

# 10th Annual Surgery, Intervention, and Engineering Symposium

DECEMBER 15TH, 2021



## "AI-Powered Computational Cardiology"

**Natalia Trayanova, PhD, FHRS, FAHA**

Murray B. Sachs Endowed Chair  
Professor of Biomedical Engineering and Medicine  
Director, Alliance for Cardiovascular  
Diagnostic and Treatment innovation (ADVANCE)  
Johns Hopkins University





## VANDERBILT INSTITUTE FOR SURGERY AND ENGINEERING

**The Vanderbilt Institute for Surgery and Engineering (VISE)** is a trans-institutional entity that promotes the creation, development, implementation, clinical evaluation and commercialization of methods, devices, algorithms, and systems designed to facilitate interventional processes and their outcomes. Its expertise includes imaging, image processing and data science, interventional guidance delivery and therapeutics, modeling and simulation, and devices and robotics. VISE facilitates the exchange of ideas between physicians, engineers, and computer scientists. It promotes the training of the next generation of researchers and clinicians capable of working symbolically on new solutions to complex interventional problems, ultimately resulting in improved patient care.

As part of its mission, VISE organizes a seminar series held bi-weekly that features both internal and external speakers. Our annual Symposium in Surgery, Intervention, and Engineering is the culmination of the fall semester series and it is an opportunity for VISE members to show and discuss the various collaborative projects in which they are involved. We hope this event will be the catalyst for new collaborative efforts.

Visit our website <https://www.vanderbilt.edu/vise/>



## **Master of Engineering (ESI) Program in Engineering in Surgery and Intervention**

Over the past several decades, dramatic breakthroughs in biomedical science have been witnessed within laboratory research, but the ability to translate those discoveries and make new discoveries has been a challenge and has been often characterized as the bottleneck of clinical translation.

At Vanderbilt University, we believe that the fundamental constraints associated with clinical translation can be dramatically improved with the training of engineers intimately familiar with medical procedures and trained in the inception of novel technology-based platforms.

VANDERBILT UNIVERSITY OFFERS A GRADUATE ENGINEERING PROGRAM THAT WILL EQUIP ENGINEERS TO IMPROVE TRANSLATION OF TECHNOLOGY FOR SURGERY AND INTERVENTION.

You can read all about the new degree in our program guide, *What is Innovation in Procedural Medicine? Getting an Engineering Degree in Surgery and Intervention.*  
[https://hubs.la/H0\\_wB2g0](https://hubs.la/H0_wB2g0)

# "AI-Powered Computational Cardiology"

**Presented by**  
**Natalia Trayanova, PhD, FHRS, FAHA**

Murray B. Sachs Endowed Chair  
Professor of Biomedical Engineering and Medicine  
Director, Alliance for Cardiovascular  
Diagnostic and Treatment Innovation  
(ADVANCE)  
Johns Hopkins University



## Keynote Speaker

**Natalia Trayanova PhD, FHRS, FAHA**



Murray B. Sachs Endowed Chair  
Professor of Biomedical Engineering and Medicine  
Director, Alliance for Cardiovascular  
Diagnostic and Treatment Innovation (ADVANCE)  
Johns Hopkins University

## Keynote Abstract

Simulation-driven engineering has put rockets in space, airplanes in the sky, and self-driving cars on the road. Computational approaches, however, have rarely been applied to human health, and trial-and-error is often used to decide on interventions for patients with life-threatening diseases. Working to change this, we have developed personalized imaging-based heart “digital twins”, which digitally replicate the patient’s heart electrical function. We also use machine learning approaches to incorporate additional clinical data in the applications of the heart digital twin technology.

The heart digital twins are models based on patient’s heart scans and clinical data, and are used to simulate the individual patient’s irregular heart rhythm – a major cause of patient morbidity and mortality. We apply the digital twin technology to diagnose which patients with heart disease are likely to develop arrhythmias and thus are at risk of dying suddenly. A digital heart twin is capable of predicting adverse cardiac events as it simulates the effect of potential stressors. Using such a tool, the patient’s risk of sudden cardiac death can be assessed, and a precise decision can be made regarding the benefit-vs-complications of implanting a defibrillator device that can shock the patient back into normal heart rhythm.

We also use the personalized heart digital technology to develop precise treatment for patients suffering from arrhythmias. For each patient, my team determines the location of perpetrator tissue in the heart, so that it can be destroyed by ablation, restoring the heart’s normal rhythm. A mock of the ablation is performed to ensure arrhythmias will not re-emerge post-procedure. This approach not only eliminates the process of trial-and-error in treating heart rhythm disorders but also prevents repeat procedures, which are common in arrhythmia management.

# Biography

Dr. Trayanova is the Murray B Sachs Professor in the Department of Biomedical Engineering at Johns Hopkins University and a Professor of Medicine at the Johns Hopkins School of Medicine. She directs the Alliance for Cardiovascular Diagnostic and Treatment Innovation, a research institute aimed at applying predictive data-driven approaches, computational modeling, and innovations in cardiac imaging to the diagnosis and treatment of cardiovascular disease. She also directs the Computational Cardiology Laboratory.

Using a personalized simulation and machine learning approaches, Dr. Trayanova has developed new methods for predicting risk of cardiac arrest and improving the accuracy of atrial and ventricular catheter ablation therapies. Through her first-of-its-kind personalized virtual hearts, she is pioneering advances in personalized medicine for patients with cardiovascular disease, which promise to profoundly influence clinical decision-making and the delivery of patient care. She is currently conducting FDA-approved clinical trial in simulation-driven treatment for cardiac arrhythmias.

Dr. Trayanova has published over 400 scientific papers, many of them in journals of high impact. She has also given over 300 invited talks, keynotes, and plenary lectures. She is the inventor on 45 patents and patent applications. Her work has received world-wide recognition, and she is the recipient of numerous honors and awards. For her groundbreaking work in computational cardiology, in 2013, she received the NIH Director's Pioneer Award, the most prestigious recognition of innovation in medical research. In 2019, she was inducted in the Women of Technology International Hall of Fame, an honor conferred only on 5 women each year from around the world. Also in 2019, she received the Distinguished Scientist Award from Heart Rhythm Society. In 2020, she was elected Fellow of the National Academy of Inventors, and received the Douglas Zipes Lectureship Award, bestowed by the Heart Rhythm Society.

Trayanova is also a Fellow of: European Society of Cardiology, American Institute for Medical and Biological Engineering; Heart Rhythm Society; American Heart Association; Biomedical Engineering Society; and International Academy of Medical and Biological Engineering. Her work has been featured by a number of news outlets, including a TEDx talk.





