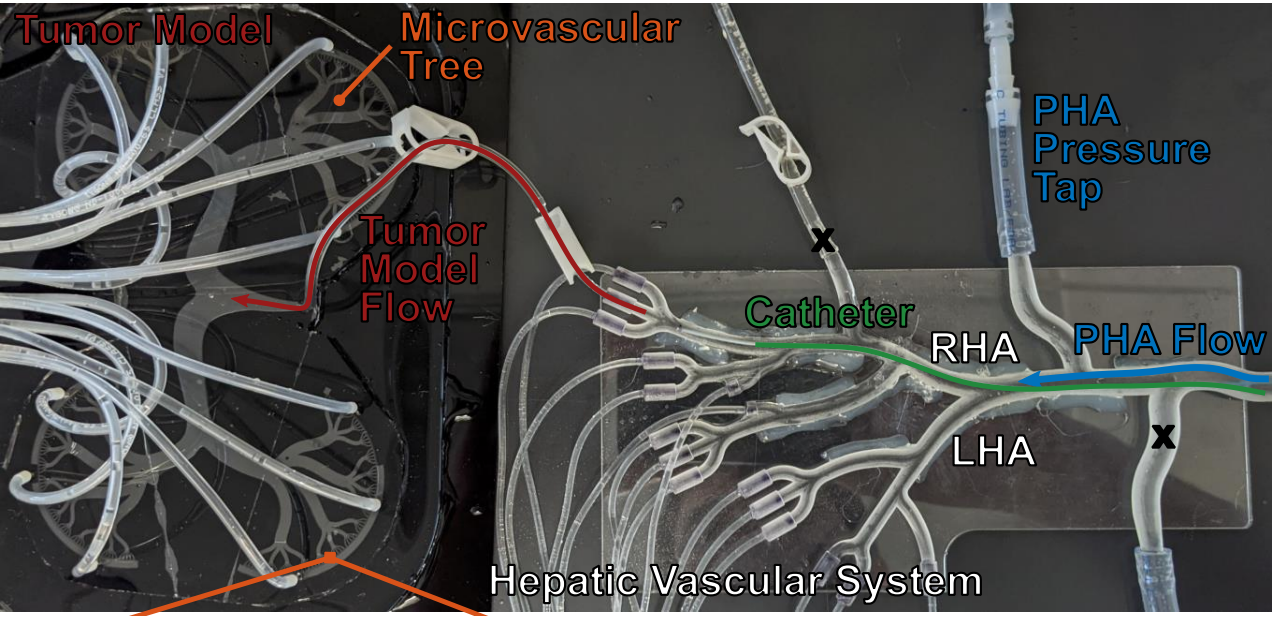
Novel Hepatic Tumor Microvascular Model for Evaluating the Deposition Characteristics of Y-90 Microspheres



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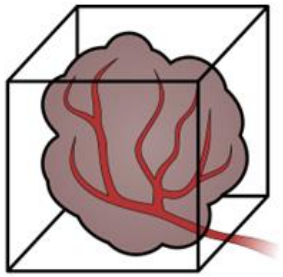
Disclosures

- ABK Biomedical Incorporated
  - Co-Founder
  - Chief Medical Officer (Employee)
  - Shareholder

Y-90 DEPOSITION IS DIFFICULT TO EVALUATE IN VIVO



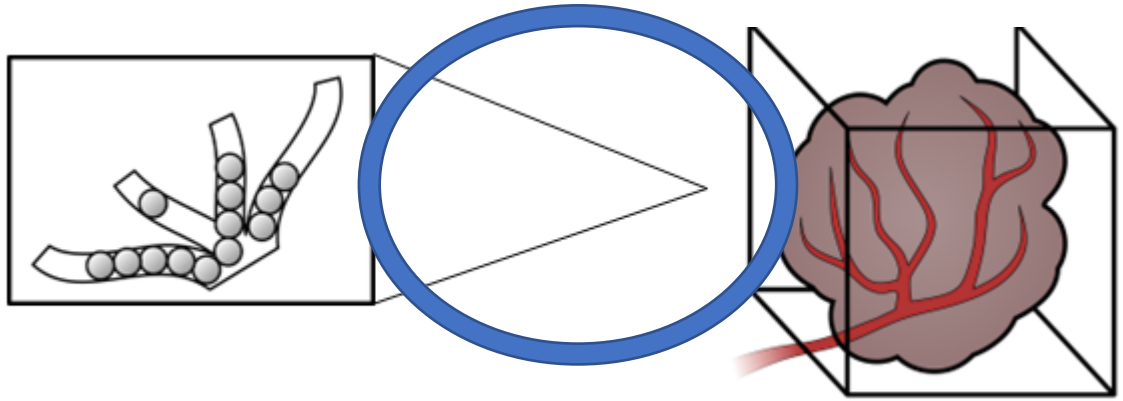
- How are microspheres distributed?
- How does administration method affect distribution and depth of penetration?
- At what arterial level does implantation occur?

We should instead do this type of evaluation on a standardized in vitro model that captures hepatic vascular anatomy and matches physiologic pressures and flow rates

Adhere to 3 R's Guidance for Ethical Animal Research

Reduction:	Any strategy that will result in fewer animals being used in research.
Refinement:	Modification of experimental procedures to minimize pain.
Replacement:	Methods which avoid or replace the use of animals in research.

In Vitro



In Vivo

https://i.ytimg.com/vi/H5ANZo5a6RE/maxresdefault.jpg

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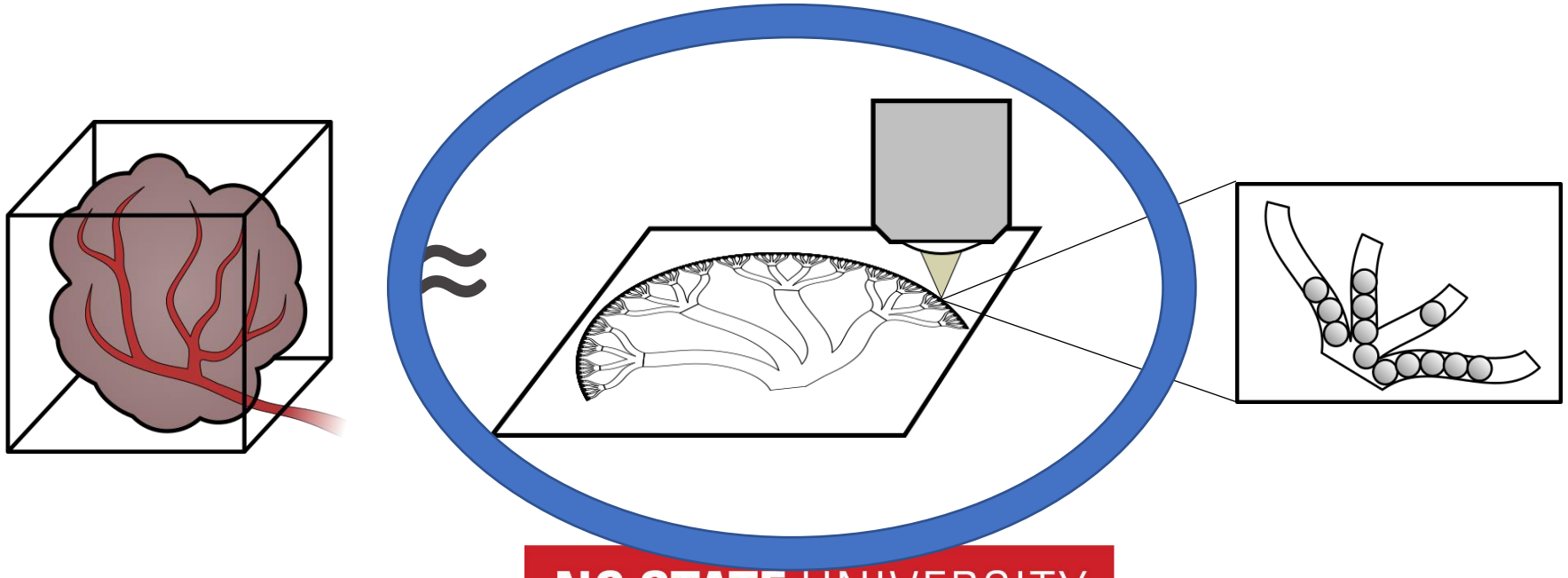
In Vitro Model Development with physiological flow dynamics



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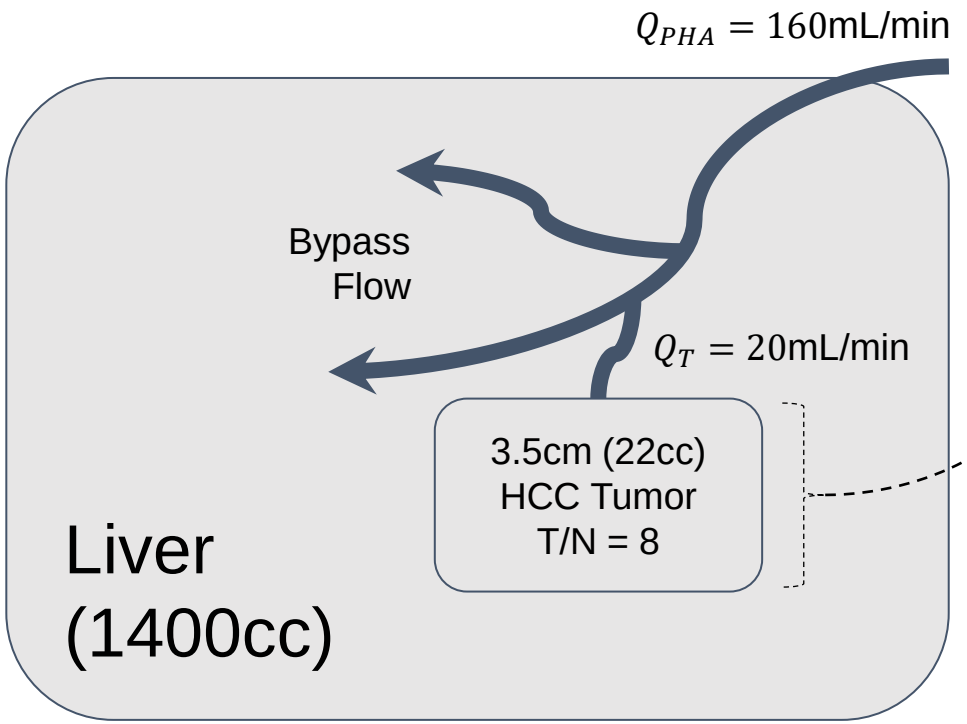
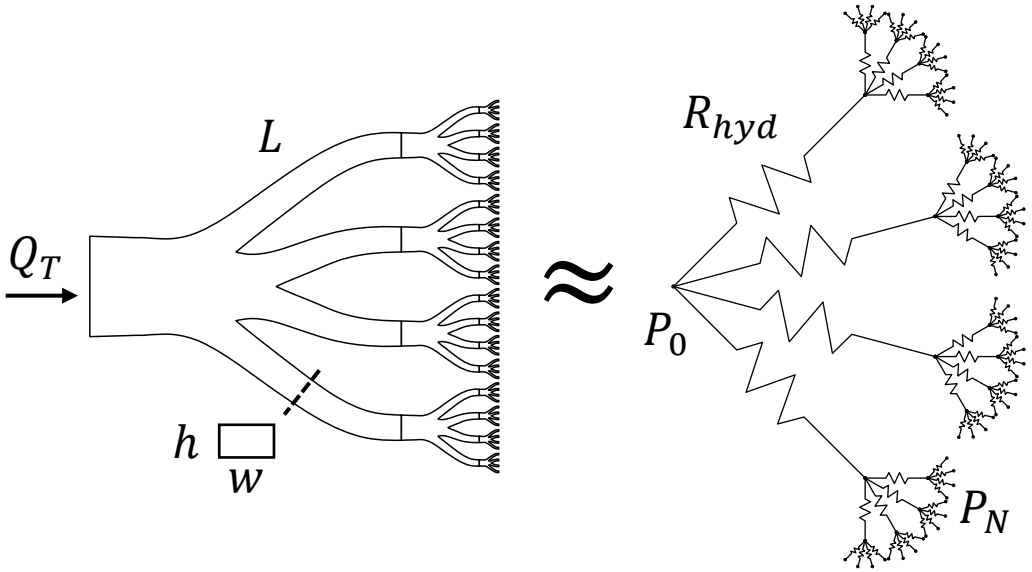
NCS MODEL IS DESIGNED TO REPRESENT A 3.5CM HCC TUMOR

- Simple flow partition yields tumor flow target of 20mL/min



$$Q_T = Q_{PHA}(T/N)\frac{V_{tumor}}{V_{liver}}$$

- The tumor is represented by a branching vascular structure



- Model branches from single inlet that is 1 mm diameter to 6400 outlet arterioles each 18μm wide

Microvascular Tumor Model Fabrication

Planar branching microfluidic mold: 4.5cm (48cc) tumor in a 1400cc liver, total hepatic flow rate of 160mL/min, tumor flow of 20mL/min, a four-compartment model with a T/N ratio of 4.

