A Parallel Plate Flow Chamber to Investigate Endothelial Glycocalyx Remodeling After Pneumonectomy

Natasha Cruz-Calderon, Lydia Masse, Gillian Miller, Taylor Paradis & Samantha Raskind

Meet the team

Gillian Miller BME 22'- Tissue Engineering/Drug delivery

Taylor Paradis BME & ME 22'- Biomaterials

Lydia Masse BME '22- Tissue Engineering/Drug Delivery

Natasha Cruz-Calderon BME 22'- Tissue Engineering/Drug Delivery

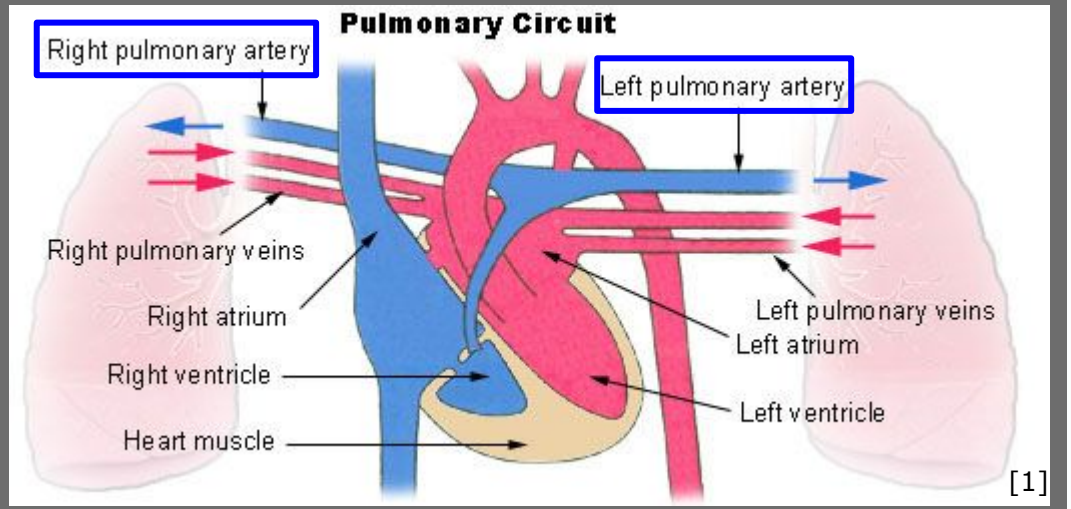
Samantha Raskind BME 22'- Tissue Engineering/Drug Delivery

Solomon Mensah- Postdoctoral Fellow, 2020, Worcester Polytechnic Institute

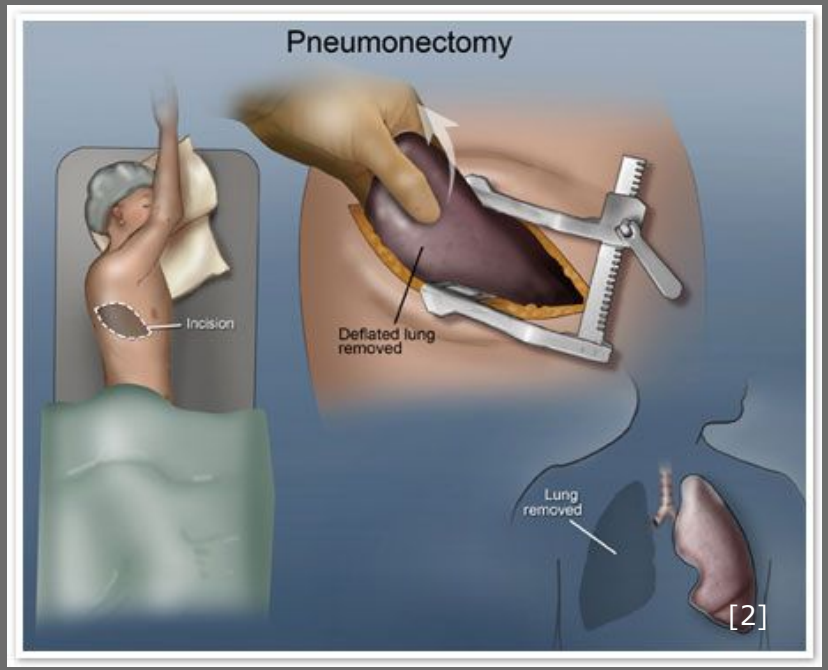
Kristen Billiar- Professor & Department Head, Worcester Polytechnic Institute

External Advisor: Dr. Aaron Waxman - Director, Pulmonary Vascular Disease Center, Brigham's & Women's Hospital

Lung Physiology and Pneumonectomy



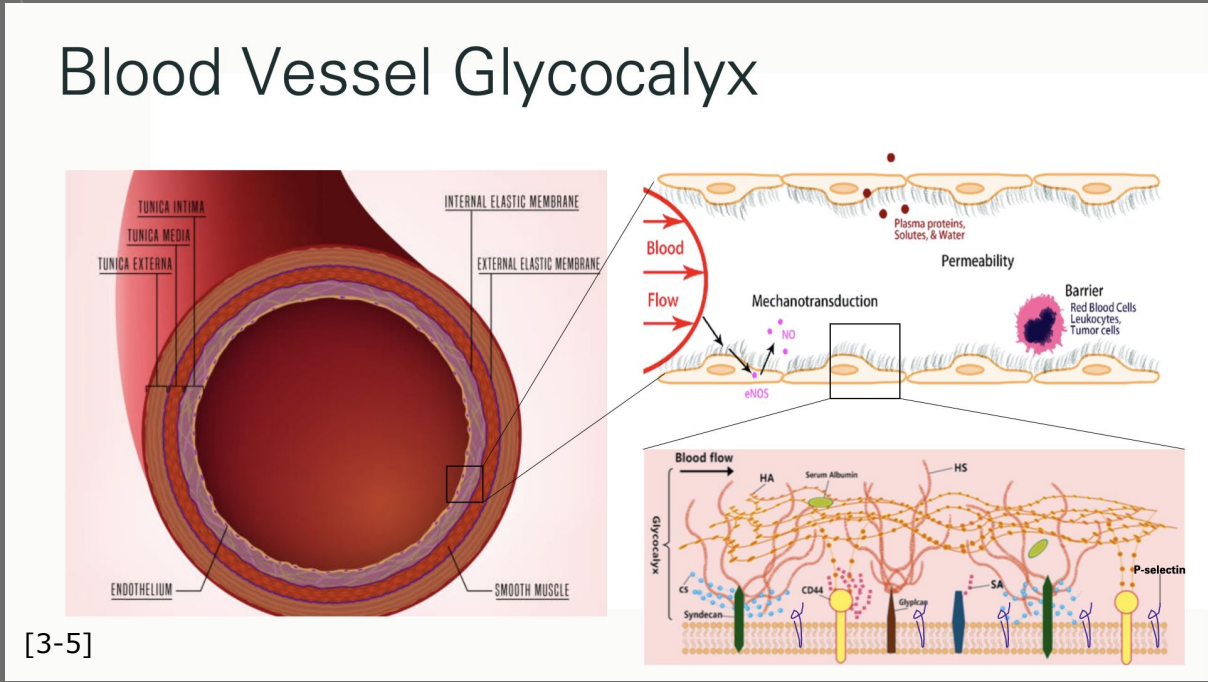
[1]



