Cumulative Shear In-Vitro Model

A Senior Project
Presented to
the Faculty of the Engineering Department
California Polytechnic State University - San Luis Obispo

In Partial Fulfillment
of the Requirements for the Degree
Bachelor of Science

by

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# 1.0                  Executive Summary

The goal of this project was to build an in-vitro model simulating blood flow through the brachial artery by using synthetic tubing to resemble varying levels of endothelial plaque buildup. This model will allow for a hemodynamic analysis of flow profile by modeling pressure and flow waveforms that would normally be obtained via a blood pressure cuff.

This model was required to be functional and compact, under 6 square feet. It needed to use test tubing that had similar compliance to arteries, between 1.0 and 1.7 ml/mmHg. The flow rate needed to be between 300 to 500 ml/min and flow intermittently with 0.5 seconds on and 0.3 seconds on. Through these requirements the pressure ranges measured across the sample were to be within physiological constraints of 80 to 200 mmHg, relating to the low end of diastolic and a high systolic blood pressure respectively.

Through testing of the final prototype these requirements were achieved, and the data obtained from these flow profiles with varying synthetic tubing was used to further explain the relationship between shear rate of blood flow and subclinical atherosclerosis. We hope that the information gathered from this model can one day lead to a minimally invasive medical device that can detect arterial plaque buildup in patients.

# 2.0                  Statement of Work

**Abstract**

       This Statement of Work covers the design and manufacturing of the Cumulative Shear In Vitro Model. The following document contains information on the project background, importance of the product, objects, key deliverables, and project management plan.

# Introduction

The goal of our model is to find a reliable method of subclinical atherosclerosis detection by measuring the pressure drop across an artery. Using this, the internal roughness of the artery tubing can be calculated. The roughness will be verified using confocal microscopy. This value will lead to a set range of flow values wherein laminar flow becomes turbulent in arteries, causing shear rate to drastically decrease. As this decrease is ultimately related to atherosclerosis, early detection could prove life saving for millions of patients worldwide. Successful execution of this in vitro model could lead to the development of a medical device that could noninvasively detect subclinical atherosclerosis.

# Background

Atherosclerosis is a buildup of plaque between the layers of arterial walls. It's a prevalent disease in the U.S., with 3 million cases diagnosed annually; with today's methods, it's difficult to detect. Arterial endothelial cells require a threshold shear rate to release nitric oxide, allowing for vasodilation. Plaque inhibits this, causing stiff arteries that are prone to disease. Accurate pressure drop measurement across an artery is key for early diagnosis of atherosclerosis, as it allows for determination of corresponding cumulative shear rate and endothelial cell function level. (Refer to Intellectual Property Assessment)

# Objectives

This project aims to develop an In Vitro model that has the ability to quantify the effects of parameters on cumulative shear. It includes an enclosed chamber that can hold pressure, tubing system, test samples modeling arterial plaque buildup, bucket to hold water for the system, pump, and a Biopac and computer to measure pressure differences. The customer requires the device to be compact, output accurate values within physiological ranges, be cost effective and be able to withstand multiple uses. (Refer to Product Specifications Matrix)

The cost will be measured by the overall cost of material. To keep the model compact we will test different setups of the model and measure the space it takes up in cubic feet. We will test the efficiency of different sample materials and look at the output ranges to check if it is within physiological values. We will run continuous tests to measure the accuracy of the device and compare the devices output with known accurate values. The level of knowledge required will be measured based on the equipment needed to measure the pressure values. We will program the pump to either give continuous or intermittent waveforms and measure the effect of the

waveforms on output values. The accessibility will be measured based on if it can be opened and resealed again to change test samples.

## Project Management

The design process we will follow will include project planning, product definition, conceptual design and product development. Project planning includes creating a PERT chart, identifying the critical path, and creating a budget. Product definitions gathering customer requirements and determining product engineering specifications. The conceptual design phase includes generating and evaluating product designs, choosing a final design and refining it to match customer needs. The product development phase will include creating the product, performing tests with it and making final changes. (Refer to Network Diagram)

The next step in the design process is to create conceptual design ideas based on our customer feedback analysis and refine the final design choice. Later we will obtain roughness ratings on samples using confocal microscopy, determine value of pressure drop indicating turbulent flow in a vessel and modify the model to include test samples within physiological ranges.

The Program Evaluation Review Technique chart includes three main phases: concept design, product development and post development analysis. Each phase must be completed before we can move on to the next phase of the project. Our critical path included the following deliverables: project budget, materials research, refine current design, develop schematic model, preliminary design review, concept design presentation, adjust variables to be within physiological ranges, function prototype, measure roughness with confocal microscope, calculate data from Biopac results and create final presentation and poster.

## Conclusion

This project is mainly to quantify the effects of cumulative shear on arteries and its relation to predicting a major cardiovascular event. This document outlines the necessary components to execute the project. The next steps are to develop a schematic of the in vitro model and prepare for the preliminary design review.

## 3.0 Network Diagram
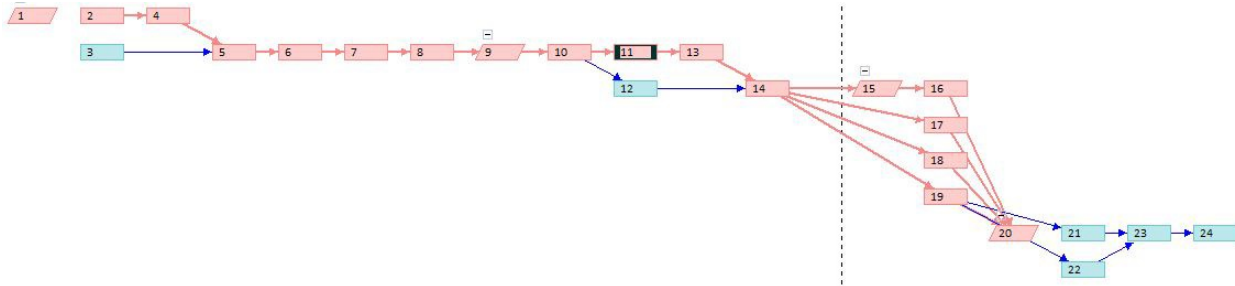


| # | Task | Duration | Start | Finish | Predecessors |
|---|------|----------|-------|--------|--------------|
| 1 | ◢ Concept Design | 26 days | 10/1 | 11/5 | |
| 2 | Create Project Budget | 8 days | 10/1 | 10/10 | |
| 3 | Define Product Goals and Outcomes | 3 days | 10/1 | 10/3 | |
| 4 | Research Materials | 6 days | 10/3 | 10/10 | 2 |
| 5 | Refine Current Design | 6 days | 10/10 | 10/17 | 3,4 |
| 6 | Develop a Schematic for Model | 4 days | 10/17 | 10/22 | 5 |
| 7 | Preliminary Design Review | 6 days | 10/22 | 10/29 | 6 |
| 8 | Concept Design Presentation | 5 days | 10/30 | 11/5 | 7 |
| 9 | ◢ Product Development | 61 days | 11/5 | 1/28 | 8 |
| 10 | Purchase Materials | 1 day | 11/5 | 11/5 | 8 |
| 11 | Control Waveform and Timing for Pump | 54 days | 11/5 | 1/17 | 10 |
| 12 | Make Compact Model | 29 days | 12/5 | 1/14 | 10 |
| 13 | Adjust Variables to Fit into Physiological Ranges | 6 days | 1/14 | 1/21 | 11 |
| 14 | Functional Prototype Demo, Test Plan Report, Test Plan Presentation | 5 days | 1/22 | 1/28 | 12,13 |
| 15 | ◢ Testing Phase | 7 days | 1/29 | 2/6 | 14 |
| 16 | Test 1: Chamber | 7 days | 1/29 | 2/6 | 14 |
| 17 | Test 2: Tubing system | 7 days | 1/29 | 2/6 | 14 |
| 18 | Test 3: Flow Rate | 7 days | 1/29 | 2/6 | 14 |
| 19 | Test 4: Arterial Samples | 7 days | 1/29 | 2/6 | 14 |
| 20 | ◢ Post Development Analysis | 36 days | 2/6 | 3/26 | 16,17,18,19 |
| 21 | Use Confocal Microscope to Measure Roughness in Sample Tubes | 11 days | 2/7 | 2/21 | 19 |
| 22 | Obtain Data Utilizing Biopack | 11 days | 2/7 | 2/21 | 19 |
| 23 | Calculate Data Using BioPac/Confocal | 6 days | 2/20 | 2/27 | 21,22 |
| 24 | Create Final Presentation and Poster | 14 days | 2/20 | 3/10 | 23 |