# Participating Laboratories

# Participating Laboratories



## **Advanced Robotics and Mechanism Applications (ARMA) Laboratory**

**PI: Nabil Simaan, Ph.D.**  
Professor of Mechanical Engineering  
and Otolaryngology,  
Vanderbilt University

ARMA is focused on advanced robotics research including robotics, mechanism design, control, and telemanipulation for medical applications. We focus on enabling technologies that necessitate novel design solutions that require contributions in design modeling and control. ARMA has led the way in advancing several robotics technologies for medical applications including high dexterity snake-like robots for surgery, steerable electrode arrays for cochlear implant surgery, robotics for single port access surgery and natural orifice surgery. Current and past funded research includes transurethral bladder cancer resection (NIH), trans-oral minimally invasive surgery of the upper airways (NIH), single port access surgery (NIH), technologies for robot surgical situational awareness (National Robotics Initiative), Micro-vascular surgery and micro surgery of the retina (VU Discovery Grant), Robotics for cochlear implant surgery (Cochlear Corporation). We collaborate closely with industry on translation our research. Examples include technologies for snake robots licensed to Intuitive Surgical, technologies for micro-surgery of the retina which lead to the formation of AURIS surgical robotics Inc., the IREP single port surgery robot which has been licensed to Titan Medical Inc. and serves as the research prototype behind the Titan Medial Inc. SPORT (Single Port Orifice Robotic Technology).

Web site: <http://arma.vuse.vanderbilt.edu>

Lab YouTube Channel: <http://www.youtube.com/user/ARMAVU/videos>

Contact: [nabil.simaan@vanderbilt.edu](mailto:nabil.simaan@vanderbilt.edu)

# Participating Laboratories



## **Biomedical Elasticity and Acoustic Measurement (BEAM) Laboratory**

**PI: Brett Byram, Ph.D.**

Associate Professor of Biomedical Engineering,  
Vanderbilt University

The Biomedical Elasticity and Acoustic Measurement (BEAM) lab is interested in pursuing ultrasonic solutions to clinical problems. Brett Byram and the BEAM lab's members have experience with most aspects of systems level ultrasound research, but our current efforts focus on advanced pulse sequencing and algorithm development for motion estimation, beamforming and perfusion imaging. The goal of our beamforming work is to make normal ultrasound images as clear as intraoperative ultrasound, the gold-standard for many applications. We have recently demonstrated non-contrast tissue perfusion imaging with ultrasound at clinical frequencies, and we are working to integrate our beamforming and perfusion imaging methods to enable transcranial functional ultrasound in adult humans.

Contact: [brett.c.byram@vanderbilt.edu](mailto:brett.c.byram@vanderbilt.edu)

# Participating Laboratories



## Biomedical Image Analysis for Image Guided Interventions (BAGL) Laboratory

PI: Prof. Jack H. Noble, Ph.D.

Assistant Professor of Electrical & Computer Engineering

Director of Graduate Student Recruitment

Vanderbilt University

Biomedical image analysis techniques are transforming the way many clinical interventions are performed and enabling the creation of new computer-assisted interventions and surgical procedures. The Biomedical Image Analysis for Image-Guided Interventions Lab (BAGL) investigates novel medical image processing and analysis techniques with emphasis on creating image analysis-based solutions to clinical problems. The lab explores state-of-the-art image analysis techniques, such as machine learning, statistical shape models, graph search methods, level set techniques, image registration techniques, and image-based bio-models. The lab is currently developing novel systems for cochlear implant procedures including systems that use image analysis techniques for (1) comprehensive pre-operative surgery planning and intra-operative guidance and (2) post-operative analysis to optimize hearing outcomes. The lab is also developing novel segmentation and registration techniques for image guided brain tumor resection surgery.

Contact: [jack.noble@vanderbilt.edu](mailto:jack.noble@vanderbilt.edu)

# Participating Laboratories



## Biomedical Modeling (BML) Laboratory

PI: Michael I. Miga, Ph.D.

Harvie Branscomb Professor

Professor of Biomedical Engineering

Professor of Radiology and Radiological Sciences

Professor of Neurological Surgery

Professor of Otolaryngology

Vanderbilt University

The focus of the Biomedical Modeling Laboratory (BML) is on new paradigms in detection, diagnosis, characterization, and treatment of disease through the integration of computational models into research and clinical practice. With the continued improvements in high performance computing, the ability to translate computational modeling from predictive roles to ones that are more integrated within diagnostic and therapeutic applications is becoming a rapid reality. With respect to therapeutic applications, efforts in deformation correction for image-guided surgery applications in brain, liver, kidney, and breast are being investigated. Other applications in neuromodulation, ablative therapies, neoadjuvant chemotherapy, and convective chemotherapy are also being investigated. With respect to diagnostic imaging, applications in elastography, strain imaging, model-based chemotherapeutic and radio-therapy tumor response parameterizations are also of particular interest. The common thread that ties the work together is that, throughout each research project, the integration of mathematical models, tissue mechanics, instrumentation, and analysis are present with a central focus at translating the information to directing therapy/intervention or characterizing tissue changes for diagnostic value.

Contact: [michael.i.miga@Vanderbilt.Edu](mailto:michael.i.miga@Vanderbilt.Edu)

# Participating Laboratories



## **Brain Imaging and Electrophysiology Network (BIEN) Laboratory**

**PI: Dario J. Englot, M.D., Ph.D.**

Assistant Professor of Neurological Surgery, Neurology, Radiology, Electrical Engineering, and Biomedical Engineering, and Director of Functional Neurosurgery  
Vanderbilt University

The BIEN lab integrates human neuroimaging and electrophysiology techniques to study brain networks in both neurological diseases and normal brain states. The lab is led by Dario Englot, a functional neurosurgeon at Vanderbilt. One major focus of the lab is to understand the complex network perturbations in patients with epilepsy, by relating network changes to neurocognitive problems, disease parameters, and changes in vigilance in this disabling disease. Multimodal data from human intracranial EEG, functional MRI, diffusion tensor imaging, and other tools are utilized to evaluate resting-state, seizure-related, and task-based paradigms. Other interests of the lab include the effects of brain surgery and neurostimulation on brain networks in epilepsy patients, and whether functional and structural connectivity patterns may change in patients after neurosurgical intervention. Through studying disease-based models, the group also hopes to achieve a better understanding of normal human brain network physiology related to consciousness, cognition, and arousal. Finally, surgical outcomes in functional neurosurgery, including deep brain stimulation, procedures for pain disorders, and epilepsy, are also being investigated.

Contact: [dario.englot@vumc.org](mailto:dario.englot@vumc.org)

# Participating Laboratories



## Computer Assisted Otologic Surgery (CAOS) Laboratory

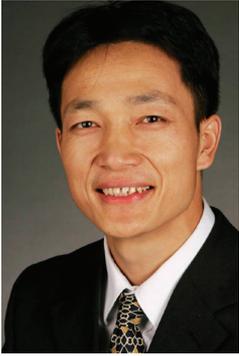
PI: Robert F Labadie, M.D., Ph.D.