[2]

Endothelial Glycocalyx

- The glycocalyx is responsible for numerous physiological functions
  - Protects the endothelial cells
  - Regulates exchange between bloodstream and endothelial cells
- Disturbed flow in the arteries can cause damage to the endothelial glycocalyx



[3-5]

Need Statement

- **Need:** develop a device that more accurately models pulmonary arteries and mimics pneumonectomy conditions to investigate cellular changes in the endothelial glycocalyx

- **Clinical Significance:** replicating pneumonectomy conditions in vitro would allow for potential explanations to pneumonectomy conditions to be studied and future therapies targeting these aspects developed

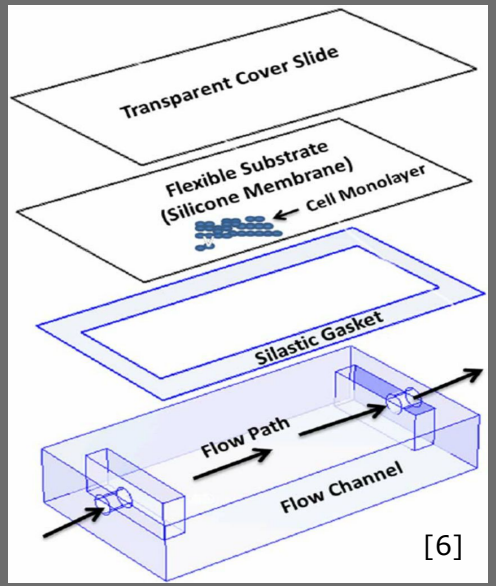
Project Objectives

1. Develop a device that models the geometries and bifurcation of the pulmonary arteries
2. Investigate the effect of increased shear stress & flow on HLMVEC
3. Analyze cell coverage, discontinuity in the endothelial layer, and function of cells after pneumonectomy conditions

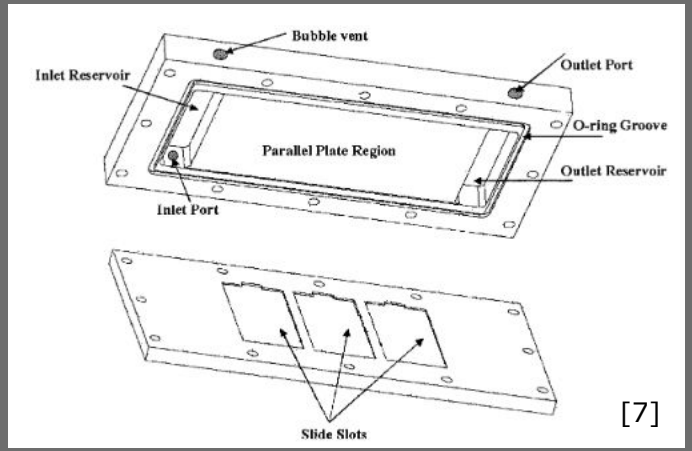
Functional & Performance Specifications

	Function	Performance
Model Type	❖ A model that allows for controlled flow, is biocompatible, and models arteries	➢ Glass slides: 10 mm x10 mm ➢ Angles of Bifurcation: RPA-MPA= 125°, LPA-MPA= 112° ➢ Diameters: MPA= 29.5 mm, RPA= 19.8 mm, LPA= 22.1 mm ➢ Material: acrylic with teflon gasket
Cell Type	❖ A cell type that models response to the change in flow and shear stress	➢ Human Lung Microvascular Endothelial Cells
Pneumonectomy	❖ Blood flow cut off to one pulmonary artery to model a pneumonectomy procedure	➢ Model Right, and Left pneumonectomy and Control/No pneumonectomy ➢ The distance the artery will be cut is 1-2 cm
Blood Flow	❖ A constant blood flow (cardiac output) in all experimental models	➢ 171.6 cm^3/s is average blood volume flow for the pulmonary arteries
Shear Stress	❖ A pump to create controlled, laminar flow and shear stress on cells	➢ Cells on slide will be stained and imaged after experiments ➢ The normal shear stress for the pulmonary arteries is approximately 5-10 dynes/cm^2

