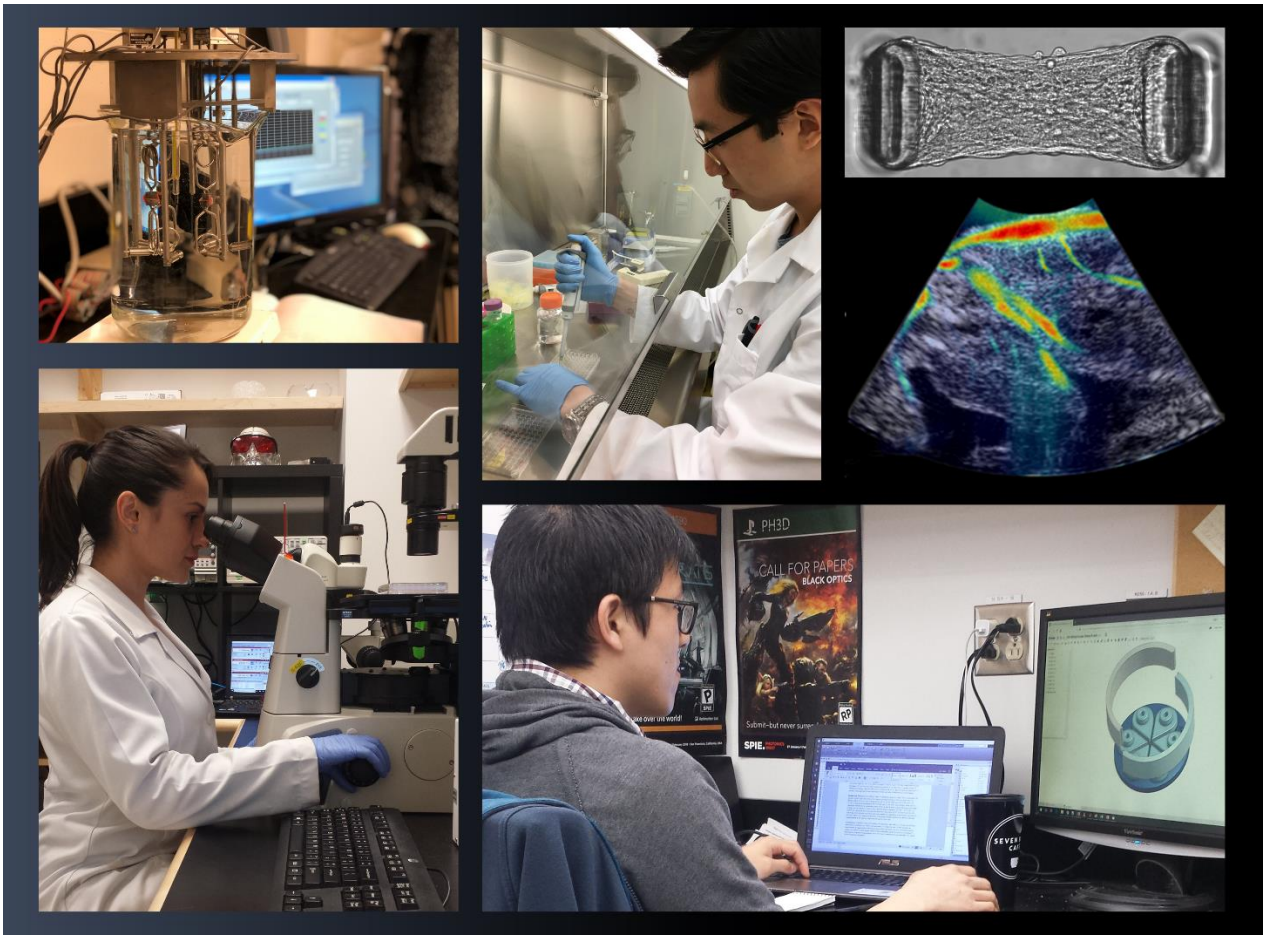
School of Biomedical Engineering

Research Day 2019



Scientific Program

DALHOUSIE UNIVERSITY

DALHOUSIE UNIVERSITY

May 3rd, 2019

Dear Colleagues:

It is my pleasure to welcome you to the 17th Annual Research Day of the School of Biomedical Engineering at Dalhousie University!

This is the premiere day of the year for our School, an exciting time for our students to present their research to the public and their peers, and a great opportunity for us all to share in their discoveries. I encourage each of you, and especially the students, to participate and engage with each other through helpful comments and questions. During the breaks, lunch and the reception there will be plenty of time to continue with spirited discussion.

This year I have the great pleasure to welcome our two Keynote Distinguished Speakers, Kullervo Hynynen, PhD, from Sunnybrook Research Institute and University of Toronto, who will present work from his lab on "Healing the Brain using Focused Ultrasound", and Jack Fairbank, PhD, Senior Product Development Engineer at Siemens Healthineers, who will present "Point-of-Care and Near-Patient Tests – Engineering Challenges in Bringing Handheld Diagnostic Devices to Market".

Dr. Hynynen is Professor in the Department of Medical Biophysics at the University of Toronto and the Director of the Physical Sciences Platform at the Sunnybrook Research Institute, Toronto, Canada. He received his MSc from the University of Kuopio, Finland and his PhD from the University of Aberdeen, UK. Dr. Hynynen currently holds a Tier 1 Canada Research Chair in Imaging Systems and Image Guided Therapy. In Toronto, his lab studies the use of focused ultrasound for ablation and to enhance the permeability of the blood-brain barrier. He has been facilitating the clinical testing of thermal ablation of essential tremor and several clinical trials on blood-brain barrier permeability enhancement.

