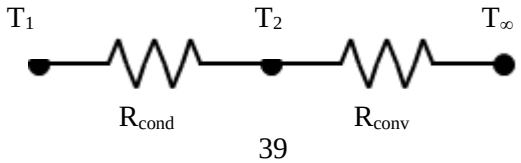
5.2.6 Temperature Analysis

Introduction
The purpose of this memo is to prove that it is feasible to maintain a physiologically relevant fluid temperature throughout an *in vitro* vascular model.

Problem
Our *in vitro* model's purpose is to imitate a biological vascular system so that experiments can be performed and refined before being performed in a living subject. In order for the model to be effective in its purpose, it must be as physiologically relevant as possible.

There are many important variables to consider when creating a physiologically relevant model, but one of the most vital variables our team must consider is the temperature of the fluid in our model. Many fluids behave differently with changes in temperature. In order to ensure that our model is relevant, we need to prove that fluids throughout our entire model are within a physiologically relevant range.

Approach:
Since we do not have a working model to test, the temperature drop of the fluid in our model must be estimated mathematically. Heat loss can be estimated by creating a thermal resistance network (Figure 1) to model the system and using it to calculate total thermal resistance.



The thermal resistance due to conduction through the vessel can be found using Equation 1, where k is the conduction coefficient of the model material, L is the length of the vasculature, r_2 is the outer radius of the vasculature, and r_1 is the inner radius of the vasculature.

$$R_{cond} = \frac{(\ln \frac{r_2}{r_1})}{(2\pi k L)} \quad (1)$$

The thermal resistance due to free convection from the vessel to the ambient air can be found using Equation 2, where h is the convection coefficient of air, L is the length of the vasculature, and r_2 is the outer radius of the vasculature.

$$R_{conv} = \frac{1}{(2\pi r_2 h)} \quad (2)$$

Since the thermal resistors are in series, they can be summed to find the total equivalent thermal resistance of the system. Using the parameters defined in Table 7, it is possible to calculate the total equivalent thermal resistance of the system.

Table 7: Parameters for Equation 1

Parameter	Value
k_{glass}	1.05 $\frac{W}{m \cdot K}$
h_{air}	10 $\frac{W}{m^2 \cdot K}$
L	0.127 m
r_2	2.01 mm
r_1	1.50 mm
T_1	37 °C
T_∞	25 °C

R_{eq}= 65.84 K/W

Once the total resistance has been found, this value along with the temperatures from Table 7 can be used to find heat loss in Equation 3.

$$q = \frac{(T_1 - T_\infty)}{R_{eq}} \quad (3)$$

q= 182.3 mW

Once we have a value for heat loss, we can use this to find the temperature drop of the fluid in the model using Equation 2, where c_p is the specific heat of the fluid, V is volume of the fluid, and ρ is density of the fluid. These parameters are quantified in Table 8.

$$q = c_p \cdot \rho \cdot V \cdot (T_1 - T_2) \quad (4)$$

Table 8: Parameters for Equation 2

Parameter	Value
c_p	2.43 $\frac{kJ}{kg \cdot K}$

ρ	$\rho = 1.26 \frac{g}{cm^3}$
V	8.98×10^{-7} m^3
T_1	37 °C

T_2= 36.94 °C

This equation shows that there is very little temperature drop in the fluid as it flows through the system.

Conclusion
The result of this estimation is very promising. Since there is minimal temperature drop in the fluid as it flows through the model, insulation of the model is likely unnecessary. This allows the model design to be simplified and allows for better visualization of flows within the model.

Since the model has not been developed, assumptions had to be made for several factors. Glass was chosen as the vessel material as a conservative estimate because glass conducts heat better than the polymers being considered. Glycerin was chosen as the fluid for the model because it has a lower specific heat than water so it doesn't take as much heat to change its temperature. Due to these assumptions, this is a conservative estimate, so the measured temperature drop in the system will likely be smaller than calculated.

This estimation can be easily proved empirically when the model is created by measuring the temperature as it flows both in and out of the model.

6 Proposed Design

Description
We have created in vitro models that we can use to show how our design will operate. Data that proves the efficacy of the fluid we will use in our design shows that we will create fluid mixtures that replicate human blood. Showing a LabView block diagram proves that we have the ability to program our DAQ. Data on a student made mold material that can be optimized to human vessel properties shows that our team is capable of improving in vitro modeling materials.

Resources
Many resources were used in the process of developing this capstone report. Online literature has been a major resource for the team as well as the faculty liaison, Dr. Becker. Our capstone professor, Dr. Trevas, has given the team many ideas, including the promising CMC for the fluid material. The Bioengineering Devices Lab (BDL) is where the testing the building of the project has taken place, along with the materials needed for this project.

Tubing and pressure transducers will also be used when conducting this experiment but since this experiment will be conducted in the Wettaw building, there will be access to both of these materials and therefore do not need to be bought for this experiment. The pump that was chosen will also be constructed rather than being bought, this will save a considerable amount of money for the total cost of this project. If grant money does come in for the programmable pump, then it will most likely be bought, which will allow future students and faculty use of the pump, although this experiment can be done without the need for such a high priced tool. A data

acquisition system will also be used to allow for storing of all of the data that is gained from this experiment, access to this tool will also be made available through the Wettaw building.

