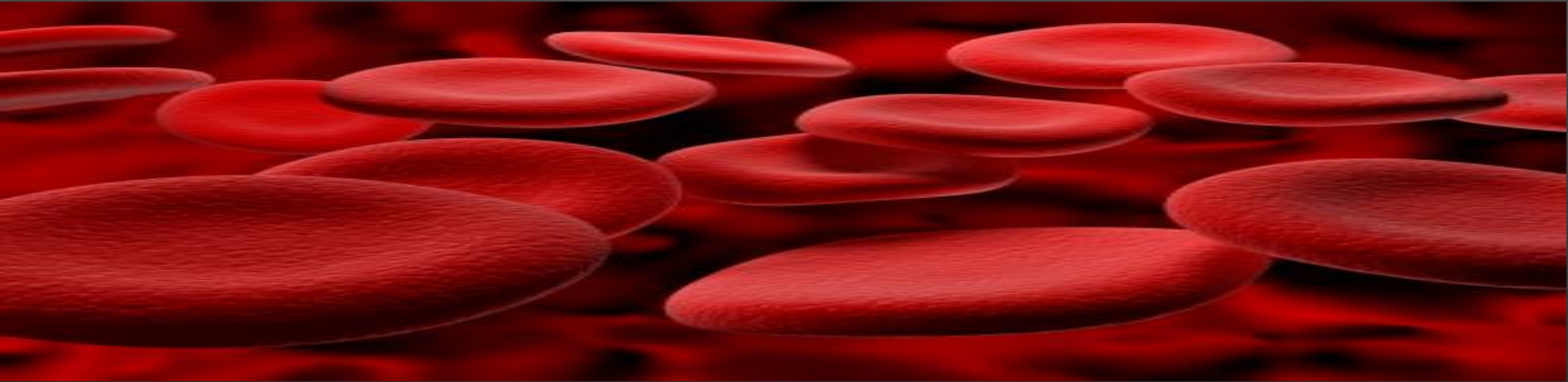


# Team Aggregation Domination Oral Report 2



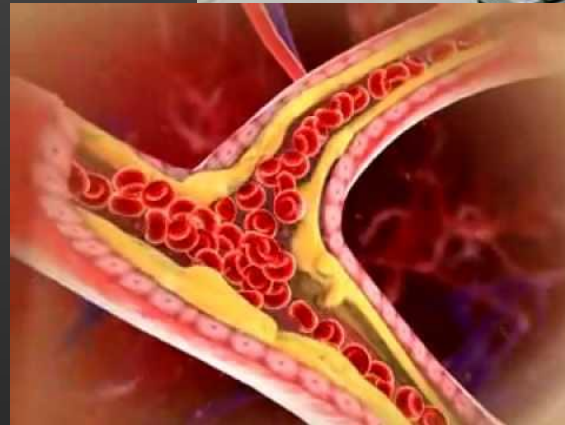
Kelly Hainline, Morgan Satterlee, Kevin Humphrey, and Cortnee Weinrich

# Agenda

- ❖ Background and Problem Statement
- ❖ Mechanism
- ❖ Goals
- ❖ Flow Experiment Protocol
- ❖ Results and Analysis
- ❖ Future Work