Professor of Otolaryngology - Head and Neck Surgery,  
Professor of Biomedical Engineering,  
Vanderbilt University Medical Center

The aim of the CAOS lab is to develop novel methods and tools to improve otologic surgery. Our multi-disciplinary team consists of members with both surgical and engineering backgrounds and expertise in Otolaryngology, Audiology, Mechanical Engineering, Electrical Engineering, and Computer Science. We use a variety of medical image analysis, image-guidance and robotic techniques in an effort to decrease the invasiveness of surgery, make surgical procedures safer, and improve patient outcomes. Some of our current projects include: minimally-invasive cochlear implantation surgery, cochlear implant programming based on medical image analysis, assessment of electrode placement and audiological outcomes in cochlear implant patients, robot-assisted bone milling for inner ear access, patient-specific modeling and planning for robotic surgery, natural orifice middle ear endoscopy, and thermal monitoring of surgical procedures.

Contact: [robert.labadie@vanderbilt.edu](mailto:robert.labadie@vanderbilt.edu)

# Participating Laboratories



## **Computational Flow Physics and Engineering (CFPE) Lab**

**PI: Haoxiang Luo, Ph.D.**  
Professor of Mechanical Engineering  
Vanderbilt University

The Computational Flow Physics and Engineering Lab is within the Multiscale Modeling and Simulation (MuMS) center located in Music Row on 17th Ave South. We use computational modeling and high-performance computing techniques to solve fluid (i.e., liquids or gases) flow problems and also the problems involving interaction between fluids with solid/tissue structures. The study of these problems can be used for surgical planning, noninvasive diagnostics, and design of biomedical and bioinspired devices. The current research thrusts in the lab include: 1) computational modeling of vocal fold vibration and interaction with glottal aerodynamics for surgery planning of voice disorders and other airway diseases, 2) computational modeling of cardiovascular flows such as the heart valve fluid-structure interaction, 3) aerodynamics and aeroelasticity of biological wings (e.g., insects and birds) and hydrodynamics of fish, and 4) particle-laden flows in electrochemical systems for applications in energy storage and water deionization.

Contact: [haoxiang.luo@vanderbilt.edu](mailto:haoxiang.luo@vanderbilt.edu)

# Participating Laboratories



## Diagnostic Imaging and Image-Guided Interventions (DIIGI) Laboratory

PI: Yuankai (Kenny) Tao, Ph.D.  
Assistant Professor of Biomedical Engineering,  
Vanderbilt University

The Diagnostic Imaging and Image-Guided Interventions (DIIGI) Laboratory develops novel optical imaging systems for clinical diagnostics and therapeutic monitoring in ophthalmology and oncology. Biomedical optics enable non-invasive subcellular visualization of tissue morphology, biological dynamics, and disease pathogenesis. Our ongoing research primarily focuses on clinical translation of therapeutic tools for image-guided intraoperative feedback using modalities including optical coherence tomography (OCT), which provides high-resolution volumetric imaging of weakly scattering tissue; and nonlinear microscopy, which has improved molecular-specificity, imaging depth, and contrast over conventional white-light and fluorescence microscopy. Additionally, we have developed optical imaging techniques that exploit intrinsic functional contrast for in vivo monitoring of blood flow and oxygenation as surrogate biomarkers of cellular metabolism and early indicators of disease. The majority of our research projects are multidisciplinary collaborations between investigators in engineering, basic sciences, and medicine.

Contact [yuankai.tao@vanderbilt.edu](mailto:yuankai.tao@vanderbilt.edu)

# Participating Laboratories



## Grissom Laboratory: MRI-Guided Focused Ultrasound

PI: William Grissom, Ph.D.

Associate Professor Biomedical Engineering,  
Vanderbilt University

A major research focus of the Grissom laboratory is MRI guidance of high intensity focused ultrasound surgery. MRI-guided high intensity focused ultrasound surgery (FUS) is a promising technique for the next generation of non-invasive therapy systems. One important feature of FUS lies in its ability to apply ultrasound from outside the body, without any skin puncture or incision. The ultrasound energy can be focused to a point within the body, with minimal heating of the intervening tissues. MR imaging is used both for treatment planning and to provide temperature measurements during the procedure. The temperature maps are used both to dynamically control the FUS beam during the procedure, and to assess thermal dose afterwards. Our group is focused on the development of MR imaging methods for FUS surgery guidance, including real-time temperature imaging sequences, algorithms to reconstruct temperature maps, and MRI-based methods to autofocus ultrasound beams through bone and inhomogeneous tissue. We also are interested in the development of imaging techniques to exploit novel temperature contrast mechanisms, and algorithms to dynamically and automatically steer and control the power of the FUS beam. Applications include ablation of uterine fibroids and diffuse adenomyosis, anti-tumor immune response modulation of breast cancer, modulation of drug uptake in pancreatic cancer, and tumor and tissue ablation in the brain for functional neurosurgery, and neuromodulation.

Contact: [will.grissom@vanderbilt.edu](mailto:will.grissom@vanderbilt.edu)

# Participating Laboratories



## **The biomedical data Representation and Learning lab**

**PI: Yuankai Huo, Ph.D.**

Assistant Professor of Computer Science

Assistant Professor of Computer Engineering

Vanderbilt University

The HRLB lab aims to facilitate data-driven healthcare and improve patient outcomes through innovations in medical image analysis as well as multi-modal data representation and learning. Our current focus efforts on quantifying high-resolution and spatial-temporal data from microscopy imaging techniques, including renal pathology, cancer pathology, cytology, computational biology. The quantitative imaging information is associated with molecular, genetic, and clinical features for precise diagnosis and treatment.

Contact: [yuankai.huo@vanderbilt.edu](mailto:yuankai.huo@vanderbilt.edu)

# Participating Laboratories



## Joos Laboratory- Ophthalmology Research

PI: Karen Joos, M.D., Ph.D.

Joseph and Barbara Ellis Professor of Ophthalmology  
and Visual Sciences,

Vanderbilt University Medical Center,  
Biomedical Engineering, Vanderbilt University

The surgical research program is designed to investigate the development of innovative surgical methods and the improvement of existing techniques to improve the outcomes of ophthalmic surgery. Approaches include the development and integration of a novel intraocular B-scan OCT probe with surgical instruments to improve visualization of structures during ophthalmic surgery, and the integration of the imaging probes with robot-assisted control for precise tissue manipulation. The Joos laboratory has ongoing NIH-funded collaborations with Dr. Nabil Simaan's and Dr. Kenny Tao's laboratories.