# 4.0 Indications for Use

Our Cumulative Shear In-Vitro Model is indicated to better define the relationship between shear rate and how it relates to endothelial dysfunction to better predict Subclinical Atherosclerosis in patients with asymptomatic or potential heart disease.

The information gathered from our Cumulative Shear in Vitro Model could lead to a medical device indicated for use in patients who are judged by a cardiologist or heart specialist to possibly be in the early stages of Subclinical Atherosclerosis and as a low risk and minimally invasive means of detecting arterial plaque buildup or blockage to further evaluate the patient.

# 5.0 Budget

| Item Description | Product Number | Purpose | Associated Task | Planned | | | | Notes | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Unit | Quantity | Cost/Unit | Total Cost | | | |
| Arterial Sample | N/A | Compliance Testing | 13 - Physiological Ran | EA | 1 | $0.00 | $0.00 | Obtain free sample | | |
| Artificial Blood | N/A | Model Arterial Bloodflow | 13 - Physiological Ran | N/A | 1 | $0.00 | $0.00 | Mixture of household products? | | |
| Plexiglas | 8560K275 | Hold Pressure for Model | 5 - Refine Current Des | 6"x12 | 6 | $5.37 | $32.22 | One will be cut into two pieces | | |
| Sealant | 7327A21 | Seal Chamber | 5 - Refine Current Des | ~16o | 1 | $0.00 | $0.00 | Already purchased | | |
| Signal Generator | 200382AFA | Drive Pump | 5 - Refine Current Des | EA | 1 | $12.59 | $12.59 | | | |
| O-ring | 9557K189 | Seal Chamber | 5 - Refine Current Des | 10 | 1 | $5.79 | $5.79 | | | |
| Sample Tubing | 5234K98 | Compliance Testing | 13 - Physiological Ran | 1ft | 10 | $0.89 | $8.90 | Soft Latex | | |
| Flow Meter | KFG-3007 | Measure Flow Rate | 13 - Physiological Ran | EA | 1 | $100.00 | $100.00 | | | |
| Water Storage | N/A | Store Water for Model | 5 - Refine Current Des | EA | 1 | $0.00 | $0.00 | Tupperware - Already purchased and usable | | |
| 1/4" Male Fittings | AO-45505-19 | Model Tubing | 5 - Refine Current Des | EA | 25 | $0.53 | $13.30 | Maybe not needed | | |
| 1/4" Female Fitting | AO-45502-20 | Model Tubing | 5 - Refine Current Des | EA | 25 | $0.47 | $11.80 | Maybe not needed | | |
| Brass Wing Nuts | 99862A520 | Secure Chamber | 5 - Refine Current Des | 5 | 1 | $8.00 | $8.00 | | | |
| Diaphragm Pump | N/A | Pump Water | 13 - Physiological Ran | 1 | 1 | $60.00 | $60.00 | | | |

The total cost of our project was approximately $110 after all necessary purchases. In our budget, we did not list the pump at first for two reasons: it can be extremely expensive for a pump sufficient for our experiment and we already have a functioning pump (although it may cause issues after a waveform generator is incorporated). This has changed, as a sponsor for a project that will begin after ours has purchased the pump for our project. The flow meter has been listed as $40 on our budget but was not purchased; in order to obtain the accuracy required in our specifications, we would need to spend upwards of $100 just to achieve a range of +/- 5%, which can also be obtained by manually measuring the flow rate.

# 6.0            Customer Requirements

1. Design a functional in vitro model
2. Create models of brachial artery with plaque buildup that is similar to artery compliant
3. Make model more compact and functional
4. Control flow rate and waveform timing
5. Obtain values within physiological constraints
6. Explain and define relationship between shear rate and endothelial dysfunction
7. Use confocal microscope to measure roughness in sample tubes

# 7.0            Specification Development

Our major engineering specifications are outlined and quantified below:

| Spec # | Parameter Description | Requirements or Target (units) | Tolerance | Risk | Compliance |
|---|---|---|---|---|---|
| 1 | Accuracy (ΔPressure) | ± .1 PSI | N/A | H | T, A, I |
| 2 | Flow Rate | 400 ml/min | ± 100.0 | M | T |
| 3 | Pressure in Chamber | 3.48 PSI at Systole<br><br>2.32 PSI at Diastole | ± .2 (blood pressure varies significantly) | L | A, I |
| 4 | Size (Overall) | 6 ft$^2$ | Max. | L | S, I |
| 5 | Weight (Overall) | 20lb | Max. | M | T, A, S |
| 6 | Production Cost | $200 | Max. | L | A |

| 7 | Sample Compliance | 1.775 ml/mm Hg (Normal)<br><br>1.072 ml/mm Hg (Diseased) | ± .5 | H | T, A |
|---|---|---|---|---|---|
| 8 | Intermittent Flow Timing | .5s off (diastole), .3s on (systole) | ± .05 | M | T |
| 9 | Pressure Ranges | 80 mmHg to 200 mmHg | N/A | L | T, I |

Risk: H (high), M (medium), L (low)
Compliance: T (test), A (analysis), I (inspection), S (similarity)

## 8.0 Total Available Market and Competitive Advantage Matrix

There are currently 28.2 million diagnosed with cardiovascular disease, and about 647,000 people die from cardiovascular disease each year; this is the highest cause of death in the US.

Assuming a unit price of $2000 for current models (see Competitive Advantage Matrix) and considering there are only about 6200 active hospitals in the US currently (each hospital may have 8 models), the total market would be about $99.2 million. Since this market is based on models sold to hospitals, room for growth is not as easily accounted for and could change abruptly based on many factors.

| | Itamar | Endothelix | Cumulative Shear Model |
|---|---|---|---|
| FDA Approved | Yes | Yes | No |
| Testing Time | 15 min | 15 min | TBD |
| Invasiveness | Non-invasive | Non-invasive | Non-invasive |
| Automation | Non-automated | Fully automated | TBD |
| Platform | Peripheral Arterial Tonometer | Temperature under curve | Sphygmomanometer |
| Warnings | No audio or visual guides | Audio and visual guides | TBD |
| Fingernail Clipping | Cllipping required | Clipping not required | TBD |

Itamar and Endothelix are compared to the Cumulative Shear In-Vitro model, which is in the stages of being modeled and therefore many features have yet to be determined. Once the final stages of design are completed and the model moves into the phase where it is converted to a commercial product, these features will be implemented.