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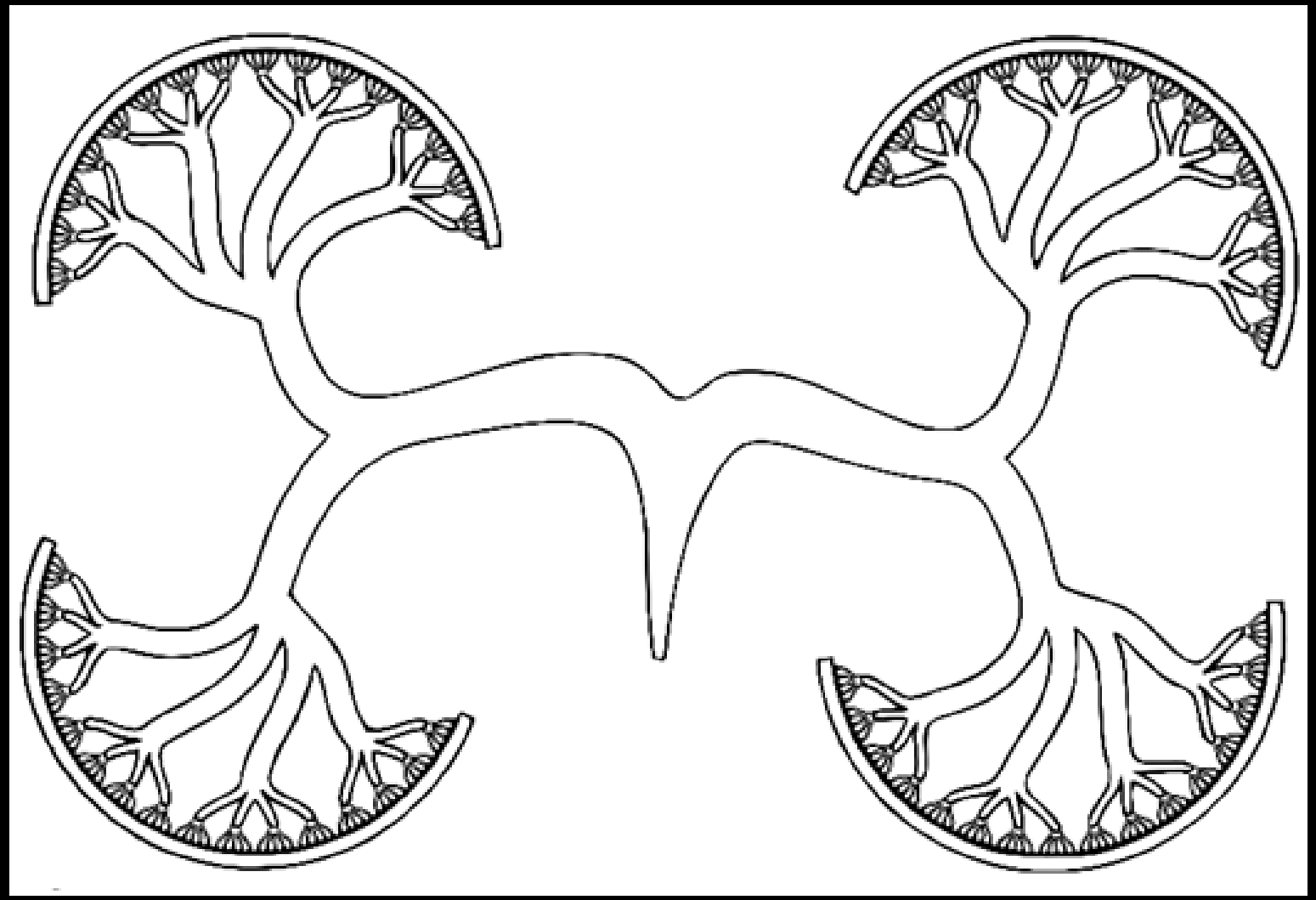


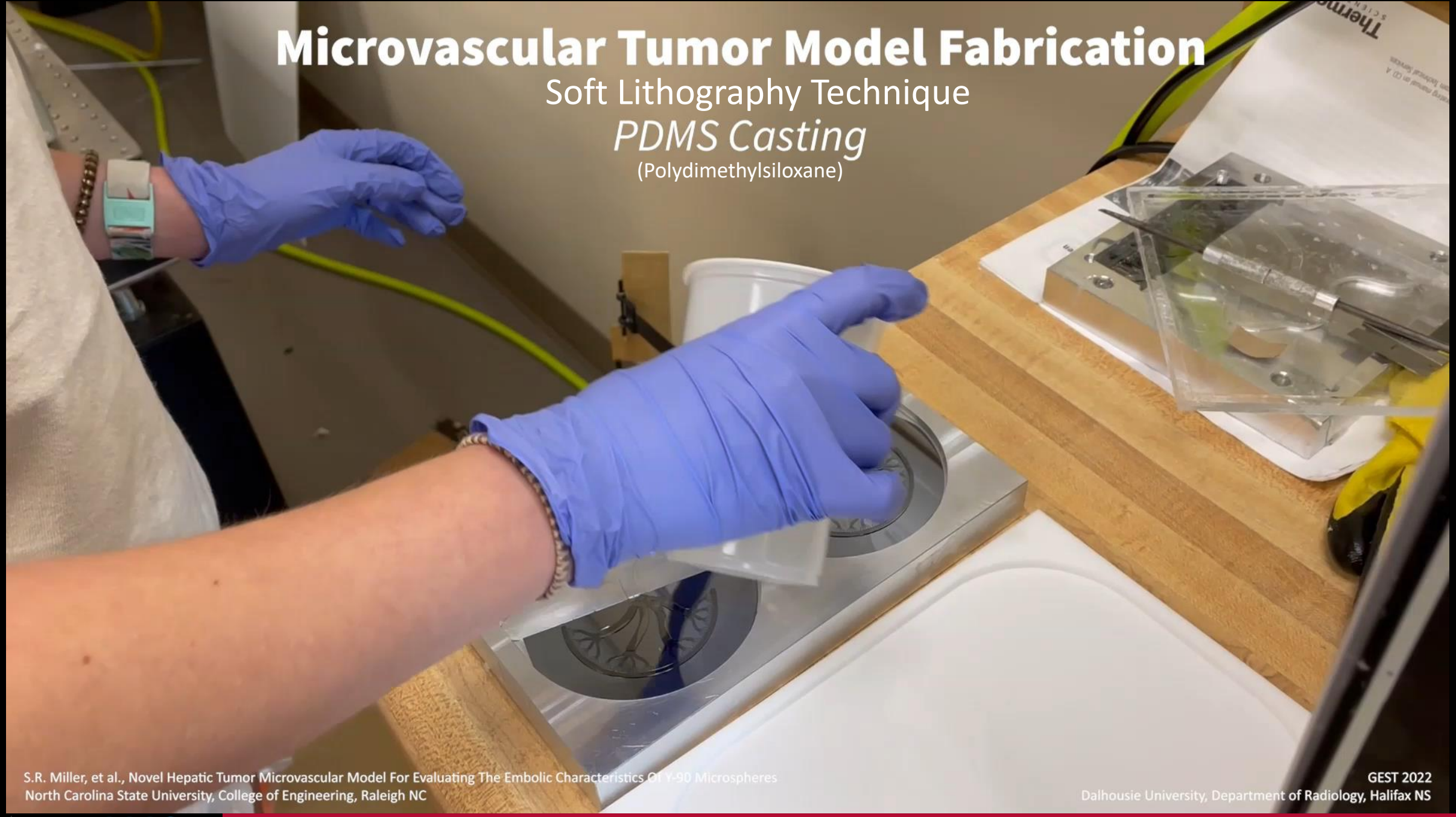
Four microvascular trees connected
by a mesoscale vascular manifold

Microvascular Tumor Model Fabrication

Soft Lithography Technique

PDMS Casting

(Polydimethylsiloxane)