Contact: [karen.joos@vumc.org](mailto:karen.joos@vumc.org)

# Participating Laboratories



## Laboratory for the Design and Control of Energetic Systems

PI: Eric Barth, Ph.D.  
Professor of Mechanical Engineering,  
Vanderbilt University

The Laboratory for the Design and Control of Energetic Systems seeks to develop and experimentally apply a systems dynamics and control perspective to problems involving the control and transduction of energy. This scope includes multi-physics modeling, control methodologies formulation, and model-based or model-guided design. The space of applications where this framework has been applied includes nonlinear controllers and nonlinear observers for pneumatically actuated systems, a combined thermodynamic/system dynamics approach to the design of free piston green engines of both internal combustion and external heat source varieties, modeling and model-based design and control of monopropellant systems, and energy-based approaches for single and multiple vehicle control and guidance. Most recent research efforts have focused on high efficiency hydraulic accumulators for regenerative braking in hybrid vehicles, a vibration energy harvester for bridge monitoring, and MRI compatible pneumatically actuated robots.

Contact: [eric.j.barth@vanderbilt.edu](mailto:eric.j.barth@vanderbilt.edu)

# Participating Laboratories



## Laboratory for Organ Recovery, Regeneration and Replacement (LOR3)

PI: Matthew Bacchetta, M.D., MBA, MA  
H. William Scott, Jr. Chair in Surgery,  
Professor of Surgery,  
Vanderbilt University Medical Center

Laboratory for Organ Recovery, Regeneration and Replacement (LOR3) aims to solve the most pressing issues in the areas of whole-organ transplantation and recovery, mechanical circulatory support, and extracorporeal membrane oxygenation. Organ transplantation remains limited by the shortage of suitable donor organs available to meet the needs of end-stage organ disease patients. Better technological platform for organ rehabilitation can expand upon the limited donor organ supply by salvaging and recovering those that were rejected due to injuries or poor quality. Furthermore, a more durable mechanical technology for supporting the native organ function would not only better bridge patients to recovery and transplant, but also provide permanent support, destination therapy for these severe disease patients. Toward these goals, our lab is: 1) developing and translating a xenogeneic cross circulation platform to provide ex vivo physiologic support to explanted human lungs and livers for extracorporeal organ recovery, repair, and regeneration using a pig bioreactor; 2) developing a durable, ambulatory mechanical cardiopulmonary support technology for end-stage lung and heart disease patients, particularly for pulmonary hypertension using a clinically relevant disease model in sheep. We utilize these large animal models to refine and develop these technological platforms, with the ultimate goal of translating them toward clinical applications.

Contact: [matthew.bacchetta@vumc.org](mailto:matthew.bacchetta@vumc.org)

# Participating Laboratories



## Mawn Laboratory

PI: Louise Mawn, M.D.  
Associate Professor Ophthalmology,  
Vanderbilt University

The laboratory of Dr. Louise Mawn of the Vanderbilt Eye Institute exists in collaboration with Dr. Robert Galloway of Biomedical Engineering, Dr. Bennett Landman of Electrical Engineering, and Dr. Seth Smith of the Imaging Institute, focuses on improving understanding, treatment and imaging of orbital disease. Specific goals include improving orbital surgery using minimally invasive techniques and image guidance. The surgical and medical treatment of disease of the orbit is challenging in part because of the difficulty reaching the space behind the eye. The orbit houses the optic nerve; disease of the optic nerve is the leading cause of irreversible blindness worldwide. The laboratory uses anatomical studies, imaging technology and biomedical engineering to improve approaches to the optic nerve and retrobulbar space.

Contact: [louise.mawn@vanderbilt.edu](mailto:louise.mawn@vanderbilt.edu)

# Participating Laboratories



## Medical-image Analysis and Statistical Interpretation (MASI) Laboratory

PI: Bennett Landman, Ph.D.

Professor and Department Chair

*Electrical and Computer Engineering (primary),  
Computer Science, Biomedical Engineering,  
Vanderbilt University*

Principal Scientist of ImageVU

*Vanderbilt University Institute of Image Science,  
Radiology and Radiological Sciences, Vanderbilt Brain Institute,  
Psychiatry and Behavioral Sciences, Biomedical Informatics,  
Neurology, Vanderbilt University Medical Center*

Biomarker Core Co-Lead

*Vanderbilt Alzheimer's Disease Research Center*

Three-dimensional medical images are changing the way we understand our minds, describe our bodies, and care for ourselves. In the MASI lab, we believe that only a small fraction of this potential has been tapped. We are applying medical image processing to capture the richness of human variation at the population level to learn about complex factors impacting individuals. Our focus is on innovations in robust content analysis, modern statistical methods, and imaging informatics. We partner broadly with clinical and basic science researchers to recognize and resolve technical, practical, and theoretical challenges to translating medical image computing techniques for the benefit of patient care.

Contact: [bennett.landman@vanderbilt.edu](mailto:bennett.landman@vanderbilt.edu)

# Participating Laboratories



## Medical Engineering and Discovery (MED) Laboratory

PI: Robert, J. Webser, III, Ph.D.  
Richard A. Schroeder Professor in Mechanical Engineering, Professor of Electrical Engineering, Professor of Otolaryngology, Urologic Surgery, Neurological Surgery, and Medicine  
Vanderbilt University

The Vanderbilt School of Engineering's Medical Engineering and Discovery (MED) Laboratory pursues research at the interface of surgery and engineering. Our mission is to enhance the lives of patients by engineering better devices and tools to assist physicians. Much of our current research involves designing and constructing the next generation of surgical robotic systems that are less invasive, more intelligent, and more accurate. These devices typically work collaboratively with surgeons, assisting them with image guidance and dexterity in small spaces. Creating these devices involves research in design, modeling, control, and human interfaces for novel robots. Specific current projects include needle-sized tentacle-like robots, advanced manual laparoscopic instruments with wrists and elbows, image guidance for high-accuracy inner ear surgery and abdominal soft tissue procedures, and swallowable pill-sized robots for interventions in the gastrointestinal tract.

Contact: [robert.webster@vanderbilt.edu](mailto:robert.webster@vanderbilt.edu)

# Participating Laboratories



## Medical Image Computing (MedICL) Laboratory

PI: Ipek Oguz, Ph.D.

Assistant Professor of Computer Science

Assistant Professor of Electrical and

Computer Engineering

Vanderbilt University

The goal of the Medical Image Computing Lab is to develop novel algorithms for better leveraging the wealth of data available in medical imagery. We are interested in a wide variety of methods including image segmentation, image registration, image prediction/synthesis, and machine learning. One of our current clinical applications is Huntington's disease, where we are interested in improving the prediction of clinical disease onset through longitudinal segmentation of subcortical and cortical anatomy from brain MRI's. We are also interested in multiple sclerosis, where we work on improving our understanding of both the inflammatory disease process through lesion quantification and a potential complementary neurodegenerative component through cortical thickness studies. Additional application areas include retinal OCTs and diffusion MRI in Aicardi-Goutières syndrome.

