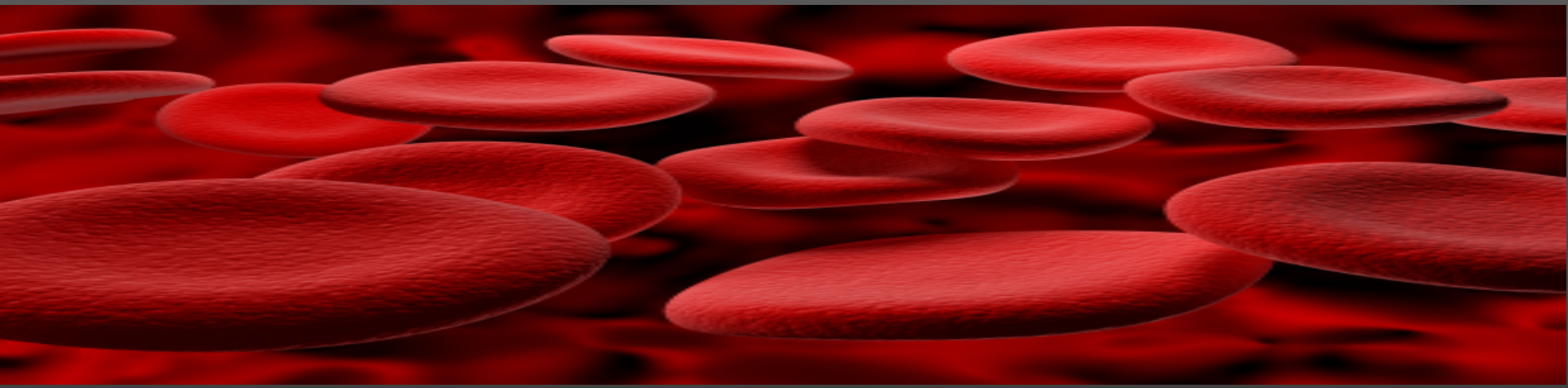
Team Aggregation Domination Oral Report 3

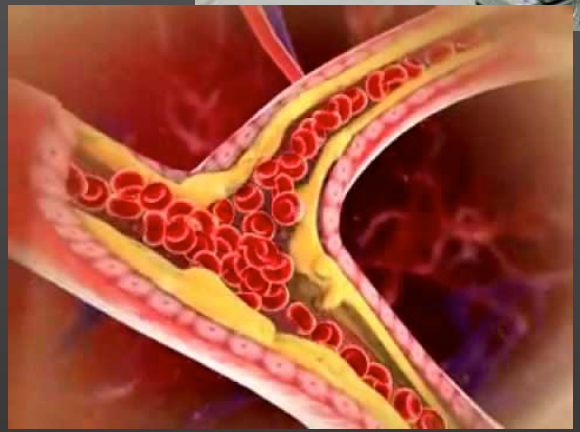


Kelly Hainline, Morgan Satterlee, Kevin Humphrey, and Cortnee Weinrich

Agenda

- ❖Background and Problem Statement
- ❖Mechanism
- ❖Previous Work
- ❖Tissue Damage Protocol
- ❖Results and Analysis
- ❖Future Work

sissupply.com



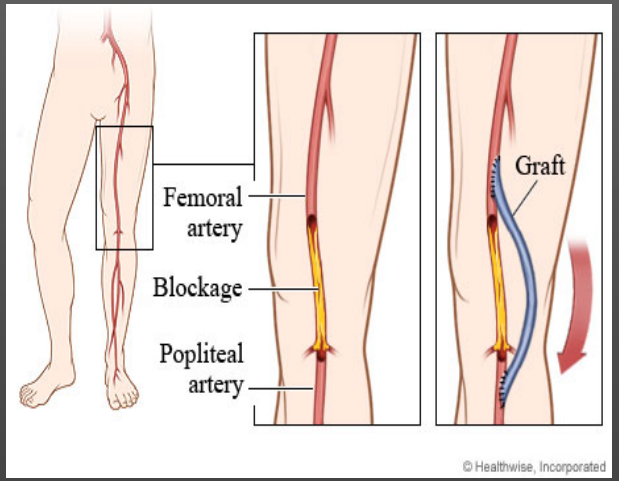
Youtube.com

Background

Vascular bypass graft failure rates can be as high as 43% depending on the type of operation.

This failure is thought to be caused by the inflammatory response induced from trauma during transplantation.

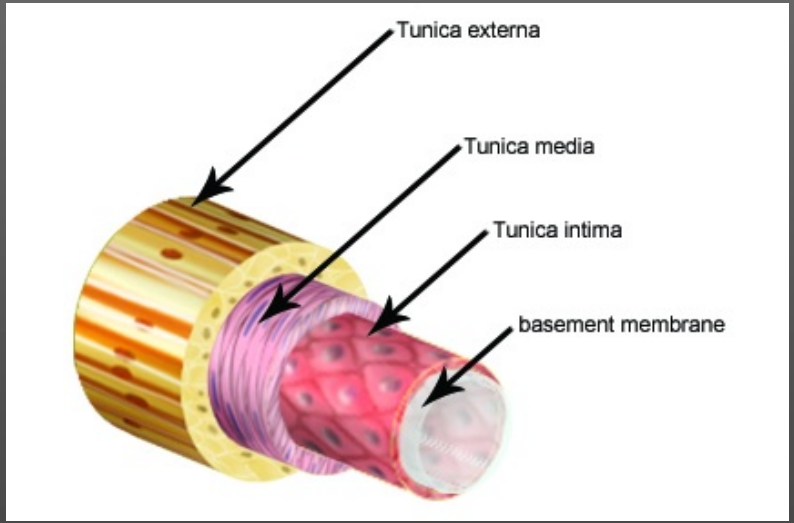
Scientists have developed an map kinase inhibitor that moderates endothelial cellular processes such as proliferation, stress response, and apoptosis. Vascular bypass graft patency has been shown to improve with treatment using this MK2 inhibitor.