Dr. Fairbank is one of our Alumni and I'm very proud as his PhD supervisor that he's returning as our distinguished academic speaker today. He has a combined degree in Engineering Physics and Management at McMaster University; a PhD in Biomedical Engineering in respiratory cell mechanics at Dalhousie University, with post-doc experience at Harvard and McGill Universities; and business strategy at Oxford University. He now works in Ottawa for Siemens Healthineers in the development of their epoc™ Blood Analysis System. He previously worked in Oxford, UK, for Alere (now Abbott Diagnostics).

I want to sincerely thank all those who help make this day run smoothly. Thank you in advance to our judges of today's presentations, and a very heartfelt thank you to our shining young students, who both moderate and present their work in the sessions detailed in the following pages. Without them there would be no celebration today. Finally, thank you to Sandra Pereira who always works tirelessly in support of our fine School. This day is a highlight for me, and I hope for all of you.

Welcome to all and please enjoy the day!

Geoffrey Maksym, Ph.D.
Professor and Director

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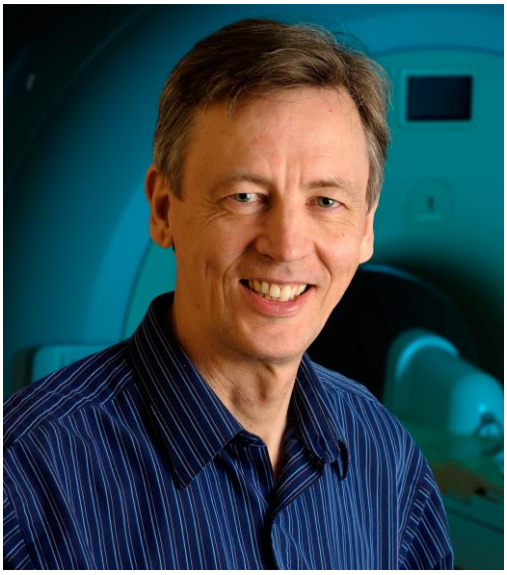
School of Biomedical Engineering

Research Day 2019

DISTINGUISHED ACADEMIC LECTURE



Kullervo Hynynen, PhD

Professor, Department of Medical Biophysics, University of Toronto

Director of the Physical Sciences Platform, Sunnybrook Research Institute

"Healing the Brain using Focused Ultrasound"

“Healing the Brain using Focused Ultrasound”

Kullervo Hynynen, PhD

Department of Medical Biophysics, University of Toronto and Sunnybrook Research Institute, Toronto, Ontario, Canada. email: khynynen@sri.utoronto.ca

Biography: Kullervo Hynynen, Ph.D. is Professor in the Department of Medical Biophysics at the University of Toronto and the Director of the Physical Sciences Platform at the Sunnybrook Research Institute, Toronto, Canada. He received his MSc from the University of Kuopio, Finland and his PhD from the University of Aberdeen, UK. He accepted a faculty position at the University of Arizona, where he built a therapeutic ultrasound program and developed several ultrasound devices from ideas to clinical trials and was the first to integrate focused ultrasound transducers with an MRI scanner. He joined the faculty at Harvard University and Brigham and Women’s Hospital in Boston in 1993. There he founded the Focused Ultrasound Laboratory and developed MRI-guided ultrasound surgery methods for clinical testing. These included MRI-guided breast tumor, uterine fibroid and brain ablation devices. He transferred the technology to InSightec for commercialization. He and his team also discovered how to safely enhance the permeability of the blood-brain barrier (BBB) using focused ultrasound and established the safety and efficacy of the method in pre-clinical models. In 2006, he moved to Toronto where he holds a Tier 1 Canada Research Chair in Imaging Systems and Image-Guided Therapy. In Toronto, he has continued his research on brain treatments using focused ultrasound for ablation and to enhance the permeability of the BBB. He has been facilitating the clinical testing of thermal ablation of essential tremor and several clinical trials on BBB permeability enhancement.

Abstract: When combined with imaging-guidance, focused ultrasound (FUS) provides means for localized delivery of mechanical energy deep into tissues. This focal energy deposition can modify tissue function via thermal or mechanical interactions with the tissue. MRI-guided hemi-spherical phased array technology with CT-based beam modulation has made FUS treatments of brain tissue through intact skull possible in the clinical setting. Thermal ablation of a target in the thalamus has been shown to be effective in the treatment of essential tremor and is now FDA approved. The impact of ultrasound exposure can be potentiated by intravascular microbubbles that can enhance blood-brain barrier (BBB) permeability for a wide variety of molecules, particles and even cells. The ability to modulate the BBB has been shown to be effective in treatments of many diseases in animal models with initial patient trials showing clinical feasibility. In this talk, the progress in utilizing ultrasound phased array technology for brain treatments will be reviewed and its further potential discussed.

School of Biomedical Engineering

Research Day 2019

DISTINGUISHED INDUSTRY LECTURE

Jack Fairbank, PhD

Senior Product Development Engineer, Siemens Healthineers

"Point-of-Care and Near-Patient Tests – Engineering Challenges in Bringing Handheld Diagnostic Devices to Market"

"Point-of-Care and Near-Patient Tests – Engineering Challenges in Bringing Handheld Diagnostic Devices to Market"

Jack Fairbank, PhD

Senior Product Development Engineer, Siemens Healthineers, Ottawa, Canada.