Implementing this project will be rather simple, nothing that needs to be done in setting up the system requires expensive tools, so there is no cost in implementing the experiment. Although there might be some time associated with putting everything together such as the heat source, pressure transducers, and tubing, and making sure that the data from the pressure transducers are correctly interpreted and stored into the data acquisition system.

Assembly

Figures 17 and 18 show the assembly and exploded views of the tube cast mold.

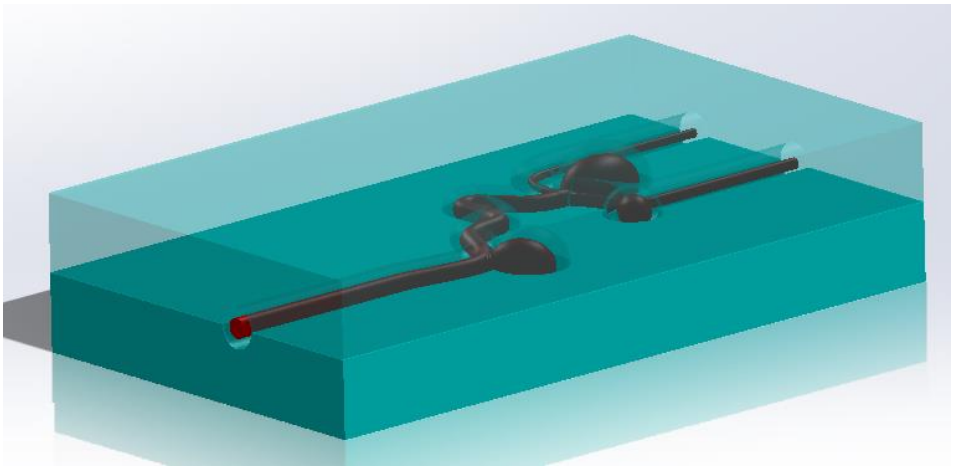


Figure 17: Assembly View of Cast Mold

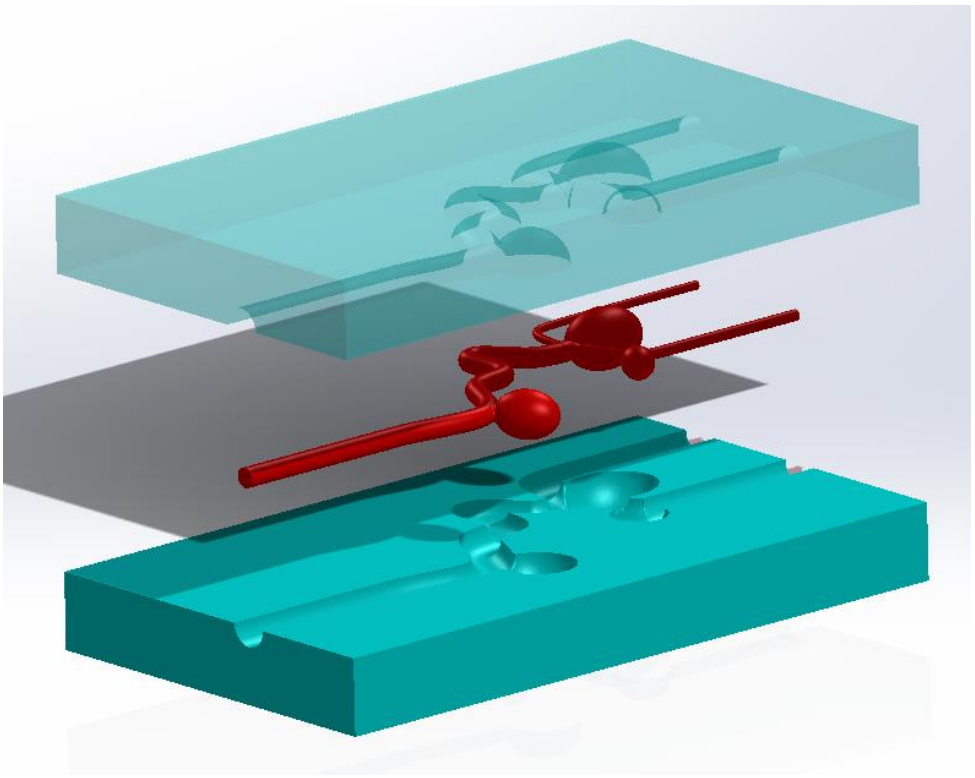
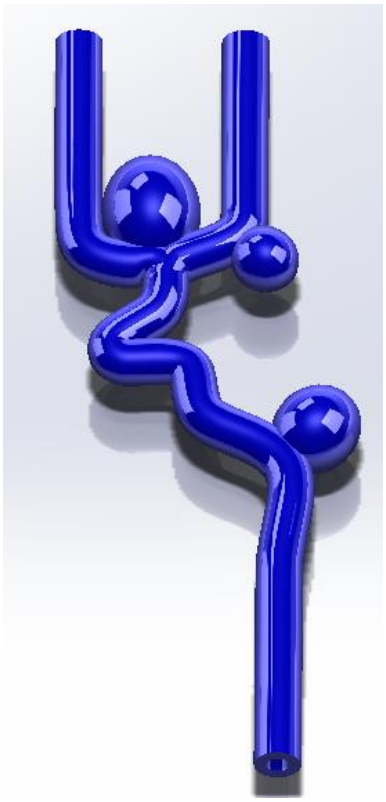


Figure 18: Exploded View of Cast Mold

Filling this mold with the desired casting material will result in our tube model. This cast is shown in Figures 19 a and b.