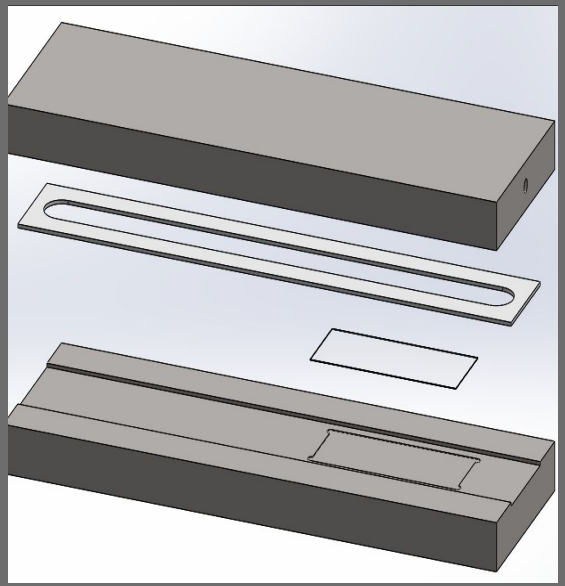
Parallel Plate Flow Chamber Research



Design in Literature #1



Design in Literature #2

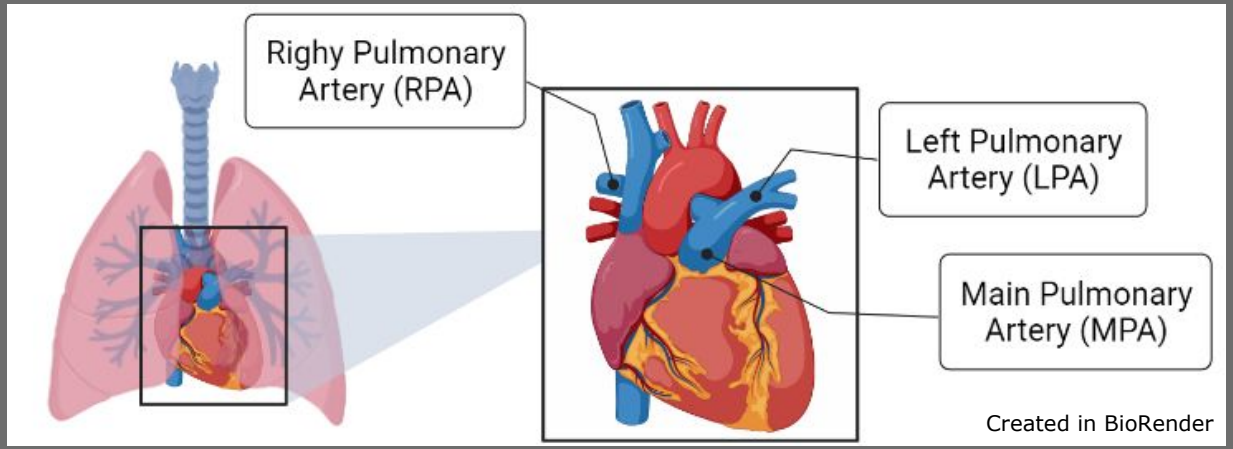


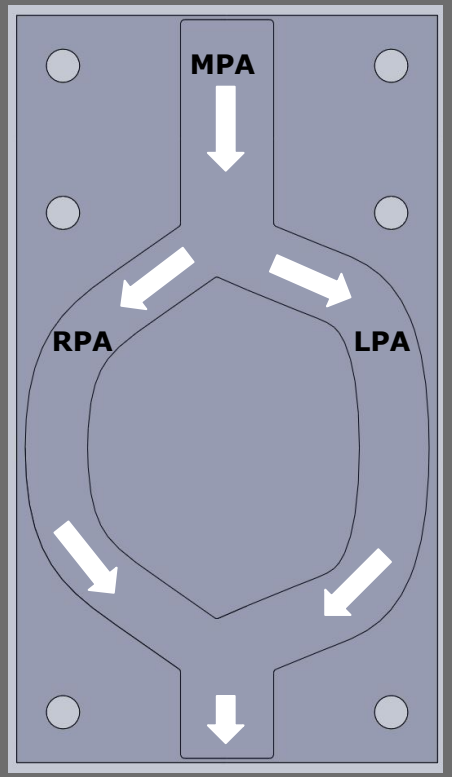
Previously Used Model

Pugh Analysis

Designs	Design From Literature #1	Design From Literature #2	Previously Used Model
Affordability	0	0	0
Functionality	0	0	0
Leak Prevention	1	1	1
Multiple Testing Points	0	1	-1
Ease of Machining	1	1	1
Ability to Manipulate Flow Path	-1	-1	1
Total Score	1	2	2