Biography: Dr. Fairbank's main interest is in developing rapid medical diagnostic devices. He currently works in Ottawa for Siemens Healthineers on their epoc™ Blood Analysis System, doing technical development on both the consumable assay and the hand-held analyser. From a few drops of blood, this system measures the concentration of blood gases, electrolytes, and metabolites within one minute, helping doctors make rapid decisions in acute care settings. Previously, Dr. Fairbank worked in Oxford, UK, for Alere (now Abbott Diagnostics). There he helped develop a hand-held electronic system, called the DDS2, that detects a series of drugs in a saliva sample. The DDS2 is now in use by police forces around the world for roadside driver-impairment testing. Dr. Fairbank trained in engineering physics at McMaster University; respiratory biophysics at Dalhousie University, Harvard University, and McGill University; and business strategy at Oxford University.

Abstract: This talk will provide an industry-perspective on the rapidly growing field of point-of-care and near-patient tests. Within a few minutes these technologies measure or detect the presence of substances in a biological sample such as blood or urine to assist time-sensitive medical decision-making. I'd like to share with you some of the product development experience I gained, and engineering challenges faced, in bringing two hand-held tests to market: the Alere DDS2 Mobile Drug Testing System and, more recently, the Siemens epoc™ Blood Analysis System. The epoc™ and systems like it are a cornerstone of Canada's contribution to the global rapid diagnostics market, which must continue growing if our healthcare systems are to cope with ageing populations and chronic disease monitoring.

Previous Winners of the Community Builder Prize in Biomedical Engineering

2008

Marianne Ariganello

2011

Adrian West

2013

J. Michael Lee

2015

Eleanor Seaman-Bolton

2017

Rishima Agarwal

2018

Kristin Robin Ko

Previous Winners of the Annual Teaching Prize in Biomedical Engineering

2008
Geoff Maksym

2009
J. Michael Lee

2010
Jeremy Brown

2011
Paul Gratzer

2012
Rob Adamson

2013
Janie Astephen-Wilson

2015
Daniel Boyd

2016
Sarah Wells

2017
Jeremy Brown

2018
John Frampton

Previous Winners of the George W. Holbrook Prize in Biomedical Engineering

2010
Richard Roda

2011
Graeme Harding

2013
Matthew Walker

2014
Pouya Amiri

2015
Lauren Kiri

2016
Brandon Scott

2017
Kristin Robin Ko

2018
Rishima Agarwal

Previous Winners of the Allan E. Marble Prizes in Biomedical Engineering

2002
Sean Margueratt

2003
Anna Dion

2005
Doctoral: Mark Glazebrook
Pre-doctoral: Carolyn Lall

2006
Doctoral: Scott Landry
Pre-doctoral: Scott MacLean

2007
Doctoral: Janie Astephen
Pre-doctoral: Andrew Moeller

2008
Doctoral: Marianne Ariganello
Pre-doctoral: Vargha Talebi

2009
Doctoral: Jack Fairbank
Pre-doctoral: Jennifer Krausher

2010
Derek Rutherford

2012
Del Leary

2013
Andre Bezanson

2014
Caitlin Pierlot

2015
Arash Momeni Boroujeni

2016
Dan MacDougal

2017
Brett Dickey

School of Biomedical Engineering

Research Day 2019 Scientific Program

Friday, May 3, 2019
Kenneth C. Rowe Management Building, Room 1020

Morning Reception	
8:00 am to 8:45 am	**Student & Faculty Check-In**
8:45 am to 8:55 am	**Welcome: Dr. Geoff Maksym, Director, School of Biomedical Engineering**
8:55 am to 9:00 am	**Opening Remarks: Dr. Alice Aiken, Vice President, Research & Innovation**

Scientific Session 1 (Chairs: Andy Huang and Nick Campbell)	
9:00 am to 9:15 am	***"A rendering pipeline and software architecture for processing and visualization of optical coherence tomography data in a clinical setting"*** **Josh Farrell (PhD Student), D. MacDougall and R. Adamson**
9:15 am to 9:30 am	***"Nanomechanical mapping of collagen fibrils under tension"*** **Chris Peacock (MASc Student) and L. Kreplak**
9:30 am to 9:45 am	***"Minimally invasive in-vivo functional ultrasound imaging using a 40 MHz phased array endoscope: mapping the auditory response in rats"*** **Chris Samson (PhD Student), T. Landry and J.A. Brown**

Coffee Break (9:45 am – 10:00 am)

Scientific Session 2 (Chairs: Breagh Devereaux and Matt Mallay)	
10:00 am to 10:15 am	***"A new 3D imaging technique demonstrated on a 128-element, crossed electrode endoscope"*** **Katherine Latham (PhD Student), C. Samson, J. Woodacre, E. Simpson, R.J. Zemp and J.A. Brown**
10:15 am to 10:30 am	***"Assessing repeatability and approaches to reducing variability in oscillometry and the effects on respiratory system impedance"*** **Jonathan Tjong (PhD Student), M. Alamer, E. Gillis, S. DeLorenzo, V. Dai, A. Dubeau, R. Foong, M. Brydges, T.J. Moraes, M.R. Sears, G.L. Hall, P. Subbarao and G.N. Maksym**
10:30 am to 10:45 am	***"Understanding the role of ECM in prostate cancer progression using 3D cell culture"*** **Nicky Tam (MASc Student), G. Dellaire and J.P. Frampton**
10:45 am to 11:00 am	***"Capacity of four different power meters to evaluate the radiant power from fourteen light curing units"*** **Stella Braga (PhD Student), S. Juckes, B. Sullivan, C.J. Soares and R.B. Price**