Figures 19: Casted Vascular Tube

7 IMPLEMENTATION

7.1 Manufacturing

A two part casting system is necessary to create a compliant *in vitro* model for aneurysm treatment. This process requires an outer mold to construct the outer wall of the model, and an inner core to shape the inner vasculature. The inner core sits within the outer mold and is held concentric via support mounts. The hydrogel material, BAM, is then poured into the mold and allowed to cure. Once cured, the inner core is removed. The model can then be attached to the pump to continuously run CMC through the vessels.

7.1.1 Manufacturing Details

The two part mold consists of inner core and an outer mold of the vasculature. With extensive literature research, the team was able to create an accurate SolidWorks assembly of the ICA and MCA vasculature and placement of three aneurysms. The correct dimensions are considered for the vessel diameter, vessel curvature, vessel lengths, and aneurysm diameters. The lengths at the end of the vessel system are extended in order to incorporate the support mounts. With this model, the team is able to 3D print (MakerBot Replicator+ 5th Generation, MakerBot Industries, Brooklyn, NY) the inner core and support mounts (**Figure 20**). The outer mold mimic the accurate vasculature shape, however, the diameters are all increased to 10 mm to create at least a 2.5 mm vessel wall thickness. The team will utilize Computer Numerical Control Machining (Tormach PCNC 770 Series 3, Tormach, Waunakee, WI) to mill the vessel system into wax blocks for the outer mold (**Figure 21).**

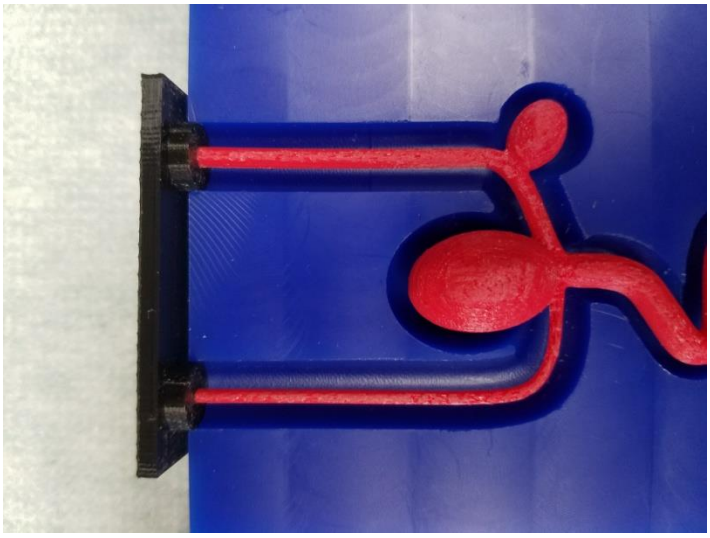


Figure 20: 3D printed core within support mounts

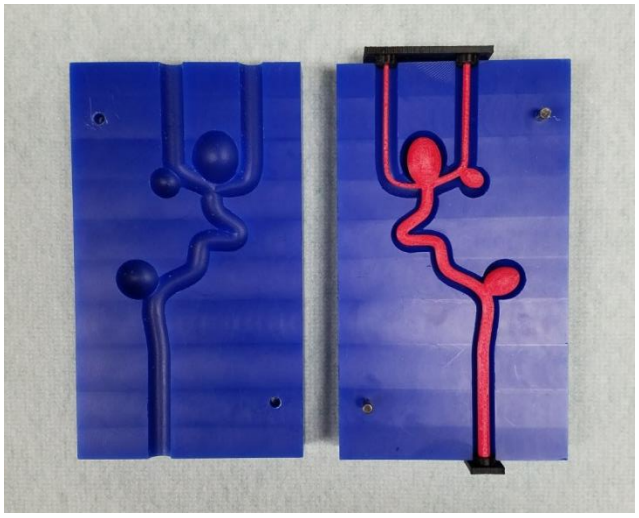


Figure 21: 3D printed core within outer wax mold

Once all of the components of the mold are built, the casting process can begin. Place the inner core of the model into the mold. Secure the inner core with the support mount on the distal end of the model. Clamp the two halves of the mold together around the inner core and place the mold vertically so that the distal end of the model is on the bottom. Pour un-cured polyacrylamide/alginate into the proximal end of the mold using a funnel until the mold is full (**Figure 22).** Place the second support mount on the proximal end of the model to fully secure the inner core. Allow the polyacrylamide/alginate to cure overnight. Once cured, remove the inner core from the model. In order to remove the inner core from the model, the inner core can be broken at its bifurcations and removed in pieces. DI water can also be injected into the model to lubricate the model and aid in the extraction of the inner core. Once the inner core has been removed, expose the model to UV-C light (254 nm wavelength) for 15 minutes. This sterilizes the model and increases its shelf life.