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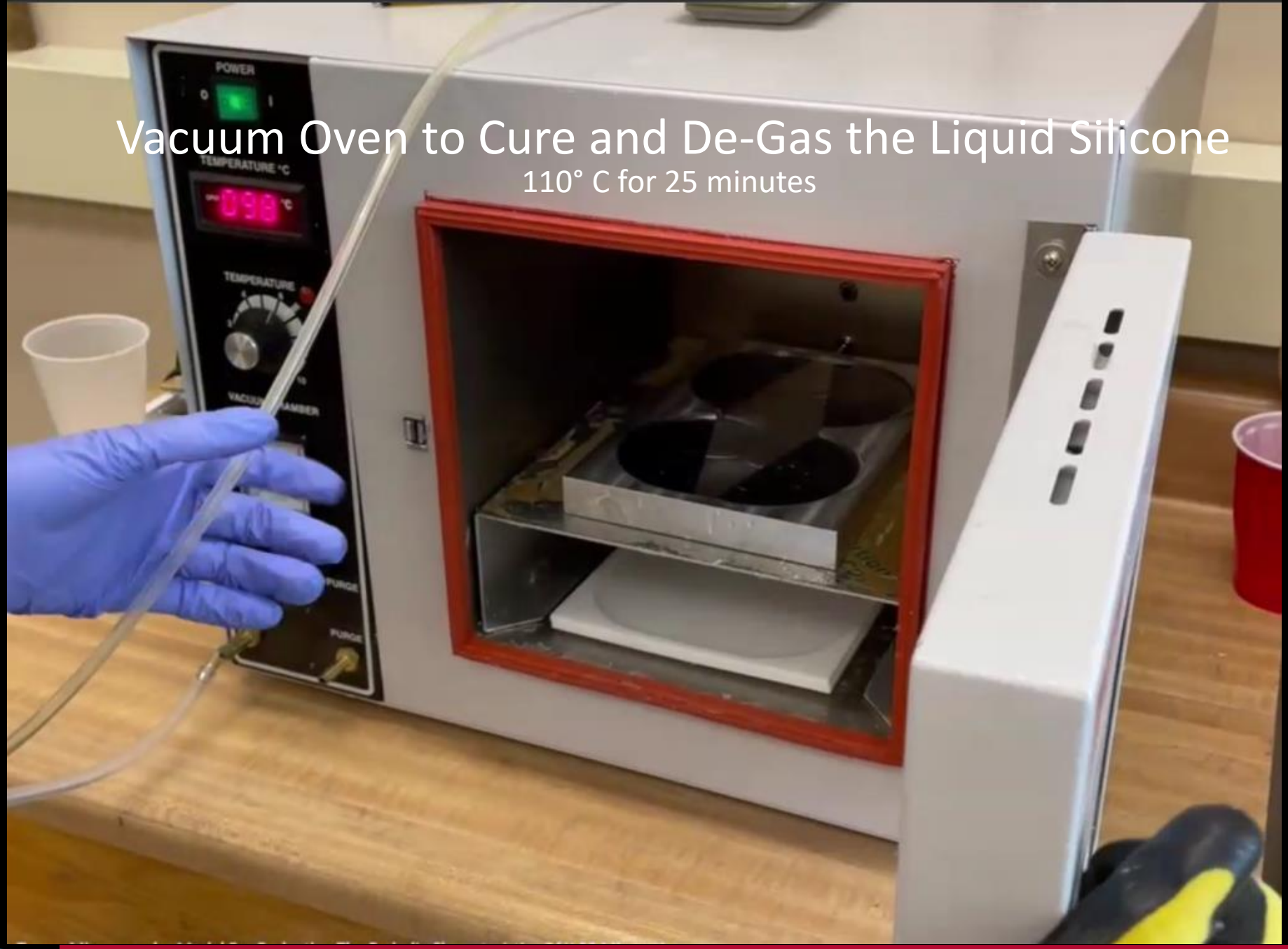
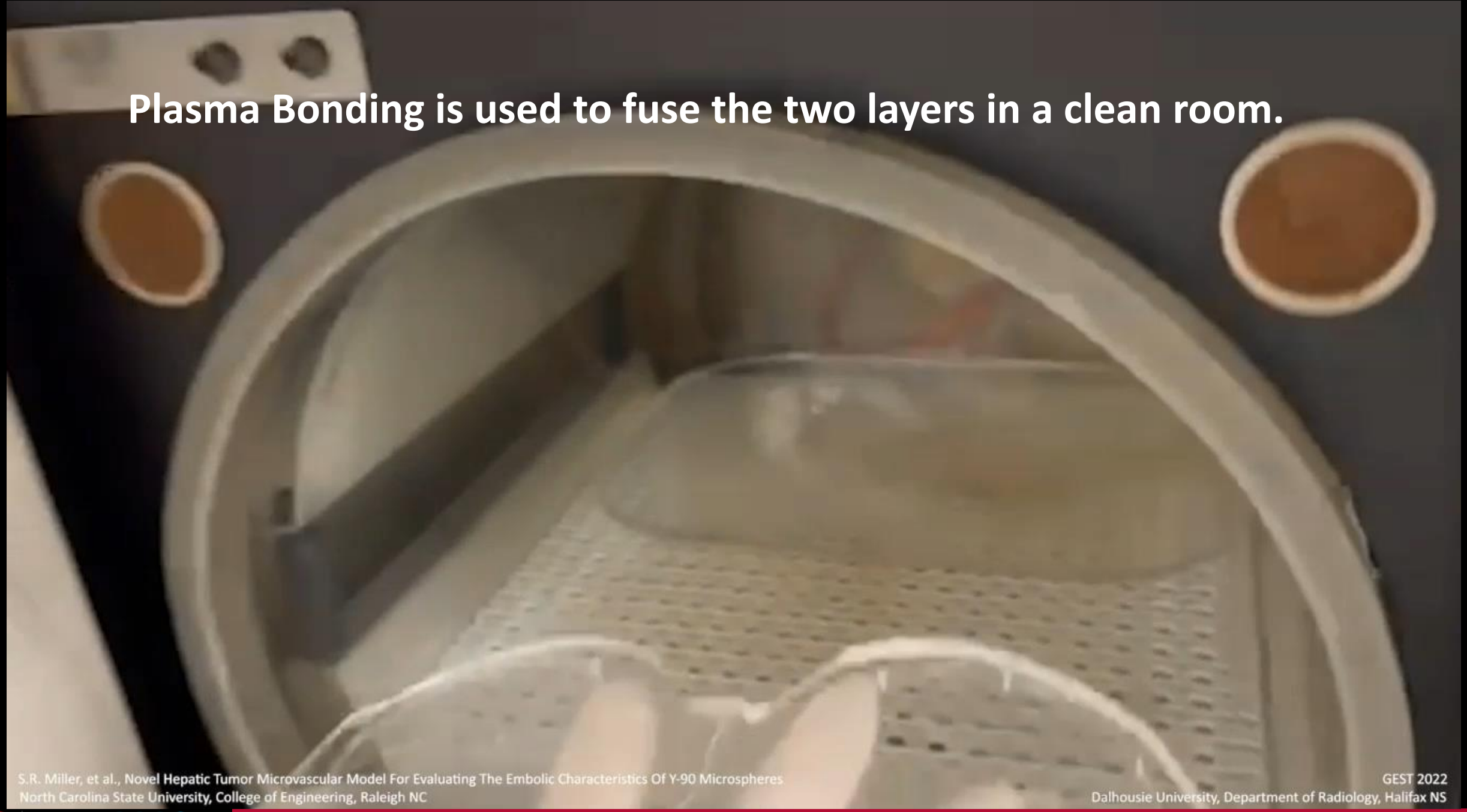
Vacuum Oven to Cure and De-Gas the Liquid Silicone

110° C for 25 minutes



Plasma Bonding is used to fuse the two layers in a clean room.



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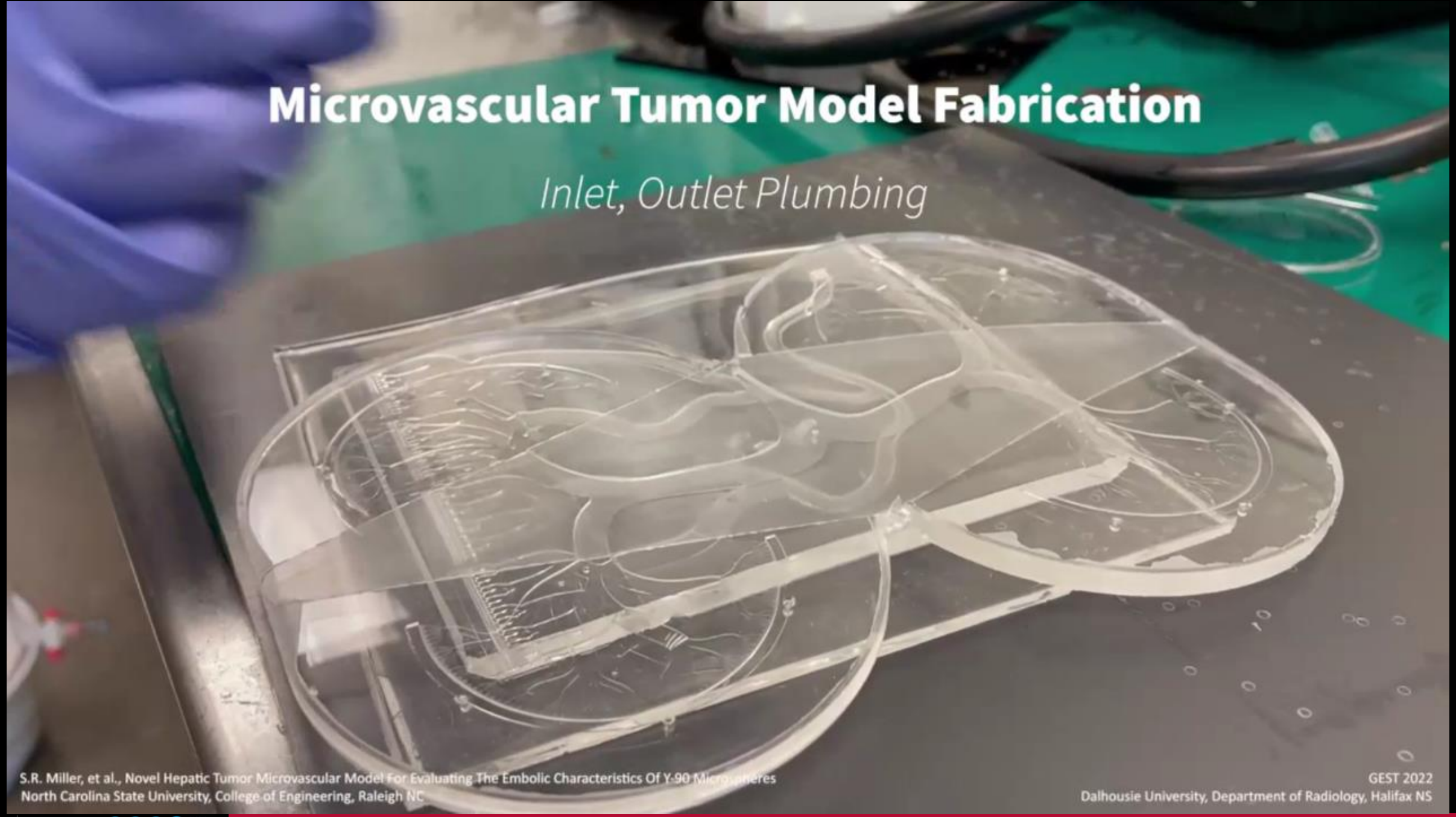
Microvascular Tumor Model Fabrication