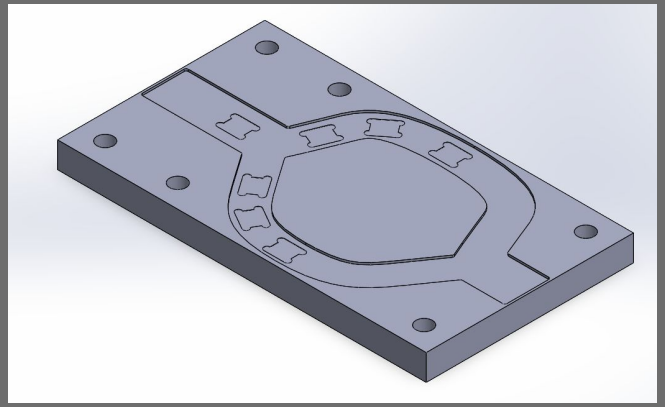
Modeling and Flow Simulations



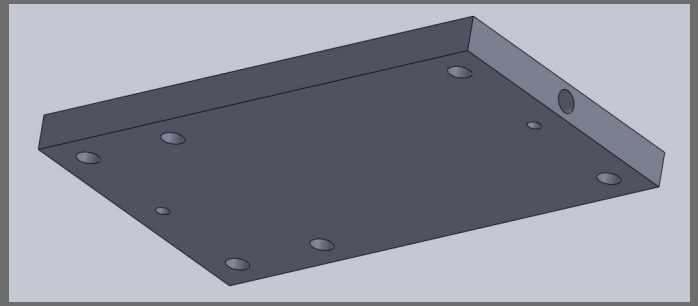


Assembly

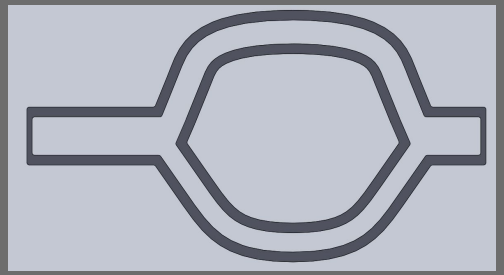
Bottom Plate



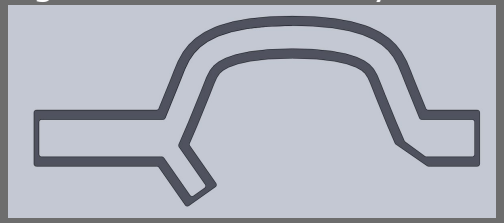
Top Plate



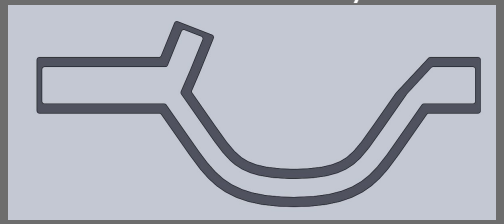
Control Gasket



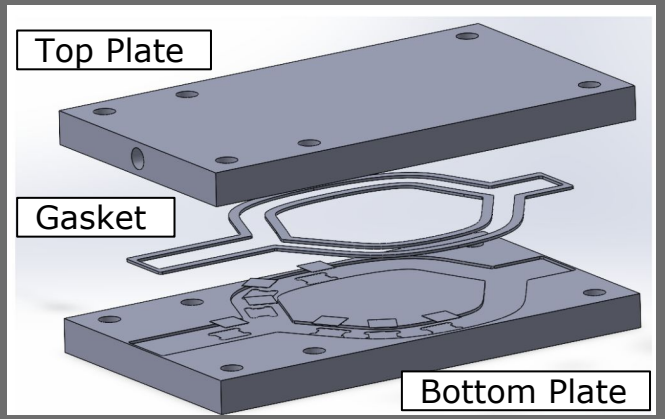
Right Pneumonectomy Gasket



Left Pneumonectomy Gasket

