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Developing an Automated Platform for Breast Cancer Biopsy Imaging

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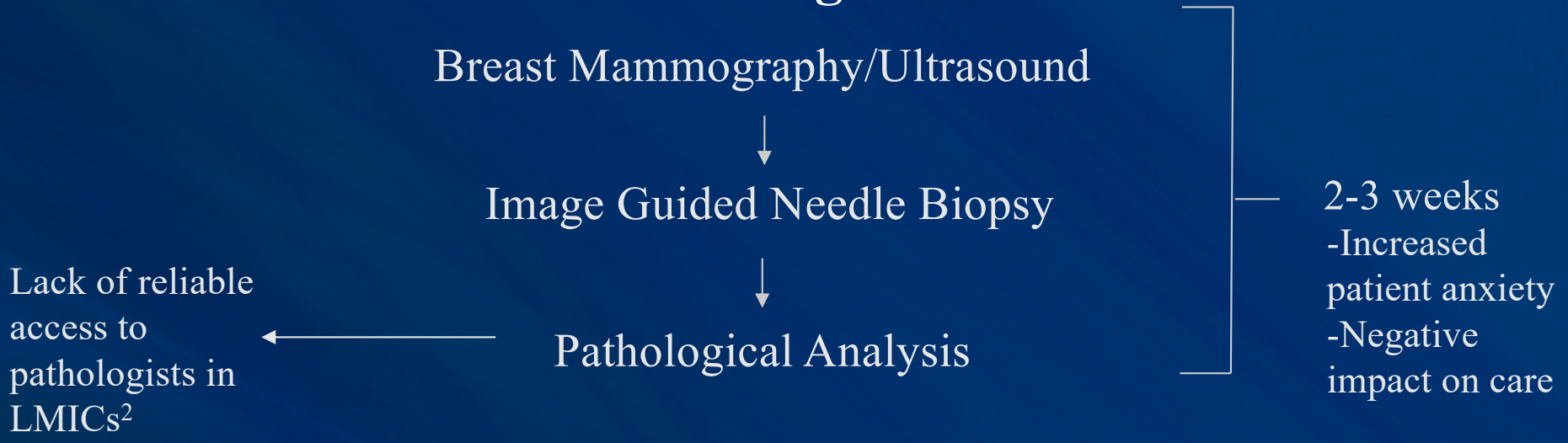
Contents

- Introduction
- Prior Work
- Platform Design
- Results
- Future Work

Introduction

Approximately 1 in 8 women will be diagnosed with invasive breast cancer in their lifetime and 1 in 39 women will die from breast cancer[1].

The Screening and Diagnosis Paradigm



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Introduction

Our Solution: Rapid assessment by leveraging fluorescently tagged HS-27 inhibitor to bind to the surface of heat shock protein 90 (Hsp90) which is overexpressed on aggressive breast cancer cells[3]. Currently, HS-27 is applied by manually staining biopsy specimen[4].

Manual Staining Protocol Disadvantages

Inconsistent Processing Times

Lack of Standardization

Biopsy prone to breakage

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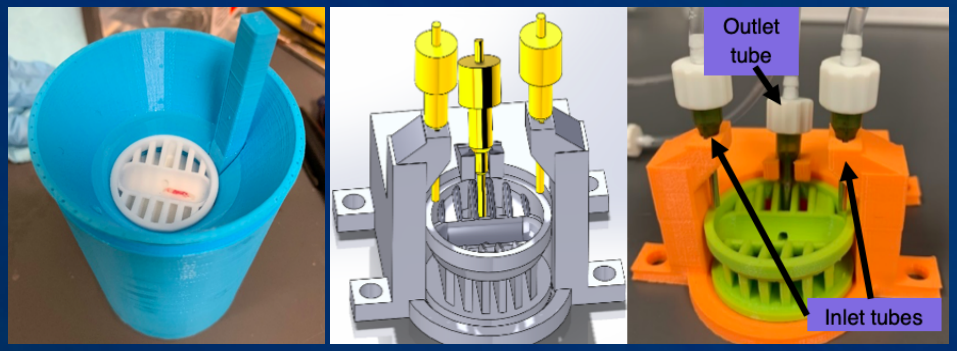
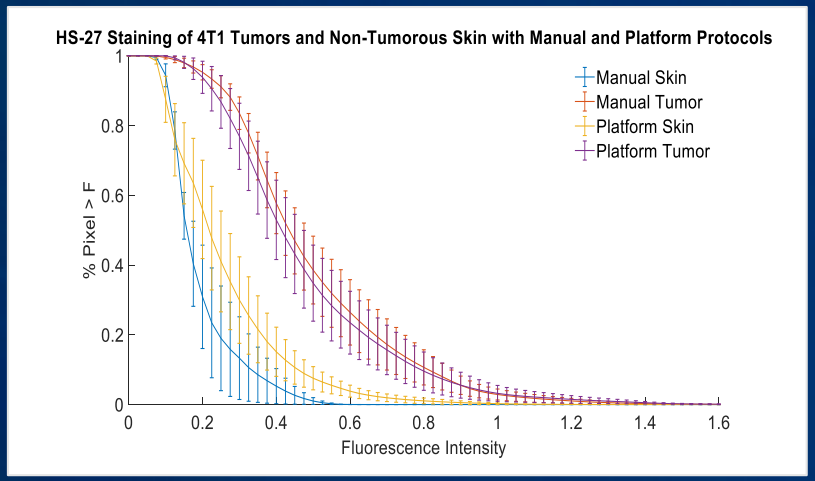
Prior Work