Inlet, Outlet Plumbing



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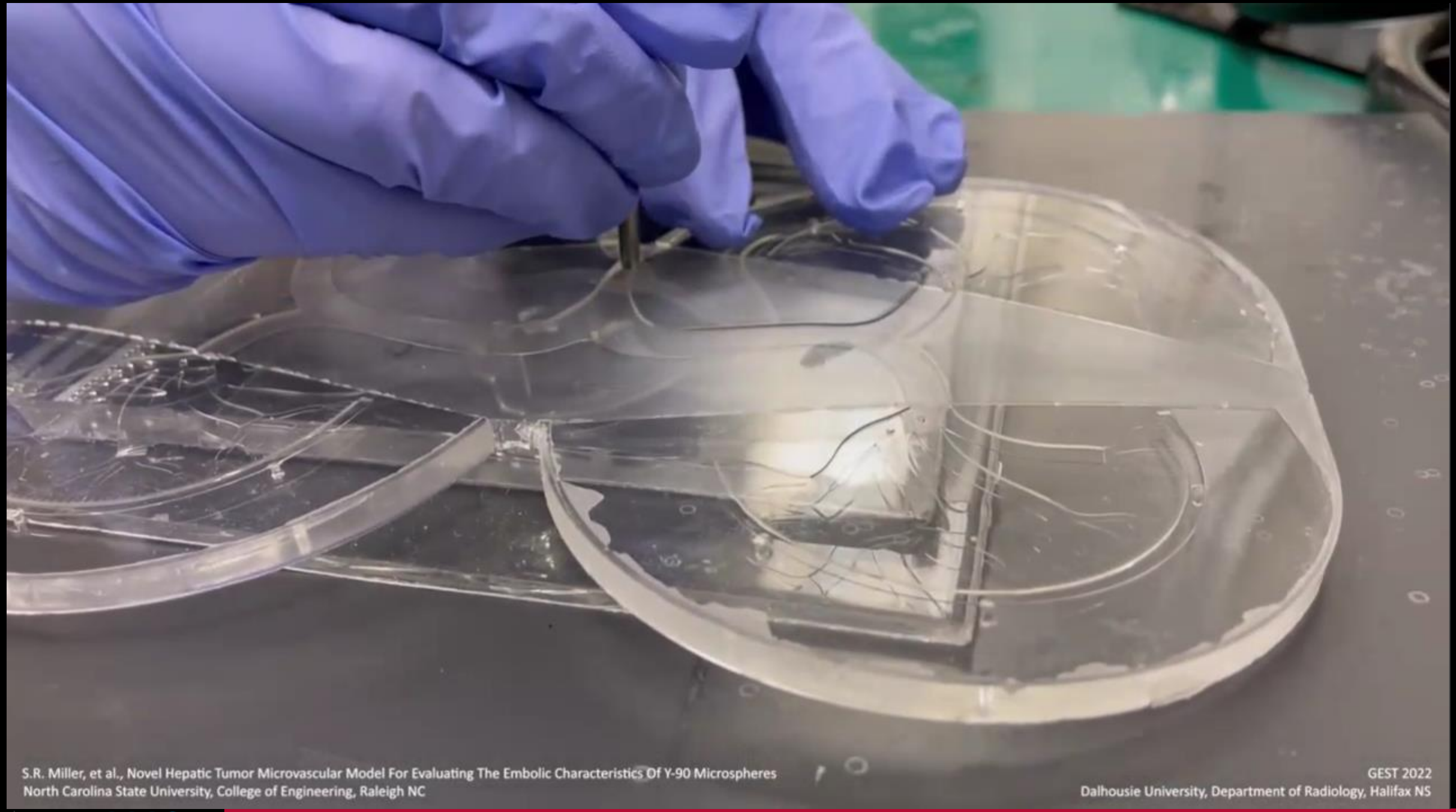
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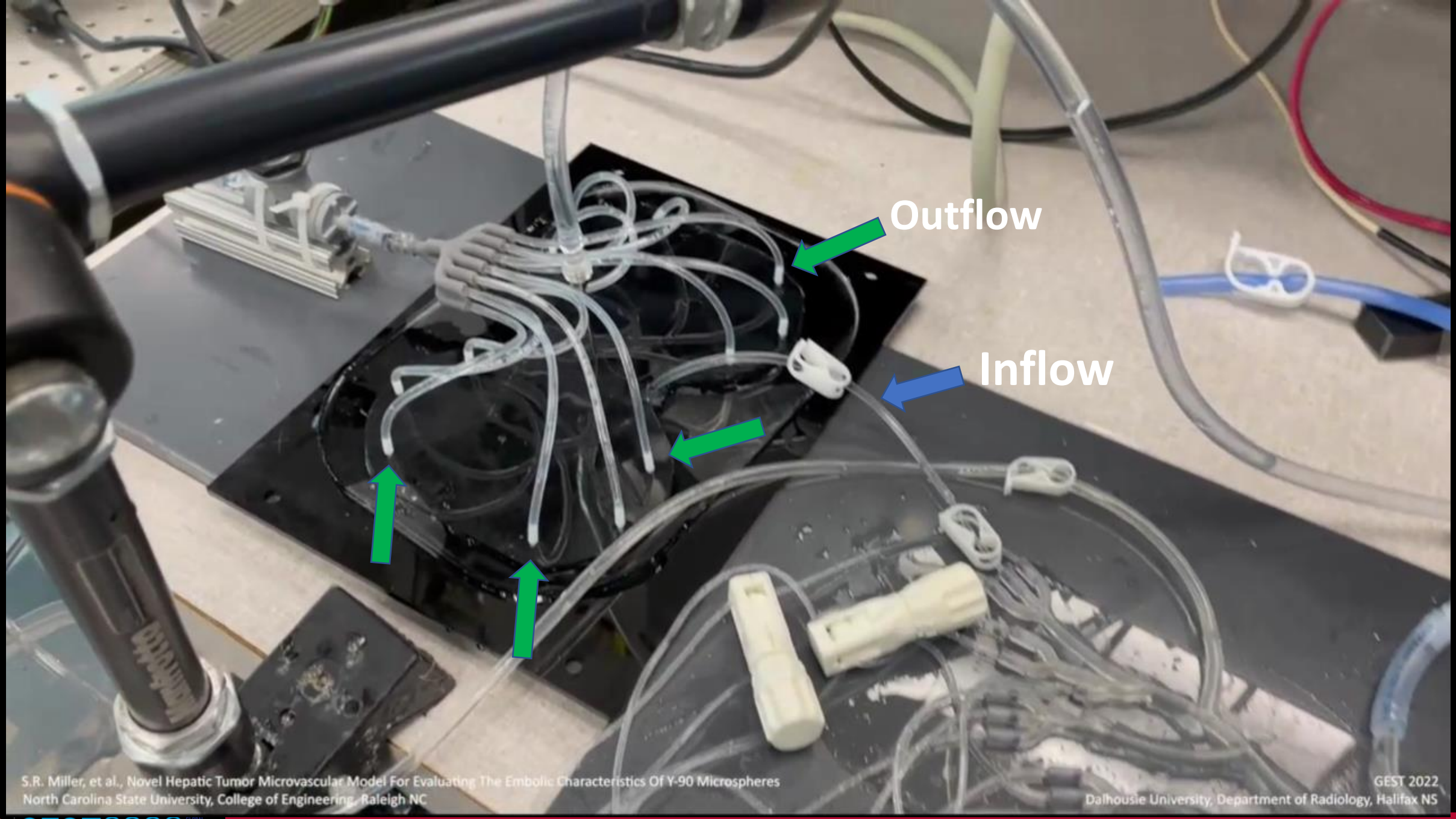
Outflow
Inflow
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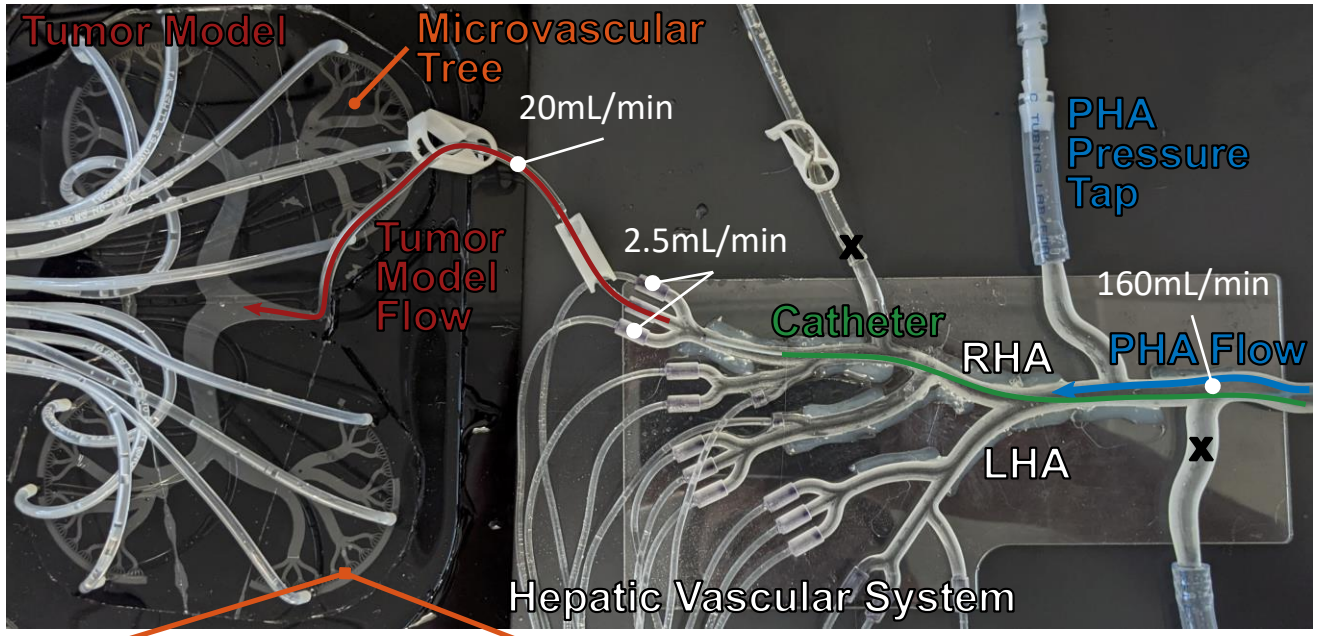
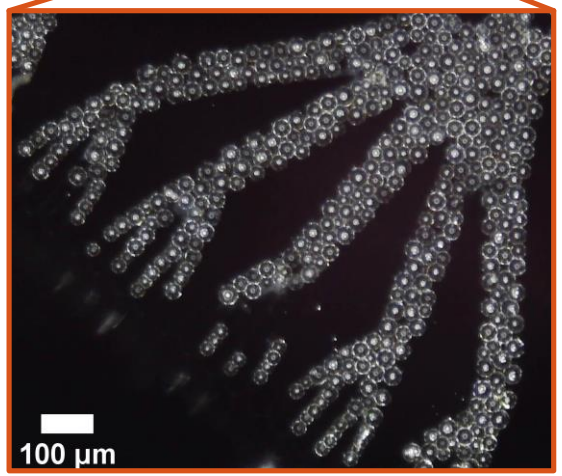
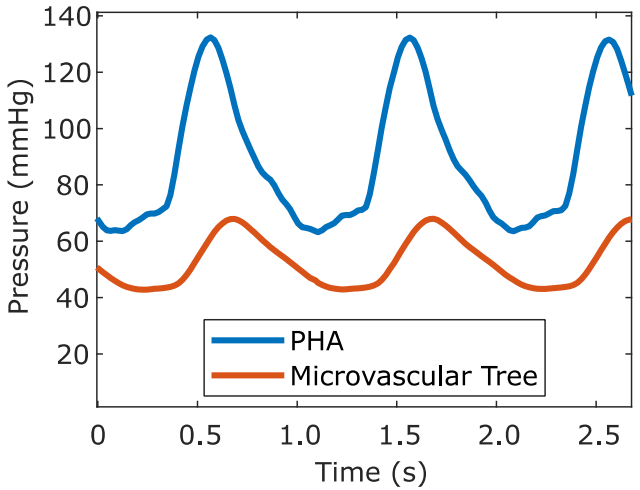
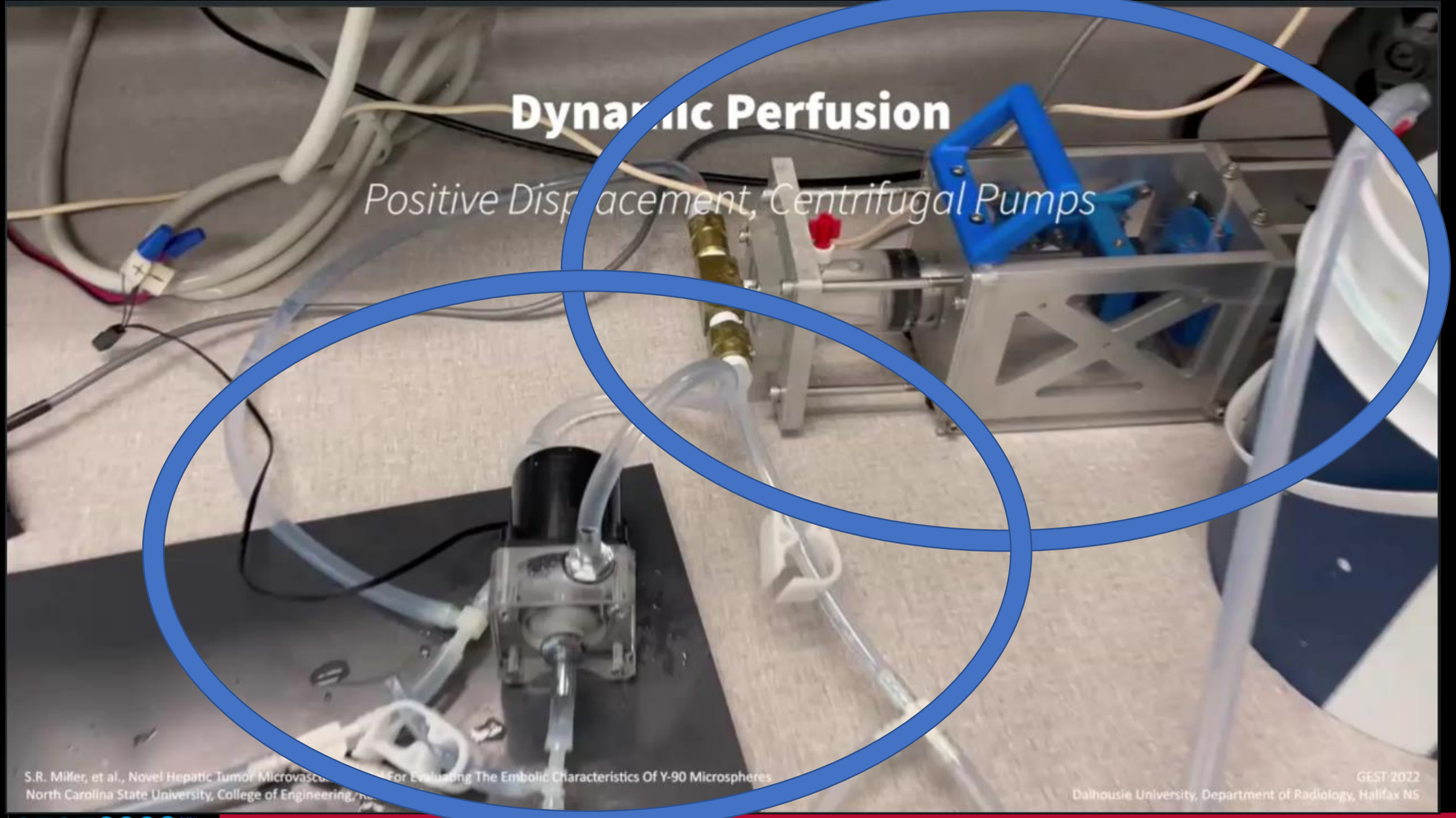
Tumor Model is attached to a Hepatic Vascular System

