UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2019 Mary Gates Hall

Online Proceedings

2H

MEDICAL IMAGING AND DEVICES

Session Moderator: Eric Seibel, Mechanical Engineering

MGH 251

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Optimizing Diffusion Weighted MRI for Non-Contrast Enhanced Breast Cancer Detection

Michaela Del Priore, Senior, Bioengineering
Mentor: Savannah Partridge, Radiology
Mentor: Debosmita Biswas, Radiology

Dynamic-contrast enhanced (DCE) MRI has a very high sensitivity for breast cancer detection. However, the high costs, long scan-times and safety issues associated with injecting gadolinium-based contrast agents prompt the need to explore non-invasive, non-contrast-based diffusion-weighted imaging (DWI) as a possible alternative. DWI reflects the microscopic cellular environment and at high sensitizations (b-values), DWI can highlight malignant breast tissues without the aid of gadolinium. Acquiring images at high b-values increases image distortions and lengthens scan times. By simulating these high b-value images, lesion conspicuity can be increased while minimizing scan time and maintaining image quality. The purpose of this study was to compare lesion conspicuity across b-values and between acquired (aDWI) and computed (cDWI) DWI. Twenty women with invasive breast cancer were enrolled to undergo a research DWI scan. aDWI was acquired at multiple b-values of b=0/100/800/1500/2500 s/mm^2. Apparent diffusion coefficient (ADC) maps were generated and cDWI images were then computed for b-values ranging from b=200-2500s/mm^2 using: S_b = $S_1$00 e$^-$$\Delta$b*ADC.$Lesioncontrast - to - noiseratio(CNR)wascalculatedforbothaDWIandcDWIatetovisual value.CNRmeasuresacrossb-valuesfromcDWIandaDWIdemonstratedwellwithpearsonrankstest.Lesionconspicuity, asmeasuredbyCNR, increasedinbothmethodsasb-value, withnosignificantdifferencebetweenaDWIandcDWIatb-values1100 - 1500s/mm^2$, which is higher than typical diagnostic breast DWI protocols. However, lesion conspicuity likely varies with breast density and other patient and tumor characteristics. Potential advantages of cDWI include shorter scan times and flexibility to retrospectively generate images at any b-value for optimal interpretation, warranting further exploration of the value of this technique for breast imaging.

Ultrasound Imaging for Visualization of Vasculature after Spinal Cord Injury in Rodents

Takunda T (Takunda) Masike, Senior, Electrical Engr: Nanoscience & Molecular
Louis Stokes Alliance for Minority Participation, NASA Space Grant Scholar
Mentor: Matthew Bruce, Applied Physics Laboratory

Spinal cord injury (SCI) is often a life changing and debilitating condition, where the loss of sensory and motor capabilities can be accompanied with bladder, bowel, respiratory and other dysfunctions. It is known that traumatic SCI causes an almost a complete loss of blood flow at the site of injury, as well as significant hypoperfused regions surrounding the injury, resulting in progressive cell death referred to as secondary injury. Counteracting secondary injury of spinal cord tissue, referred to as "rescue-able" tissue, is an active area of neuroprotective research. Surprisingly, there are no existing techniques to detect and assess contused spinal cord tissue at risk for secondary injury clinically or pre-clinically. In this work, we present an approach to visualize and quantify the blood flow changes after SCI by imaging microbubbles, an intravascular contrasting agent, with ultrasound following intravenous injection. Nonlinear Doppler sequences were programmed on a research platform where Doppler processing separates microbubbles in the vasculature from background tissue signals. Our preliminary data demonstrate the ability to visualize changes in blood flow resulting from SCI in a rodent model. We will present results characterizing differences in blood flow associated from different injury severities. The nonlinear Doppler sequences are used to quantify the different characteristics of low velocity blood flow changes in the smaller vasculature and higher velocity blood flow changes in the larger vasculature. In addition, the passage of a bolus injection of microbubbles also highlights differences in blood flow in the contused and surrounding spinal cord tissue. Once translated, this ultrasound imaging technique could assist in detecting and monitoring local tissue perfusion at the injury site, ultimately improving SCI patient outcomes.