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## 9.0        Intellectual Property Assessment

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**Major Patent Results for Existing Designs to Note:**

**System and method for estimating arterial pulse wave velocity (10,438,355):** A method of determining arterial pulse wave velocity in a healthy artery utilizing imaging modality.
Assignee: **General Electric Company** (Schenectady, NY)

**Cardiac Simulation Device (10,229,615):** A device that uses pressurized chambers to generate ventricle and atrium contractions. This invention is designed to generate pumping action that produces accurate volume fractions and pressure gradients of pulsatile flow, similar to that of the human heart.

Assignee: **Vascular Simulations Inc.** (Wilmington, DE)

**Physiological signal stimulator and simulator (10,067,489):** An apparatus that receives programming values in order to generate electrical signals similar to the heart.

Assignee: **COMMISSIONING AGENTS, INC.** (N/A)

# Conjoint Analysis

SUMMARY OUTPUT

**Regression Statistics**

| | |
|---|---|
| Multiple R | 0.579377 |
| R Square | 0.335678 |
| Adjusted R | 0.314918 |
| Standard E | 1.943237 |
| Observatic | 232 |

ANOVA

| | df | SS | MS | F | ignificance F |
|---|---|---|---|---|---|
| Regressior | 7 | 427.4095 | 61.0585 | 16.16943 | 3.62E-17 |
| Residual | 224 | 845.8621 | 3.77617 | | |
| Total | 231 | 1273.272 | | | |

| | Coefficients | andard Err | t Stat | P-value | Lower 95% | Upper 95% | ower 95.0% | pper 95.0% |
|---|---|---|---|---|---|---|---|---|
| Intercept | 4.655172 | 0.36085 | 12.90057 | 7.67E-29 | 3.944077 | 5.366267 | 3.944077 | 5.366267 |
| Cost | 2.198276 | 0.25516 | 8.6153 | 1.26E-15 | 1.695456 | 2.701096 | 1.695456 | 2.701096 |
| Compactn | -0.57759 | 0.25516 | -2.26363 | 0.024555 | -1.08041 | -0.07477 | -1.08041 | -0.07477 |
| Sample Ma | -0.37069 | 0.25516 | -1.45278 | 0.147685 | -0.87351 | 0.13213 | -0.87351 | 0.13213 |
| Accuracy | -0.62931 | 0.25516 | -2.46634 | 0.014401 | -1.13213 | -0.12649 | -1.13213 | -0.12649 |
| Knowledge | 0.474138 | 0.25516 | 1.858202 | 0.064452 | -0.02868 | 0.976958 | -0.02868 | 0.976958 |
| Waveform | -0.09483 | 0.25516 | -0.37164 | 0.710512 | -0.59765 | 0.407993 | -0.59765 | 0.407993 |
| Container | -1.19828 | 0.25516 | -4.69618 | 4.62E-06 | -1.7011 | -0.69546 | -1.7011 | -0.69546 |

The factors that are important to the success of the product based on the ANOVA results are

- Cost
- Compactness
- Accuracy
- Container accessibility

## 11.0 Morphology

| Function | Concept 1 | Concept 2 | Concept 3 | Concept 4 |
|---|---|---|---|---|
| Securing chamber lid | O-ring - tight fit with plexiglass | Clamps (like mason jar lid) | Sealant - Silicone | Vice |
| Opening chamber lid | Handle | Sealant removal | Unlock clamps | |
| Inserting and removing tubing | Male and female connectors - screw on and off | Zip ties to secure sample tubing | Electrical Tape | Hose clamp |
| Adding/removing pressure from the system | Hand pump | Mechanical pump | | |
| Changing System Compliance | Syringe | | | |
| Changing Relative Roughness of Tubes | Glitter | Sand | Cholesterol/fat combination | |
| Verifying Hemodynamic Measure of Tube Relative Roughness | Confocal Microscope | | | |

# 12.0                    Concept Evaluation
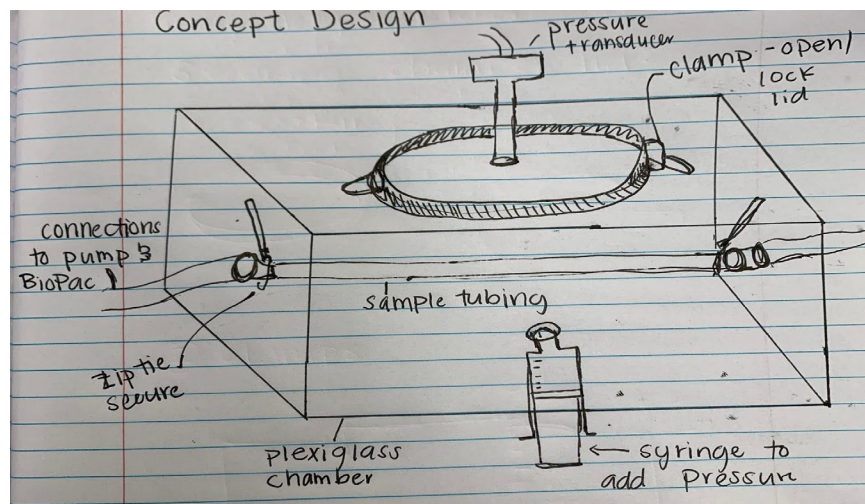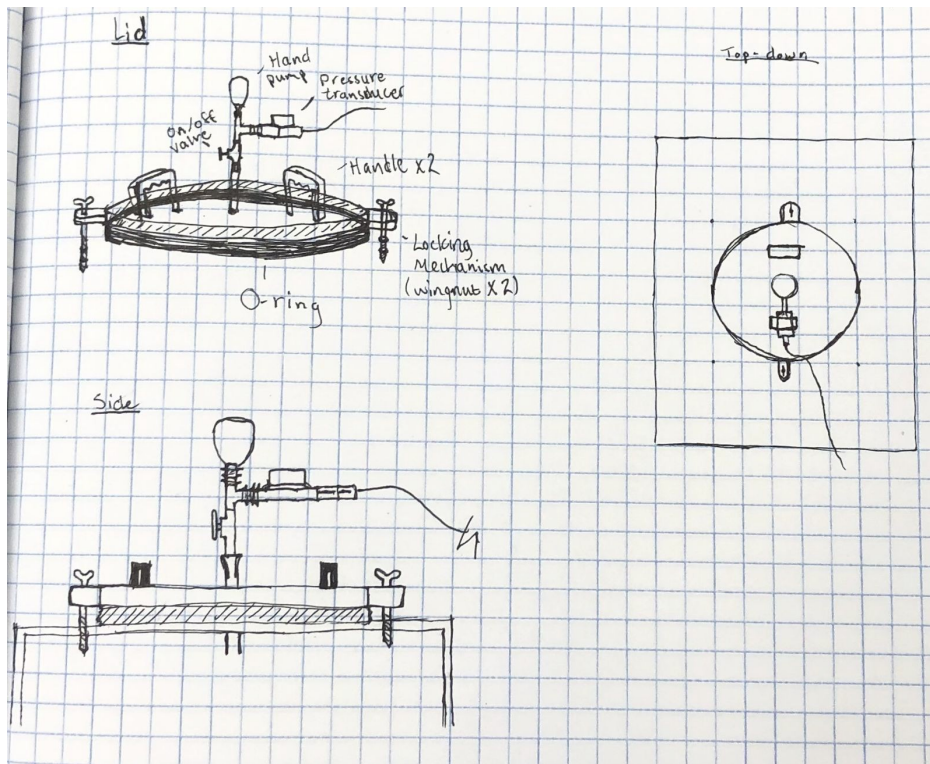
## Concept 1:



This concept uses clamps to open and close lid with an O-ring to ensure it holds pressure. A syringe would be used to add or release air to control the pressure of the chamber. The sample tubing is secured to the system tubing with zip ties to endure a tight fit.

