Developing an Organ-on-a-Chip Device to Determine the Impact of ECMO Life-Support on the Aorta

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Introduction

ECMO
Extracorporeal membrane oxygenation (ECMO) supports pulmonary function in patients with acute or chronic lung disease.

Mixing Zone
As blood is returned from the ECMO device to the distal aorta, the retrograde flow collides with antegrade cardiac output creating a mixing zone with a nonphysiologic flow pattern.

Patient Outcomes
In a study of patients weaned from ECMO, 20% had major vascular abnormalities (1). A potential explanation for these abnormalities is the nonphysiologic flow in the mixing zone.

Motivation
Despite the widespread use of ECMO, there is limited understanding of the impact of the mixing zone on vasculature cells.

The goal of this project is to determine the impact of ECMO on aortic vasculature to improve understanding of vascular abnormalities found in patients weaned from ECMO.

Approach
Develop a device to replicate the shear stress and flow conditions experienced by cells in the aorta during ECMO.

Design Methodology

1. Prototypes
   a. 3D models of the two designs with channel lengths 10mm, 15mm, & 20mm were developed

2. Prototype Fluid Simulations in Solidworks CAD
   a. Normal Blood Flow Simulations
      i. To compare shear stress to stress found in the aorta under normal conditions
   b. Laminar 2 Directional Flow Simulations
      i. To determine the location of the mixing zone
   c. ECMO Blood Flow Simulations
      i. To predict experimental shear stress and visualize the flow

3. Final Design
   a. The triangular 15mm prototype was selected due to optimal flow and shear stress

Simulation Experiment

Table 1: Simulation Shear Stress and Flow Pattern Results

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<thead>
<tr>
<th>Shape</th>
<th>Percent ECMO</th>
<th>Length</th>
<th>Shear</th>
<th>Flow</th>
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<tbody>
<tr>
<td></td>
<td>10 mm</td>
<td>15 mm</td>
<td>20 mm</td>
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<tr>
<td>Triangle</td>
<td>30%</td>
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<td></td>
<td>50%</td>
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<td>Vein</td>
<td>30%</td>
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Figure 1: ECHO Overview

Figure 2: ECHO Mixing Zone

Figure 3: Model of mixing zone in aorta and on vasculature-on-a-chip device

Benchtop Experiment

Fabrication
1. Acrylic molds were laser cut, adhered to a Petri dish, and covered in PDMS
2. Cured PDMS was cut into rectangles and a biopsy punch was used to create inlets and outlet holes
3. Devices were attached to glass cover slips using plasma bonding

Seeding Devices
- The channels were coated with 1% gelatin and incubated for 12 hours
- Channels were flushed and seeded with MDA-MB-231 cancer cells
- Seeded devices grew to confluency

Experiment
- Cells were exposed to 1 directional flow, 2 directional flow, or static conditions for 4 hours
- Cells were fixed, stained, and imaged

Results

Vasculature-on-a-Chip Device

1-Directional Flow

2-Directional Flow

Static

Figure 4: triangular (top) and vein (bottom) geometries

Figure 5: Acrylic molds in PDMS (left)

Biopsy punch creating inlets and outlets in cured PDMS (right)

Figure 6: Experimental setup for 1-Directional Flow

Areas predicted by the simulation to experience increased shear stresses by the mixing zone simulations aligned with cell detachment zones

ECMO mixing zone disrupts cell alignment

Moderate cell alignment at ECMO inlets compared to pulsatile flow conditions

Figure 7: A representative photo of the channel shows two inlet and two outlet options (A). In static conditions, we can see that there is confluence of cells covering the channels (B). We can see that there is cell detachment in areas of high shear as predicted by simulations (C, D).

Experimental results support successful replication of cell conditions during ECMO life support

Future Work

- Conduct experiment with aortic endothelial cells
- Increase cell adhesion to device to prevent cell shearing off under flow

Acknowledgements

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References