A 3D Printed Microfluidic, Tumor Organoid Testing Platform for Personalized Cancer Care and Treatment
Arman Reza (Arman) Naderi, Senior, Bioengineering
Mentor: Albert Folch, Bioengineering

Microfluidics is a field that consists of the manipulation of fluids in microchannels and chambers for a variety of biomedical applications from drug screening to the study of cell biology. Currently, the majority of microfluidic devices are made from drug-absorbent materials and manufactured using processes that are expensive, labor-intensive and time-consuming. These constraints have limited the commercialization and dissemination of microfluidic technology into healthcare markets. Digital manufacturing is a computer-based manufacturing method which integrates digital designs, automated fabrication, and device testing in order to increase fabrication efficiency. Through recent advancements in digital manufacturing technologies like 3D printing and laser cutting, and the development of non-drug absorbent resins for 3D printing, the Folch lab has been inexpensively prototyping complex 3D microfluidic platforms capable of testing the effectiveness of personalized cancer therapies that utilize multiple drug exposures. Current methods for modeling cancer lack the ability to replicate the human microenvironment in which a tumor develops, and prevent high throughput analysis of the effects of therapeutics. This need to efficiently recapitulate physiologically relevant effects of disease progression have been addressed by patient-derived tumor organoids. Composed of patient-derived cancer cells cultured in vitro, tumor organoids are a promising method for accurately modeling cancer because they serve as a representative snapshot of the types of cancer cells seen within the patient. By performing tests on tumor organoids to observe the effect of different combinatorial therapies, personalized cancer treatment regimens can be developed to most effectively treat individual patients. Combining the advantages of digital manufacturing with tumor organoids, I have been able to 3D print a microfluidic device capable of trapping and treating organoids with different combinations of drugs through the use of biocompatible, non-drug absorbent resins. This device's functionality and manufacturability demonstrates that digital manufacturing is vital for the implementation of microfluidics into healthcare industries.

Molecular Imaging of Inflammation with Ultrasound and Targeted / Non-Targeted Microbubbles
Mingxin (Ming) Ren, Senior, Bioengineering
Mary Gates Scholar, Undergraduate Research Conference Travel Awardee
Mentor: Matthew Bruce, Applied Physics Laboratory

The use of targeted microbubbles to image the molecular expression of vascular factors is an active area of ultrasound research. Combining the imaging advantages of ultrasound (e.g. cost, ease of use, availability) with the potential of molecular imaging makes targeted microbubbles especially attractive for studying the expression of vascular factors. During imaging, signals from molecularly attached microbubbles need to be separated from signals of non-attached free-flowing microbubbles in the vasculature. Thus far, different indirect approaches have been used to isolate stationary microbubbles. In this work, we present a direct approach to classify bound microbubbles in the presence of free-flowing microbubbles by processing nonlinear Doppler acquisitions. Nonlinear Doppler sequences are programmed on a research platform where Doppler processing separates low frequency stationary microbubbles signals from high frequency flowing microbubbles signals. In-vitro experiments are conducted by imaging stationary microbubbles surrounded by free-flowing microbubbles in a dialysis tube. In-vivo experiments are conducted by applying this approach to image the extent of inflammation associated with spinal cord injury (SCI), which plays a critical role in progressive tissue loss after injury. Both targeted and non-targeted microbubbles have been imaged in a rat SCI model. Targeted microbubbles were made for the inflammation marker p-selectin. Our in vivo results show successful separation of a limited number of non-targeted microbubbles adhering around spinal cord contusions. We believe this may be due to interactions between microbubbles and activated leukocytes. We expect to observe increases in bubble adherence and differences in the spatial distribution in using targeted bubbles, hopefully elucidating the extent of inflammation due to SCI. This work demonstrates the potential to separate bound targeted microbubbles from of free-flowing microbubbles to image a vascular factor for inflammation, which demonstrates practical pre-clinical ultrasound molecular imaging and opportunities for broader applications.

Engineering 3D Smooth Muscle Tubular Vessels with Controllable Architectures for Study of Structure-Function Relationships
Marcus Rhodehamel, Senior, Bioengineering
Mary Gates Scholar
Mentor: Deok-Ho Kim, Bioengineering
Mentor: Nisa Williams, Bioengineering

Current methods of modeling tissues rely on two-dimensional (2D) cell cultures which fail to incorporate the three-dimensional (3D) aspect of native tissues in the body and therefore cannot mimic tissue-specific conditions in vivo. The inability to accurately mimic the native properties of tissues in vitro makes characterizing physiological cell behavior challenging and limits the applications of these models. As such, the lack of sufficient in vitro tissue models necessitates the need for a more advanced engineered tissue models that accurately recapitulates the native morphology and function of cells in vivo. Previously developed in vitro platforms that attempt to model human vasculature in vivo have been lim-

ited in their ability to imitate the circumferential architecture of smooth muscle cells which surround the veins and arteries. Through the production of a more advanced vascular tissue engineered platform that accurately recapitulates biomimetic conditions of native tissue, we could better study cardiovascular biology, disease modeling, and drug-response in a dish. We propose the fabrication of an architecturally-controlled multi-layered 3D smooth muscle cardiovascular model that mimics the tubular structure of blood vessels in vivo to study structure-function relationships. Utilizing a thermoresponsive nanopatterned film, we are able to direct cell alignment and layer sheets of cells to create a circumferentially aligned 3D smooth muscle tissue model that mimics the physiology of the vascular tunica media. Furthermore, we have designed a fibrin gel casting method to produce tubes with a hollow intraluminal space that has mechanical properties that are physiologically relevant to human tissue. We aim to determine how anisotropic alignment of smooth muscle affects vascular compliance. This model is highly versatile in nature and can be functionalized with a wide variety of cell types to accommodate different tubular tissue structure throughout the human body.