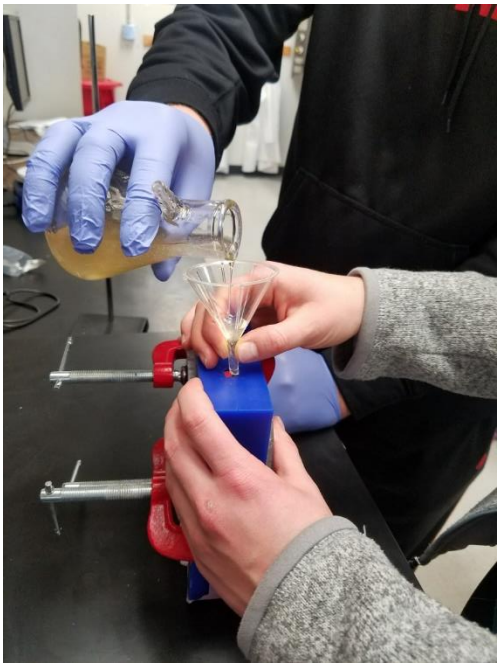


Figure 22: Pouring of hydrogel into mold

PUMP
Despite designing a pump, the team will be using a Variable-Flow Peristaltic Pump (Fisher Scientific, Waltham, MA). This pump gives constant flow rate but with the use of an actuator, the bypass can be occluded so that the flowrate will pulse into the model. This actuation be designed by a lab assistant from the BDL. The capstone team will no longer be focused on creating pulsatile flow.

DAQ
The LabVIEW vi will operate three Deltran pressured transducers (Utah Medical, Midvale, UT), a thermocouple type K, and a FTB-420 flowmeter (Omega, Norwalk, CT). A NI USB-6009 (National Instruments, Austin, TX) will be used to power the measurement tools and read their signals. Signal conditioning will be done using an op-amp with a 1k ohm resistor for the gain.

Filters
The inline filters are a Briggs & Stratton 298090 150 micron (Briggs & Stratton, Wauwatosa, WI) and a Hemo-Nate 18 micron (Utah Medical, Midvale, UT). Free samples of these filters were sent to the BDL.

7.1.2 Budget

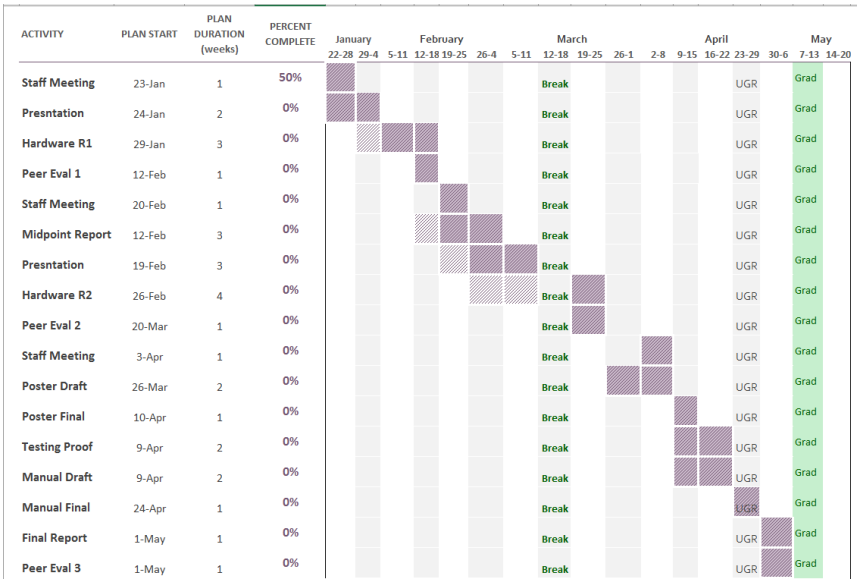
Table 9 shows the current standing budget for this project.

Table 9: Bill of Materials and Projected Budget

Product	Quantity	Cost	Total Cost
CMC [1]	1 lb	$9.24	$9.24
Clear Flex 50 [2]	3 lb	$50/3 lb	$50
3-D printed core [3]	8g	$.10/gram	$.80
3-D printed stabilizers	8g	$.10/gram	$.80
Acetone [4]	1	$8.63	$3.69
Flow Meter [5]	1	$108	$108
Fisher Scientific Pump	1	$364.19	$364.19
NI USB-6009	1	$372	$372
Total	----------	----------	$908.72