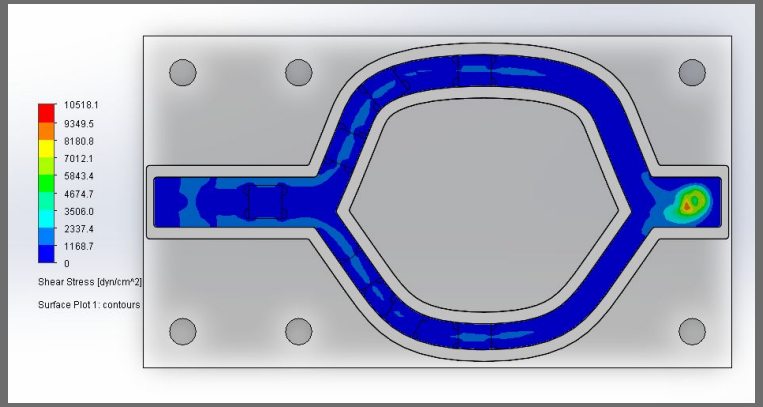


Final Assembly - Expanded View

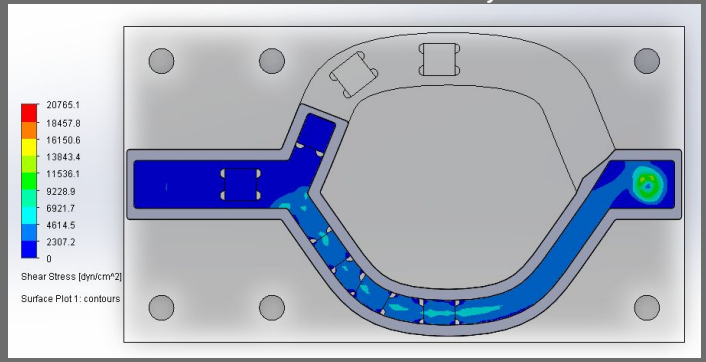


Flow Simulation Shear Stress Visuals

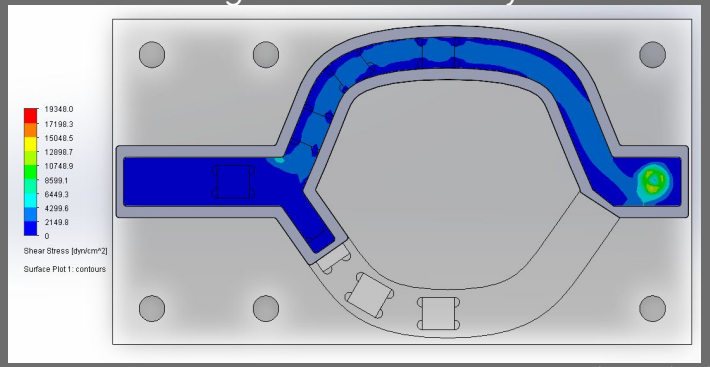
No Pneumonectomy – Control



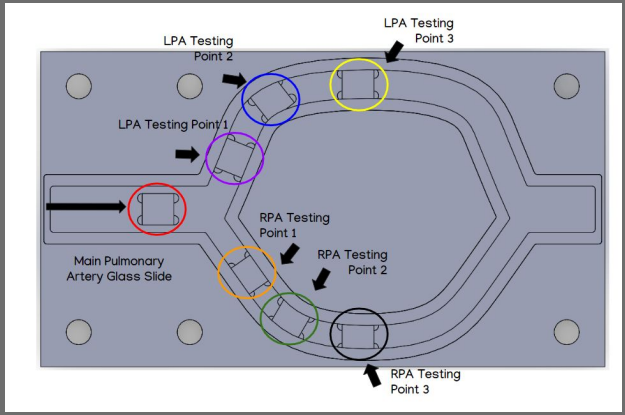
Left Pneumonectomy

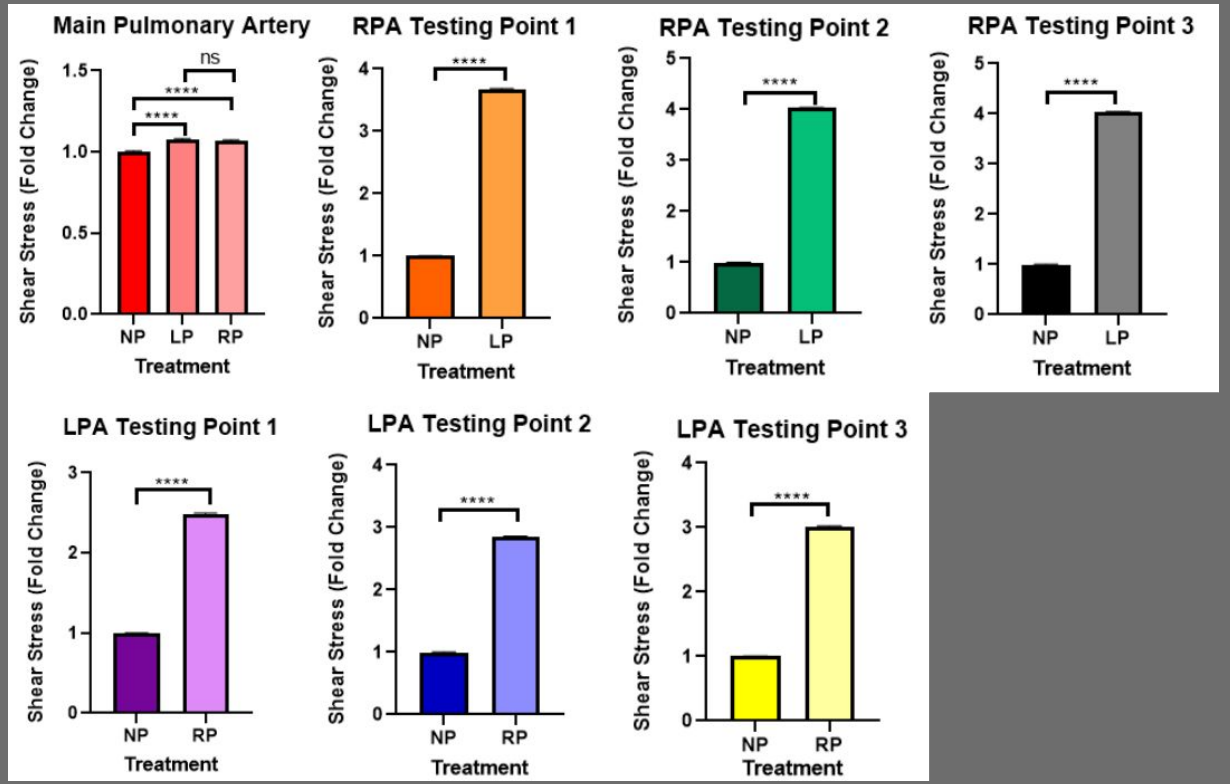


Right Pneumonectomy



2D Flow Simulation Data





Verification & Validation

