

**DESIGN OF FOCAL THERAPY PARADIGMS FOR BREAST CANCER-DERIVED  
EXTRACELLULAR VESICLE MODULATION**

**SOCIOECONOMIC FACTORS AFFECTING BREAST CANCER SCREENING**

An Undergraduate Thesis Portfolio  
Presented to the Faculty of the  
School of Engineering and Applied Science  
In Partial Fulfillment of the Requirements for the Degree  
Bachelor of Science in Biomedical Engineering

By

Emma Imbarlina

May 12, 2023

**ADVISORS**

Catherine D. Baritaud, Department of Engineering and Society

Natasha Sheybani, Department of Biomedical Engineering

## **SOCIOTECHNICAL SYNTHESIS**

Despite efforts to raise breast cancer (BrCa) awareness, mortality rates remain high among women, owing to a large number of stage IV diagnoses. Late-stage BrCa is more difficult to treat and often results in poor patient outcomes, thus it is important to develop surveillance techniques and effective stage IV treatment options. The technical report details such a design focusing on focal therapy modulation of BrCa-derived extracellular vesicles (EVs). Another factor contributing to high BrCa mortality is a lack of early detection stemming from socioeconomic disparities. To address this observation, the STS research paper investigates the degree to which President Biden's Advanced Research Projects Agency for Health (ARPA-H) may develop screening programs which consider relevant social factors and transcend socioeconomic status (SES). The tightly coupled projects, both aiming to reduce BrCa mortality among United States women, attack the problem at hand from both technical and social perspectives.

To better monitor BrCa, provide late-stage treatment, and ultimately reduce mortality, the technical report details the design of a focal therapy paradigm modulating the release of EVs, biomarkers important to cancer progression and metastasis. In leveraging these biomarkers, as well as associated miRNA, the paradigm may characterize BrCa. Aims included optimization of focal therapy modulation through evaluation of focused ultrasound (FUS) and radiotherapy, as well as a pipeline for downstream EV isolation and extracellular miRNA analysis. Cells were exposed to each therapy in vitro to understand respective modulatory effects, and expression of target miRNAs was analyzed to profile BrCa-derived EVs.

Results emphasize FUS as the optimal modulatory device for EV release and point to three miRNAs as relevant to BrCa. The developed focal therapy paradigm includes in vitro FUS

treatment, EV isolation via ultracentrifugation, RNA isolation using TRIzol reagent, and qRT-PCR for expression analysis. Expression analysis revealed mmu-miR-182 and mmu-let-7f as present across three BrCa cell lines, potentially important for tumor progression, but most notably, mmmu-miR-21a was demonstrated increased expression from stage I to stage IV BrCa. Overall, these findings and the focal therapy paradigm developed potentiate the use of liquid biopsy for BrCa diagnosis, surveillance, and miRNA-targeted drug therapy.

The STS research paper approaches the reduction of BrCa mortality from a social perspective. In light of ARPA-H's inception, the paper evaluates the ability of such an institution to provide governmental support towards early detection for lower SES women to minimize late-stage BrCa diagnosis. Considering health insurance differences, outdated screening standards, and educational factors, the investigation aims to overcome SES disparities leading to late detection through a linear Actor Network Theory model.

Findings reveal that expansion of Medicaid, though seemingly beneficial for BrCa screening rates, exacerbated differences in private and public health insurance policies due to inconsistencies nationwide. Thus, the paper suggests that Medicaid be expanded in every state, setting the stage for universal screening practice, screening programs which update consistently based on experimental findings, and educational resources made available to women of all SES. Subsequent implementation of these suggestions by ARPA-H shifts the linear Actor Network model toward earlier BrCa detection and lower mortality rates.

As shown through the tightly coupled projects, both technical and social factors must be considered to solve problems effectively. To address concerning BrCa statistics, both technical limitations regarding late-stage BrCa treatment and social barriers which perpetuate socioeconomic disparities involved in screening access must be sufficiently resolved.

## **TABLE OF CONTENTS**

### **SOCIOTECHNICAL SYNTHESIS**

#### **DESIGN OF FOCAL THERAPY PARADIGMS FOR BREAST CANCER-DERIVED EXTRACELLULAR VESICLE MODULATION**

with Nghi Tran

Technical advisor: Natasha D. Sheybani, Department of Biomedical Engineering

#### **SOCIOECONOMIC FACTORS AFFECTING BREAST CANCER SCREENING**

STS advisor: Catherine D. Baritaud, Department of Engineering and Society

### **PROSPECTUS**

Technical advisor: Natasha D. Sheybani, Department of Biomedical Engineering

STS advisor: Catherine D. Baritaud, Department of Engineering and Society