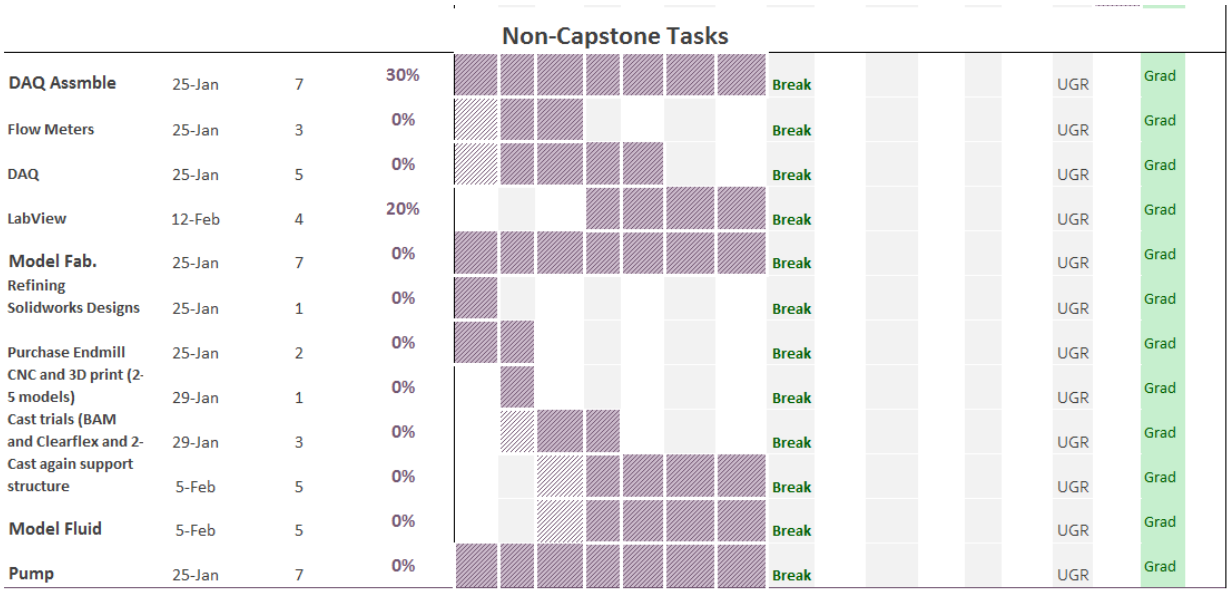
7.1.3 Schedule

The team is currently on track with schedule. There was a delay in ordering parts for the DAQ and the CMC. Figure 23 and 24 include the capstone and non-capstone deadlines for this semester.



ACTIVITY	PLAN START	PLAN DURATION (weeks)	PERCENT COMPLETE
Staff Meeting	23-Jan	1	50%
Presntation	24-Jan	2	0%
Hardware R1	29-Jan	3	0%
Peer Eval 1	12-Feb	1	0%
Staff Meeting	20-Feb	1	0%
Midpoint Report	12-Feb	3	0%
Presntation	19-Feb	3	0%
Hardware R2	26-Feb	4	0%
Peer Eval 2	20-Mar	1	0%
Staff Meeting	3-Apr	1	0%
Poster Draft	26-Mar	2	0%
Poster Final	10-Apr	1	0%
Testing Proof	9-Apr	2	0%
Manual Draft	9-Apr	2	0%
Manual Final	24-Apr	1	0%
Final Report	1-May	1	0%
Peer Eval 3	1-May	1	0%

Figure 23: Capstone Schedule



Non-Capstone Tasks			
DAQ Assmble	25-Jan	7	30%
Flow Meters	25-Jan	3	0%
DAQ	25-Jan	5	0%
LabView	12-Feb	4	20%
Model Fab.	25-Jan	7	0%
Refining Solidworks Designs	25-Jan	1	0%
Purchase Endmill	25-Jan	2	0%
CNC and 3D print (2-5 models)	29-Jan	1	0%
Cast trials (BAM and Clearflex and 2-Cast again support structure	29-Jan	3	0%
	5-Feb	5	0%
Model Fluid	5-Feb	5	0%
Pump	25-Jan	7	0%

Figure 24: Breakdown Schedule

7.2 DOE

In order to optimize the *in vitro* model, it is necessary to create a composition of BAM to correctly imitate a biologic vessel. Various compositions have previously been tested for shear modulus, elastic modulus, and viscosity. Currently, one composition is being tested to finalize the curing process. Once the curing

process is optimized, the team can begin determining the final composition of the hydrogel.

The curing process usually consists of setting the polymerizing gel under UV light to ensure sufficient cross linking. However, the opaque mold inhibits the use of the UV light for the *in vitro* model vasculature. The team allowed one trial to cure for one hour. This test was unsuccessful because the gel was not fully cured. The second trial allowed the model to cure overnight. This resulted in a more cured model, although the casted gel was plagued with air bubbles. Further steps will be taken to cast without the infringement of air bubbles. In order to ensure reproducibility, the team plans to make certain specific ingredients to the BAM composition are pure. Oxygen could play a factor in oxidizing certain materials and causing the lack in polymerization. Therefore, the team is ordering new ingredients to continue to test the curing process.

The next trial was more successful. The solution was heated to 50 C before casting. This allowed the material to be much more viscous and cure fully. The ends where the stabilizers are placed were less firm than the rest of the model which is caused by air. There was only one bubble in this trial which can be eliminated with extra shaking before letting the model sit. When the core was being removed the model stuck to itself and some holes were created. In the future, water will be used to lubricate the BAM before the core is removed.

Once the curing process is optimized, the team will continue to test various compositions of the BAM. These values will be compared to literature research on the mechanical properties of a human vessel. Once the ultimate BAM composition is finalized, the *in vitro* model will be fully optimized.

8. TESTING

All material testing was conducted with a DHR-2 Hybrid Rheometer (TA Instruments, Newark, DE). This rheometer is able to test fluids, gels, and solids in both axial and shear planes (**Figure 25**). This allows for the testing of elastic modulus, shear modulus, and viscosity.