- System is perfused with water-glycerin mixture at a rate of 160mL/min and at 140/60mmHg pressure
- Outlets adjacent to tumor are set to a specific rate.
  - i.e. 2.5mL/min: T/N = 8)








Dynamic Perfusion
Positive Displacement, Centrifugal Pumps
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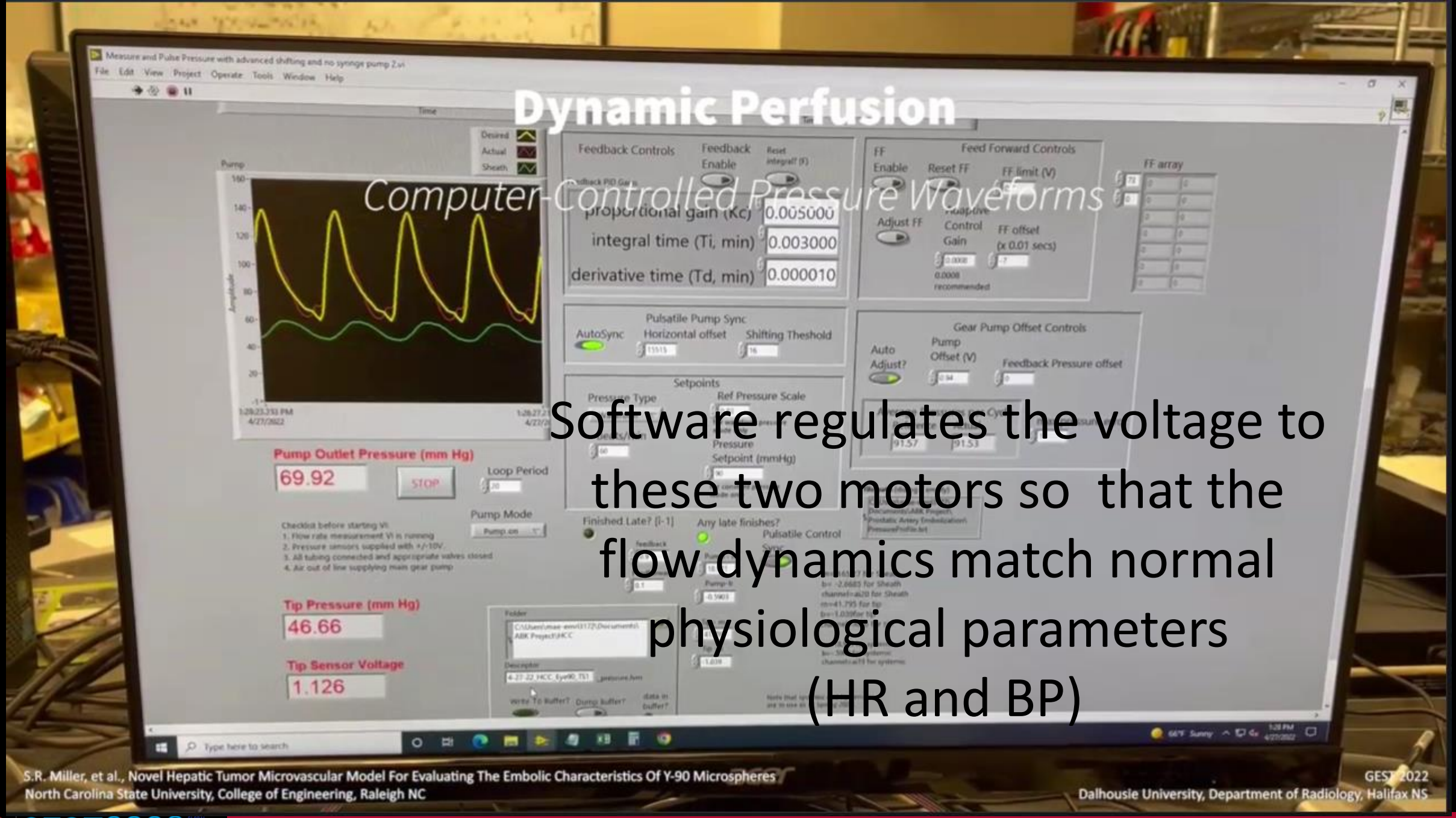
Dynamic Perfusion

Computer-Controlled Pressure Waveforms



Software regulates the voltage to these two motors so that the flow dynamics match normal physiological parameters (HR and BP)

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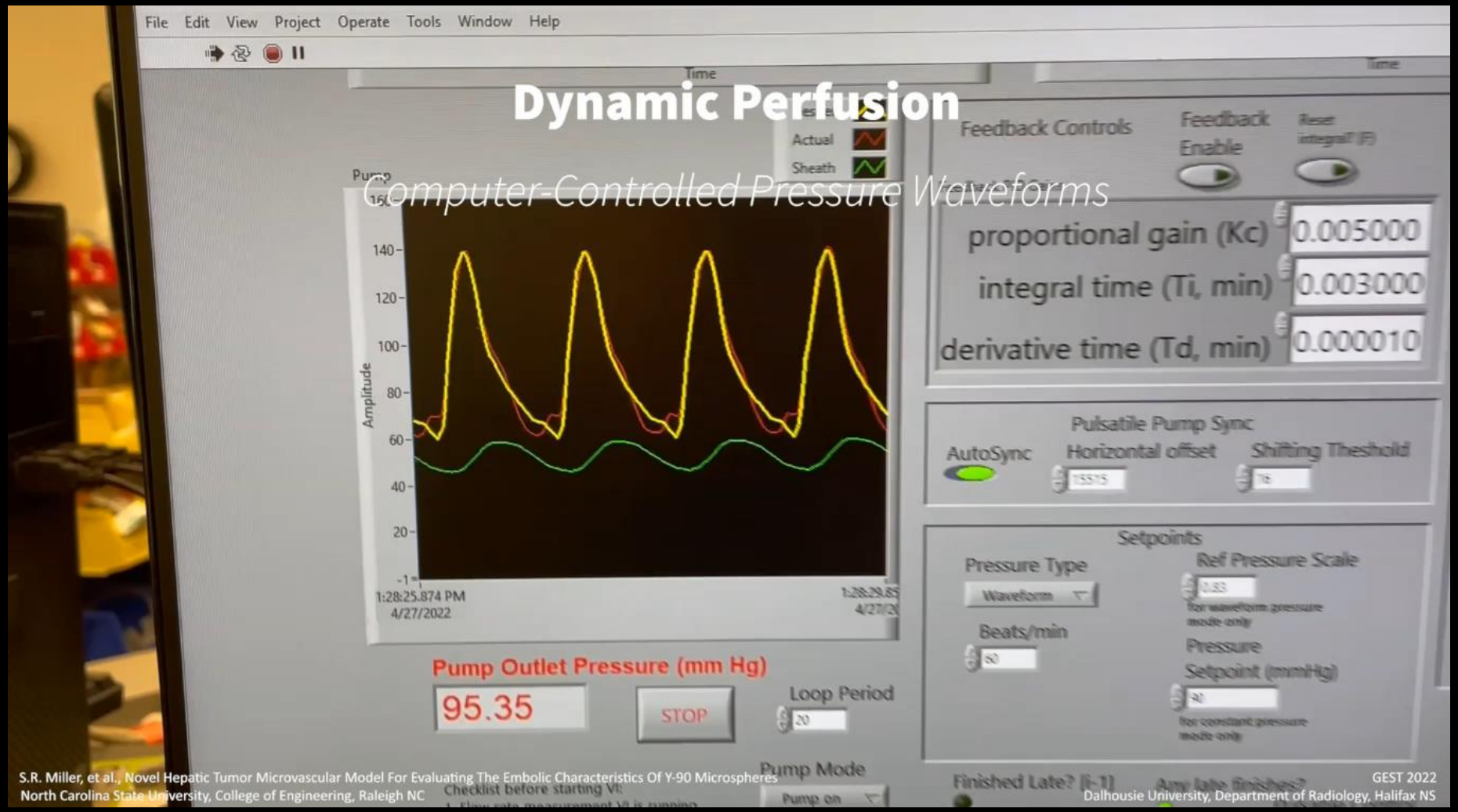
Dynamic Perfusion

Computer-Controlled Pressure Waveforms



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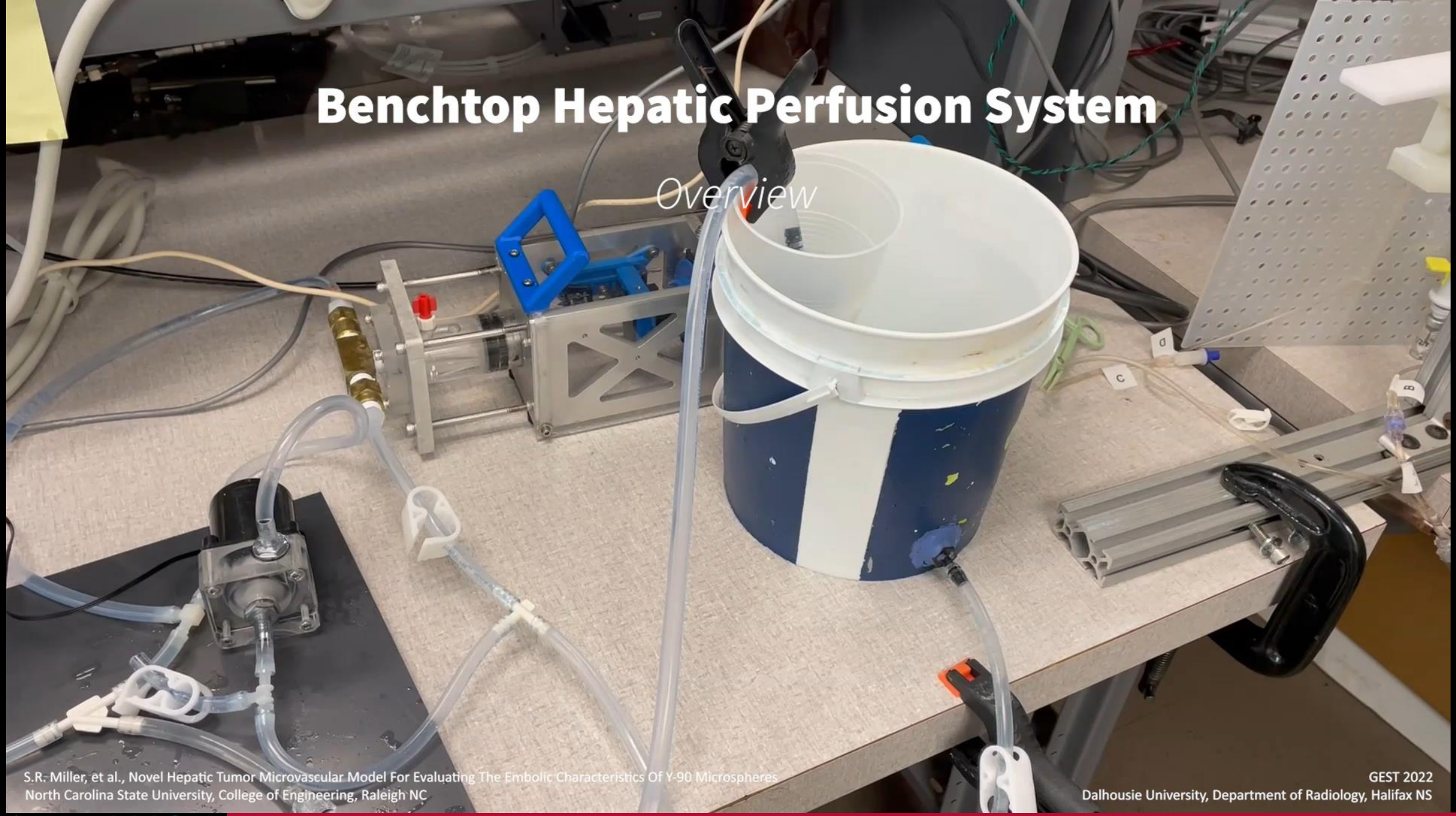
Benchtop Hepatic Perfusion System