Distinguished Academic Lecture	
11:00 am to 12:00 pm	**Dr. Kullervo Hynynen, Professor, Department of Medical Biophysics, University of Toronto and Sunnybrook Research Institute** ***"Healing the Brain with Focused Ultrasound"*** **Introduction: Dr. Jeremy Brown**

Catered Lunch (12:00 pm – 1:00 pm)

Distinguished Industry Lecture	
1:00 pm to 2:00 pm	**Dr. Jack Fairbank, Senior Product Development Engineer, Siemens Healthineers** ***"Point-of-Care and Near-Patient Tests – Engineering Challenges in Bringing Handheld Diagnostic Devices to Market"*** **Introduction: Dr. Geoff Maksym**

Scientific Session 3 (Chairs: Anas Tahir and Emile Feniyanos)	
2:00 pm to 2:15 pm	***"Fabrication and verification of an endoscopic phased array for combined photoacoustic tomography and high-frequency ultrasound imaging"*** **Taylor Landry (MASc Student), C. Samson, K. Latham, J.A. Brown and R. Adamson**
2:15 pm to 2:30 pm	***"Individuals with delayed trunk muscle reflexes have different muscle activation patterns to complete a controlled transfer task"*** **D. Adam Quirk (PhD Student) and C.L. Hubley-Kozey**
2:30 pm to 2:45 pm	***"Engineering a microenvironment for screening responses of immune cells to infectious disease therapies"*** **Alyne Teixeira (PhD Student) and J.P. Frampton**
2:45 pm to 3:00 pm	***"Performance evaluation of various 1:3 piezo-composite substrates for histotripsy applications"*** **Jeffrey K. Woodacre (PhD Student) and J.A. Brown**

Coffee Break (3:00 pm – 3:15 pm)

Career Panel Q&A	
3:15 pm to 4:00 pm	**Student Question and Answers and Career Advice with Distinguished Speakers and BME Faculty** **Chair: Dr. John Frampton** **Panel: Dr. Kullervo Hynynen, Dr. Jack Fairbank, Dr. Sarah Wells and Dr. Daniel Boyd**

Awards and Closing	
4:00 pm to 4:15 pm	**Presentation Judging (Atrium)** **Dalhousie Biomedical Engineering Society Elections (Room 1020)**
4:15 pm to 4:30 pm	**School of Biomedical Engineering Awards and Closing Remarks** **Chair: Dr. Geoff Maksym**

Closing Reception (4:30 pm – 6:30 pm)

School of Biomedical Engineering

Research Day 2019 Abstracts

SCIENTIFIC SESSION 1

A rendering pipeline and software architecture for processing and visualization of optical coherence tomography data in a clinical setting

Joshua Farrell[1], D. MacDougall[1] and R. Adamson[1,2]

[1]School of Biomedical Engineering, Dalhousie University; [2]Department of Electrical and Computer Engineering, Dalhousie University

Introduction: We demonstrate techniques for the visualization and processing of optical coherence tomography (OCT) Doppler vibrometry data for presentation in a clinically relevant and intuitive manner. We also demonstrate a suitable software framework to support such processing and visualization while being flexible, reliable, stable and supportable. Topics to be covered are: Real-time visualization of 2D OCT and in-vivo Doppler. These processing steps are implemented within a software architecture capable of supporting the range of functionality required in a clinical imaging system.

Methods: We render in-vivo Doppler middle ear images in real-time using a custom image processing pipeline centered on the use of hardware acceleration through general purpose graphics processing units (GPUs). Rendering of middle ear Doppler data consists of several processing steps throughout the pipeline such as: phase unwrapping, Doppler extraction, noise correction, accumulation, and finally colour mapping. As a first step, each acquired OCT image line is phase unwrapped relative to adjacent image lines. This allows vibrometry data to be extracted across groups of image lines through cross correlation with a known phasor centered at the excitation frequency of the acoustic tone applied to the ear being imaged. Before accumulating the extracted vibrometry data we first correct for low frequency noise introduced through patient head movement. The accumulated vibrometry data is then scaled within a vibration range of interest and converted to a colour map to be displayed. By utilizing the features within the new software framework we can easily extend this pipeline for real-time display of 2D and 3D in-vivo Doppler datasets.

Results and Discussion: We present benchmark results comparing the Doppler processing pipeline implemented within the new software architecture to that of the old system and demonstrate specific capabilities of the new software framework relevant to middle ear imaging. Design considerations in a clinical imaging system suitable for multi-site deployment are discussed.

Conclusion: The processing pipeline and supporting architecture appear well-suited to use in clinical real-time imaging applications.

Nanomechanical mapping of collagen fibrils under tension

Chris Peacock[1] and L. Kreplak[1,2]

[1]Department of Physics and Atmospheric Science; [2]School of Biomedical Engineering, Dalhousie University

Introduction: Collagen fibrils constitute the smallest repeating unit in tissues such as tendon and bone, and act as a major constituent of the matrix in which cells live and move within the bodies of mammals. The collagen fibril is a rope-like aggregate of triple-helical polypeptides, assembling with a characteristic 67nm staggering pattern known as the D-band. The function of the fibrillar structure is to withstand stress applied both at the tissue and at the cellular level. However, the current understanding of how this structure responds to applied stress has been extrapolated from experiments performed at the tissue level, rather than from direct measurements made on the fibril level. Here, I address the need to mechanically assess individual collagen fibrils under tension by using atomic force microscopy to image hydrated fibrils absorbed to a strained elastic substrate.