sissupply.com



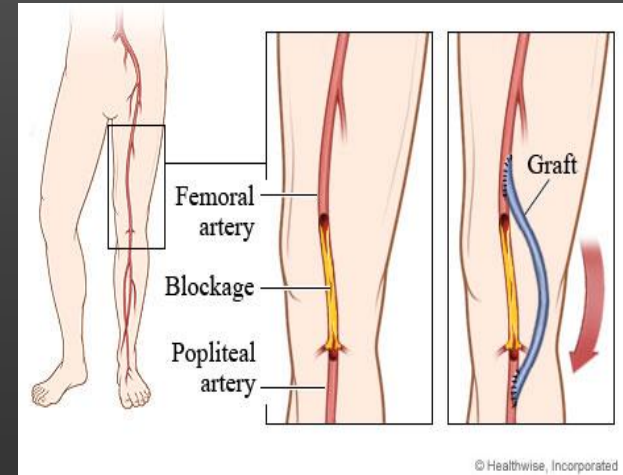
Youtube.com

# Background

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

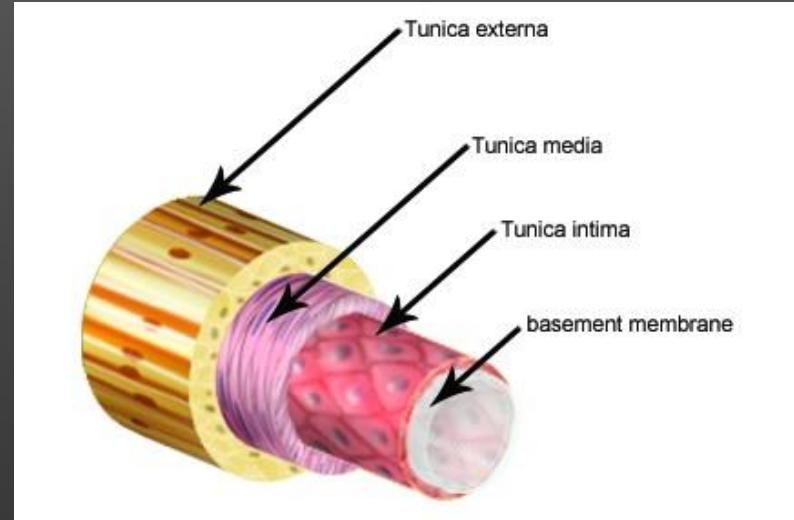
This failure is thought to be caused by the inflammatory response induced from trauma during transplantation.

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.