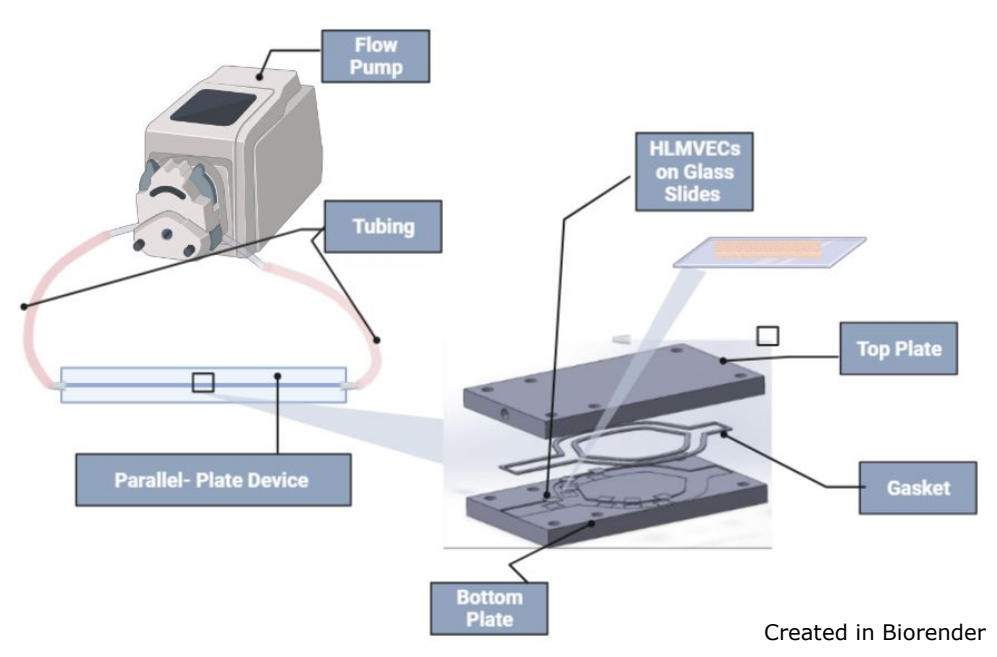
Before Alterations

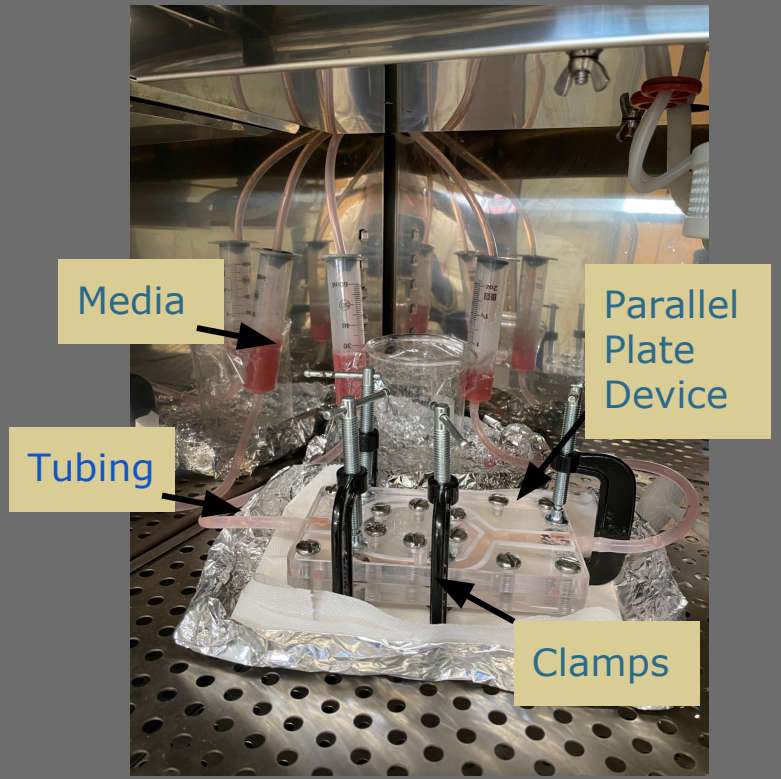
Control

Left Pneumonectomy

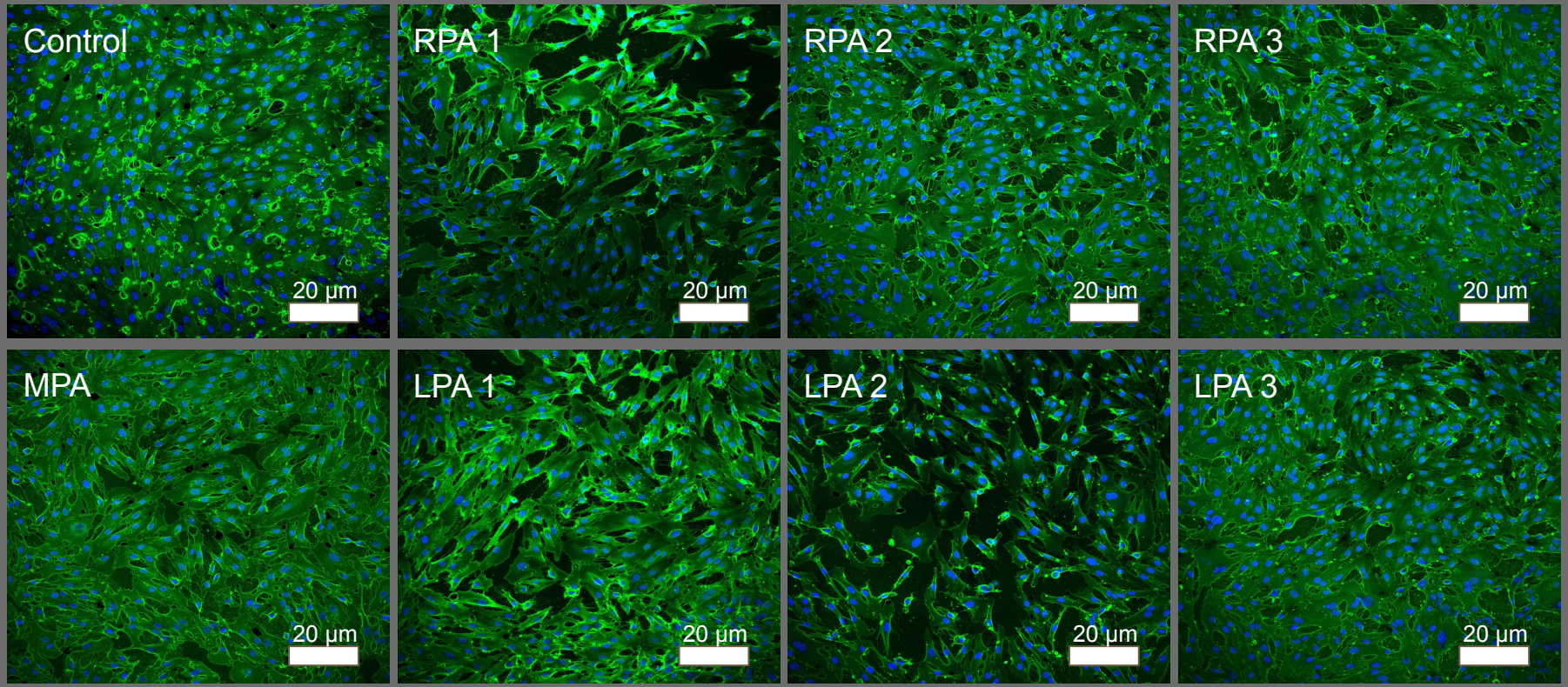
Right Pneumonectomy

Experimental Setup



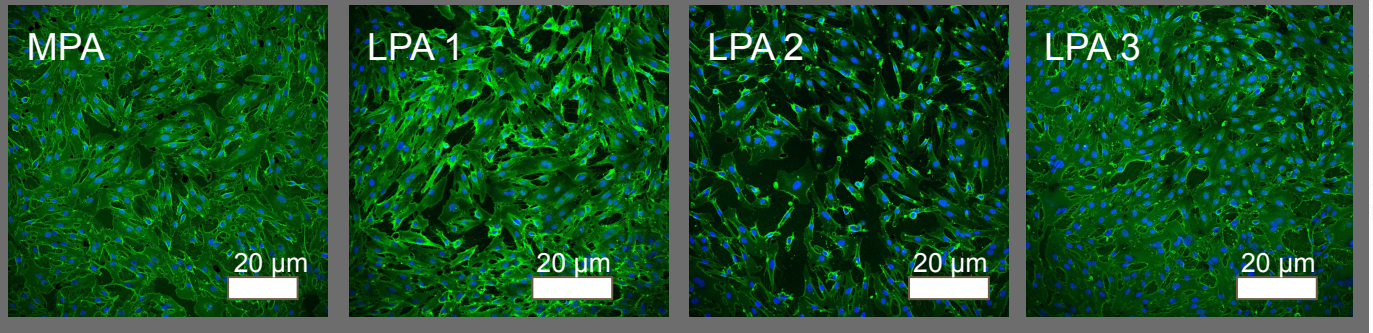


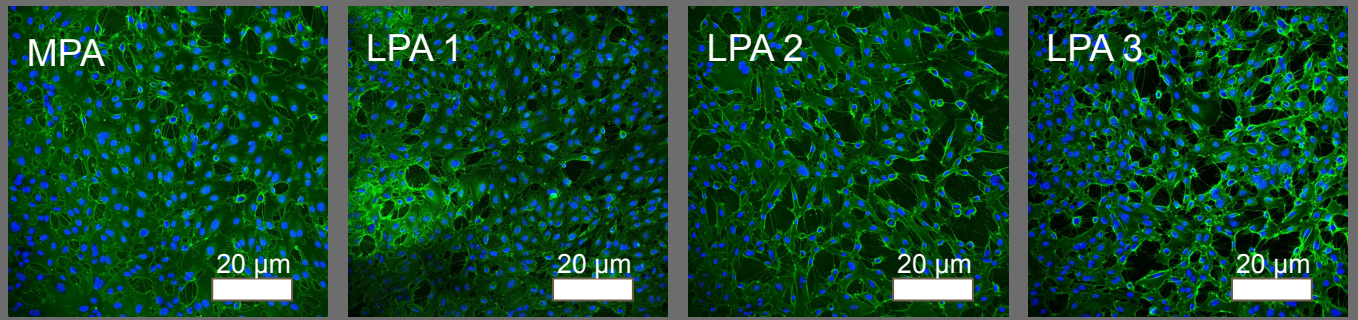
No Pneumonectomy



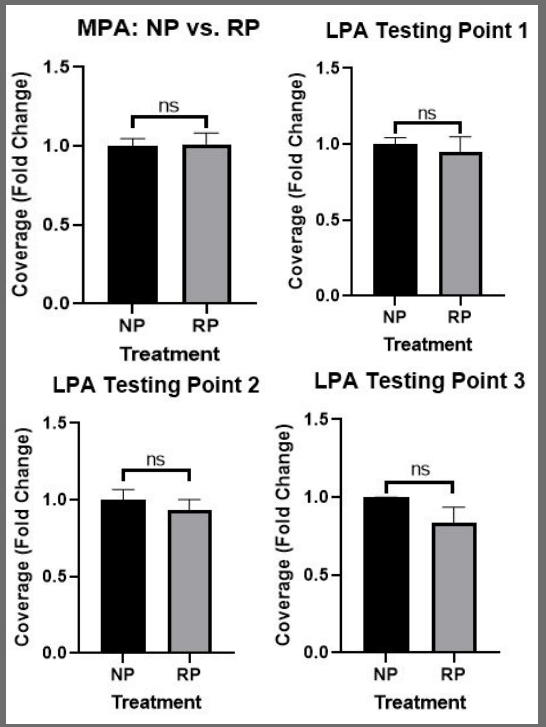
Right Pneumonectomy

No Pneumonectomy



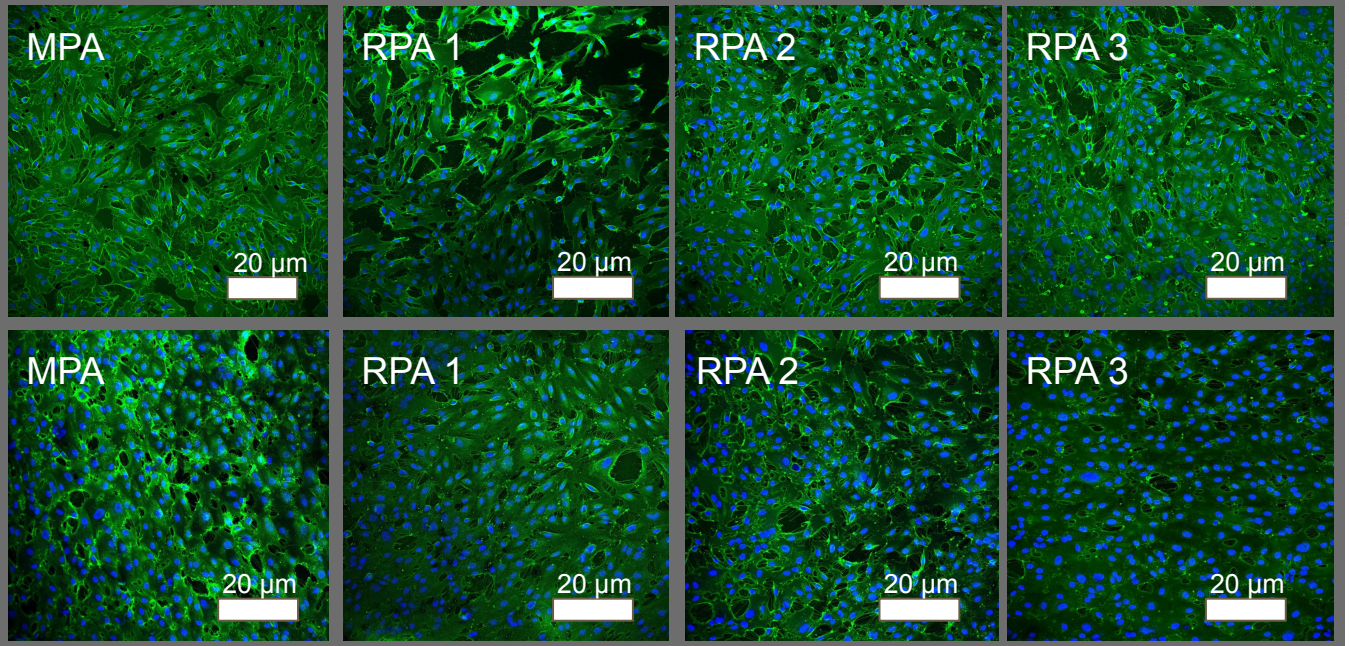