Methods: In order to image individual collagen fibrils held under tension, I designed a motorized tensile testing stage that is compatible with both an atomic force microscope and a visible light microscope. This stage is used to strain a thin PDMS sheet to which hydrated collagen fibrils are adsorbed, and to maintain tension in the sheet while obtaining atomic force micrographs. These micrographs capture the structural and mechanical properties of the strained collagen fibrils as a function of fibrillar strain.

Results and Conclusion: The collagen fibrillar structure responds inhomogeneously to applied tension through tauting and sliding of its constituent polypeptides, reconstruction mechanisms that have been suggested in previous studies but never directly observed. This deformation pathway may function not only to protect the polypeptides from developing plastic damage, but also to alter the nature of the cell-fibril interaction when the fibril is held under tension.

Minimally invasive in-vivo functional ultrasound imaging using a 40 MHz phased array endoscope: mapping the auditory response in rats

Chris Samson[1], T. Landry[1] and J.A. Brown[1,2]

[1]School of Biomedical Engineering, Dalhousie University; [2]Department of Electrical and Computer Engineering, Dalhousie University.

Introduction: Recently, functional ultrasound imaging has emerged as a new tool for monitoring changes in cerebral blood volume associated with neural activity. The combination of high spatiotemporal resolution as well as low cost and high portability have propped ultrasound to potentially become a ground-breaking imaging modality for functional imaging of the brain. To date, studies have been limited to large craniotomies, neonatal, and thin skull applications. In this study we extend the application of functional ultrasound to small burr hole surgeries by using a miniature high-frequency phased array in an endoscopic form factor.

Methods: Rats were anaesthetized and subjected to 4, 8, and 15 kHz tones at 97 dB for fixed intervals. The ultrasonic probe used for this investigation was a 64-element 40 MHz phased array packaged in a 2.5 x 3.1mm endoscopic form factor. The probe was inserted into a small 3x6.5 mm hole for functional imaging of the inferior colliculus (IC). Imaging was undertaken during these intervals by coherently compounding 16 diverging waves at a pulse repetition frequency of 40KHz on a custom 64-channel beamforming platform. Image acquisition and stimulus was synchronized and automated using a custom Python 2.7 software interface. Beamforming, SVD filtering, and post-processing was performed in MATLAB.

Results and Discussion: Increases in cerebral blood volume as high as 85% were measured in response to auditory stimuli in the IC. Mapping was performed with very high spatial resolution, 40 and 100 µm of axial and lateral resolution respectively. Strong correlations indicate neural activation in response to 4, 8 and 15 kHz tones, and the position of functional activation is in excellent agreement with the anatomical position of the IC.

Conclusion: This study shows that functional mapping through small burr hole surgeries is possible, vastly increasing the number of potential use-cases for functional ultrasound imaging.

School of Biomedical Engineering

Research Day 2019 Abstracts

SCIENTIFIC SESSION 2

A new 3D imaging technique demonstrated on a 128-element, crossed electrode endoscope

Kate Latham[1], C. Samson[1], J. Woodacre[1], E. Simpson[1], R.J. Zemp[2] and J.A. Brown[1,3]

[1]School of Biomedical Engineering, Dalhousie University; [2]Department of Electrical and Computer Engineering, University of Alberta; [3]Department of Electrical and Computer Engineering, Dalhousie University

Introduction: Crossed electrode arrays address some the challenges associated with 3D ultrasound imaging because of the large reduction in the number of elements ($2N\ vs.\ N^2$). However, creating a two-way focused 3D image is difficult with these arrays because azimuth and elevation dimensions cannot be beamformed at the same time. This typically forces a synthetic aperture approach which often sacrifices SNR to maintain frame rates.

Methods: We have developed a new 3D imaging approach that uses the flexibility of bias sensitive (i.e. pulse amplitude and polarity depend on a DC bias) substrates to create a high-quality elevation focus. The principle behind this technique is to perform conventional compound imaging in one plane while implementing a bias controllable elevation lens in a perpendicular plane. The lens is a combination of a transmit Fresnel lens with receive Hadamard coding. A 30MHz, 64x64 element crossed electrode relaxor array was fabricated on a semi-kerfed substrate. Imaging performance was tested using a custom 64 channel beamforming system with a 3D module that provides the 64 reconfigurable biasing channels.

Results and Discussion: Two-way radiation patterns in both azimuthal and elevational planes were compared with simulation results. The -6dB beamwidths were simulated to be 155µm and 170µm in the azimuth and elevation direction respectively and the secondary lobe levels were suppressed below -55dB.

Conclusion: 3D images were generated by imaging a wire phantom using a reconfigurable Fresnel lens and Hadamard receive coding to focus to a set of elevation slices and build the volume image. Imaging of tissue mimicking phantoms is ongoing.

Assessing repeatability and approaches to reducing variability in oscillometry and the effects on respiratory system impedance

Jonathan Tjong[1], M. Alamer[1], E. Gillis[1], S. DeLorenzo[2], V. Dai[2], A. Dubeau[2], R. Foong[3], M. Brydges[4], T.J. Moraes[4], M.R. Sears[5], G.L. Hall[3], P. Subbarao[2] and G.N. Maksym[1]

[1]School of Biomedical Engineering, Dalhousie University, Halifax, NS, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Telethon Kids Institute, Subiaco, Australia, [4]Hospital for Sick Children, Toronto, ON, Canada, [5]McMaster University, Hamilton, ON, Canada.