# 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

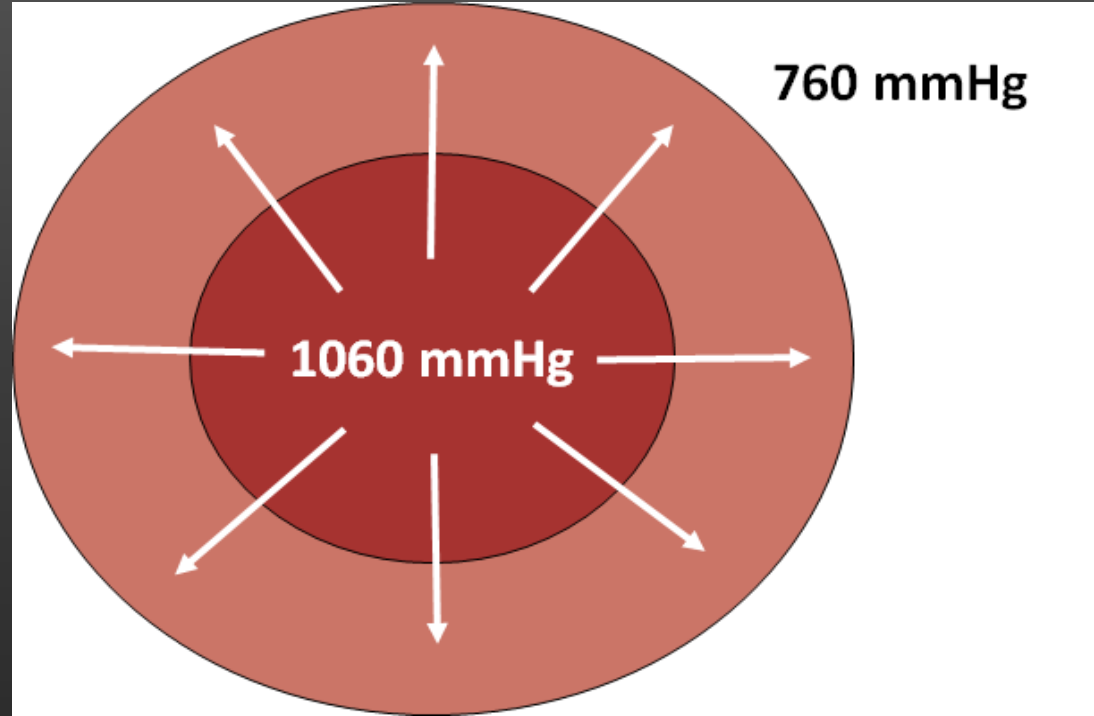
# Needs Assessment

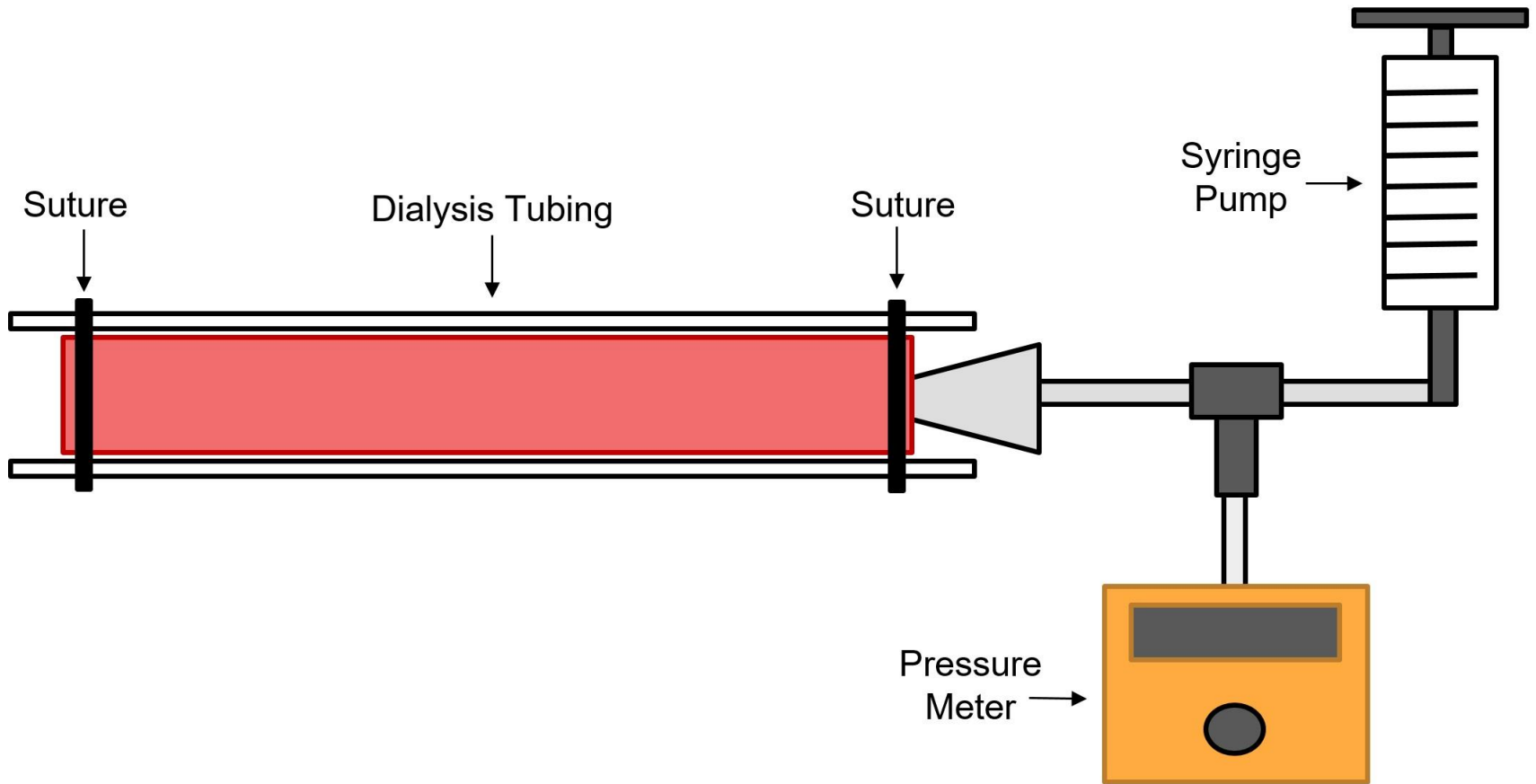


- Device should cause no toxicity to vein
- Integrate pressure release valve to prevent excess pressure
- Easily integrated into existing operating room technology
- Reasonable cost