OsteoApp: Towards Ubiquitous Osteoporosis Screening
Parker Scott (Parker) Ruth, Senior, Bioengineering, Computer Engineering
Mary Gates Scholar, UW Honors Program, Washington Research Foundation Fellow
Mentor: Shwetak Patel, Computer Science & Engineering
Mentor: Edward Wang, Electrical and Computer Engineering

Osteoporosis — a condition characterized by abnormally low bone density — primarily afflicts women over the age of 65 and is estimated to cause almost 9 million annual fractures worldwide. The current gold standard for clinical osteoporosis screening is dual-energy x-ray absorpiometry (DEXA), which can be used in combination with demographic metrics to estimate an individual's likelihood of fracturing a bone. Early detection of osteoporosis enables preventative dietary, lifestyle, and pharmaceutical interventions to improve patient outcomes. However, DEXA requires access to expensive equipment and specialized facilities. This motivates the need for an inexpensive and ubiquitous osteoporosis screening technology, bringing access to osteoporosis screening to individuals in low resource settings. In this work, I designed, implemented, and evaluated a smartphone application called OsteoApp that attempts to infer bone density indirectly by measuring the resonant properties of bone. Using my smartphone application prototype in parallel with a custom hardware setup, I collected data from retirement community members with known DEXA scan results as well as from a control group of University of Washington students. I analyzed these data to evaluate the feasibility of a smartphone-based osteoporosis screening solution.

Application of Photoplethysmograhy in the Measurement of Physiological Parameters
Sabrina Xie, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Ruikang Wang, Bioengineering

Heart rate, as an essential health indicator, can provide valuable information to evaluate the fitness level of an individual. To improve the health and wellness, an affordable, noninvasive, and robust device monitoring the condition of the heart that could track long-term physiological measurement of an individual is highly demanded. Intrinsic signal optical imaging (ISOI) technology is an innovative, simple and favorable optical technique directly used for detecting miniscule intrinsic optical signals in tissues. Here, we have developed an ISOI system and taking advantages of an intensity-sensitive algorithm to monitor blood volume change in the vasculature bed in tissues which is indicative of heart pulse throughout the day. A green (532 nm), red (650 nm) laser, and a CCD camera were implemented allowing the production of an affordable, efficient and robust heart rate monitoring device. To provide accurate evaluation for the level of health, a highly sensitive intensity-based algorithm was implemented to this device, which detect the minuscule blood volume change based on the scattered light reflected from the tissues. Parameters such as the rate of blood flow, blood pressure, blood oxygenation, and hemodynamic property were extracted from the intrinsic signal and provide information for further evaluation of the heart condition and heart diseases. Our device can be a powerful tool for medical services to track and control the progression of the disease and further lowering the cost of medical care alleviating the financial burden for the individual, communities, nations and worldwide organizations.

Medical Imaging for Realtime Diagnosis on Magic Leap One
Paul Yoo, Junior, Applied & Computational Mathematical Sciences (Discrete Mathematics & Algorithms)
Yingru (Alan) Feng, Senior, Computer Science
Mentor: Aditya Sankar, Computer science and engineering

Medical imaging techniques such as X-ray, provide clinicians intensive information on the disease/condition of patients. However, clinicians have to look away from the subject to refer to medical images, thereby losing track of their work. Thus, clinicians usually study the images prior to surgery and limit reference time to images during surgery. Furthermore, unlike X-ray, novel imaging methods (such as optical ultrasound) are not taught in medical schools, so untrained clinicians face challenges in interpreting the images. These two limitations restrict the clinicians' ability to fully utilize and

adopt advanced medical imaging techniques. In this work, we explore the possibility of using Augmented and Virtual Reality (AR/VR) in the context of medical imaging. Prior applications of AR/VR technology in medicine have been limited to AR-aided training for medical students, telepresence for interaction, as well as remote therapy. We aim to use AR as a real-time diagnostic and therapeutic tool by augmenting the clinicians' live view with various imaging modalities (such as X-ray, optical ultrasound, near-infrared). We hypothesize that providing these images in-context, and in some cases aligned with the subject, will improve the interpretation of images resulting in better guidance for diagnosis or surgery. To test this, we are creating an AR-based medical imaging/analysis application that uses techniques such as volumetric rendering and real-time image registration to augment the clinicians' view. Furthermore, clinicians can interact with the images by filtering, slicing, and reducing dimensionality, in order to better understand the images and thereby the underlying disease/condition.