Myhealth.albert.ca

Problem Statement

- Permeation of this drug is limited by vascular tissue's inherent diffusional barriers.
- The target tissues for this drug are the tunica intima and tunica media.



Carotid.net

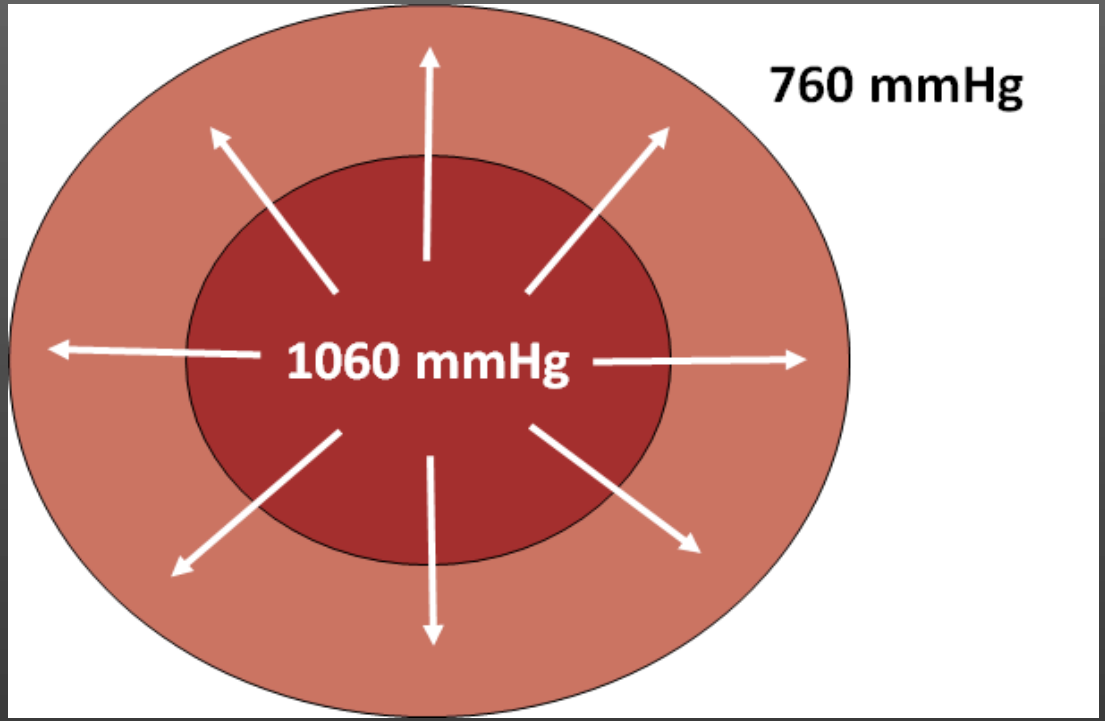
We are developing a pressurized device that will deliver prophylactic drugs into the target tissue of the vessel used for vascular bypass graft transplant