# Mechanism

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



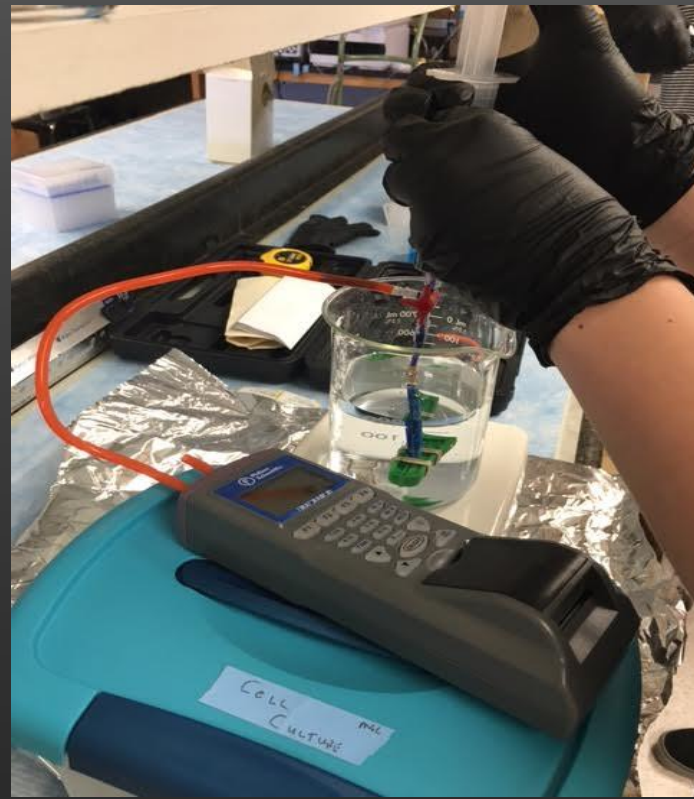
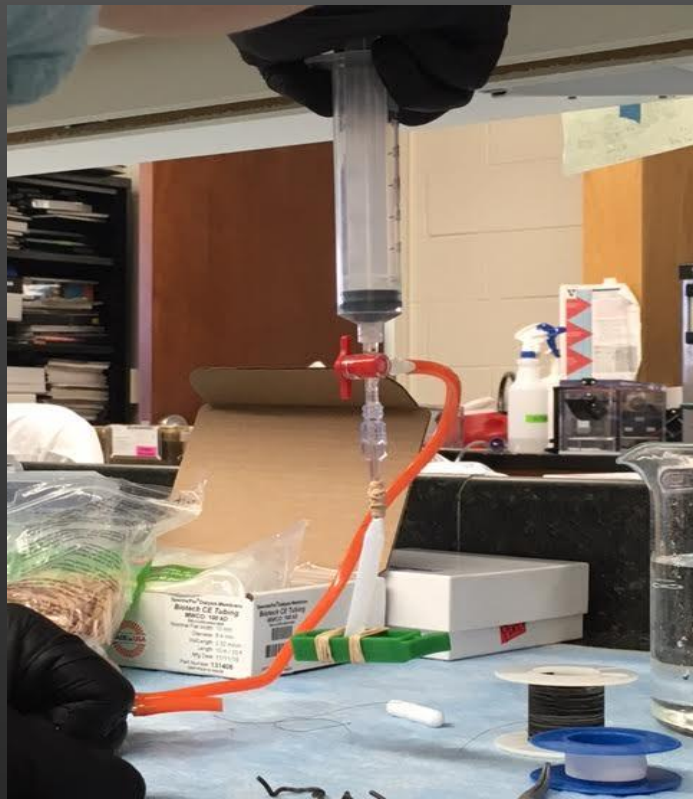