Thomas Vincent began this project by developing the biopsy collection platform and holder for staining and washing.



His results showed promise that using the platform design for staining and cleaning was as effective as the manual protocol at staining tissue with fluorescence.



The next step was to automate this process using his platform design.

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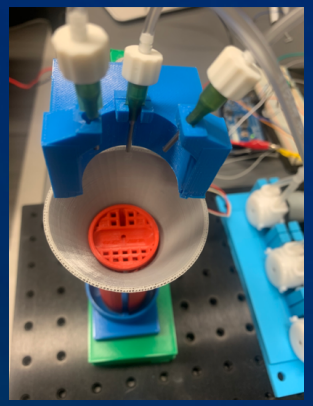
Design Needs/Specifications

Need #1: Integrity of biopsy specimen maintained	→	- Stays in platform for the whole process - Pump flow rate is less than 15 mL/min
Need #2: Can be transported by clinician	→	- Platform fits on 30 x 30 cm aluminum breadboard
Need #3: Fluorescent images are comparable to conventional microscopes	→	- Establish Wide-field and High-Resolution mode resolution within 10 microns of confocal resolution
Need #4: System can be implemented in LMIC	→	- Use Pocket Colposcope for imaging - Use PLA materials for design

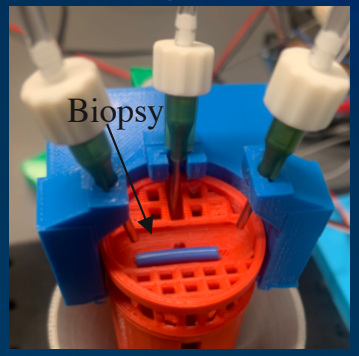
Design Proposal

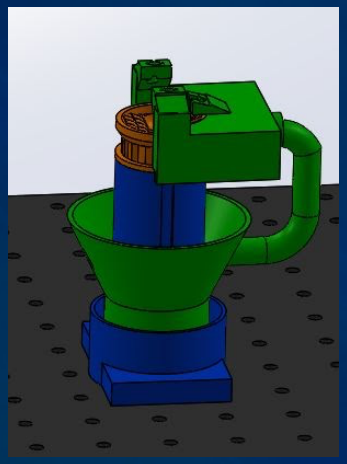
Biopsy Holder Design



Position 1:
Collection

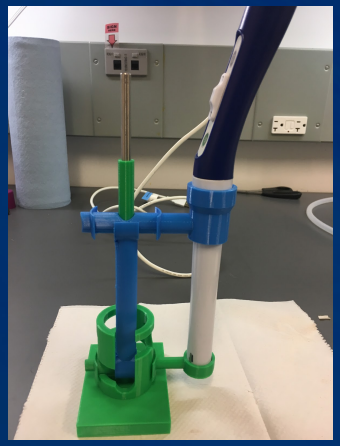
Position 2:
Staining/
Washing





Imaging Holder Design

Wide Field Mode



High Resolution Mode

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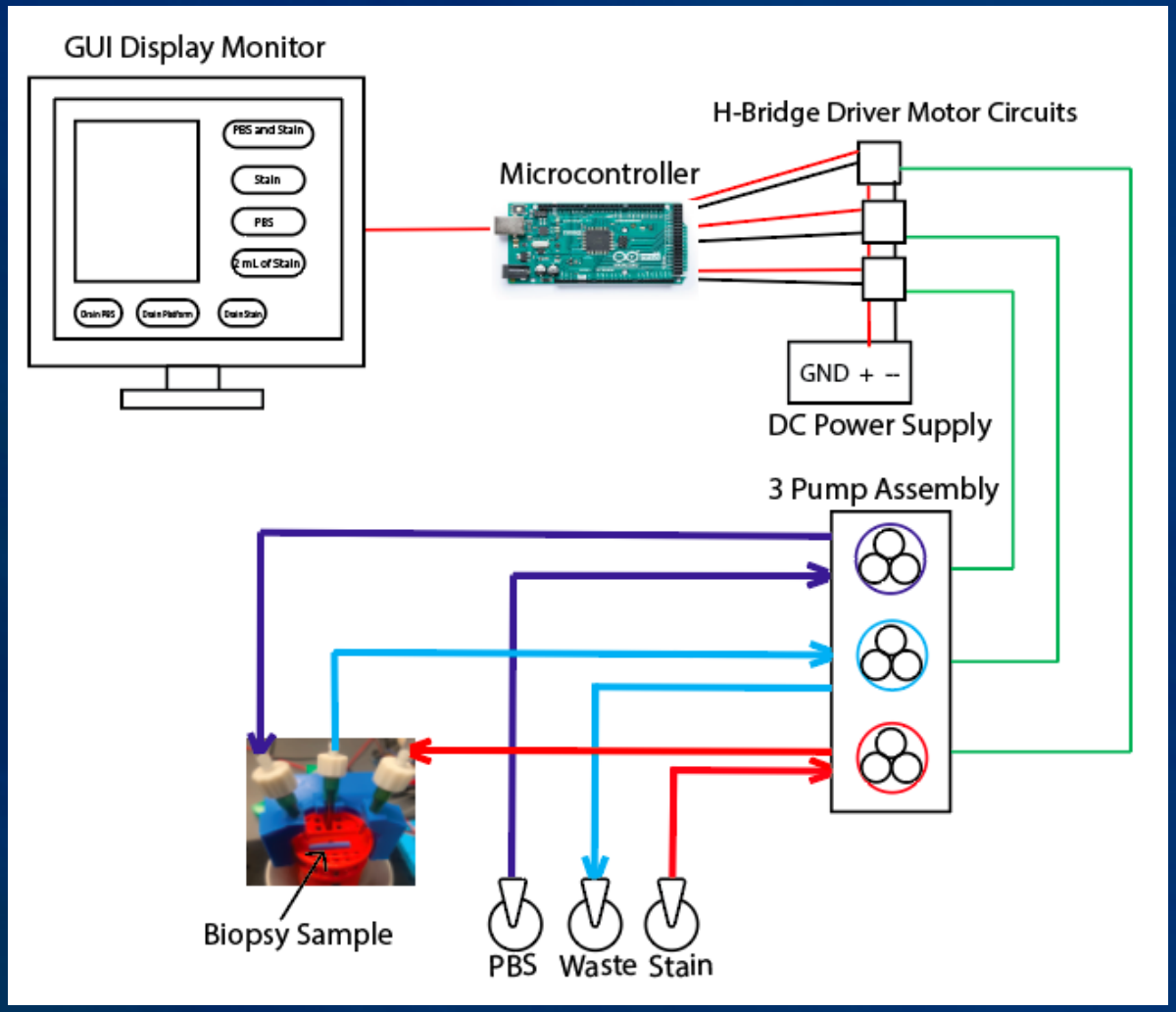
Design Proposal

Pump Automation Workflow



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Results

Flow Rate Experiment

-Biopsies of chicken breast tissue and fat

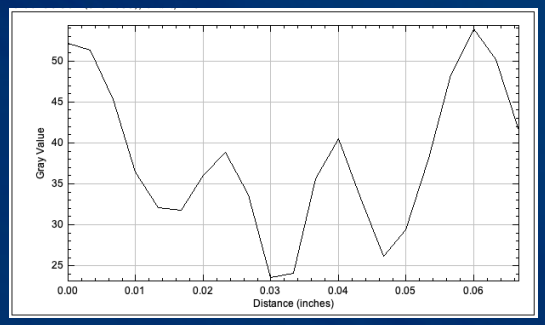