Contact: Ipek Oguz [ipek.oguz@vanderbilt.edu](mailto:ipek.oguz@vanderbilt.edu)

# Participating Laboratories



## Medical Image Processing (MIP) Laboratory

PI: Benoit Dawant, Ph.D.,  
Cornelius Vanderbilt Professor of Engineering  
Professor of Electrical Engineering  
Professor of Computer Science  
Professor of Biomedical Engineering  
Professor of Radiology and Radiological Sciences  
Director, Vanderbilt Institute for Surgery and  
Engineering (VISE)  
Vanderbilt University

The Medical Image Processing (MIP) laboratory of the Electrical and Computer Engineering (ECS) Department conducts research in the area of medical image processing and analysis. The core algorithmic expertise of the laboratory is image segmentation and registration. The laboratory is involved in a number of collaborative projects both with others in the engineering school and with investigators in the medical school. Ongoing research projects include developing and testing image processing algorithms to assist in the placement and programming of Deep Brain Stimulators used to treat Parkinson's disease and development of methods to facilitate the pre-operative, intra-operative, and post operative phases of cochlear implant procedures. The laboratory expertise spans the entire spectrum between algorithmic development and clinical deployment. Several projects that have been initiated in the laboratory have been translated to clinical use or have reached the stage of clinical prototype at Vanderbilt and at other collaborative institutions. Components of these systems have been commercialized.

Contact: [benoit.dawant@vanderbilt.edu](mailto:benoit.dawant@vanderbilt.edu)

# Participating Laboratories



## **Morgan Engineering and Imaging in Epilepsy Lab**

**PI: Vicky Morgan, Ph.D.,**  
Professor of Radiology and Radiological Sciences  
Professor of Biomedical Engineering  
Professor of Neurology  
Professor of Neurological Surgery  
Vanderbilt University

The Morgan Engineering and Imaging in Epilepsy Lab works closely with the departments of Neurology and Neurosurgery to develop Magnetic Resonance Imaging (MRI) methods to improve neurosurgical outcomes, particularly for patients with epilepsy. We directly support clinical care by developing and providing functional MRI to localize eloquent cortex in the brain to aid in surgical planning to minimize functional and cognitive deficits post surgery. Our research focuses on mapping functional and structural brain networks in epilepsy before and after surgical treatment. Ultimately, we aim to use MRI to fully characterize the spatial and temporal impacts of seizures across the brain to optimize management of epilepsy patients. The Morgan lab has on-going research collaborations with the BIEN (Englot) Lab, the Medical Imaging Processing Laboratory (Dawant), the MASI Lab (Landman) and researchers throughout the Vanderbilt Institute of Imaging Science (VUIIS).

Contact: [Victoria.morgan@vanderbilt.edu](mailto:Victoria.morgan@vanderbilt.edu)

# Participating Laboratories



## Neuroimaging and Brain Dynamics Lab

PI: Catie Chang, Ph.D.

Assistant Professor of Electrical and Computer Engineering

Assistant Professor of Computer Science

Assistant Professor of Biomedical Engineering

Vanderbilt University

The goal of our research is to advance understanding of brain function in health and disease. We develop approaches for studying human brain activity by integrating functional neuroimaging (fMRI, EEG) and computational analysis techniques. In one avenue, we are examining the dynamics of large-scale brain networks and translating this information into novel fMRI biomarkers. We also work toward resolving the complex neural and physiological underpinnings of fMRI signals. Our research is highly interdisciplinary and collaborative, bridging fields such as engineering, computer science, neuroscience, psychology, and medicine.

Contact: [catie.chang@vanderbilt.edu](mailto:catie.chang@vanderbilt.edu)

# Participating Laboratories

## Science and Technology for Robotics in Medicine (STORM) Lab



Director STORM Lab USA and PI: Keith L. Obstein, M.D.  
Division of Gastroenterology, Hepatology, and  
Nutrition, VUMC;  
Department of Mechanical Engineering,  
Vanderbilt University



Director STORM Lab UK and PI: Pietro Valdastri, Ph.D.  
School of Electronic and Electrical Engineering,  
University of Leeds;  
Department of Mechanical and Electrical Engineering  
Vanderbilt University

At the STORM Lab we strive to improve the quality of life for people undergoing endoscopy and abdominal surgery by creating miniature and non-invasive capsule robots.

The continuous quest for miniaturization has made the science fiction vision of miniature capsule robots working inside the human body a reality. Capsule robots represent a challenging paradigm for both research and learning. They embed sensors, actuators, digital intelligence, miniature mechanisms, communication systems, and power supply, all in a very small volume. Capsule robots may be autonomous or teleoperated, they can work alone or as a team, and they can be customized to fulfill specific functions.

At the STORM Lab, we are designing and creating mechatronic and self-contained devices to be used inside specific districts of the human body to detect and cure diseases in a non-invasive and minimally invasive manner—including early detection and treatment of gastrointestinal cancers (i.e. colorectal cancer, gastric cancer) and inflammatory bowel disease. Building upon these competences, we are always ready to face new challenges by modifying our capsule robots to emerging medical needs.

Contact: [keith.obstein@vanderbilt.edu](mailto:keith.obstein@vanderbilt.edu) or [p.valdastri@leeds.ac.uk](mailto:p.valdastri@leeds.ac.uk)

# Participating Laboratories



## Surgical Analytics Lab

PI: Alexander Langerman, M.D.

Associate Professor, Department of Otolaryngology,  
Vanderbilt University Medical Center

The Surgical Analytics Lab focuses on novel methods of real-time surgical data collection and analysis. Our flagship project is the Clearer Operative Analysis and Tracking (“CleOpATra”) surgical video system - a wearable camera that automatically tracks the surgical field for sustained viewing of open surgical fields.