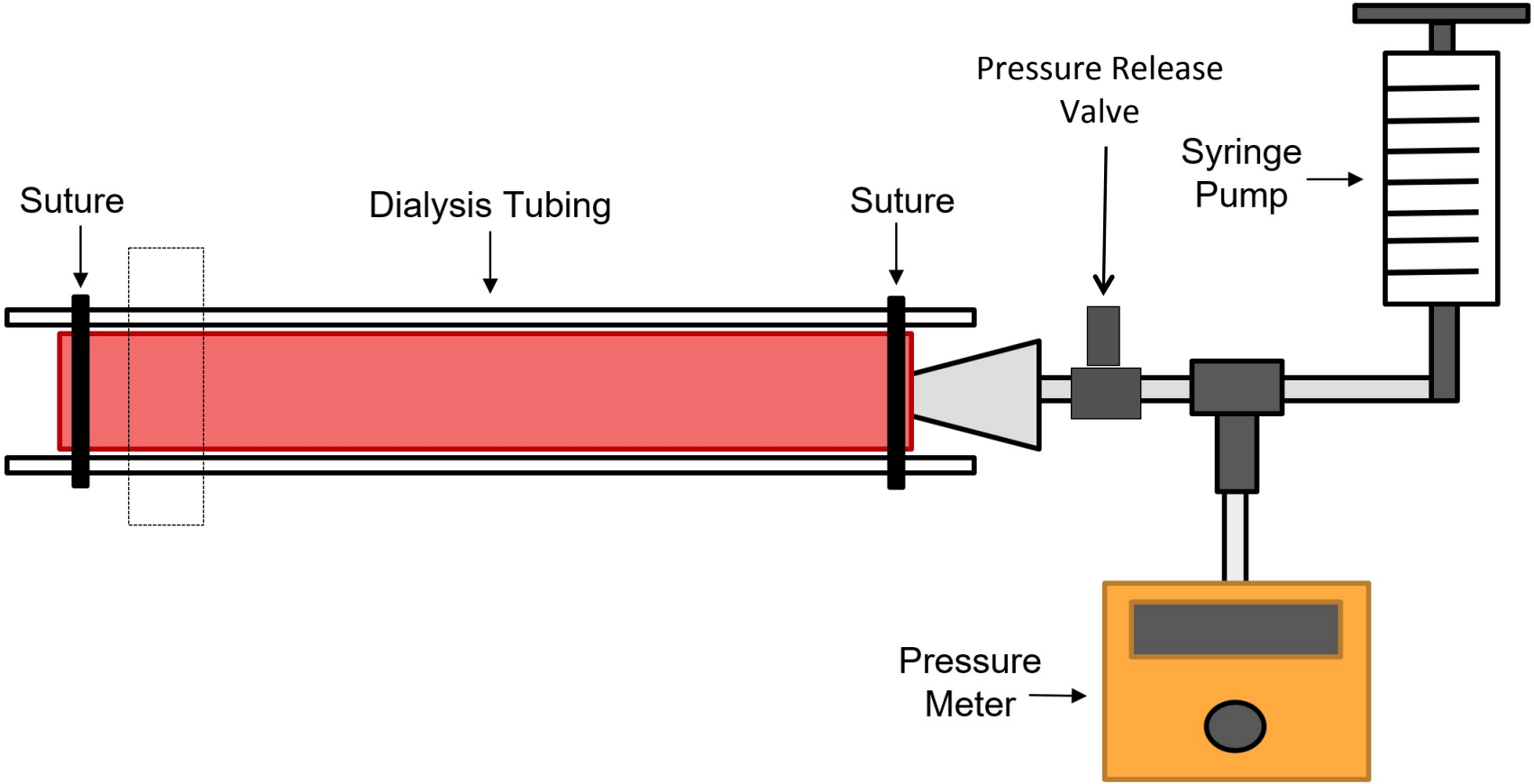
Needs Assessment

- membrane needs to maintain stiffness to reduce circumferential distension of the vessel
- pressure regulator and pressure release valve to maintain steady pressure
- vessel can be removed from membrane without incurring any damage
- easily integrated into current operating room technologies

Mechanism

- Pressure creates gradient from lumen to exterior of the vessel
- Convective circumferential flow of the drug solution into the target tissue
- Should result in a more effective mode of delivery than current method of treatment

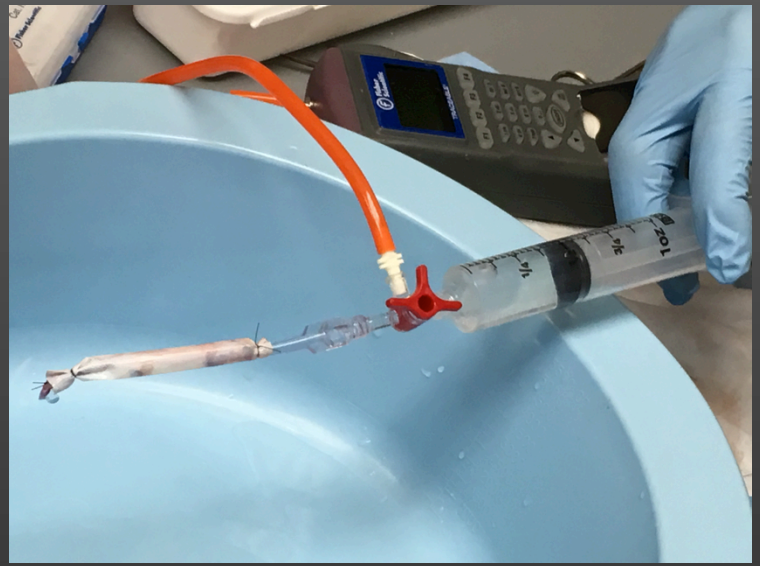



Suture
Dialysis Tubing
Suture
Pressure Release Valve
Syringe Pump
Pressure Meter

Previous Work

Initial Vein Pressurization Protocol: Proof of Concept

1. Suture vein to cannula
2. Use guidewire to pull dialysis tubing over vein
3. Suture both ends until sealed
4. Assemble three way stopcock with vein cannula, pressure meter and filled syringe
5. Pressurize to desired level



Previous Work

Take-away :

- Can reach desired pressures of 132, 300, 600 mmHg.
- Multiple sutures necessary to completely seal the dialysis tubing.
- Veins are not sturdy enough to push through dialysis tubing alone.
- Dialysis tubing did not fully support the vein wall.

Moving Forward :

- A guidewire is a necessary component to our design.
- Determine if vascular surgeons can tie strong sutures quickly.
- Develop a way to compress dialysis tubing around vein structure.

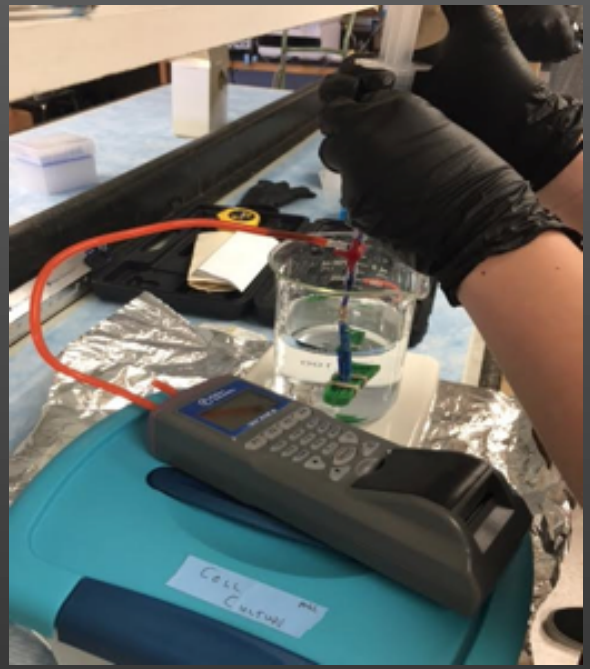
Previous Work

Dialysis Tubing Flow Test: Is Tubing Limiting the Pressure

Goal: Compare the hydraulic conductivity of veins to the dialysis tubing.

Passed a dye solution through the 100 kDa dialysis tubing and measured rate of escape.

From data, calculate hydraulic conductivity of dialysis tubing and compare to studies of vein hydraulic conductivity.