# Weekly Goals

- ❖ Ensure that flow occurs through dialysis tubing
- ❖ Find concentration over time of flow at 100 mmHg and 300 mmHg
- ❖ Test dialysis clamps to prevent device leakage



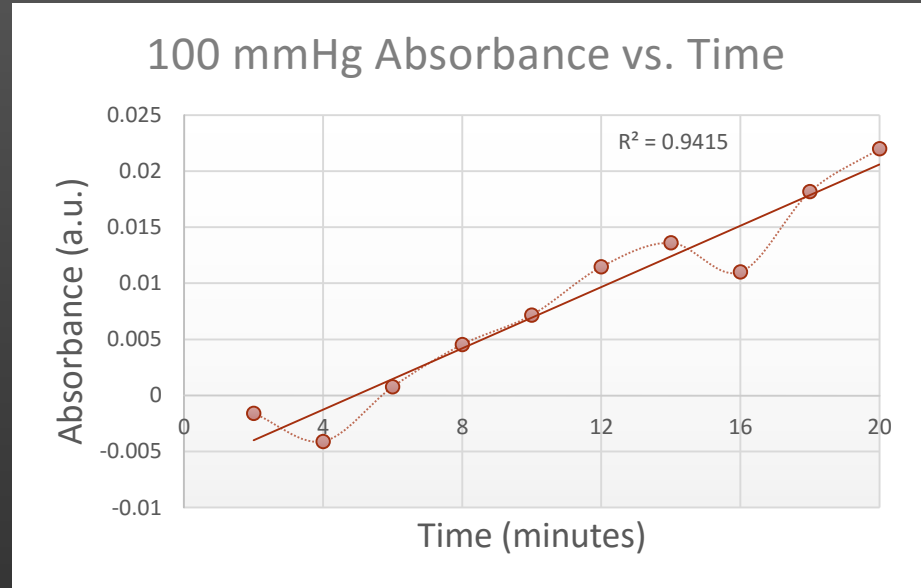
# Protocol



# Results

## 100 mmHg Flow Test Results

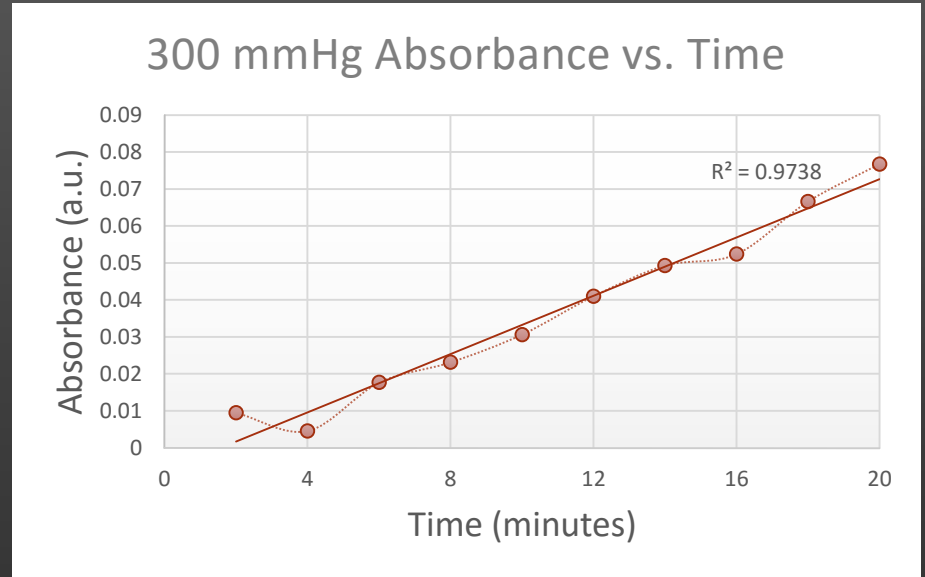
	1	2	3	Average	Relative to Background
Trypan	3.585700	OVER	3.754200	3.669950	
Background					
d	0.040500	0.043500	0.040200	0.041400	
2 min	0.039900	0.039900	0.039600	0.039800	-0.001600
4 min	0.036500	0.037500	0.037900	0.037300	-0.004100
6 min	0.041400	0.042800	0.042300	0.042167	0.000767
8 min	0.047300	0.044800	0.045700	0.045933	0.004533
10 min	0.049000	0.048300	0.048400	0.048567	0.007167
12 min	0.052300	0.054400	0.051900	0.052867	0.011467
14 min	0.056300	0.054400	0.054300	0.055000	0.013600
16 min	0.052700	0.052100	0.052400	0.052400	0.011000
18 min	0.059200	0.058700	0.060800	0.059567	0.018167
20 min	0.063600	0.063100	0.063500	0.063400	0.022000