Contact: [alexander.langerman@vanderbilt.edu](mailto:alexander.langerman@vanderbilt.edu)

# Participating Laboratories



## Vanderbilt Biophotonics Center

PI: Anita Mahadevan-Jansen, Ph.D.  
Orrin H. Ingram Professor of Engineering  
Director of Undergraduate Studies in  
Biomedical Engineering  
Professor of Neurological Surgery  
Director of the Biophotonics Center at Vanderbilt  
Vanderbilt University

The Vanderbilt Biophotonics Center is an interdisciplinary research center at the intersection of the College of Arts and Science, the School of Engineering and the School of Medicine that brings together faculty, post-doctoral fellows, graduate and undergraduate students dedicated to biophotonics research. VBC provides a state-of-the-art research facility and a collaborative environment and includes shared core facilities and resources for research that spans everything from fundamental discovery to clinical translation. Research is organized into 3 thrust areas: Clinical Photonics, Neurophotonics and Multi-scale biophotonics. Other research interests include application of optical techniques in a variety of other areas such as diabetes research, neonatology, ophthalmology, critical care, surgery, obstetrics, and orthopedics for clinical translation as well as fundamental research. Further, since many of our team are engineers and physicists, research is also focused on the discovery of new optical methodologies and the support needed to advance current technologies to new levels. Example projects include near-infrared fluorescence for the detection of the parathyroid gland in endocrine surgery, optical metabolic imaging to assess therapeutic response in breast cancers and development of infrared neural stimulation to modulate the electrical response of the nervous system without the need for genetic or other external mediators.

Contact: [anita.mahadevan-jansen@vanderbilt.edu](mailto:anita.mahadevan-jansen@vanderbilt.edu)

# Participating Laboratories



## Vanderbilt Dermatology Translational Research Clinic (VDTRC)

PI: Eric Tkaczyk, M.D., Ph.D., FAAD,  
Director, Vanderbilt Dermatology Translational Research Clinic  
Staff Physician Department of Veterans Affairs, Nashville  
Dermatology and Research Services  
Assistant Professor Department of Dermatology  
Assistant Professor Biomedical Engineering

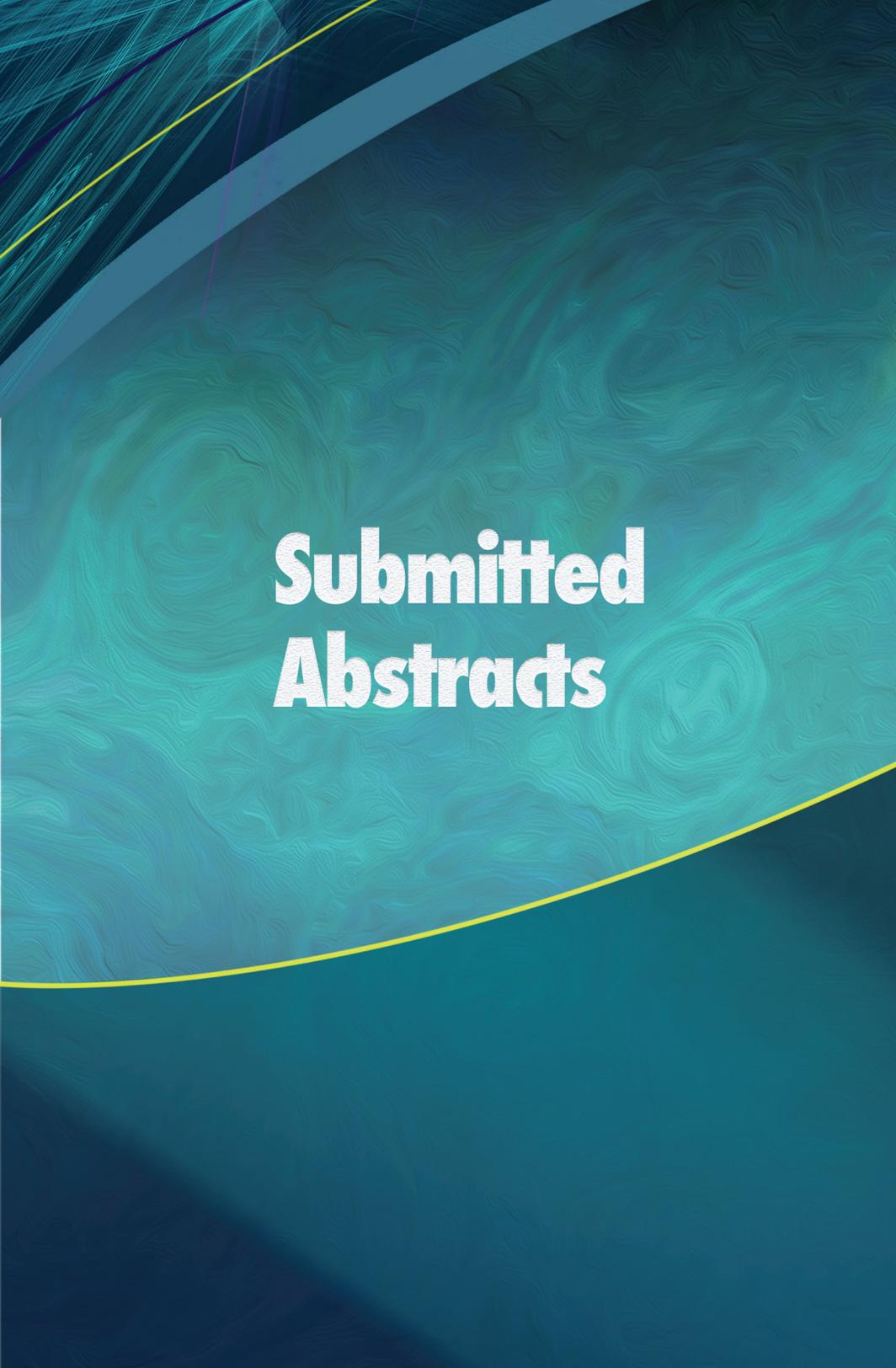
The Vanderbilt Dermatology Translational Research Clinic (VDTRC.org) was founded in 2016 (then as the Vanderbilt Cutaneous Imaging Clinic) as a platform for direct clinical translation of engineering for clinical impact in dermatology, oncology, and related specialties. The mission is seamless integration of technology-based patient care and translational research.

A major focus is the development and clinical investigation of noninvasive methods to assess graft-versus-host disease (GVHD) in bone marrow / hematopoietic stem cell transplantation (HCT) patients. Occurring in most patients following allogeneic HCT, chronic GVHD (cGVHD) is the leading cause of long-term mortality and morbidity after this life-saving procedure. Current cGVHD staging relies on physician estimation of involved skin body surface area, which suffers poor intra- and interrater reproducibility and is therefore insensitive to disease changes.

Skin manifestations of cGVHD are broadly divided into two categories – ERYTHEMA and SCLEROSIS. We use convolutional neural networks to measure ERYTHEMA from cross-polarized 3D photos calibrated in distance, color, and lighting. Additionally, we have completed initial clinical studies to assess SCLEROSIS with a unique handheld device that noninvasively measures soft tissue biomechanical properties (a modified “Myoton”). These interdisciplinary projects have benefited from the support of teams lead by strong collaborators including Professor Madan Jagasia at VUMC (CMO of the Vanderbilt-Ingram Cancer Center), Professor Benoit Dawant at Vanderbilt University (Director of VISE), and Professor Arved Vain from the University of Tartu (inventor of the Myoton and visiting professor at VUMC).