Introduction: Oscillometry (OS) assesses respiratory resistance (Rrs) and reactance (Xrs) during normal breathing. While it can be more sensitive than spirometry, it is also more variable. Post-collection quality control (QC) is sometimes conducted, but it is time-consuming and may not adequately reduce variability. We demonstrate developed an automated approach (AQC) based on reducing the coefficient of variation (CV) over repeated measurements from a large cohort of preschool children, then compared AQC against post-hoc expert manual QC (MQC) in children admitted with wheeze.

Methods: Using subjects from the Canadian Healthy Infant Longitudinal Development (CHILD) study (n=416, age 5), multifrequency OS was repeated from 4 to >8 times. After 4 measurements, minimum CV was sought from combinations of 3 measurements of Rrs until CV was below either 0.1 or 0.15 in value. Averaged CV from 5 and 11 Hz Rrs outperformed single-frequency CV, and thus this AQC method was applied to OS data from a separate cohort of children presenting at the ER with wheeze (Wheezy-ER, n=73, ages 1-6) and at follow-up (1-3 months) obtaining both OS and spirometry before and after administration of salbutamol.

Results and Discussion: In CHILD, with CV threshold set at 0.15, MQC of OS eliminated 194 subjects, while AQC only removed 9 subjects, giving feasibility >98% in 5-year-olds. For Wheezy-ER at CV<0.1, first visit feasibility was 20.5% for MQC and 78.1% for AQC. At CV<0.15, feasibility was higher at 45.2% MQC and 82.2% AQC. Interestingly, there were no significant differences in population means of Rrs or Xrs in either cohort following either MQC or AQC (p=0.99 and 0.97, respectively), with the largest change in 5Hz Rrs = -0.11 (SD 1.3) cmH20.s/L. However, the mean absolute difference was larger at 0.95 (SD 0.89) cmH20.s/L), indicating AQC affected individual tests. For comparison, feasibility of spirometry was lower at 62% and while FEV1 improved after BD, it showed no change at follow-up, but OS indicated improvements in Rrs and Xrs both with BD and in follow-up.

Conclusions: In healthy 5-year-old children, OS feasibility was >98%, in 1-6-year-old children with wheeze feasibility was >80% with automated CV reduction, and OS was sensitive to improvement in lung function following wheeze while spirometry was not. Automated quality control can replace manual quality control without affecting sensitivity, and we recommend a minimum of 4 repeated measurements until CV of any 3 measurements are less than 15% based on low-frequency resistance.

Understanding the role of ECM in prostate cancer progression using 3D cell culture

Nicky Tam[1], G. Dellaire[2] and J.P. Frampton[1]

[1]School of Biomedical Engineering, Dalhousie University; [2]Department of Pathology, Dalhousie University

Introduction: Prostate cancer progression is mediated by a wide-range of cell-cell and cell-extracellular matrix (ECM) interactions, such as cadherin switching, integrin-mediated interactions, matrix metalloproteinase expression, and chemokine signaling. The importance of the ECM, not only in providing structural support but also as a biochemical niche for cell function is evident in the differences seen in gene expression and overall behaviour of cells cultured in two dimensions compared to cells *in vivo*. While the ECM plays a clear role in tissue morphogenesis, it has been difficult to decouple the individual effects of ECM components on cell behaviour, especially in terms of metabolism and migration. This is due to the sheer complexity of the ECM and the interconnectedness of cell signaling pathways. Three-dimensional (3D) hydrogel-based cell culture systems are especially useful in this aspect, as they can recapitulate the physicochemical and biochemical cues found in real prostate tissues. Here, a hyaluronic acid (HA)-based hydrogel is used to culture microscopic 3D prostate tissues in order to study the direct effects of ECM composition on cell metabolism, phenotype expression, and migratory behaviour.

Methods: For acute cell toxicity experiments, cells were seeded in monolayer onto a 96-well plate. After cell attachment, a modified HA-based hydrogel was introduced to simulate the prostate tissue ECM. This hydrogel was synthesized by introducing reversible disulfide crosslinks between HA chains through carbodiimide chemistry. Acute cell toxicity was evaluated over three days of monolayer culture in the hydrogel using calcein-AM and propidium iodide staining, as well as CellTiter Glo luminescent assay. Cell responses to the hydrogel environment were examined using Western Blot to probe for proteins involved in cell metabolism, such as protein kinase B and AMP-activated protein kinase; caspase 3, which is responsible for apoptosis; and LC3, a marker for autophagy.

Results and Discussion: The hyaluronic acid-based hydrogel did not negatively impact cell viability at low concentrations but appeared to affect cell viability at higher concentrations, possibly due to limited diffusivity. Markers for autophagy were detected in cells cultured in the hydrogel, but also in cells cultured under standard monolayer conditions, suggesting that cells were utilizing autophagy as a survival mechanism under low nutrient availability and as a strategy for rapidly dividing cells to scavenge resources. S6 kinase activity was expected to decrease with hydrogel concentration, due to its anabolic activity, but this was not observed even in the presence of autophagy. This, despite low protein kinase B activity suggests that baseline S6K activity may be involved in autophagy, in line with current theories of cellular metabolic control.