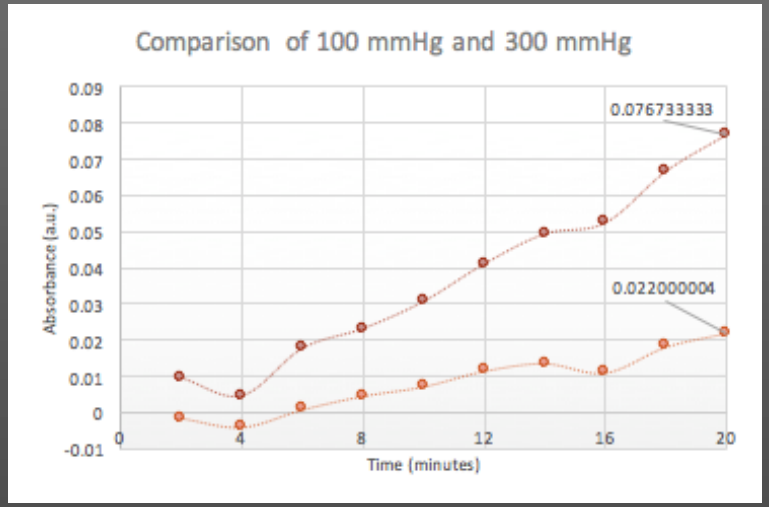


Previous Work

Conclusions:

Vena cava were tested hydraulic conductivity of 1.23*10^-7 (cm/(s*mmHg)) (Vargas 1986) meaning approximately 80% of the pressure drop is across the vein wall.

Additionally, the sutures do not leak up to pressures of 300 mmHg.



Red: 300 mmHg, Orange: 100 mmHg

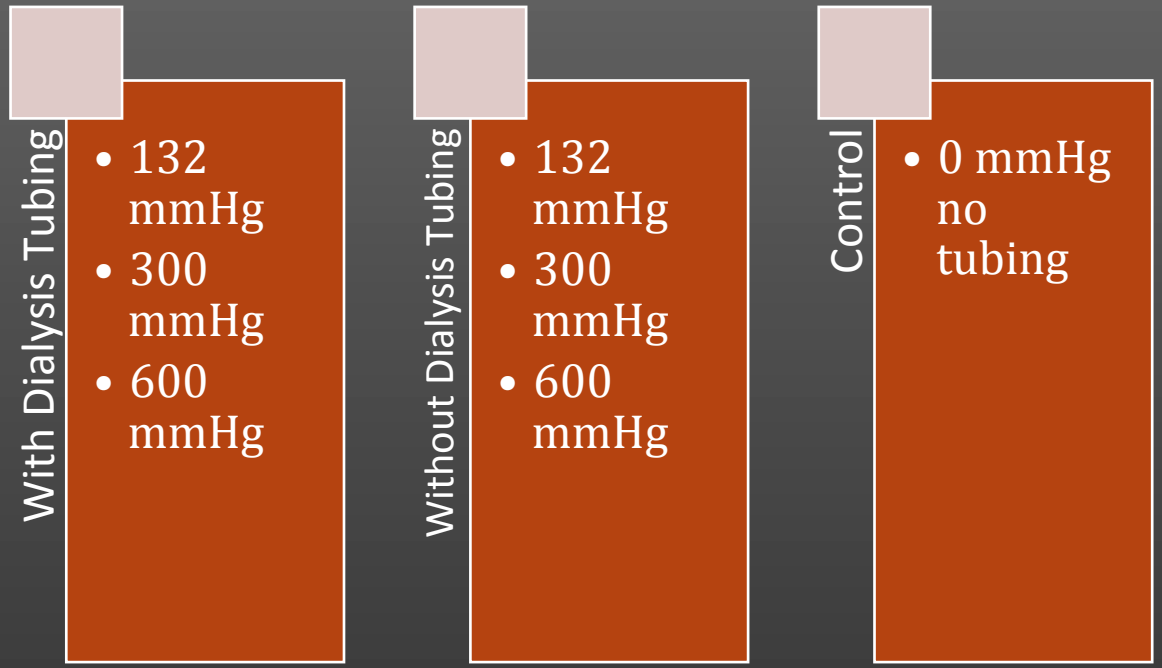
	100 mmHg	300 mmHg
Hydraulic Conductivity (cm/(s*mmHg)	7.16E-07	4.70E-07

Weekly Goals

- Create a positive control for the tissue damage assay
- Determine if optical microscopy is sufficient to assess damage

Tissue Damage Assessment

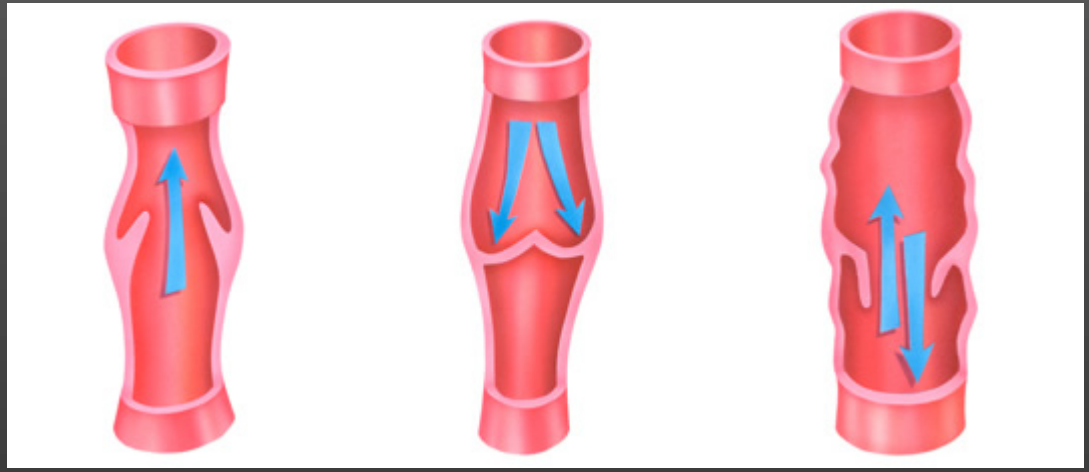
- ❖Evaluate pressure induced tissue damage
- ❖7 trials using improved prototype design
- ❖Immunohistochemistry to analyze tissue damage



Positive Control

- During a vascular bypass procedure, doctors distend the vein in order to prevent vasospasms as well as to blow out the valves that are inherent to vein structure.