# Concept 2:
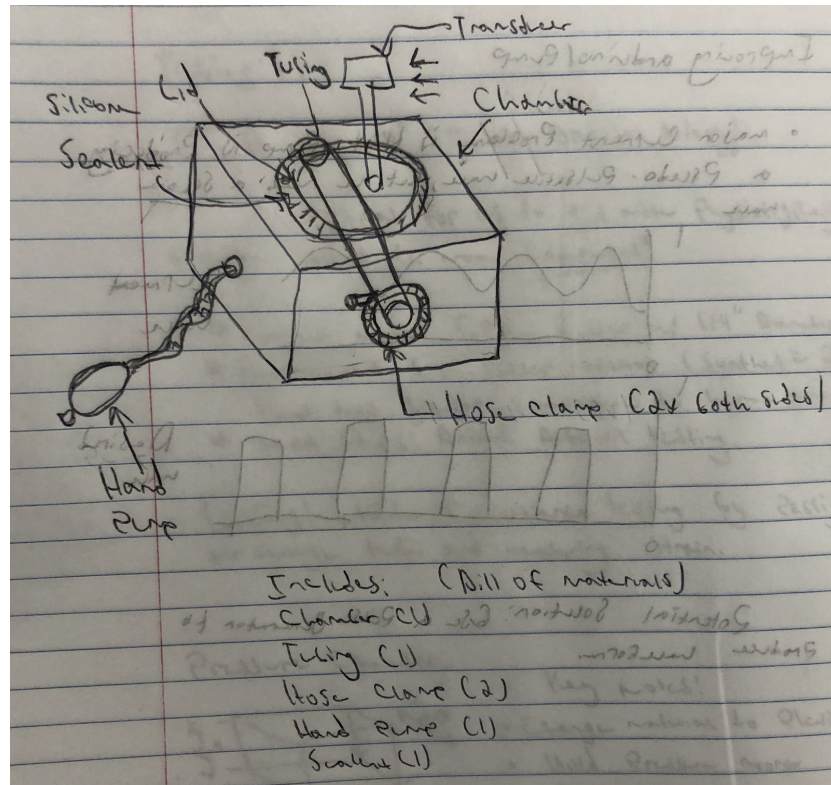


This concept utilizes silicone sealant to effectively seal lid to chamber and maintain pressure. The sealant is removed by a compound that dissolves it when lid needs to be opened. A hose clamp is used to clamp the tubing and hold it to chamber wall. Pressure is increased or decreased via a manual hand pump.

# Concept 3:



This concept uses wingnuts to ensure seal against O-ring for maintaining pressure within the chamber. The lid would have handles for easy placement and lifting, while middle of lid has a connection to pressure transducer/hand pump to alter and measure pressure inside the chamber. The wingnut with O-ring design prevents any pressure leak due to threaded connection.

## 13.0                        Pugh Matrix

| Issue: Choose a chamber design | | Baseline | Clamped | Sealed | Wingnut |
|---|---|---|---|---|---|
| Accessibility | 30 | Datum | 1 | -1 | 1 |
| Feasibility | 15 | | 1 | -1 | 0 |
| Compliance with Physiology | 30 | | 0 | 1 | 0 |
| Maintain Pressure | 25 | | -1 | 1 | 1 |
| Total | | | 1 | 0 | 2 |
| Weighted Total | | | 20 | 10 | 55 |

- Analysis of the Pugh Chart shows concept design #3 to be the most effective
- It allows for a highly accessible, securely fastened chamber with little chance of pressure or water leaks
- The feasibility and compliance with physiological characteristics are average, but the other designs are not much better in either regard

## 14.0                        Front Runner

- Plexiglass chamber with an O-ring sealing mechanism (wing nut design) on top to allow for changing samples
  - Pressure in chamber changeable through syringe in front of chamber
  - Hand pump on top of the lid to change compliance
  - Pressure transducer on top of lid
  - Samples will be thin-walled rubber tubing
  - Cost of Chamber: $56.93
- Diaphragm pump to pump water through chamber
  - Cost of Generator and Pump: $1,100 - obtained from sponsor so not included in budget

- Water flows into graduated cylinder, volume over time is calculated to determine flow rate
  - Cost of Flow Measurement: $0

Dimensioning:
- Chamber
  - 6" x 6" x 10"
  - Lid will be 4.5" diameter
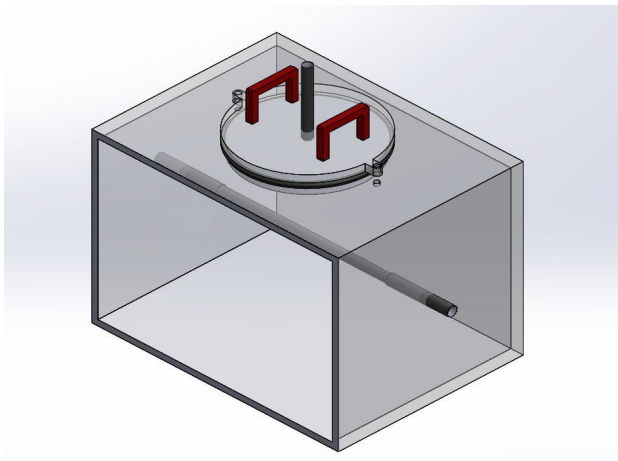- Overall System
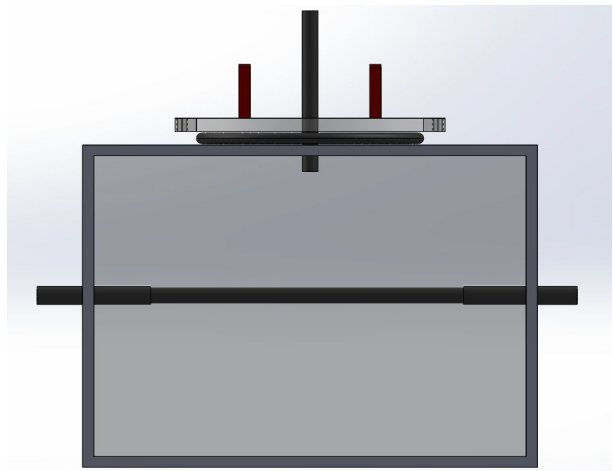  - 4ft²
  - Compact, mobile design

Total Cost: $56.93

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## 15.0        Conceptual Model

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## CAD Design:

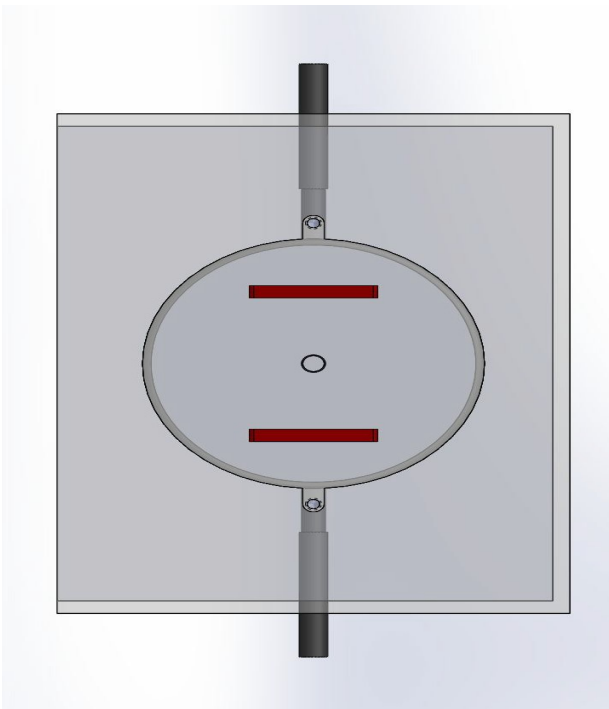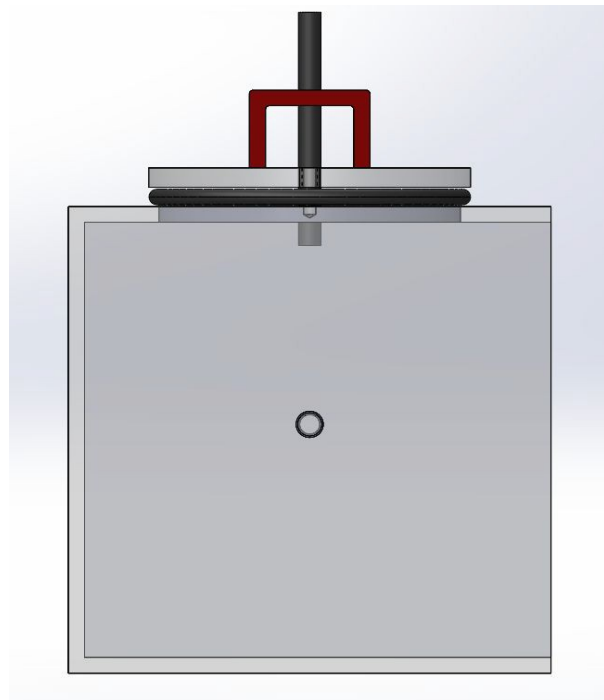| Isometric View | Front View |
|:---:|:---:|



Note: Front of chamber removed in drawings for visual purposes. Front panel will be identical to the back panel and sealed in place.

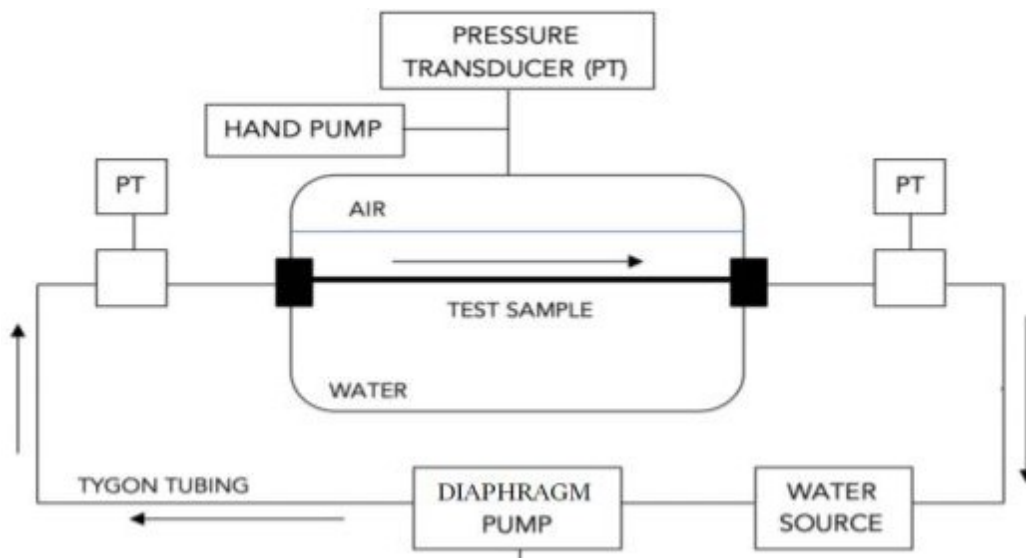| Top View | Side View |
|---|---|
|  |  |

## Schematic of Total System:



Schematic of Total System:

- Waveform Generator to control pump

- Pump drives water flow through samples
- Pressure driven via diaphragm pump
- Pressure Transducer takes pressure drop readings
- Flow Meter to measure flow rate

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## 16.0            Mathematical Model

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Darcy's Equation:

$$\frac{p_1}{y} + z_1 + \frac{v_1^2}{2g} + h_A - h_R - h_L = \frac{p^2}{y} + z_2 + \frac{v_2^2}{2g}$$

$$h_L = \frac{p_2 - p_1}{y}$$

For our model, we can assume $z_1$, $\frac{v_1^2}{2g}$, $h_A$, $h_R$, $z_2$ and $\frac{v_2^2}{2g}$ are equal to 0.

Darcy's equation can be used to calculate head loss. Head loss (hl) is a loss in pressure head due to the viscosity of a fluid and obstructions of flow.

In this calculation the following assumptions are made:
1. No energy is added to the system therefore $h_A = 0$.
2. No energy is returned therefore $h_R = 0$.
3. The elevation of both pressure transducers is equal therefore $z_1 = z_2$.
4. The flow is incompressible and the diameters at each end of the tube are equal therefore $v_1 = v_2$.
5. Head loss can then be calculated by the difference in pressures over the specific weight of the fluid.

Energy Loss:
$$h_L = f \times \frac{L}{D} \times \frac{v^2}{2g}$$

'f' is the friction factor of a sample and is used to determine turbulent versus laminar flow on a Moody diagram. Solve for linear velocity 'v' with equation for flow rate

from the continuity equation:

$$Q = Av$$

Once linear velocity is determined using the flow rate equation, the friction factor can be calculated.

Reynold's Number:

$$N_R = \frac{\rho v D}{\mu}$$

The Reynold's number can then be calculated using the density, fluid velocity, inner tube diameter, and dynamic viscosity.

The Reynold's number and friction factor then allows us to use a moody diagram via triangulation to determine laminar vs turbulent flow and then estimate shear rate. Greater energy losses and lower shear rate corresponds to turbulent flow.

Compliance:

$$C = \frac{3\pi r^3 L}{2hE}$$

Compliance is used to determine how similar our sample tubing is to a human brachial artery; on average, a healthy brachial artery has a compliance of approximately 1.775 ml/mmHg and a diseased artery has a compliance of approximately 1.072 ml/mmHg.