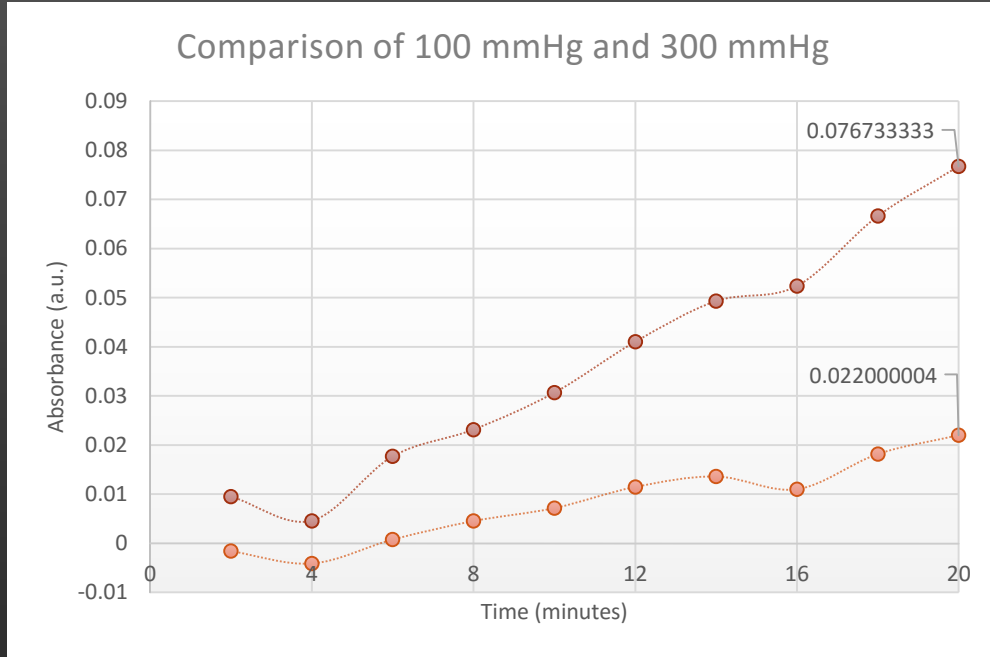
# Results

## 300 mmHg Flow Test Results

	1	2	3	Average	Relative to Background
Trypan	3.335000	3.498100	3.476800	3.436633	
Background	0.040100	0.040100	0.040400	0.040200	
2 min	0.064800	0.042300	0.042000	0.049700	0.009500
4 min	0.045700	0.044500	0.044100	0.044767	0.004567
6 min	0.067400	0.052200	0.054000	0.057867	0.017667
8 min	0.060700	0.064800	0.064500	0.063333	0.023133
10 min	0.069400	0.071400	0.071700	0.070833	0.030633
12 min	0.081400	0.078700	0.083500	0.081200	0.041000
14 min	0.088900	0.088600	0.091000	0.089500	0.049300
16 min	0.092200	0.092600	0.092900	0.092567	0.052367
18 min	0.107600	0.104700	0.108100	0.106800	0.066600
20 min	0.116100	0.117600	0.117100	0.116933	0.076733



# Results



To make sure there were no leaks we compared the data and saw what we expected (3x increase in absorbance).

# Data Analysis

Goal: To compare hydraulic conductivity of dialysis tubing with veins.