- The vein we acquired this week had already been distended, so we were unable to run our tissue damage assessment.
- Rather we used the distended vein graft as a positive control for this assay



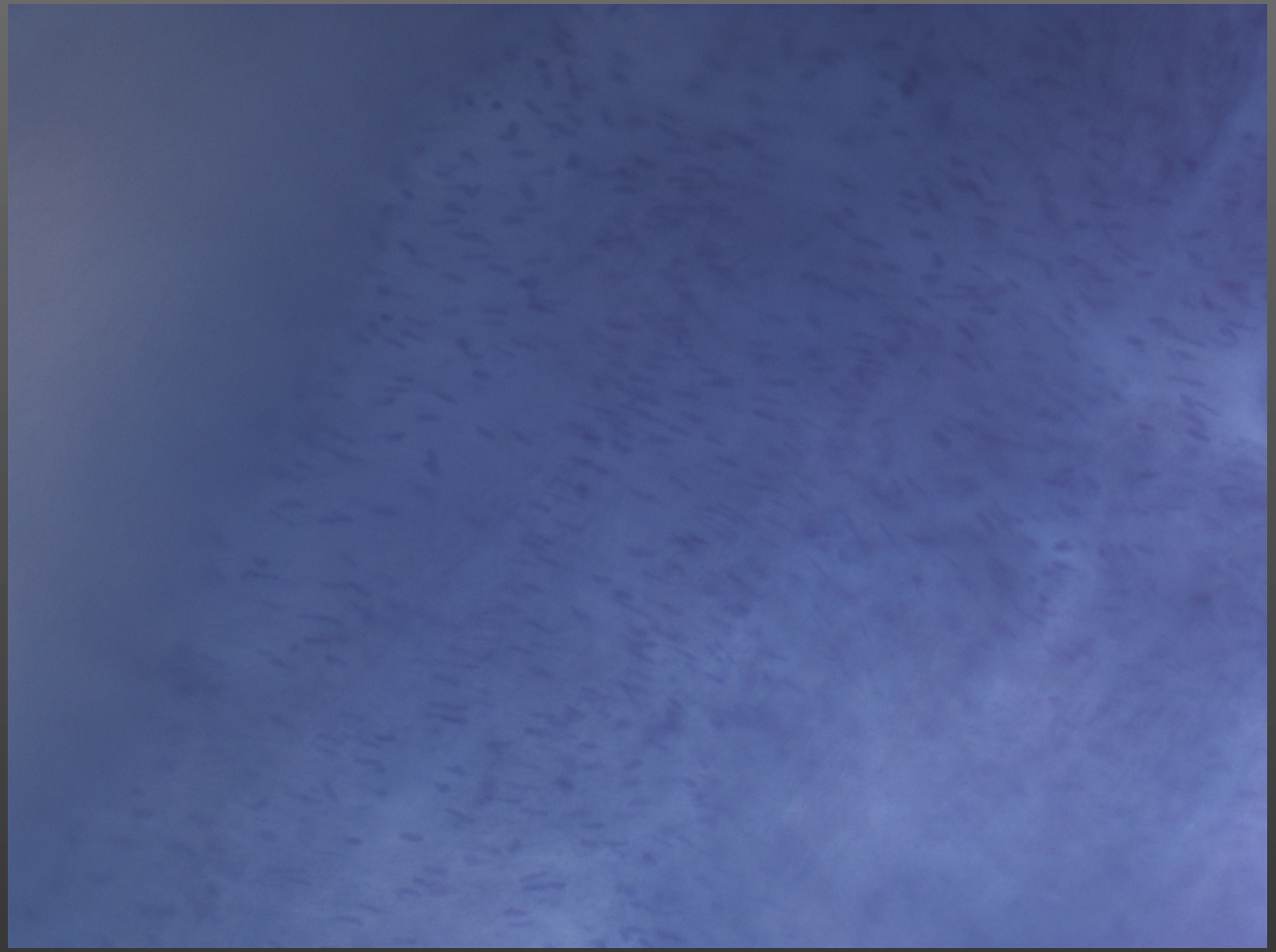
Veinsandlasercenterofnj.com

Protocol

- The vessel was flayed to expose the endothelial tissue
- The lumen endothelial tissue was covered with 200 microliters of 2% Evans Blue Dye
  - Dye stains the nuclei of intact endothelium and allows us to visualized the damaged areas where the basement membrane is exposed
- The dye was washed off using PBS++ after 10 minutes, and the vessel was imaged using an optical microscope