After calculating the compliance of the tubing we used for samples, we determined that the compliance of a healthy sample (no added material) was around 1.240 ml/mmHg (30% difference) and the compliance of a diseased sample was around .8976 ml/mmHg (16.2% difference).
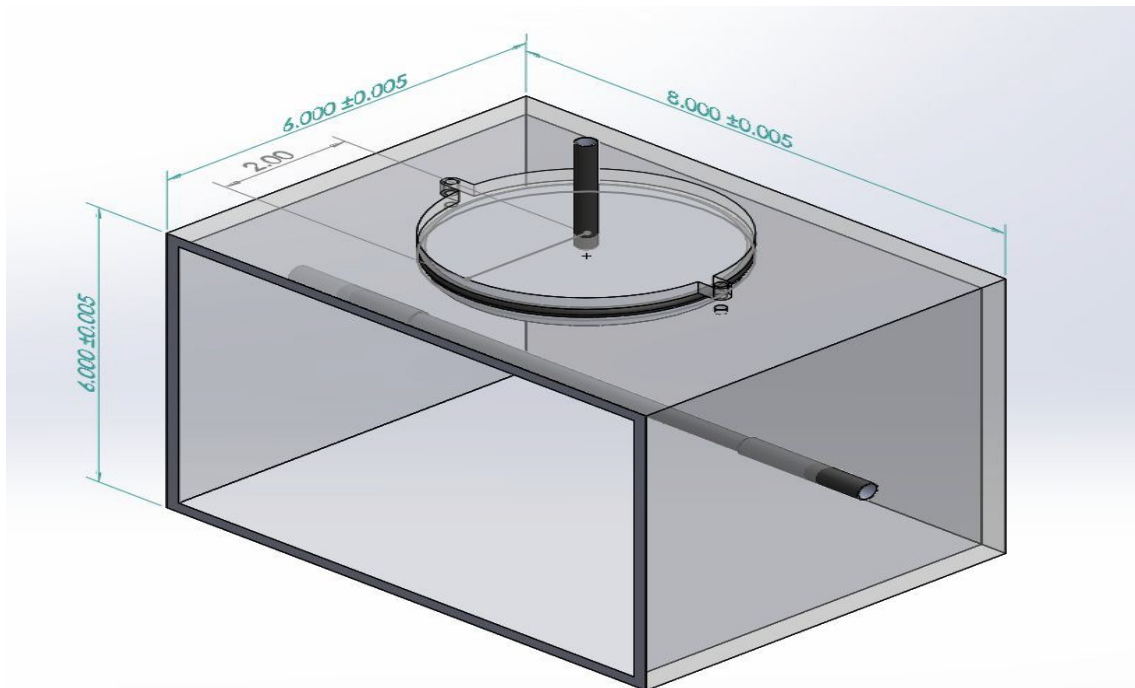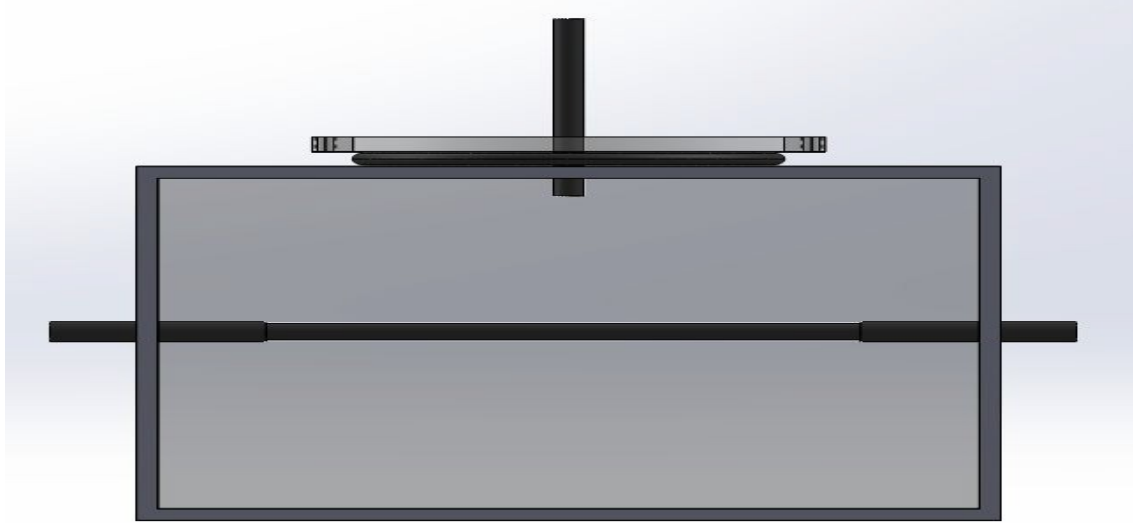
# 17.0 Detailed Design

## Dimensioned Tubing:
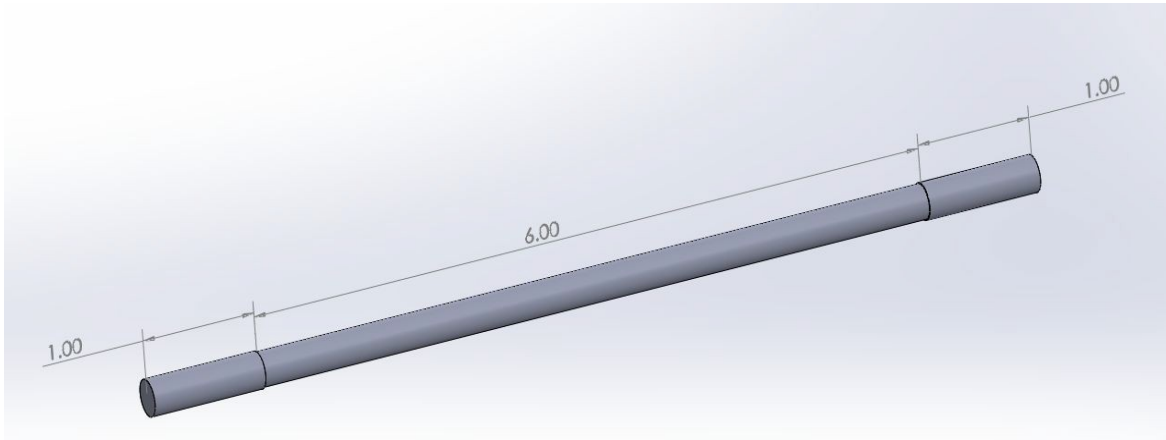


## Isometric of Design:



## Front View of Design:

# Side View of Design:



Materials
- Chamber: Plexiglass walls and lid, brass bolts, rubber O-ring, rubber tubing (top of chamber), silicone caulk for sealant
- Sample: Pig artery, rubber tubing

- Total Cost: $56.93

<u>Dimensions</u>
- Sample Tubing: ¼" inner diameter, 1/32" wall thickness
  - Pig arteries are similar but not exact
- Chamber: 6" tall, 6" wide, 10" long
  - ¼" diameter holes drilled at center of each end (samples)
  - ¼" diameter hole drilled at center of one of the long panels, located 1" above the base (syringe)
- Lid: 4.5" diameter
  - .5" radius semicircles extended on both sides parallel to sample tubing in chamber
  - ⅜" holes drilled/tapped for wing bolt placement in center of semicircles
  - ¼" hole drilled through center of lid (tubing)

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## 18.0            Bill of Materials

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| Quantity | Part Description | Part Number | Source |
|---|---|---|---|
|  | CHAMBER |  |  |
| 7 | Acrylic | 8560K275 | McMaster Carr |
| 1 | Acrylic Cement | 10315 | Amazon |
| 2 | Brass Wing-nuts | 99862A520 | McMaster Carr |
| 1 | Bolt Adhesive | 1452853 | Dr. Whitt |
| 1 | Rubber Sheet | 203193498 | Home Depot |
| 2 | 10/32 E-Z Lock Inserts | 240-332-BR | E-Z Lock |
|  | SYSTEM |  |  |
| 1 | Signal Generator | 200382AFA | Amazon |

| 2 | Sample Tubing | 5234K98 | McMaster Carr |
|---|---|---|---|
| 1 | Water Storage | N/A | |
| 1 pack | ¼" Male Fittings | AO-45505-19 | McMaster Carr |
| 1 pack | ¼" Female Fittings | AO-45505-20 | McMaster Carr |
| 1 | NF100 Liquiport pump | 112021043 | KNF |