Conclusion: Cell-matrix interactions are difficult to study due to the complexity of the ECM and overlapping cell signaling pathways. By using a tissue engineering approach to systematically study how ECM affects cell behaviour, we can get a better understanding of the driving forces that favour the development of aggressive prostate cancer phenotypes.

Capacity of four different power meters to evaluate the radiant power from fourteen light curing units

Stella Braga[1,2], S. Juckes[1], B. Sullivan[1], C.J. Soares[2] and R.B. Price[1]

[1]Department of Dental Clinical Sciences, Dalhousie University; [2]Department of Operative Dentistry and Dental Materials, Federal University of Uberlandia.

Introduction: Every year, over 6.5 Billion dollars are spent in the USA alone on light cured dental restorations, yet there is currently no monitoring of the dental curing light in dental offices and few offices have a meter that can monitor their curing light. This study evaluated the reliability of three commercially available power meters compared with an integrating sphere attached to a fiber-optic spectrometer to measure the radiant power from fourteen dental light curing units (LCUs).

Methods: The radiant power from fourteen contemporary light-emitting diode LCUs was evaluated using two laboratory-grade power meters: integrating sphere (IS; LabSphere) attached to a fiber-optic spectrometer (Ocean Optics) (control), PM-Pro150 BB (PM; Coherent) and the hand-held dental radiometers Bluephase Meter II (BM; Ivoclar Vivadent) and MSC15-W (MS; Gigahertz-Optik/Ultradent). The LCUs tested were: six single-peak blue lights (two Elipar DeepCure-S lights (3M Oral Care), a LED.D (Woodpecker), a SmartLite Focus (Dentsply), a SmartLite Pro (Dentsply) and a Spark Curing Light (Dental Spark), as well as eight broad-spectrum multipeak lights (a Bluephase G4 (Ivoclar Vivadent), a Bluephase Style (Ivoclar Vivadent), a Bluephase Style 20i (Ivoclar Vivadent), four VALO Cordless (Ultradent) and a VALO Grand (Ultradent)). One measurement was made for each LCU using IS, PM and MS. Three measurements were made for each LCU using BM and the average was calculated. The power values were fitted comparing each power meter with the integrating sphere. The percentage differences in radiant power were calculated relative to the IS results.

Results and Discussion: The BM was manufactured and designed to evaluate the Ivoclar Vivadent broad-spectrum multipeak lights. Thus, as expected, lower discrepancies were found using similar broad-spectrum multipeak LCUs. Most LCUs evaluated using PM showed higher radiant power values than IS, ranging from 0.7% for the Bluephase Style 20i to 13.5% for the SmartLite Focus, except for the low power LED.D (-10.8%). All LCUs evaluated using the MS power meter exhibited radiant power values lower than reported by the IS (range -0.5% to SmartLite Pro to -17.9% to LED.D). All power meters exhibited good correlation with IS, but the best correlation was found with the PM power meter.

Conclusions: When compared to the measured radiant power measured using the integrating sphere attached to a fiber-optic spectrometer, the PM- Pro150 BB provided the most similar data. Regarding the hand-held dental radiometers, MS- MSC15-W had the best correlation and may be recommended for use in dental offices by dentists.

School of Biomedical Engineering

Research Day 2019 Abstracts

SCIENTIFIC SESSION 3

Fabrication and verification of an endoscopic phased array for combined photoacoustic tomography and high-frequency ultrasound imaging

Taylor Landry[1], C. Samson[1], K. Latham[1], J.A. Brown[1,2] and R. Adamson[1,2]

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Introduction: In previous work, our group has demonstrated the use of an endoscopic 64-element, 45 MHz phased ultrasound array and a 64x64 -element crossed electrode array for 3D ultrasound. In the present study we adapt these two endoscopes for use in photoacoustic tomography (PAT) imaging. PAT is an emerging modality in which the absorption of pulsed light generates an acoustic shock wave that is imaged by an ultrasound transducer. PAT is particular useful in imaging vasculature since haemoglobin is a strong absorber of light. Integrating PAT into intrasurgical ultrasound endoscopes provide surgeons with the ability to image blood vessels so as to reduce bleeding and more clearly identify tumor margins.

Methods: The two ultrasound probes were modified by attaching custom-made fiber bundles around the periphery of the square probes. Light from an 808 nm pulsed diode bar laser with 500 µJ of pulse energy and a 1KHz repetition rate was coupled into the other end of the fiber bundles to provide illumination. The system was verified in a set of gelatin/silica/intralipid phantoms that mimic the ultrasonic and acoustic properties of brain tissue.

Results and Discussion: We report lateral and axial resolution and bandwidth for photoacoustic and B-mode imaging of hair targets with the two transducers.

Conclusions: The system demonstrates that photoacoustic tomography can be successfully integrated into high-frequency ultrasound micro-endoscopy devices for intrasurgical imaging.

Individuals with delayed trunk muscle reflexes have different muscle activation patterns to complete a controlled transfer task

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Introduction: Theoretical models suggest if spinal stability were to become impaired it could be compensated for by changing the recruitment patterns of trunk muscles. The purpose of this study was to determine whether those with slow (SRL) or fast reflex (FRL) would have different muscle activation patterns during a dynamic transfer task.