Results

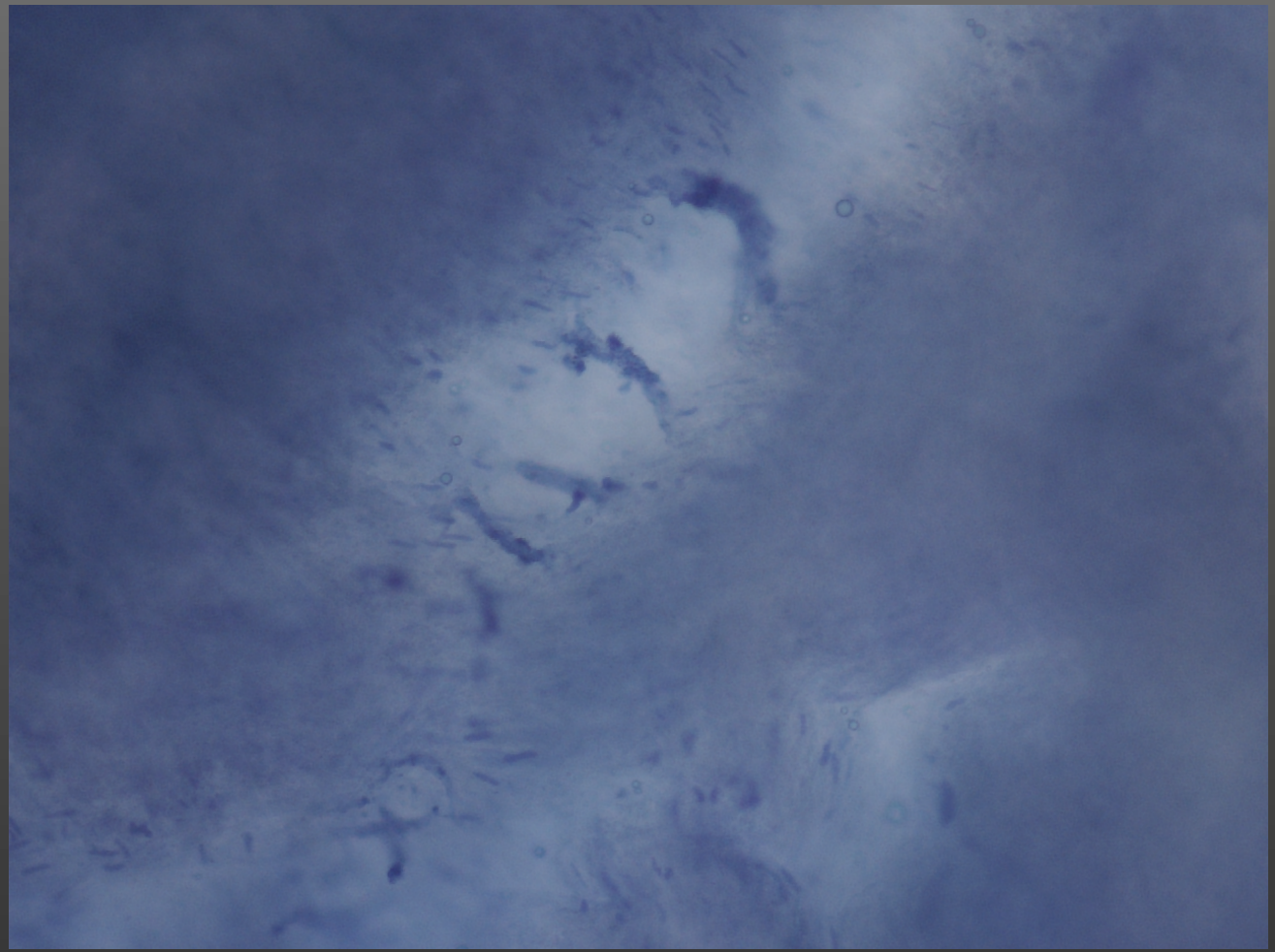
Intact Endothelium

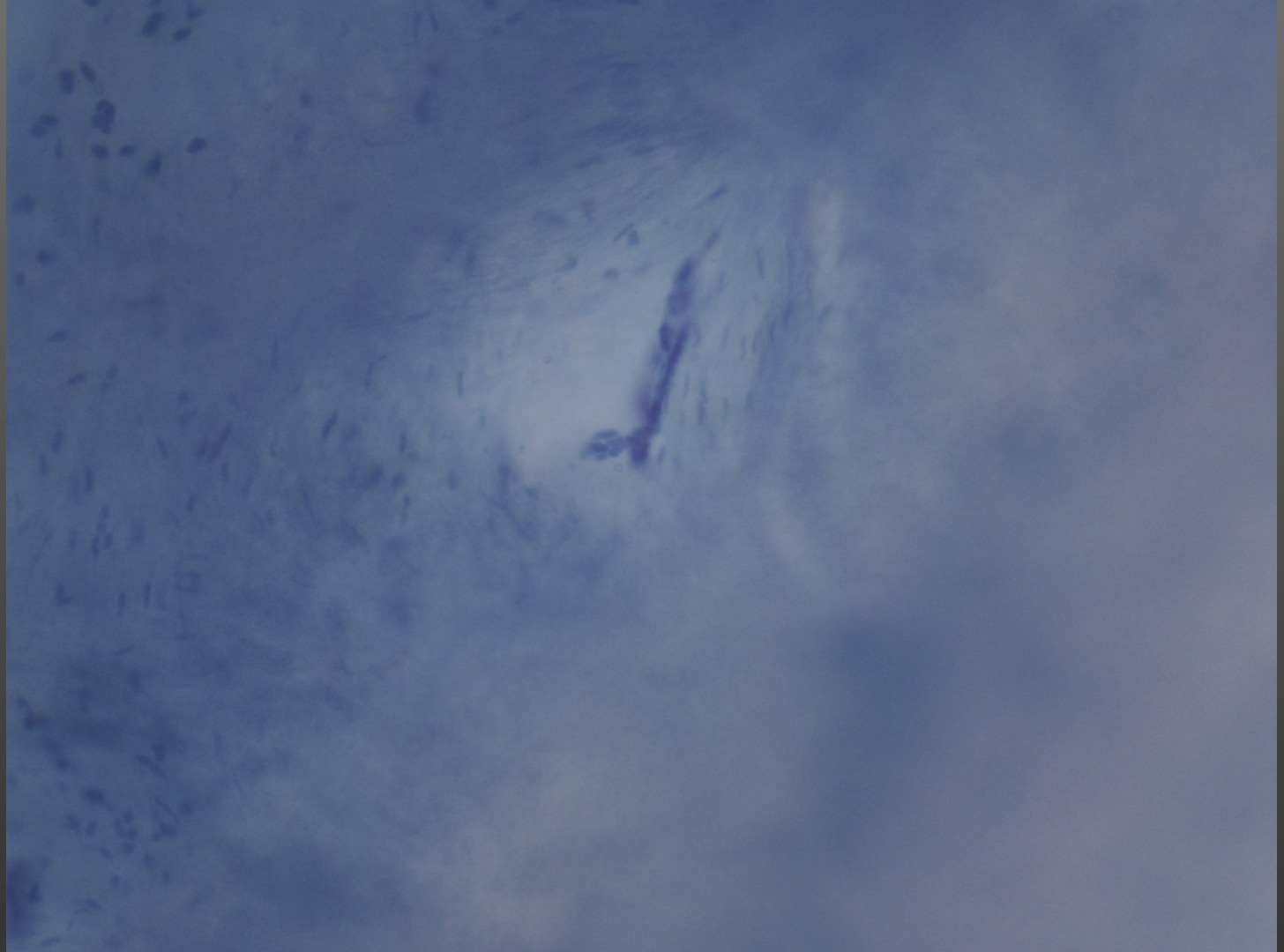


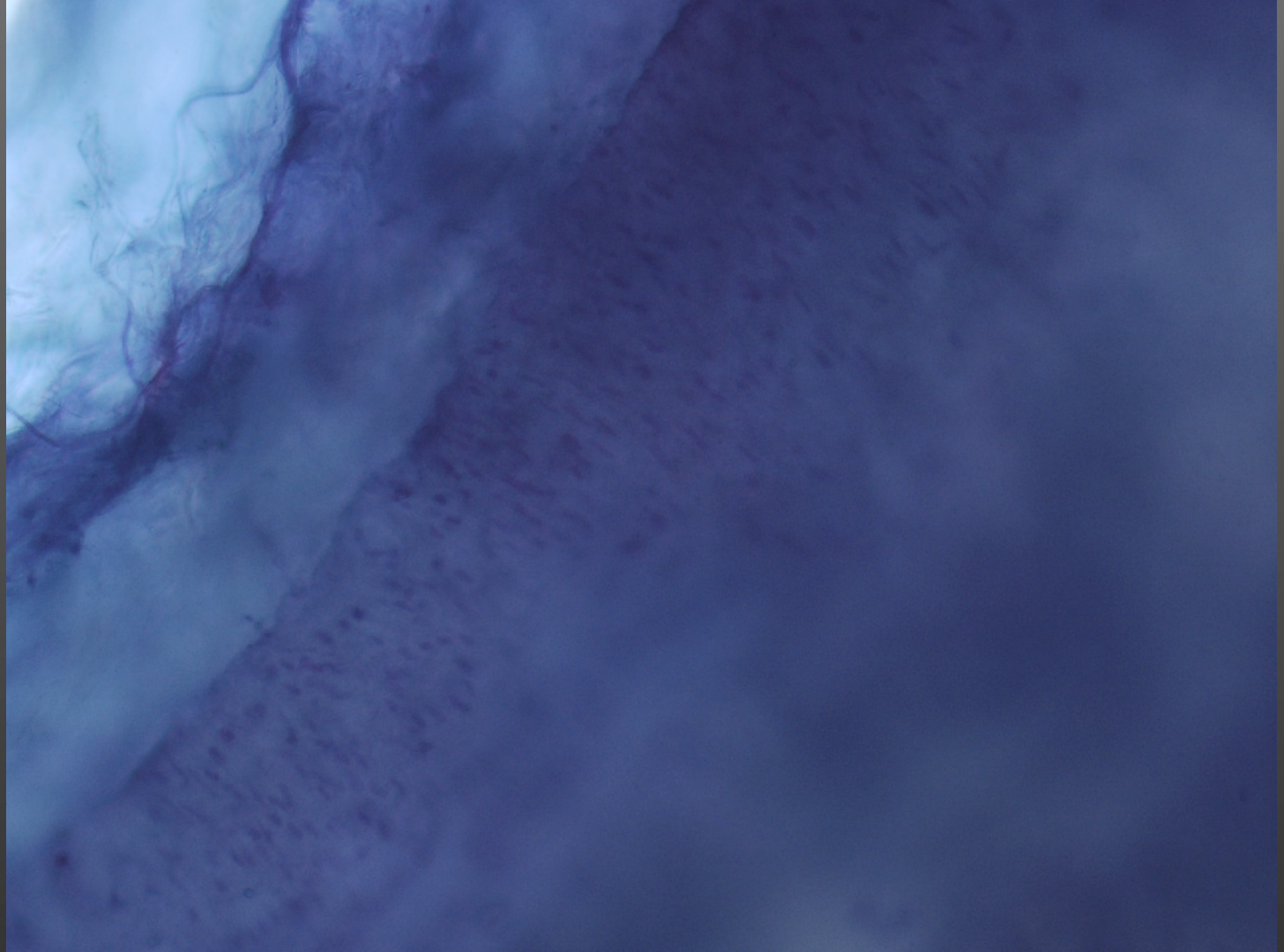
Results

Damaged Endothelium

Visible Basement Membrane





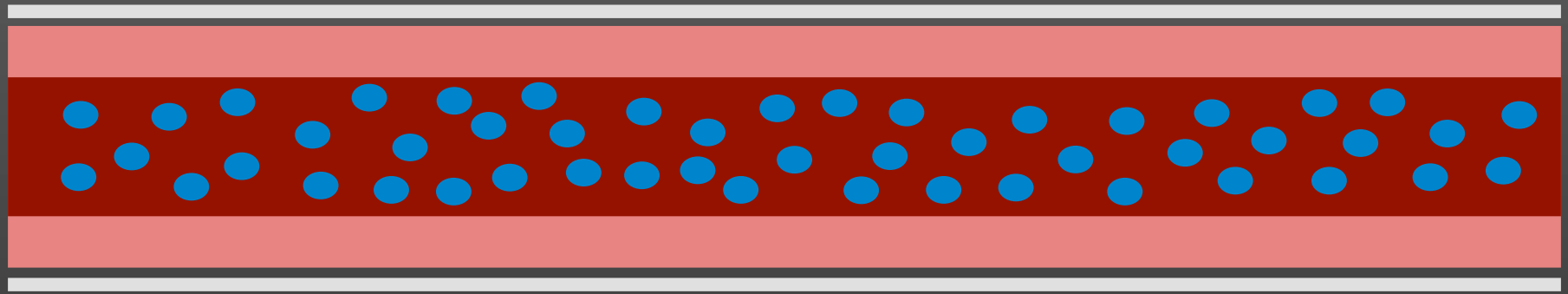


Results

- We will be able to use Evans Blue Dye to qualitatively assess tissue damage caused by the pressurization of our device

- The tissue will be evaluated on the following grounds:
  - Cobblestone morphology
  - Cuboidal contact
  - No visualized basement membrane

Future Tasks – Flow Experiment



1. Add comparable fluorescence molecule to solution
2. Pressurize the system
3. Section of vessel and add OCT compound
4. Freeze with dry ice and cryosection for imaging

Future Tasks

- Continue Pressure Induced Tissue Damage Assessment at varying pressures and controls
- Address safety benchmarks
- Efficacy trials for decreased graft failure rates
  - MK2 inhibitors decrease incidence of vein graft failure and occlusion (J. Alexander, Duke 2010)

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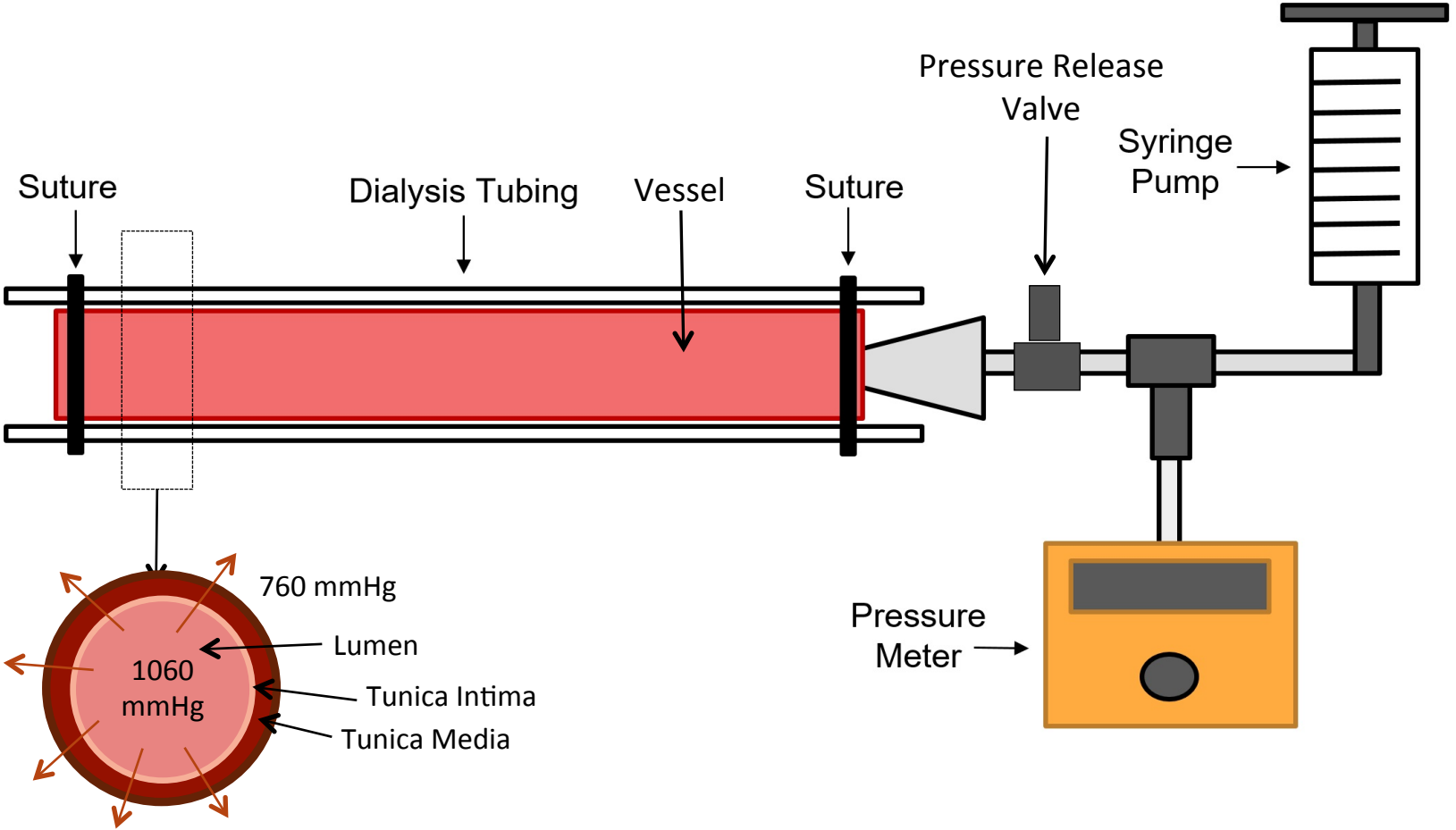
Questions


Suture
Dialysis Tubing
Vessel
Suture
Pressure Release Valve
Syringe Pump
760 mmHg
Lumen
1060 mmHg
Tunica Intima
Tunica Media
Pressure Meter