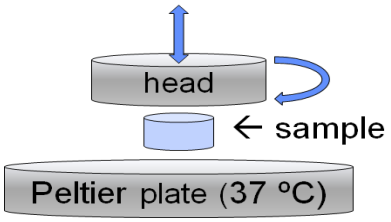


Figure 25: Rheometer testing setup

Elastic and shear modulus tests were conducted for the vessel material and a viscosity test was conducted for the blood substitute. For the vessel material shear modulus testing, data points were taken using the following test conditions:

3 samples
20mm cylindrical parallel plate head geometry
Constant temperature of 37 ºC
Constant compressive axial force of 0.1 N
Test duration of 60 seconds
Strain rate sweep from 1 to 100 radians per second
Each sample was tested 5 times
Set up concentrically

For the vessel material elastic modulus testing, data points were taken using the following test conditions:

5 samples
Tension test head geometry
Ambient temperature
Constant axial translation rate of 50µm/s
Test ran until material failure
Each sample was tested once

For the blood substitute viscosity testing, data points were taken using the following test conditions:

3 samples
20mm cylindrical parallel plate head geometry
0.25mL sample volume
Constant temperature of 37 ºC
Shear rate sweep from 15 to 105 1/s incrementing every 10 1/s
Each sample was tested 5 times

Using these procedures, a range of values was created for the vessel material's moduli (**Table 10**) and for the blood substitute's viscosity (**Figure 26**).

Table 10: Testing Results

	Elastic Modulus (kPa)	**Shear modulus (kPa)**
PAAM-Alg	20.7 - 51.0	0.890 - 5.37
ClearFlex	196 - 623	325 - 673
Blood Vessel [x (banks)]	38.4 - 578	----------

The range of the data was created by altering the vessel materials composition. After every series of tests for a given composition, the change in moduli values was analyzed. Depending on how much the moduli data changed, the next samples of vessel material's composition were changed accordingly. This was done to help get the vessel material to physiologically relevant moduli values.

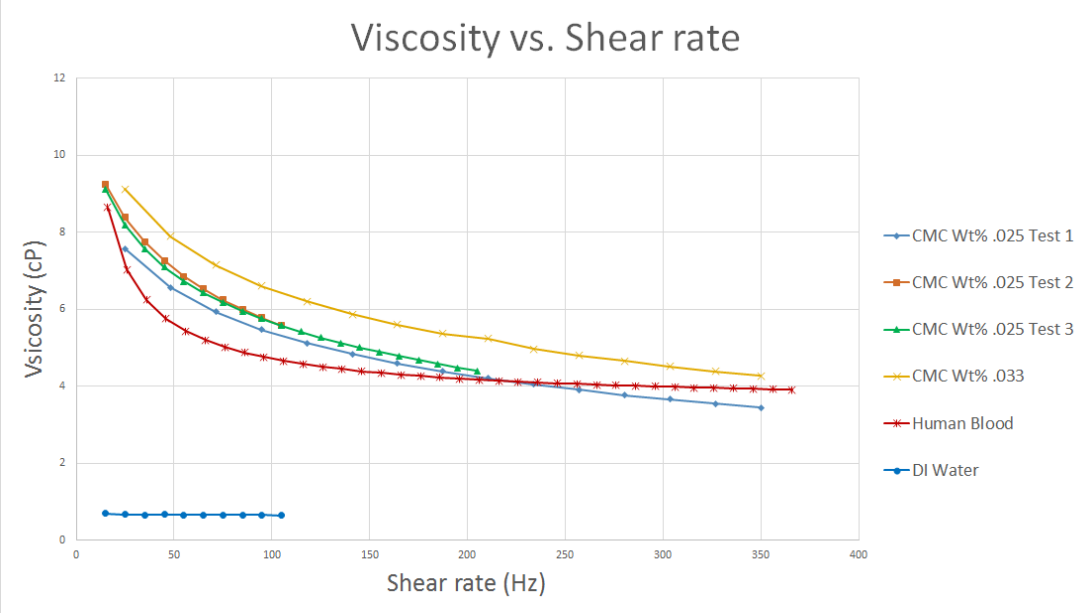


Figure 26: Tested CMC, Shear Rate vs. Viscosity

A value of 0.033wt% CMC was obtained from literature, and served as the starting point of the experiment. After testing the samples, the weight percent CMC of the following samples was adjusted accordingly to closely fit the curve of real blood data from literature. The samples consisting of 0.025wt% CMC had the closest fitting viscosity to blood, and can be seen above in (Figure 26).

Although the initial formulations of the materials tested were not within an acceptable range, iterative changes to the materials were implemented until the material was within the acceptable range. Thus, the testing was a success, as the final formulations of the vessel material and the blood substitute were consistently measured within a physiological range.

9 CONCLUSIONS

9.1 Contributors to project success

Our project has interchangeable components to the design. This allowed each member of the team to be responsible for aspects and the options available for the respective aspect. When looking at the team charter, the purpose and goals of this project were completed. Although there is still room for improvement, the project has been completed and deemed satisfactory of all requirements by the client.

Below is a section of the Team Charter [10] outlining the goals of the project.

> "Project goals: Create a vessel model for testing aneurysm treatment medical devices.
>
> Process goals: To perform thorough up-front work, including gathering all customer needs and objectives, brainstorming and researching possible options, analyzing all top choices for benefits and shortcomings, and building and testing proof of concepts and prototypes.
>
> Quality goals: To create a model that closely resembles human properties, is useful for testing bioengineering devices, and is better than the current solution.
>
> Team members will commit to putting in their best work for this project, and collectively we are aiming to exceed project expectations and earn an A for the project." [10]

The process goal of performing thorough work related to the customer needs, objectives, concepts, and testing was completed. The core for the model is physiologically accurate and is adjustable depending on future needs of the project. The 3D printed core allows for more detail than the hand-sculpted wax core originally used. The cost of the project stayed within the designated budget. The goals of this project were accomplished by utilizing many resources available from the university.