Overview



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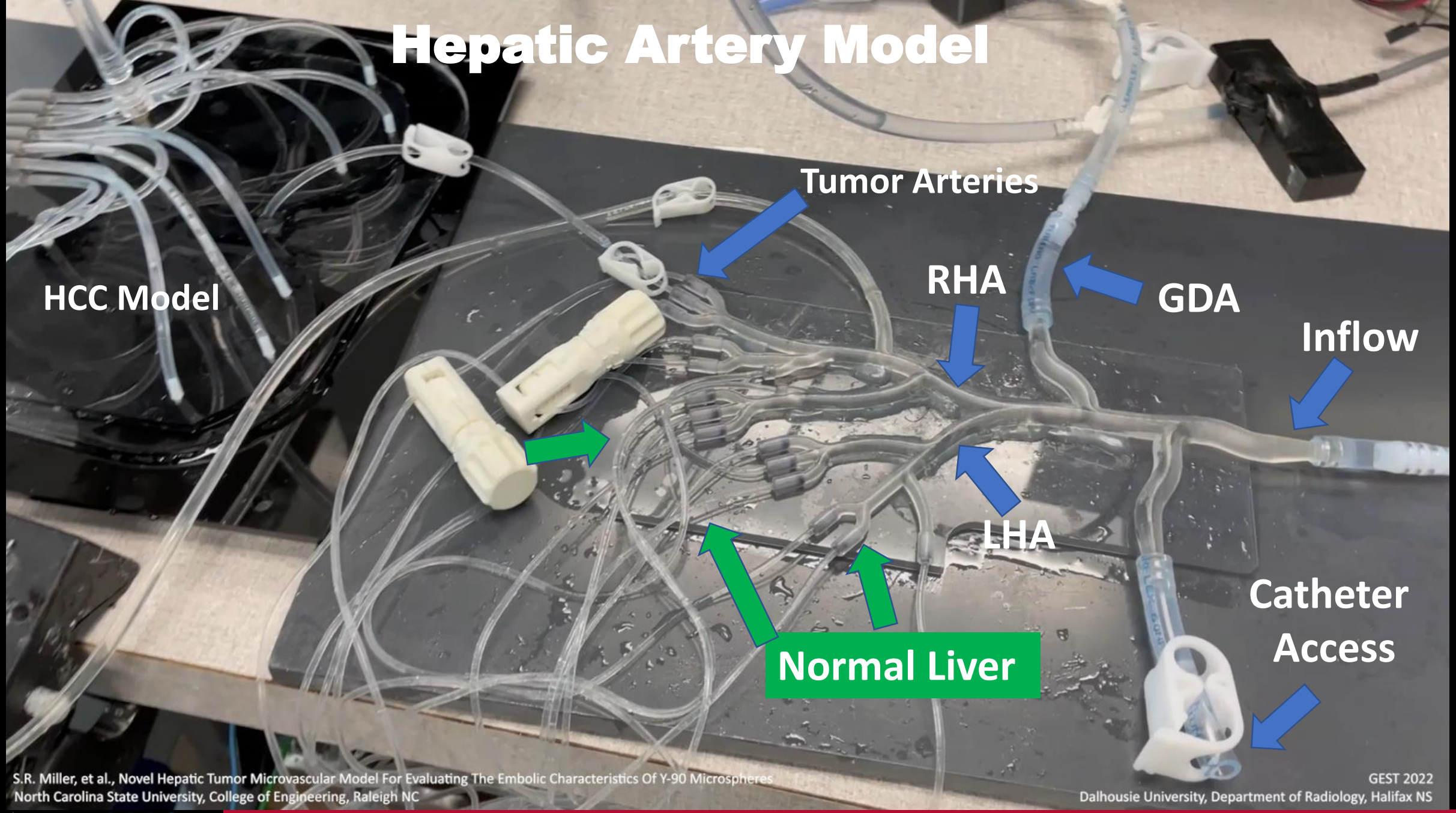
Hepatic Artery Model



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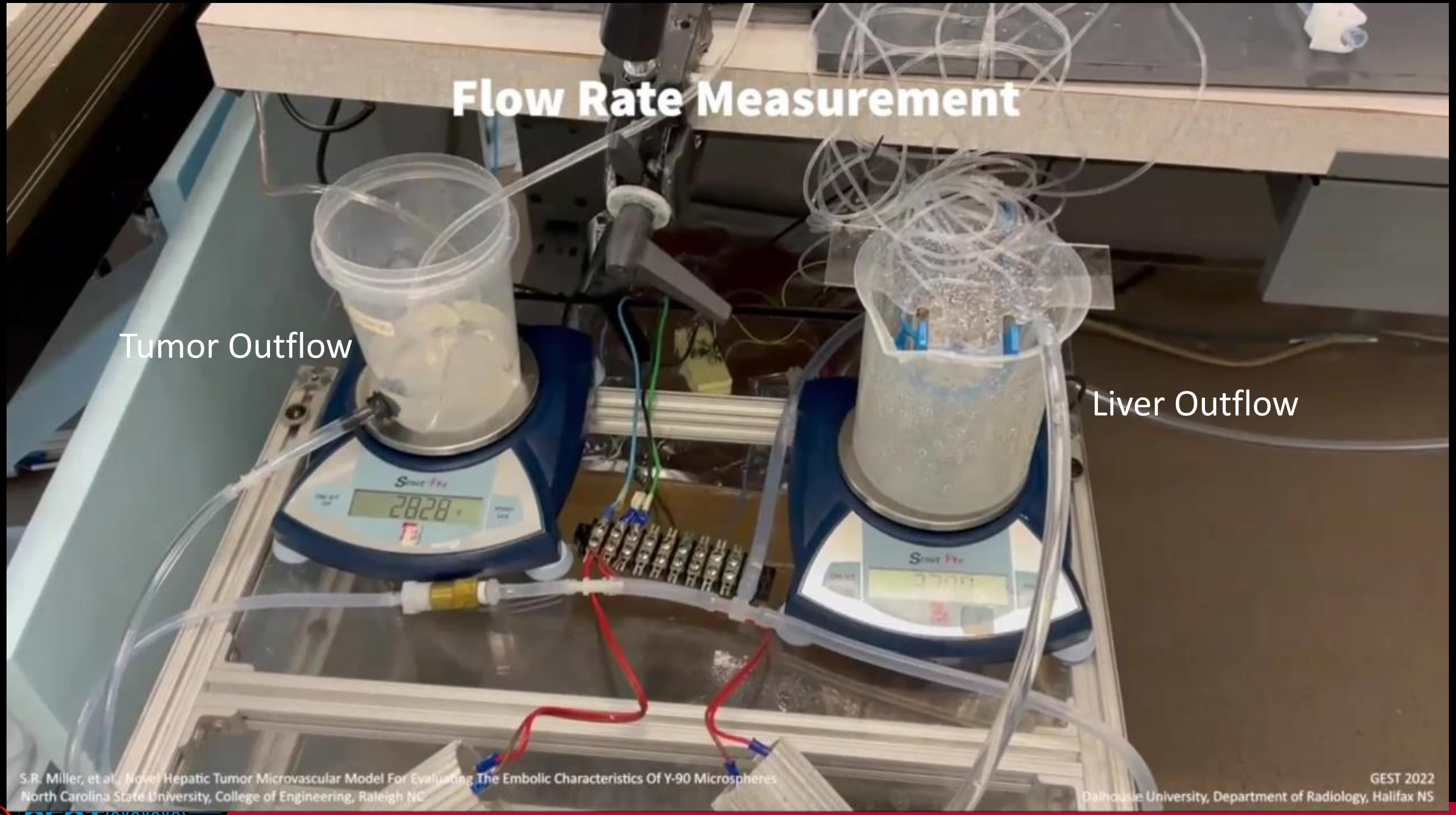
Flow Rate Measurement
Tumor Outflow
Liver Outflow
2828
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Microsphere Administration

Catheter Insertion

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Microsphere Administration

Computer-Controlled Syringe Pump

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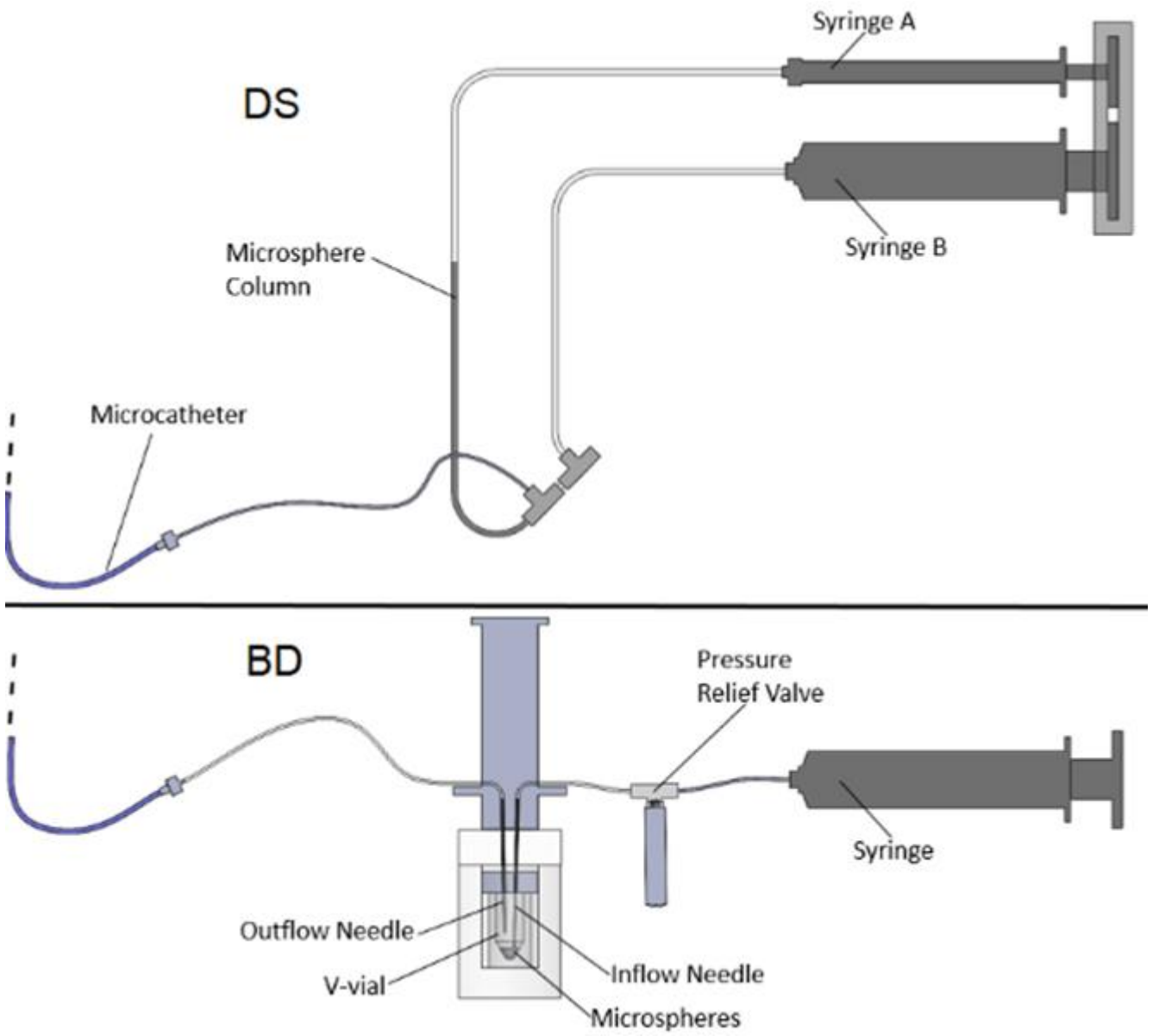
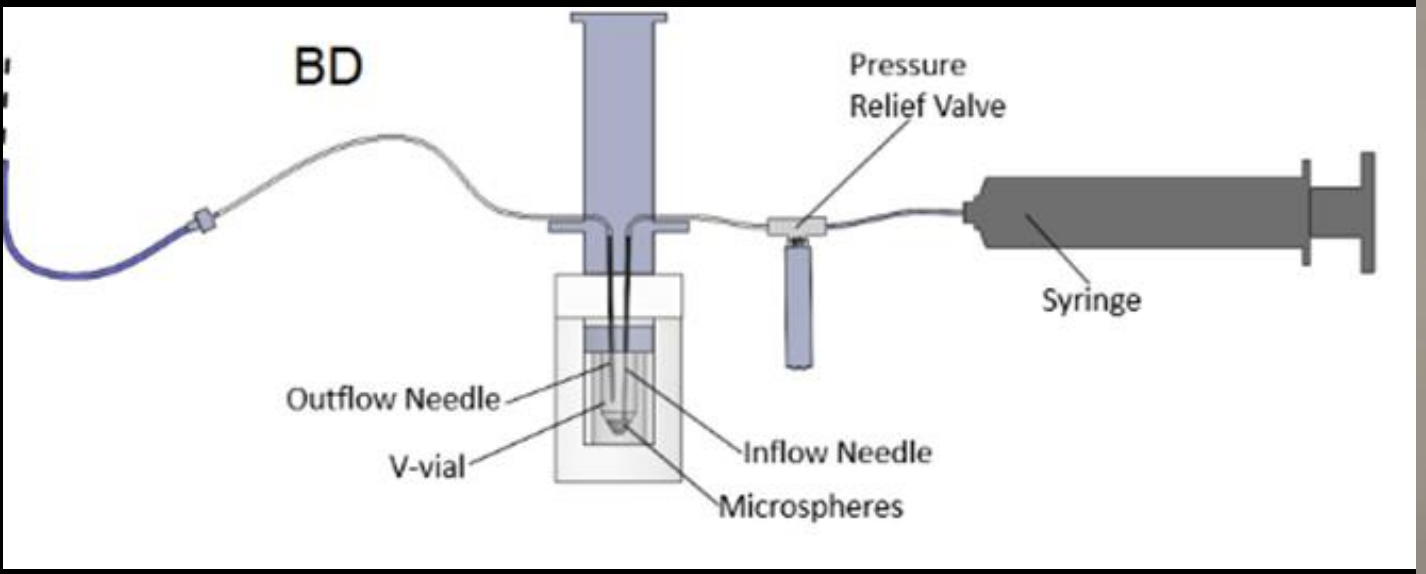
Dual Syringe System (DS)