Contact: [eric.tkaczyk@vumc.org](mailto:eric.tkaczyk@vumc.org)



The background is a vibrant teal color with a complex, wavy, marbled texture. A thick, dark blue curved line sweeps across the top left, and a bright yellow curved line sweeps across the bottom. In the top left corner, there are several thin, intersecting lines in shades of purple and yellow.

# **Submitted Abstracts**

# 1. Therapeutic MK2 inhibition blocks pathological vascular smooth muscle cell phenotype switch

J. William Tierney,<sup>1</sup> Brian C. Evans,<sup>1</sup> Joyce Cheung-Flynn,<sup>2</sup> Bo Wang,<sup>1</sup> Juan M. Colazo,<sup>1,3</sup> Monica E. Polcz,<sup>1,4</sup> Rebecca S. Cook,<sup>1,5</sup> Colleen M. Brophy,<sup>2</sup> and Craig L. Duvall<sup>1</sup>

<sup>1</sup>Department of Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, USA. <sup>2</sup>Division of Vascular Surgery, Department of General Surgery, Vanderbilt University Medical Center, Nashville, Tennessee, USA. <sup>3</sup>Medical Scientist Training Program, Vanderbilt University School of Medicine, Nashville, Tennessee, USA. <sup>4</sup>Department of General Surgery and <sup>5</sup>Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, Tennessee, USA.

Vascular procedures, such as stenting, angioplasty, and bypass grafting, often fail due to intimal hyperplasia (IH), wherein contractile vascular smooth muscle cells (VSMCs) dedifferentiate to synthetic VSMCs, which are highly proliferative, migratory, and fibrotic. Previous studies suggest MAPK-activated protein kinase 2 (MK2) inhibition may limit VSMC proliferation and IH, although the molecular mechanism underlying the observation remains unclear. We demonstrated here that MK2 inhibition blocked the molecular program of contractile to synthetic dedifferentiation and mitigated IH development. Molecular markers of the VSMC contractile phenotype were sustained over time in culture in rat primary VSMCs treated with potent, long-lasting MK2 inhibitory peptide nanopolyplexes (MK2i-NPs), a result supported in human saphenous vein specimens cultured *ex vivo*. RNA-Seq of MK2i-NP-treated primary human VSMCs revealed programmatic switching toward a contractile VSMC gene expression profile, increasing expression of antiinflammatory and contractile-associated genes while lowering expression of proinflammatory, promigratory, and synthetic phenotype-associated genes. Finally, these results were confirmed using an *in vivo* rabbit vein graft model where brief, intraoperative treatment with MK2i-NPs decreased IH and synthetic phenotype markers while preserving contractile proteins. These results support further development of MK2i-NPs as a therapy or blocking VSMC phenotype switch and IH associated with cardiovascular procedures.

## 2. Automatic Segmentation of Intracochlear Anatomy in MR Images Using a Weighted Active Shape Model

Yubo Fan [1], Rueben A. Banalagay [2], Nathan D. Cass [3], Jack H. Noble [2], Kareem O. Tawfik [3], Robert F. Labadie [3], and Benoit M. Dawant [2]

[1] Department of Computer Science, Vanderbilt University [2] Department of Electrical and Computer Engineering, Vanderbilt University [3] Department of Otolaryngology - Head & Neck Surgery, Vanderbilt University Medical Center

There is evidence that cochlear MR signal intensity may be useful in prognosticating the risk of hearing loss after middle cranial fossa (MCF) resection of acoustic neuroma (AN), but the manual segmentation of this structure is difficult and prone to error. This hampers both large-scale retrospective studies and routine clinical use of this information. To address this issue, we present a fully automatic method that permits the segmentation of the intra-cochlear anatomy in MR images, which uses a weighted active shape model we have developed and validated to segment the intra-cochlear anatomy in CT images. We take advantage of a dataset for which both CT and MR images are available to validate our method on 132 ears in 66 high-resolution T2-weighted MR images. Using the CT segmentation as ground truth, we achieve a mean Dice (DSC) value of 0.81 and 0.79 for the scala tympani (ST) and the scala vestibuli (SV), which are the two main intracochlear structures.

### **3. Multi-modality Differentiation between myxofibrosarcoma and myxoma using radiomics and machine learning models**

**Can Cui<sup>1</sup>, Samuel R. Johnson<sup>2</sup>, Cullen P. Moran<sup>2</sup>, Katherine S. Hajdu<sup>2</sup>, Joanna Shechtel<sup>3</sup>, John J. Block<sup>3</sup>, Brian Bingham<sup>4</sup>, David Smith<sup>3</sup>, Leo Y. Luo<sup>4</sup>, Hakmook Kang<sup>5</sup>, Jennifer L. Halpern<sup>2</sup>, Herbert S. Schwartz<sup>2</sup>, Ginger E. Holt<sup>2</sup>, Joshua M. Lawrenz<sup>2</sup>, Benoit M. Dawant<sup>6</sup>**

<sup>1</sup>Department of Computer Science, Vanderbilt University, Nashville, TN 37235, USA  
<sup>2</sup>Department of Orthopedic Surgery, Vanderbilt University Medical Center, Nashville, TN, 37235, USA <sup>3</sup>Department of Radiology, Vanderbilt University Medical Center, Nashville, TN, 37235, USA <sup>4</sup>Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, TN, 37235, USA <sup>5</sup>Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, 37235, USA <sup>6</sup>Department of Electrical and Computer Engineering, Vanderbilt University Medical Center, Nashville, TN, 37235, USA

Myxofibrosarcoma is a rare, malignant myxoid soft tissue tumor. It can be challenging to distinguish it from myxoma, a benign tumor, in clinical practice as there exists imaging and histologic feature overlap between these two entities. Some previous works used radiomics features of T1-weighted MRI images to differentiate myxoid tumors, but few have used multi-modality data. In this project, we collect a dataset containing 20 myxomas and 20 myxofibrosarcomas, each with a T1-weighted image, a T2-weighted image, and clinical features. Radiomics features from multi-modality images and clinical features are used to train multiple machine learning models. Our experiment results show that the prediction accuracy using the multi-modality features surpasses the results from a single modality. The radiomics features Gray Level Variance and Gray Level Non-Uniformity Normalized extracted from the Gray Level Run Length Matrix (GLRLM) of the T2 images and age are the top three features selected by the LASSO feature reduction model.