SolidWorks and 3D printing have proven to be very helpful tools for the project. SolidWorks allowed for a parametric core design coupled with 3D printing allowing for an accurate design that can be quickly and cost effectively created. The machine shop manufactured the CNC outside blocks for the casting portion of the project quickly and accurately.

9.2 Opportunities/areas for improvement

After implementing changes from the post-mortem report, the ground rules and coping strategies were followed and worked well. The team was more focused and productive during meetings. Better communication about upcoming deadlines in the class helped the team more efficiently layout our schedule and work.The team charter currently works as intended, and no changes are planned to be made to it.

In the team charter we included the following segment in our potential barriers section.

> "One possible barrier is that four of the members already work for the client and have access to more of the product development, so the other two need to make sure they are caught up and able to contribute to these efforts. They should be included in all research meetings related to the project and a part of every decision. Everyone will have access to the lab and

keys will be made for the other two team members. All preceding research will be shared." [10]

The Wettaw building ran out of keys so only the members who previously had keys were able to have access to the lab. This did not interfere with the progress of the project. The members without keys were able to coordinate when the lab would be unlocked if they needed access.

Another area improved on was staying focused during the group meetings. This was a difficult improvement to make throughout the semester since the team get along and liked each other. The team would get distracted in irrelevant conversation. As the semester progressed and became busier the meetings were tailored more specifically delegating project tasks.

Planning ahead on reports and other requirements is another aspect the team could have improved upon. Even though the team completed all the capstone requirements, it still felt rushed during certain parts of the process.

The blood substitute proved to be accurate in modeling the viscosity of blood throughout the model. Although the substitute did not match the curve exactly to the specification of blood, the reason for this is that the solution does not have as high thixotropic properties to that of blood. During testing a variety of CMC powders were used, and what was noticed is that the CMC with a higher molecular weight had a higher amount of thixotropic properties, and better fit the curve. Moving forward with the solution, a higher molecular weight of powder could be tested to improve accuracy of the substitute.

The flow loop that collects data and puts flows through the *in-vitro* model is complete and operates. A simpler set up for the flow loop would include a programmable pump and a higher quality DAQ. Both improvements are expensive. For the purposes of testing aneurysm treatments, the flow loop does not need to be improved.

The casting material remains the main improvement to be made on this project. Trials of the material continued to be unsuccessful and a backup ClearFlex 50 two-part model was made using the team's 3-D printed core. This proved the functionality of the design but was not as physiologically accurate as the original model of PAAM-Alg. The casting material will continue to be tested in the lab until it can be use for the *in-vitro* model.

There are suggested improvements that can be made to the PAAM-Alg material. Altering the formulation of the material itself did not yield the large changes in moduli that the team anticipated, but adding a new component to the material and creating a composite would potentially alter the material properties significantly. A biomimetic approach to creating a composite-type material would likely have the best results. Another approach would be to purchase an alginate that has more reactive sites on each alginate chain. This would allow the alginate to have increased cross-linking, which would increase the moduli values of the material. Additionally, ensuring the purity of the PAAM-Alg cross-linking agent will also improve the curing process of the vessel system.

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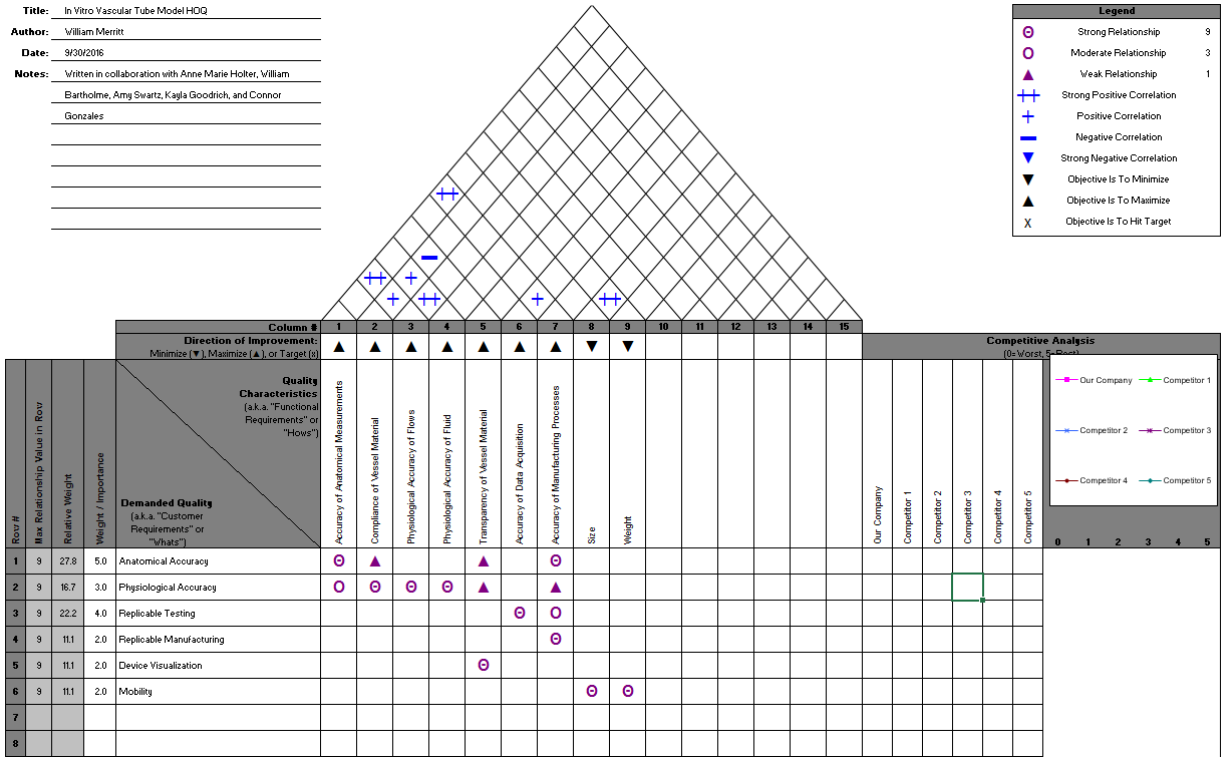
APPENDIX