-Most critical condition at the outlet tube with fat biopsy

-No horizontal turbulence detected below 15 mL/min

Resolution of Pocket Colposcope using Imaging Holder

-Intensity Line Profile using ImageJ

-Resolvable if two smaller peaks are ½ the value of the maximum intensity



Distance from target resolution slide (mm)	Overall Resolution (um)	Field of View (mm)
4 (High Resolution)	5.52	6.20
22 (Wide Field)	17.54	26.3

Parameters of standardized wide-field and high resolution modes using imaging platform

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Future Work

- Check platform for stain residue
- Compare manual to automated staining protocol using 4T1 tumors from mice studies
- Add battery power as a power source
- Insulate wiring between microcontroller, circuit, and pumps
- Modify platform to be able to stain and wash multiple biopsies at once

References

1. Breast Cancer Facts and Figures 2017 & 2018. *American Cancer Society* (2017).
2. Crouch, B. T. *et al.* Exploiting heat shock protein expression to develop a non-invasive diagnostic tool for breast cancer. *Scientific Reports* **9,** (2019).
3. Barrott, J. J. *et al.* Optical and Radioiodinated Tethered Hsp90 Inhibitors Reveal Selective Internalization of Ectopic Hsp90 in Malignant Breast Tumor Cells. *Chemistry & Biology* **20,** 1187–1197 (2013).
4. Crouch, B. *et al.* Leveraging ectopic Hsp90 expression to assay the presence of tumor cells and aggressive tumor phenotypes in breast specimens. *Scientific Reports* **7,** (2017).

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