Equations used:

$$\text{Flow Rate (cm}^3\text{/sec)} = \frac{\text{Absorbance}_{\text{peak}}}{\text{Absorbance}_{\text{Trypan}}} * \frac{\text{Volume}_{\text{bath}}}{\text{Time}_{\text{peak}}}$$

$$\text{Surface Area (cm}^2\text{)} = 2 * \text{pi} * \text{radius} * \text{length}$$

$$\text{Hydraulic Conductivity} \left( \frac{\text{cm}}{\text{sec} * \text{mmHg}} \right) = \frac{\text{Flow Rate}}{(\text{Surface Area}) * (\text{Pressure})}$$

# Data Analysis

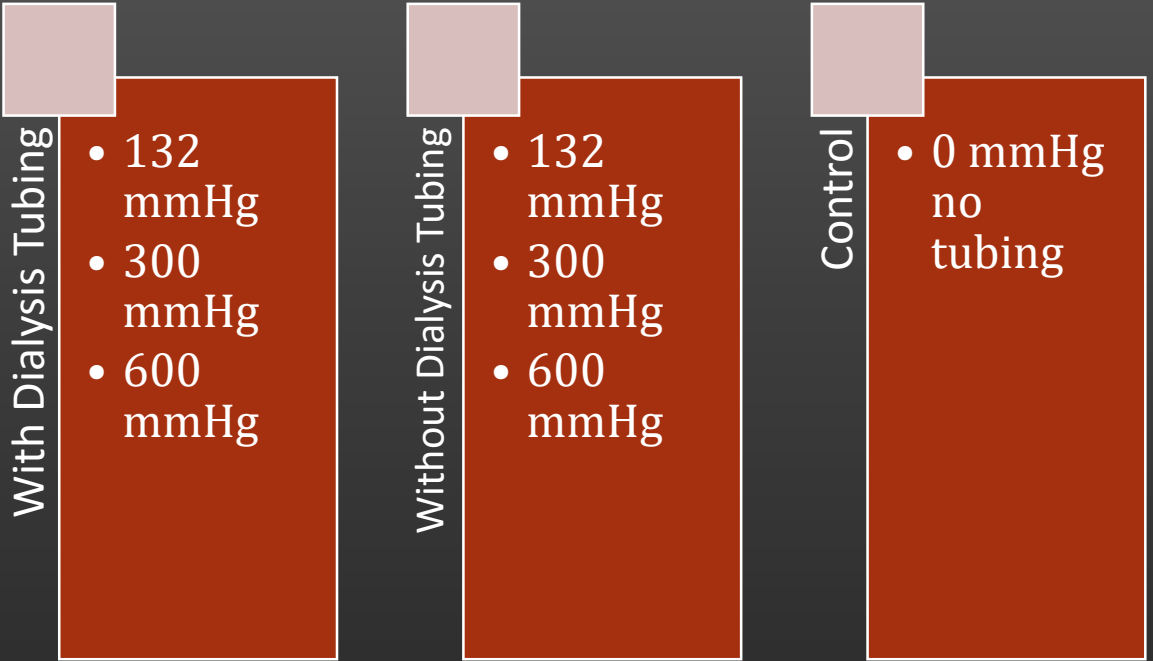
	100 mmHg	300 mmHg
Hydraulic Conductivity	7.160E-07	4.701E-07

From Vargas et al. (1986) it was found that vena cava endothelium had a hydraulic conductivity of about  $1.23 \cdot 10^{-7}$  cm/s\*mmHg.

# Future Tasks

## Pressure-Induced Tissue Damage Assessment

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



# Future Tasks

- ❖ Histology to address depth of drug permeation
  - ❖ Compare to today's standard
  - ❖ Evans Blue Dye
- ❖ Fluorescence assay to address depth of drug permeation
- ❖ Address safety benchmarks (??)
- ❖ Efficacy trials for decreased graft failure rates
  - ❖ MK2 inhibitors decrease incidence of vein graft failure and occlusion (J. Alexander, Duke 2010)



# Questions