Appendix A: QFD



Title: In Vitro Vascular Tube Model HOQ
Author: William Merritt
Date: 9/30/2016
Notes: Written in collaboration with Anne Marie Holter, William Bartholme, Amy Swartz, Kayla Goodrich, and Connor Gonzales

Legend

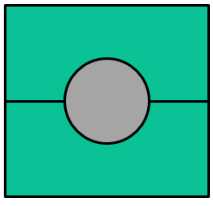
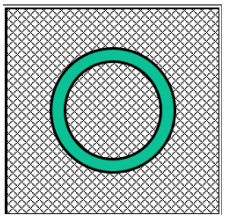
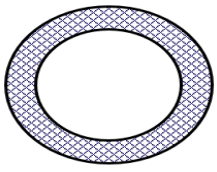
⊙	Strong Relationship	9
O	Moderate Relationship	3
▲	Weak Relationship	1
++	Strong Positive Correlation	
+	Positive Correlation	
−	Negative Correlation	
▼	Strong Negative Correlation	
▼	Objective Is To Minimize	
▲	Objective Is To Maximize	
X	Objective Is To Hit Target	

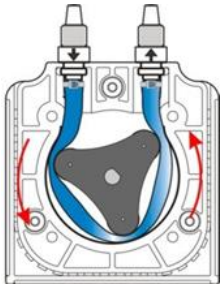
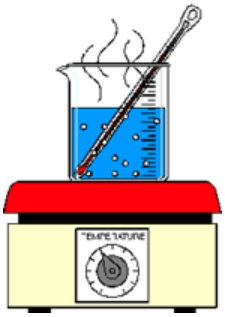
Row #	Max Relationship Value in Row	Relative Weight	Weight / Importance	Demanded Quality (a.k.a. "Customer Requirements" or "Whats")	Column #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Competitive Analysis (0=Worst, 5=Best)					
				Quality Characteristics (a.k.a. "Functional Requirements" or "Hows")	Direction of Improvement: Minimize (▼), Maximize (▲), or Target (x)	▲	▲	▲	▲	▲	▲	▲	▼	▼							Our Company	Competitor 1	Competitor 2	Competitor 3	Competitor 4	Competitor 5
						Accuracy of Anatomical Measurements	Compliance of Vessel Material	Physiological Accuracy of Flows	Physiological Accuracy of Fluid	Transparency of Vessel Material	Accuracy of Data Acquisition	Accuracy of Manufacturing Processes	Size	Weight												
1	9	27.8	5.0	Anatomical Accuracy		⊙	▲			▲		⊙														
2	9	16.7	3.0	Physiological Accuracy		O	⊙	⊙	⊙	▲		▲														
3	9	22.2	4.0	Replicable Testing							⊙	O														
4	9	11.1	2.0	Replicable Manufacturing								⊙														
5	9	11.1	2.0	Device Visualization						⊙																
6	9	11.1	2.0	Mobility									⊙	⊙												
7																										
8																										

3	9	22.2	4.0	Replicable Testing						Θ	O																
4	9	11.1	2.0	Replicable Manufacturing							Θ																
5	9	11.1	2.0	Device Visualization					Θ																		
6	9	11.1	2.0	Mobility								Θ	Θ														
7																											
8																											
9																											
10																											

Target or Limit Value	0 ↑ Ø5mm	0.4 ↑ 0.2 %	2.5 ↑ 0.5 mL/s	3.5 ↑ 0.5 cP, 37 ↑ 2°C	15% Opacity	Pressure ↑ 0.2 %, Temperature ↑ 25 %	0 ↑ 0.1mm from design	36"x36"x24"(LxWxH)	≥75lbs						
Difficulty (0=Easy to Accomplish, 10=Extremely Difficult)	5	6	5	3	4	3	8	4	7						
Max Relationship Value in Column	9	9	9	9	9	9	9	9	9						
Weight / Importance	300.0	177.8	150.0	150.0	144.4	200.0	433.3	100.0	100.0						
Relative Weight	17.1	10.1	8.5	8.5	8.2	11.4	24.7	5.7	5.7						

Appendix B: Component Reference Pictures

Vasculature	Wax Mold Cast 	3D Printed Cast 	3D Printed Vasculature 	
Pumps	Sink	Programmable	Roller	

				
Temperature Control	Hot Plate and Flask 	Solar Water Heater 	Body Heat 	
Fluid	Glycerin 	Powdered Milk 	Cow Blood 	CMC