Right Pneumonectomy

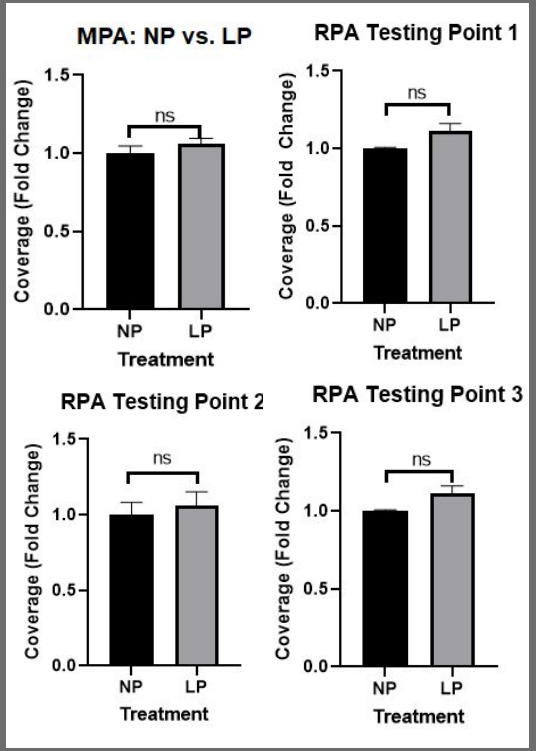


Left Pneumonectomy

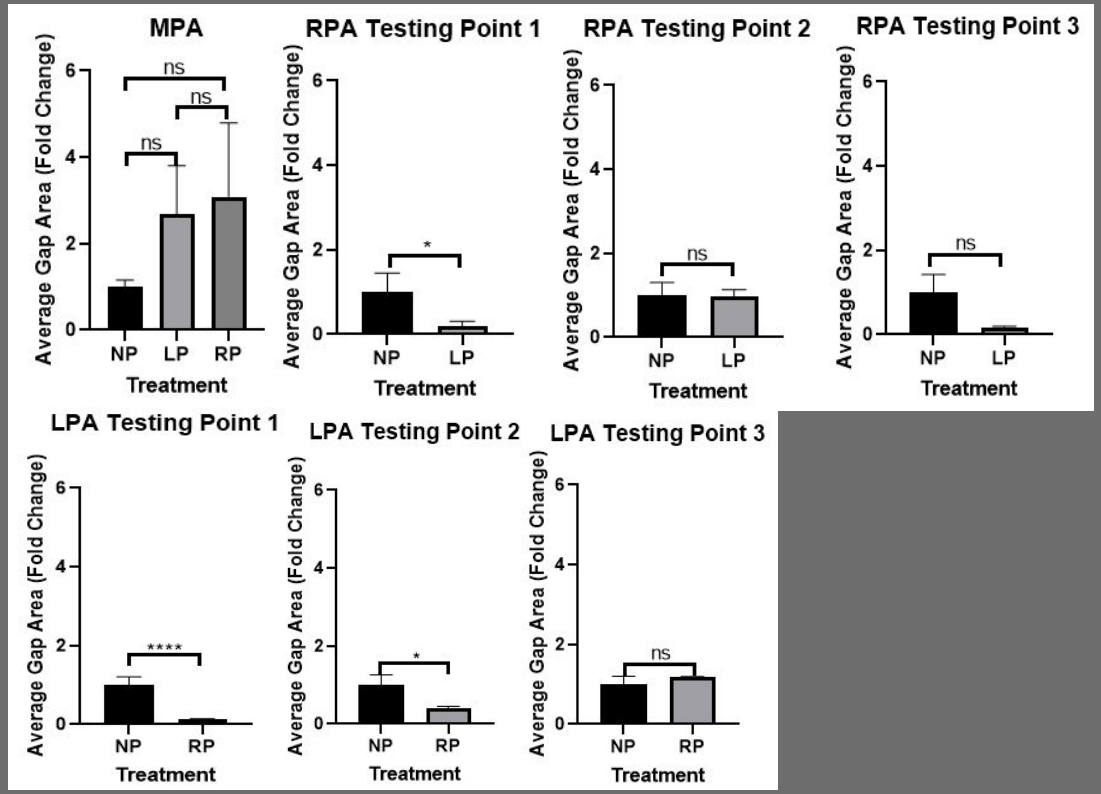
No Pneumonectomy



Left Pneumonectomy



Analysis of Discontinuity in the Endothelial Layer



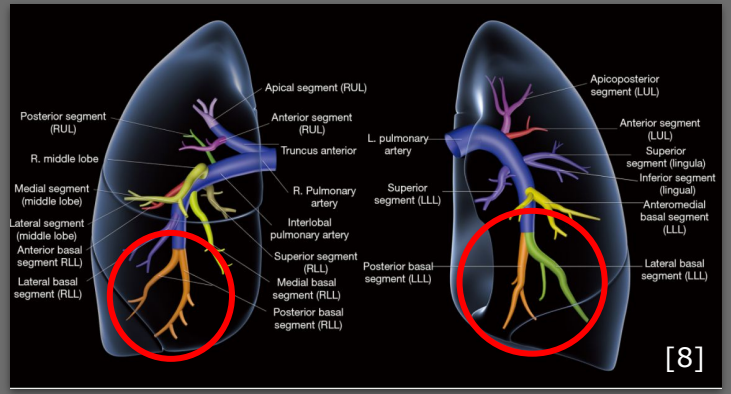
- We hypothesized that the discontinuity would increase after a pneumonectomy
- More experiments are required to support the hypothesis