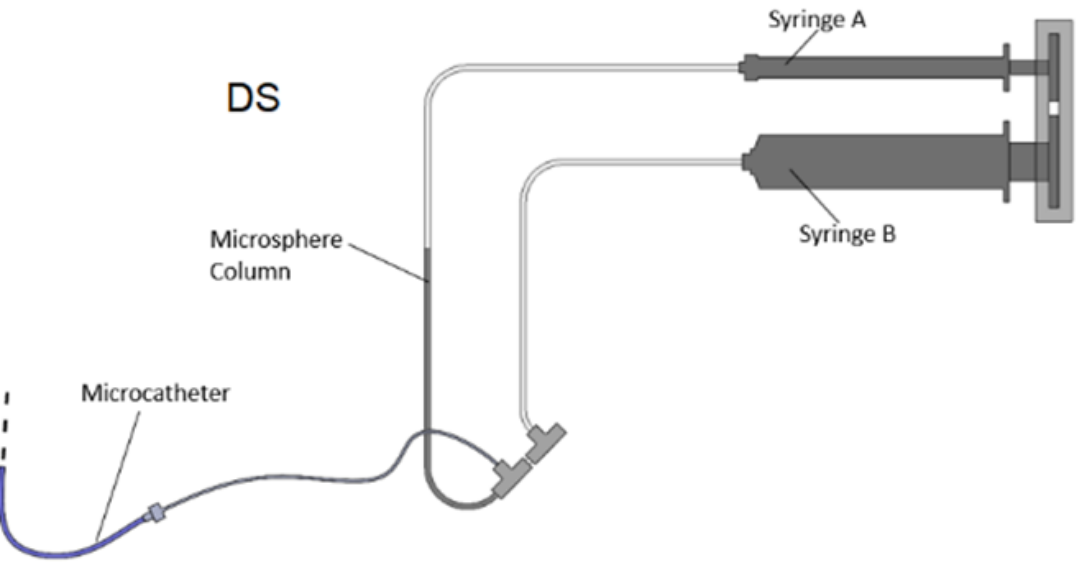
Bolus Delivery System (BD)



Bolus Delivery (BD) Injection

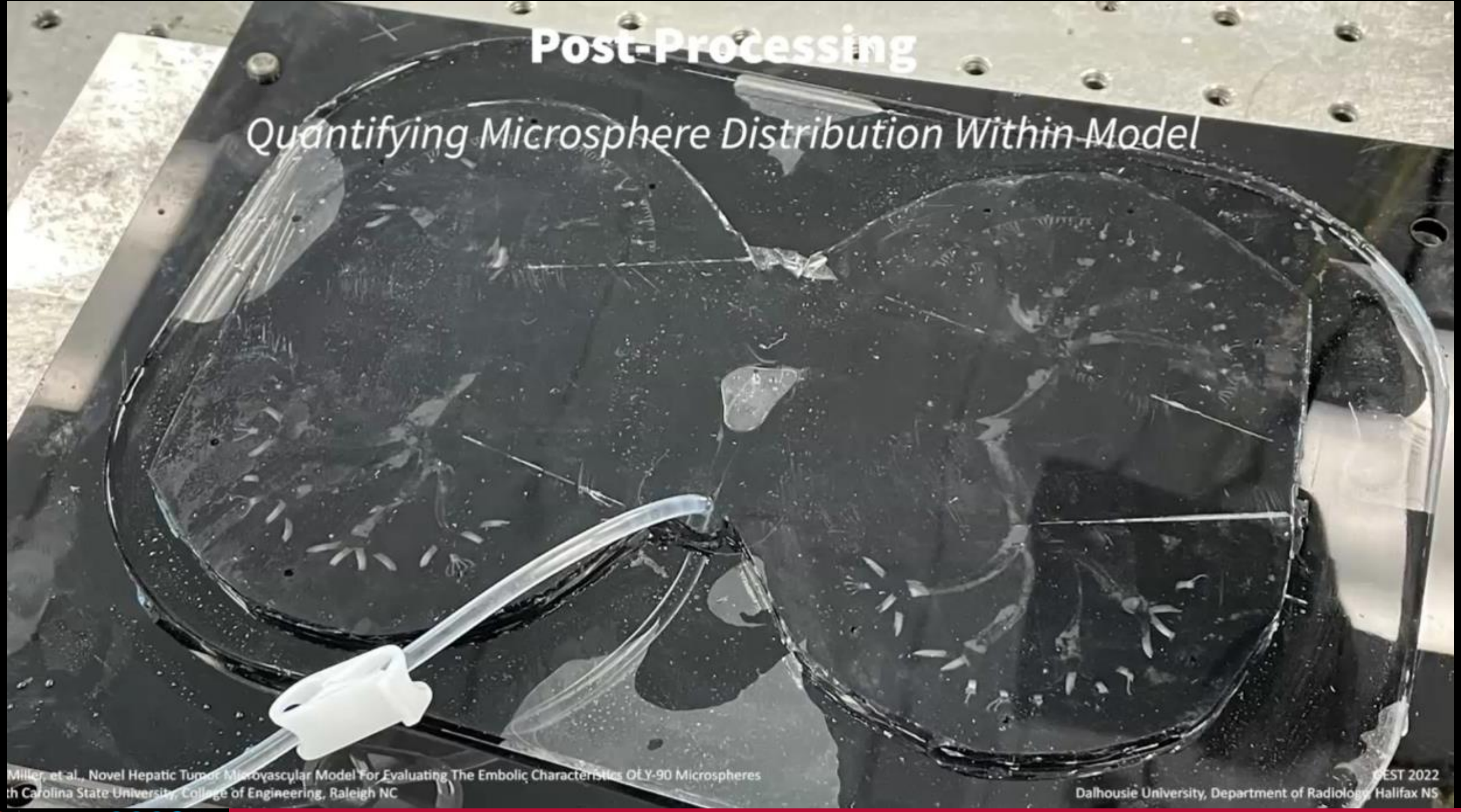


Dual Syringe (DS) Injection



Post-Processing

Quantifying Microsphere Distribution Within Model



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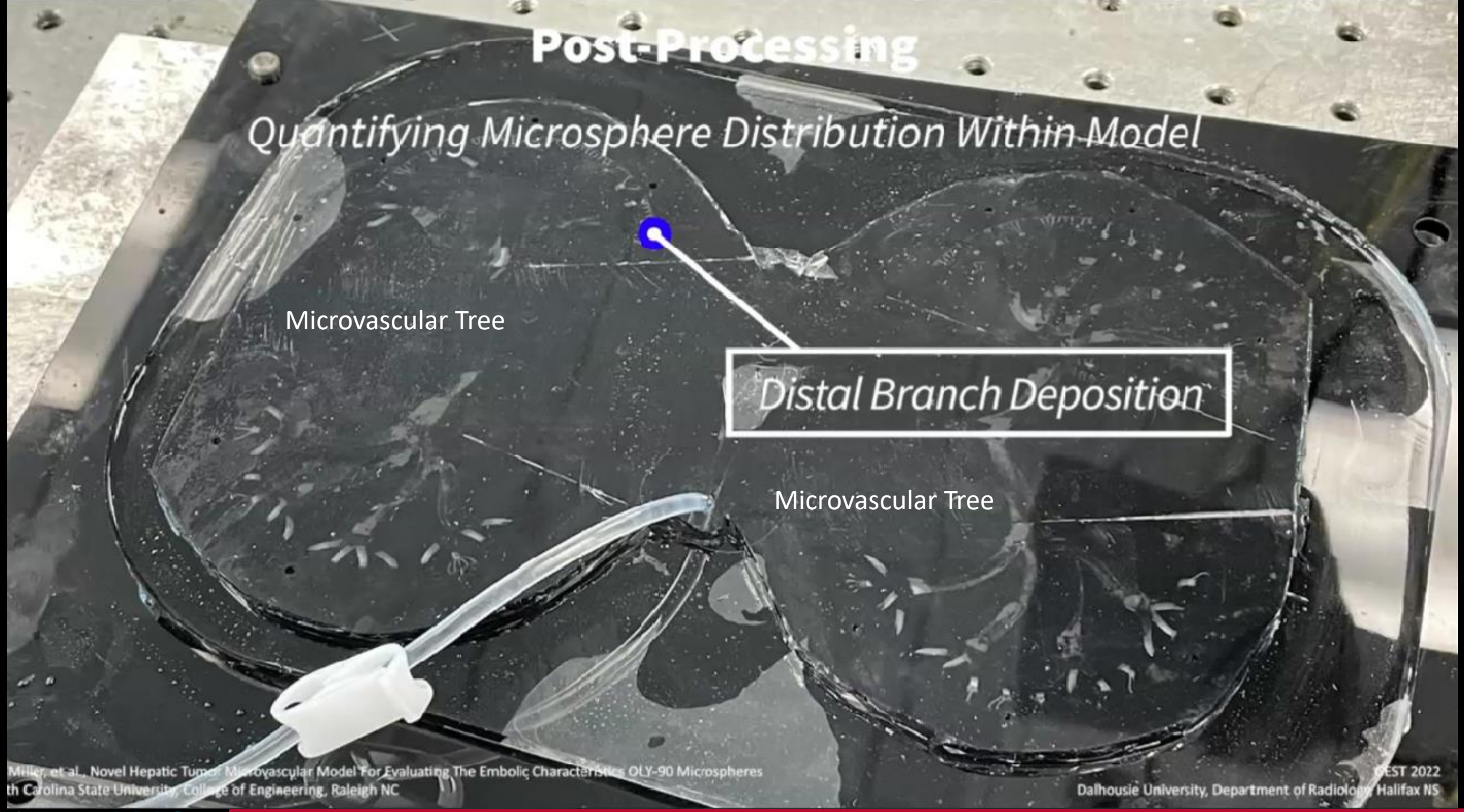
Post-Processing