Methods: Data were collected from 60 male active military participants. Electromyographic (EMG) data were digitized at 2000Hz from 12 bilateral trunk sites. To test reflexes, participants were exposed to perturbations from 3˚ extension to 12˚ flexion (or visa-versa) at 120˚/s. For this test reflex latency, time to detected reflex (mean±2 standard deviations), was measured. To test muscle activation patterns, participants performed a controlled transfer task. Spatial-temporal analysis of EMG data were determined from principal component (PC) analysis on time and maximum amplitude normalized ensemble average waveforms. Participants were separated into two onset groups (SRL or FRL) relative to a median split for reflex latency. Mixed Model ANOVAs (group, muscle) tested for main effects and interactions for each PC score (α=0.05).

Results and Discussion: Participants in the SRL and FRL were not different for demographics, or spatial-temporal task performance (trunk motion or movement time). PC analysis explained >95% of the waveform variance. For abdominals, PC1 showed SRL had higher activation amplitudes than FRL. For back extensors, PC1 captured SRL had lower activation amplitudes than FRL. For PC2, SRL was less responsive to the changing lateral flexion moment than FRL.

Conclusion: These results reflect sustained co-activation in response to the flexion moment (PC1 abdominals) or the lateral flexion moment (PC2 back extensors) produced by the task. Co-activation would increase active stiffness of the trunk reducing displacement from sudden loading, consistent with a compensation for delayed production of reflexive stiffness.

Engineering a microenvironment for screening responses of immune cells to infectious disease therapies

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Introduction: Immunotherapies such as vaccines have been the most effective medical interventions for prevention and treatment of infectious diseases. However, the high cost and long timeframe for research and development of vaccines remain a challenge to be overcome. To address this drawback, I propose to develop a pre-clinical screening platform designed to identify optimal vaccine formulations. This platform uses polymers that form aqueous two-phase systems (ATPS) to confine immune cells and vaccine reagents together in microdroplets. Compared to conventional screening methods, these microdroplets can produce outputs with high sensitivity in a shorter time and using smaller amounts of cells and reagents.

Methods: A small library of pre-selected ATPS solutions was evaluated: albumin, dextran (Dex), Ficoll, poly(2-ethyl-2-oxazoline), poly (ethylene glycol) (PEG), and poly (ethylene oxide) (PEO). The most biocompatible polymers were selected to confine the immune cell lines RPMI 8226 (B cells) and Jurkat (T cells). The effect of phase-separating polymers on immune cell viability and activation were assessed by calcein-AM/propidium iodide staining, and enzyme-linked immunosorbent assay (ELISA), respectively. Immune cells were stimulated to secrete cytokines against the model antigen ovalbumin (OVA) and various vaccine adjuvants. The immune responses were evaluated by direct ELISA and enzyme-linked immunospot (ELISPOT). In parallel, cytokine stability and partitioning were measured by sandwich ELISA.

Results and Discussion: The ATPS-polymers PEG and albumin (Albumax BSA) performed best with immune cells. Culturing Jurkat T cells in Albumax BSA solution for 72 hours resulted in 98% cell viability. Cell viability was slightly lower when the cells were cultured in Dex solution compared to Albumax BSA (~ 97%). Although PEO exhibited superior cell viability compared to PEG, the latter had more appropriate handling properties. Thus, the PEG-BSA and PEG-Dex systems were selected for further examination. Jurkat T cell and RPMI 8226 cell activation were assessed by IL-2 and IL-6 secretion, respectively. The ATPS solutions did not stimulate either IL-2 or IL-6 secretion over 24 hours, which suggests that PEG, BSA or Dex solutions themselves did not activate the cells. The immune responses to antigen/adjuvants and the formation of well-defined colored spots during ELISPOT assay were superior when cells were cultured in ATPS microdroplets compared to culture medium. Finally, preliminary examination of cell and biomolecule partitioning suggests that immune cells and cytokines remain confined within the ATPS microdroplets, increasing the efficiency and sensitivity of biochemical reactions, and ultimately, improving immunotherapy screening.

Conclusions: This study demonstrated that PEG-Dex and PEG-BSA systems can confine immune cells and cytokines within microdroplets without significantly compromising cell viability and activation. Using these systems to screen immunotherapy agents may facilitate the cost-effective development of vaccine formulations.

Performance evaluation of various 1:3 piezo-composite substrates for histotripsy applications

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Introduction: The new generation of high-intensity ultrasound transducers for histotripsy tissue ablation involves pushing the limits of both transducer fabrication and electronics design. For future histotripsy applications, it may be necessary to ask for more pressure beyond what our current devices can provide. In this work, we examine options to increase the overhead on histotripsy transducers by considering two new materials for composite fabrication, single crystal PIN-PMN-PT and CTS 3257 high-dielectric piezoelectric in place of the currently used PZT5A.

Methods: Simulations of each piezoelectric were performed using the KLM method, and 1:3 dice-and-fill composites designed to couple well to aluminum were fabricated based on these results. The electrical impedance was measured and compared to simulations both before and after coupling to a lens, while preliminary pressure measurements were also taken using a hydrophone to determine the maximum drive voltage possible before saturation.

Results and Discussion: KLM simulations and measured impedances of composites suggest CTS 3257 HD can deliver much more acoustic power per input volt compared to PIN-PMN-PT and PZT5A. PIN-PMN-PT, however, should be able to operate at a much higher voltage before saturation is reached. Preliminary measurements of pressure per volt and saturation point for the various substrates is ongoing, however, a large variation output pressure results from variation in bonding layer uniformity to the focusing lens.

Conclusions: The importance of maintain cleanliness and flatness of surfaces cannot be overstated when bonding piezoelectric to lens. Further work should be done to determine the acceptable amount of variation while avoiding impacting of performance.