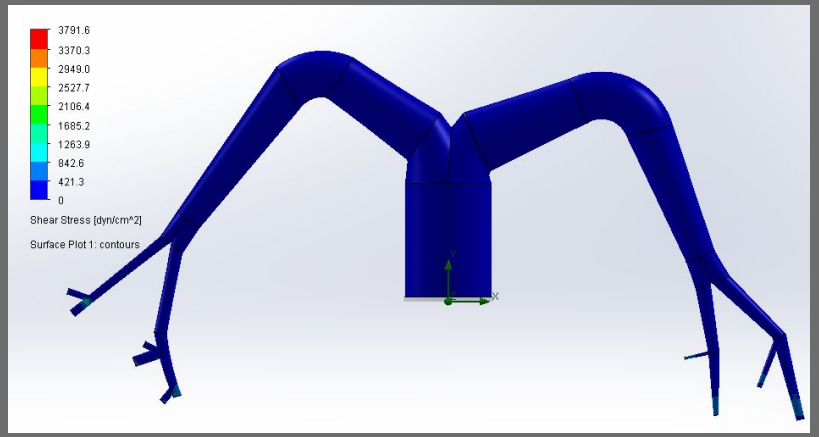
Discussion

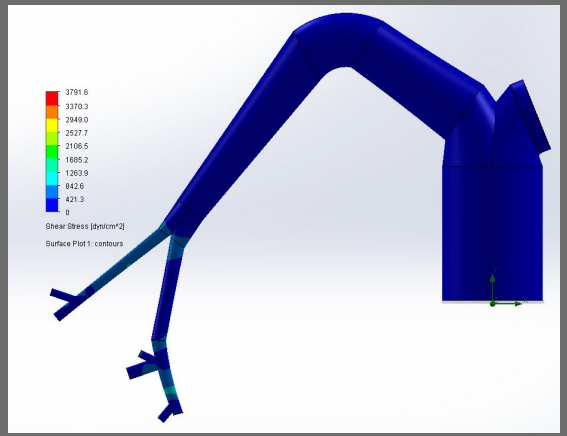
- We hypothesized that after a pneumonectomy the increase in shear stress would cause discontinuity in the endothelial layer and decrease cell coverage
- Flow simulations results showed a large increase in shear stress magnitude supported by the literature and hypothesis
- The coverage data collected indicated the possibility of loss of cellular function under pneumonectomy conditions
    - Although we can see trends in the data, more experiments and more cell analysis needs to be done in order to prove significance

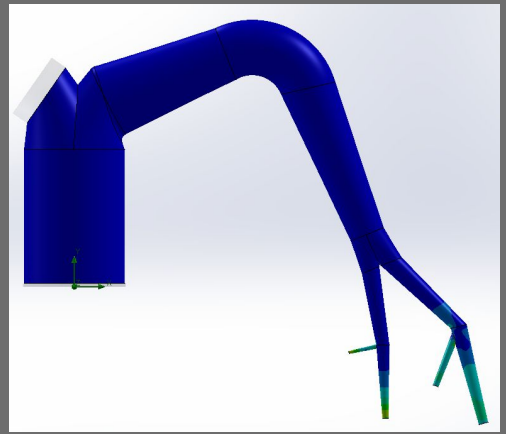
Future Direction - 3D Model

Alternative 3D Model Design – Solidworks

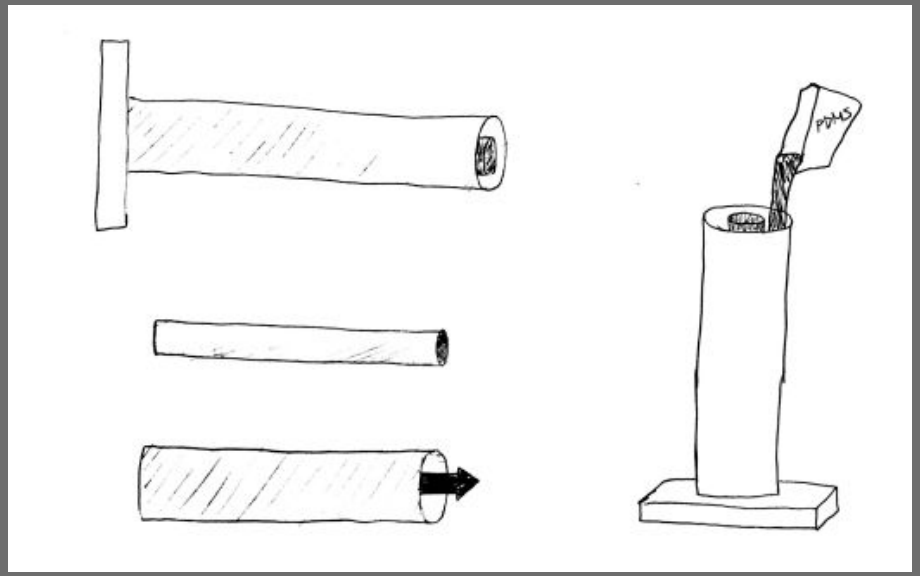


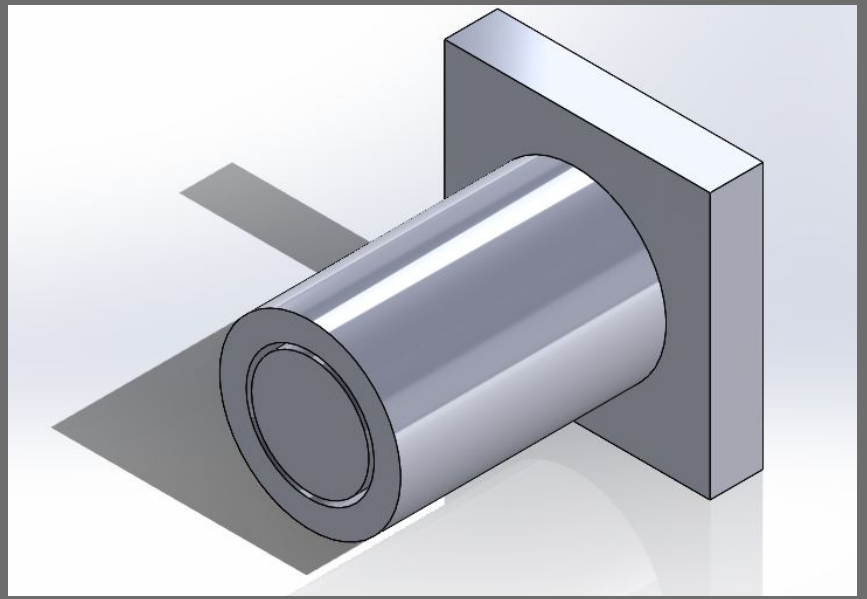






Alternative 3D Model Design - Fabrication





Alternative 3D Model Design - Recommendations

- Difficulties
  - Time and budget constraints
  - 3D printing availability
  - Technical problems
- Possible Solutions
  - Ensure sole focus
  - Different materials

Acknowledgements

- WPI Advisors: Solomon Mensah & Kristen Billiar
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- WPI Washburn & Goddard Machine Shop
- WPI BME Department: Lisa Wall, Rob Kirch, and Victoria Bicchieri

WPI

Thank you!

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