## 19.0         Prototype Manufacturing Plans

**Chamber Manufacturing**

1. Each of the 7 acrylic pieces (#8560K275) need to be cut to size using a laser cutter
   a. 2 6" x 6" pieces with ¼" radius holes centered
   b. 3 6" x 8" pieces
   c. 1 6" x 8" piece with a 4.5" diameter circle cut out of the center
   d. 1 4.5" circle with 2 0.5" circular sticking out on either side as shown in the detailed CAD drawing. In the circular lid a ¼" radius hole is cut from the center
2. The chamber is assembled with the acrylic cement (#10315) to connect the plexiglass pieces at the edges to put together the chamber as shown in the detailed design CAD drawing.
3. Male fitting (#AO-45505-19) connected to a female fitting (#AO-45505-20) are secured with the sealant into the holes of the 6" x 6" pieces at their center.
4. Rubber sheet (#203193498) is cut to the size of the lid and holes are cut in same place as on lid
5. 2 ¼ inch holes are drilled in the top directly across from each other of the circle and the E-Z lock inserts (#240-332-BR) are gently hammered into place so that they are flush with the top of the chamber

**Sample Tubing Manufacturing**

1. Sample Tubing (#5234K98) is cut to 7" piece
2. Epoxy or gorilla glue is inserted into one end and spread throughout the tube using a long metal rod

3. The rod is dipped into substance (i.e. sand or glitter) and pushed through the tube again rubbing it against the edged
4. This is repeated at the other end of the tube and can be done multiple times to increase the amount of substance lining the walls of the tube

**Connecting Entire System**
1. Tubing is connected to the outlet of the chamber and then a pressure transducer that connects to the Biopac is placed
2. Tubing is connected to the other side of the pressure transducer and the flow meter which is connected with tubing to the water source
3. From the water source comes more tubing which connected the system to the pump, which is connected to the waveform generator via wires
4. The system is completed by attaching the other end of the pump with another pressure transducer to the inlet
5. Pressure transducers (including one on top of the chamber) are all connected to channels of the Biopac, which displays data on the computer system

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## 20.0               Test Protocols

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We will need to test the chamber to make sure it is properly sealed. We will fill the chamber with water and check for leaks in the sealant between the plexiglas pieces. It will be easy to tell if water is leaking from the chamber immediately and we will reseal areas needing attention. To test if the chamber can hold pressure, we will pressurize the chamber with the hand pump. We will check if the chamber holds pressure using the pressure transducer on the lid. It needs to maintain a pressure of at least 200 mmHg. Once the chamber passes the water and pressure test, we can move on to testing arterial samples.

We will also need to ensure the tubing throughout the entire system does not leak water, specifically where fittings are connected to the tubing. We will be able to visibly see any leaks. If tests fail, we will replace fittings, add sealant and try again.

The flow rate must be within the range of 400 ml/min ± 100. This will be read by the flow meter and we can alter the pump until we are within this range.

To test arterial samples, the sample will be attached to the fittings on the sides of the chamber using dental floss. The chamber will be filled with water, the lid will be

secured with the wingnuts and the chamber will be pressurized. We will start the pump for the liquid to be pumped through the system and record the pressure difference using the Biopac. The pressure drops will be recorded for one minute. Recorded pressure needs to be in physiological ranges between 50 and 200 mmHg. In order to obtain this, we will adjust chamber pressure in increments of 5 mmHg. If physiological ranges are still not recorded, then we will change arterial samples.

To determine Relative roughness of sample material inside arteries the last confocal microscope will be used. This experimentally determined surface roughness can then be utilized to confirm hand calculations. This test will be conducted by gluing various samples (sand and glitter) to a microscope slide and setting the microscope to the proper settings. Photons are emitted from the microscope and are then reflected back creating a 3-d topographical map. The surface roughness is then determined from the relative area of this map.

All testing will be done in the ATL building and imaging room, no special training is required. We will be using the whole system, including the Biopac, chamber, tubing, and sample arteries.

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## 21.0          Operations Manual Overview

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SYSTEM
- Pressure transducers must be flushed with water (removing the cap and letting water flow through) to accurately read pressure
- Chamber filled with water to control compliance of system
- Lid is taken off by two wing-bolts located on top of chamber; once removed, samples may be inserted into the two fittings on either side. Once replaced, seal lid with O-ring and ensure that it is airtight
- To increase the pressure in the chamber, twist the luer lock for the syringe to close and take the syringe off; fill with air, put the syringe back on and open the luer lock.

PUMP
- The pump mechanism is controlled by a battery pack; turn the switch to 'on' to begin pumping

- After incorporation, the waveform generator will be the connection between the battery pack and pump. Set desired duty cycle and frequency to control square wave.

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## 22.0          Testing Data and Analyses

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|  | Test 1 | Test 1 | Test 2 | Test 2 |
|---|---|---|---|---|
| Sample | Friction Factor | Shear Rate | Friction Factor | Shear Rate |
| 1 - Sand | 0.055456177 | 394.4892953 | 0.057340765 | 393.3589535 |
| 2 - Sand | 0.079565334 | 441.9636517 | 0.081328045 | 421.617499 |
| 3 - Sand | 0.049393655 | 291.6281896 | 0.049156699 | 375.2734843 |
| 4 - Sand | 0.060233866 | 376.4038262 | 0.063700281 | 366.2307498 |
| 5 - Glitter (fine) | 0.050619973 | 362.8397243 | 0.042041298 | 368.4914334 |
| 6 - Epoxy | 0.034095404 | 377.534168 | 0.024773771 | 361.7093825 |
| 7 - Baseline 1 | 0.029894883 | 367.3610916 | 0.031126433 | 367.3610916 |
| 8 - Baseline 2 | 0.032115608 | 358.318357 | 0.029416093 | 359.4486988 |
| 9 - Glitter 1 (Chunky) | 0.03241938 | 310.8440006 | 0.032208358 | 311.9743424 |
| 10 - Glitter 2 (Chunky) | 0.121030608 | 394.4892953 | 0.097220727 | 397.8803207 |