Quantifying Microsphere Distribution Within Model



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Post-Processing

Digital Microscopy of Microsphere Deposition

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Post-Processing

Quantifying Distal Penetration, Distribution of Microspheres

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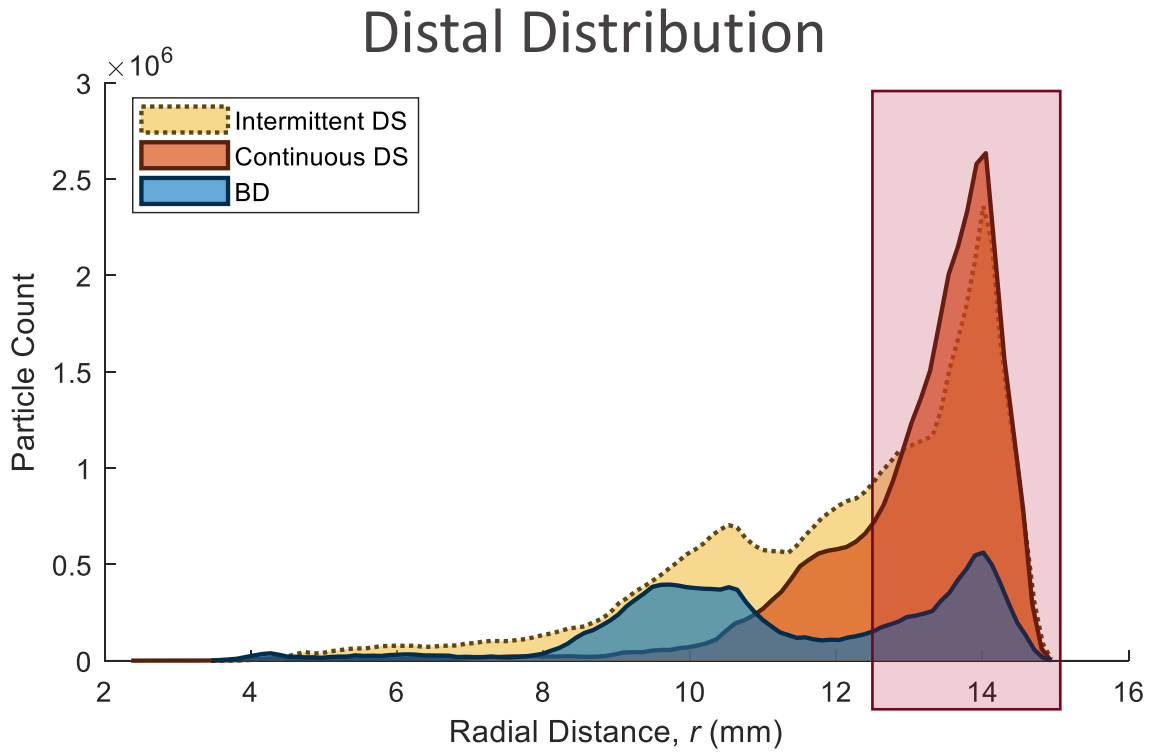
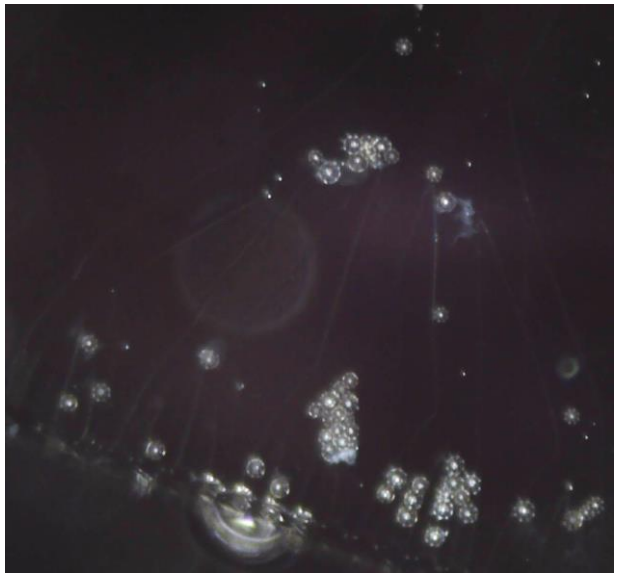
ADMINISTRATION METHOD AFFECTS DISTAL DISTRIBUTION

- DS system showed greater deposition in the most distal vessels



Dual Syringe

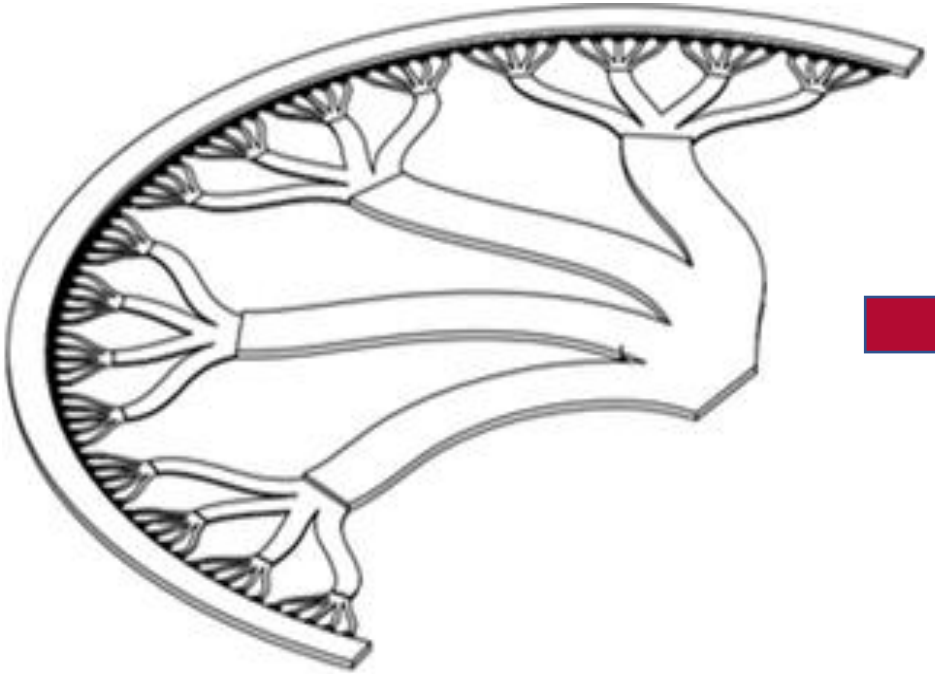
Bolus Delivery



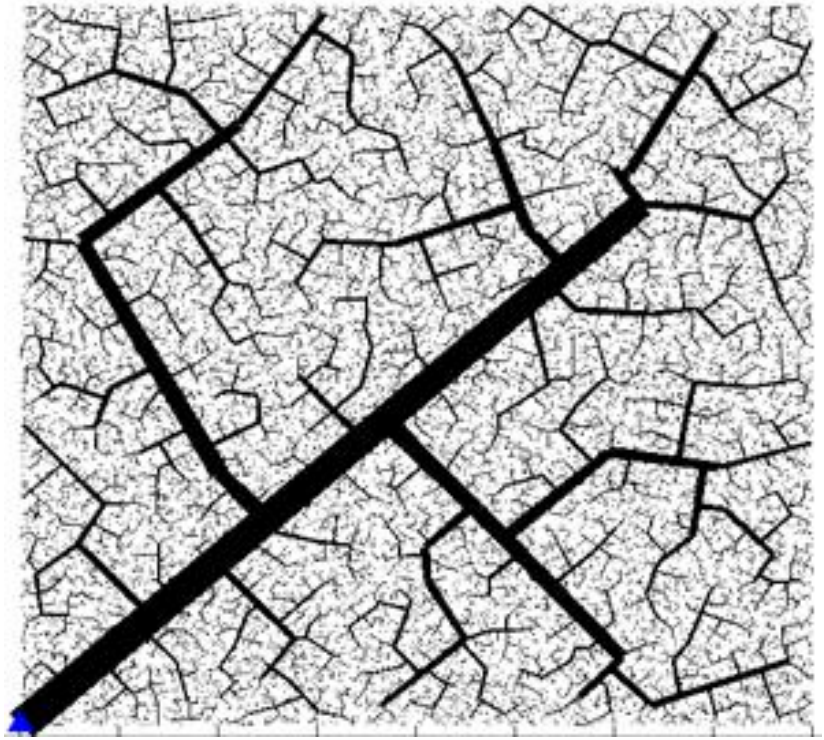
HCC In Vitro Model Future Work

- Variation of Key Parameters:
  - Pressure and flow rates
  - Tumor to Normal Ratios
- Transportable Version
- Reusable Version

HCC In Vitro Model Future Work



Current Model



Future Space Filling Model

NCS University Contact Information

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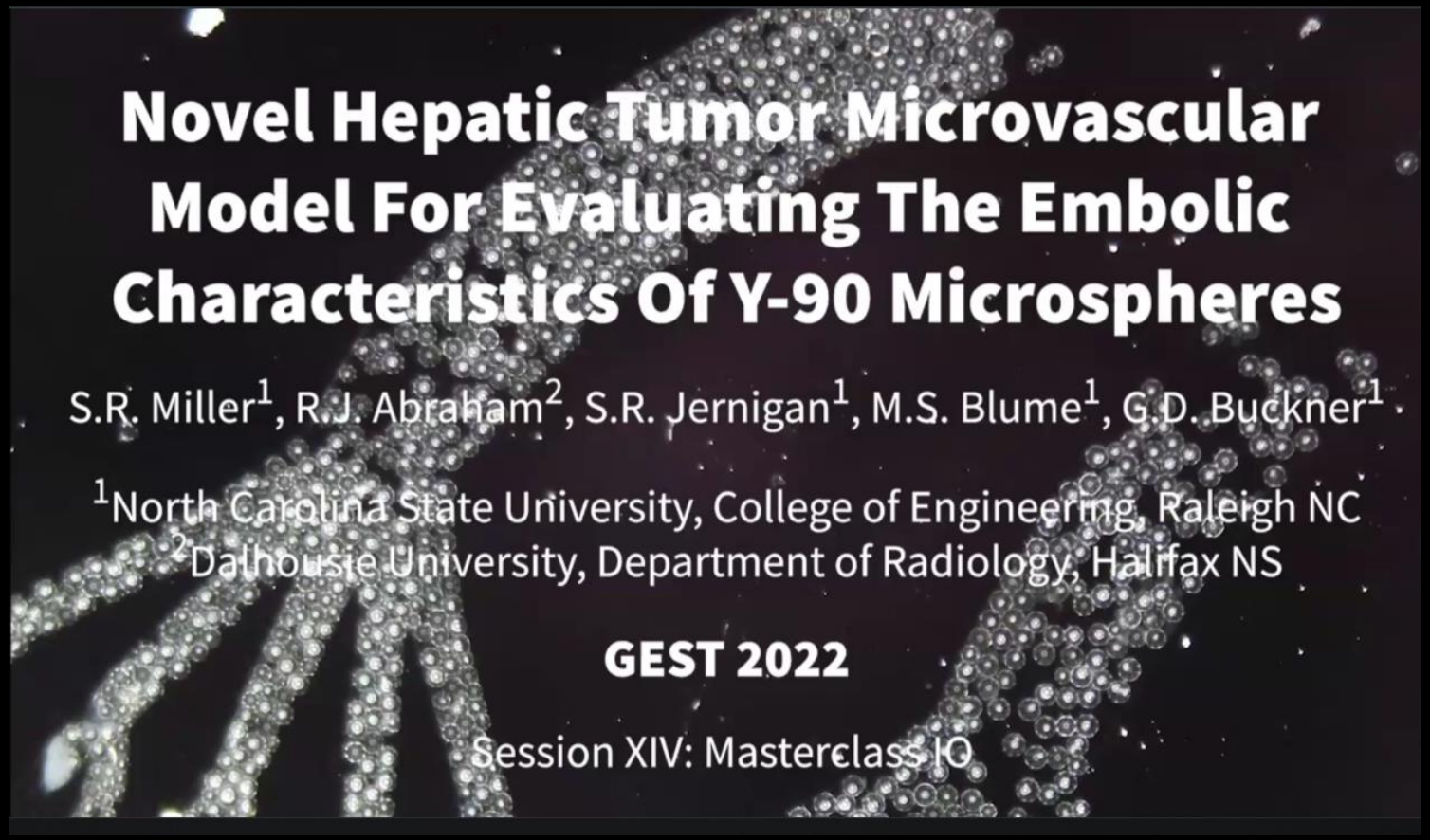

Contact Information

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