Reynolds number Re

28
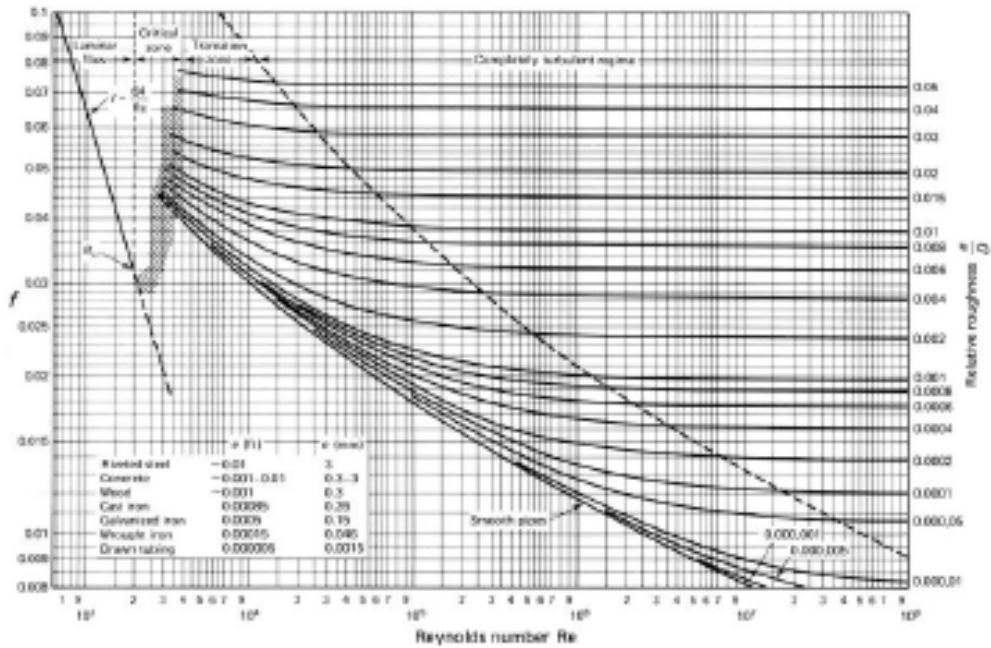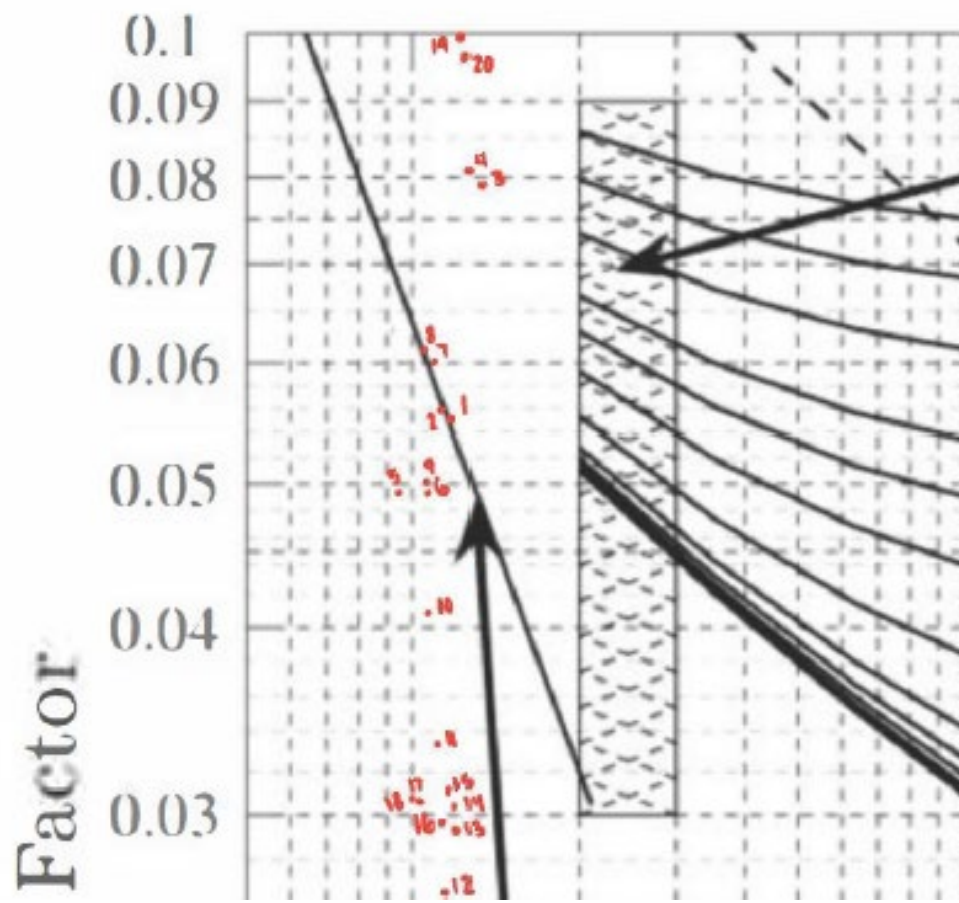
The first image is a Moody Diagram; by obtaining Reynold's Number and the friction factor of a given sample, we are able to determine whether the flow through the sample is laminar or turbulent. In all 10 samples, we found that the flow was laminar, and were therefore able to use the equation

$$SS = \frac{4\mu Q}{\pi r^3}$$

to determine the shear rate of each sample. As seen in the table, the shear rate somewhat correlated with an increase in friction factor; since the equation does not account for head loss in the system, however, the friction factor has a much better correlation with pressure drop within the samples. In the second image, all 10 samples are placed within the laminar flow region of the Moody Diagram. Since each sample was tested twice, #1 and #2 are for Sample 1, #3 and #4 are for Sample 2, etc.

## 23.0                  Conclusions

Using Darcy's equation and energy loss, we were able to calculate the friction factor from the pressure differences obtained in our tests. We were able to see that friction factor increased with the addition of sand or glitter material in relation to the baseline reading. This is obtained from the pressure readings suggesting that this factor can be measured noninvasively with a pressure cuff in a future device.

We can also relate this friction factor to the shear rate of an artery. By using a moody diagram, we were able to determine if it is laminar or turbulent flow. Based off of this we can use the appropriate shear rate equation to establish a relationship between pressure and flow. It is known that low wall shear stress correlates to abnormal flow in a tube.

In conclusion, our data shows a significant increase in both friction factor and relative roughness of our synthetic tubing when compared to baseline, which can ultimately lead to subclinical atherosclerosis.

## 24.0　　　　　　　　　　Discussion

While the data obtained from this model is highly useful, for future testing creating a more physiologically accurate model would be critical to getting the most accurate results. Both arterial compliance and material properties of our synthetic arteries could be improved to better model human arterial hemodynamics. While our arterial compliance values were within tolerance, interpretation of data should be guarded as this was the best compliance, we could obtain using synthetic arteries. Continuation of this in-vivo model should use animal or human arteries to give the most accurate physiological waveforms possible when analyzing data. Further, the fluid running through our model was water. Using a fluid similar to that of the viscosity of blood would provide for more accurate flow profiles for hemodynamic analysis.

Being able to validate our hand calculated relative roughness with some kind of measurement was something we were unable to do. We attempted to quantify surface roughness by using a confocal microscope to calculate relative area as this was the best resource available to us at Cal Poly. However, a number of issues presented preventing testing ranging from mounting of samples to particulates falling into microscope made it infeasible to image samples. A different method to quantify roughness should be considered to provide validation to the accuracy of calculated surface roughness values.

Lastly, in this in-vitro model sand, glitter, and silicone epoxy were utilized to simulate arterial plaque. While these materials are useful to look at varying levels of roughness affect rate of shear, using a material that better resembles a calcified region of artery would allow for a more accurate comparison between blood flow shear rate changes and arterial plaque build up. While the results of our testing show that this relationship is present, improving physiological parameters would for a more accurate analysis as the wall shear stress generated from blood flow would be modeling endothelial dysfunction more accurately than our current design.

**Endothelix Competitive Advantages**

https://www.endothelix.com/physicians/competitive-advantages/

**Hospital Information for the US**

https://www.aha.org/statistics/fast-facts-us-hospitals

**Aortic Compliance in Human Hypertension**

https://www.ahajournals.org/doi/pdf/10.1161/01.HYP.14.2.129

**Cardiac Cycle: Meaning, Duration and Phases**

http://www.biologydiscussion.com/human-physiology/cardiovascular-system/cardiac-cycle-meaning-duration-and-phases/62445

**Brachial Artery Blood Flow Measurement**

https://onlinelibrary.wiley.com/doi/pdf/10.1002/dat.20565