## 4. Cross-Modality Domain Adaptation for Vestibular Schwannoma and Cochlea Segmentation

Han Liu, Yubo Fan, Can Cui, Dingjie Su, Andrew McNeil, Benoit M. Dawant

Automatic methods to segment the vestibular schwannoma (VS) tumors and the cochlea from magnetic resonance imaging (MRI) are critical to VS treatment planning. Although supervised methods have achieved satisfactory performance in VS segmentation, they require full annotations by experts, which is laborious and time-consuming. In this work, we aim to tackle the VS and cochlea segmentation problem in an unsupervised domain adaptation setting. Our proposed method leverages both the image-level domain alignment to minimize the domain divergence and semi-supervised training to further boost the performance. Furthermore, we propose to fuse the labels predicted from multiple models via noisy label correction. Our results on the challenge validation leaderboard showed that our unsupervised method has achieved promising VS and cochlea segmentation performance with mean dice score of  $0.8261 \pm 0.0416$ ; The mean dice value for the tumor is  $0.8302 \pm 0.0772$ . This is comparable to the weakly-supervised based method. In the final evaluation period, our solution has achieved dice scores of 0.799 and 0.825 and ASSD of 0.74 and 0.18 mm for VS tumor and cochlea respectively, ranking #4 in the crossMoDA challenge leaderboard.

## **5. Automated detection of electrocautery instrument in videos of open neck procedures using YOLOv3**

**Tingyan Deng, Shubham Gulati, William Rodriguez, Benoit M. Dawant, Alexander Langerman**

With the rapid development of deep learning approaches, tremendous progress has been made in computer-assisted analysis of minimally-invasive, videoscopic surgery. However, surgery through open incisions (“open surgery”), which constitutes a much larger portion of surgical procedures performed, is rarely investigated because of the difficulty in obtaining high-quality open surgical video footage. Automated detection of surgical instruments shows promise for evaluating surgical activities, and provides a foundation for quality/safety review, education, and identification of surgical performance. In this paper, we present results using YOLOv3 to successfully identify an electrocautery surgical instrument in a library of images derived from 22 open neck procedures (an 887-image training/validation set, and a 1149-image testing set) captured using a wearable surgical camera. We show that our method effectively detects the spatial bounds of the electrocautery pencil in still images and we further demonstrate the ability of our method to detect the location of this instrument in video footage. Our work serves as the first demonstration of open surgical instrument detection using first-person video footage from a wearable camera and sets the stage for further work in this field.

## 6. Segmentation of Skin Affected by Cutaneous Chronic Graft-Versus-Host Disease by U-Net Convolutional Neural Network

Andrew McNeil 1,2,3 Kelsey Parks 2,3 Xiaoyi Liu 1,2,3 Inga Saknite 3,6 Fuyao Chen 2,3,4,5 Tahsin Reasat 1 Lee Wheless 2,3 Benoit M Dawant 1 Eric R Tkaczyk 2,3,4

1 Department of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA 2 Dermatology Service and Research Service, Department of Veterans Affairs, Tennessee Valley Healthcare System, Nashville, TN, USA 3 Vanderbilt Department of Dermatology, Vanderbilt University Medical Center, Nashville, TN, USA 4 Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, US 5 School of Medicine, Yale University, New Haven, CT, US 6 Biophotonics Laboratory, Institute of Atomic Physics and Spectroscopy, University of Latvia, Riga, Latvia

Chronic graft-versus-host disease (cGVHD) is the leading cause of non-relapse long-term morbidity and mortality in the hematopoietic cell transplantation population. Skin is the most commonly and first affected organ. Surface area involvement is a key measure for staging and tracking cutaneous disease. It is typically evaluated visually, with limited availability of expert dermatologists. As a step towards addressing this gap, we developed a U-Net deep learning algorithm to segment skin affected by cGVHD. We took 360 cross-polarized stereoscopic photographs from 36 cGVHD patients. As ground truth, each region affected by cGVHD was marked by an annotator with >6 months of cGVHD training. We trained 36 U-Net models in a leave-one-patient-out validation experiment. In the unseen patient, the algorithm performed well at identifying photos with affected or unaffected skin with overall accuracy above 90%. At the pixel-level, the algorithm achieved a median Dice coefficient of 0.76 (interquartile range: 0.44 - 0.89), and median surface area error of 8.73% (3.93 - 21.52%). Without knowing the ground truth, a board-certified dermatologist assessed each segmentation for its clinical relevance, with 77% of segmentations rated as clinically acceptable to excellent.

## 7. Application to display brain shift simulation in tumor resection procedures

**Kush J. Hari (1) Rohan C. Vijayan (2) Ma Luo (1,3) Jaime Tierney (1,3) Jon S. Heiselman (1,3) Lola B. Chambless (3,4) Reid C. Thompson (3,4) Michael I. Miga (1,3,4,5)**

1. Vanderbilt University, Department of Biomedical Engineering, Nashville TN USA 2. Johns Hopkins University, Department of Biomedical Engineering, Baltimore MD USA 3. Vanderbilt Institute for Surgery and Engineering, Nashville TN USA 4. Vanderbilt University Medical Center, Department of Neurological Surgery, Nashville TN USA 5. Vanderbilt University Medical Center, Department of Radiology and Radiological Sciences, Nashville TN USA

The quality of neurosurgical planning can become compromised by soft tissue deformations that occur during surgery (i.e., brain shift). Conventional image guidance systems do not consider these intraoperative changes. In recent efforts, model-based strategies have been developed to estimate surgical load displacements and modify the patient's data intraoperatively to account for brain shift. While the efficacy of the model has been previously established, there is also an opportunity to further assist surgical planning with this pipeline. To address this, a mobile application designed for an Android tablet was developed to display simulated brain shifts that would occur during a craniotomy. The application has two primary functions to facilitate planning: a patient positioning mode and a simulation mode. The patient positioning mode allows the neurosurgeon to load the patient's preoperative MR data and create a surgical plan (i.e., head orientation and craniotomy location) for the procedure. The simulation mode then displays both the preoperative data and the model-predicted brain shift as a function of the specified orientation from the patient positioning mode. Additionally, to account for positional variations between planning and procedural implementation, the simulation mode also displays solutions with additional perturbations to the planned positioning to estimate shift possibilities. To assess the simulation mode prototype, practicing neurosurgeons were provided a prototype demonstration and interviews were performed to evaluate efficacy and design. Preliminary survey responses show that the prototype could be an impactful surgical planning tool, especially if the application could interface with the Microsoft HoloLens as a mixed reality simulation.

## **8. Breast image registration for surgery: insights on material mechanics modeling**

**Morgan J. Ringel (1), Winona L. Richey (1), Jon S. Heiselman (1, 2), Ma Luo (1), Ingrid M. Meszoely (3), Michael I. Miga (1)**

1 - Vanderbilt University 2 - Memorial Sloan-Kettering Cancer Center 3 - Vanderbilt University Medical Center

Breast conserving surgery is a common procedure for early-stage breast cancer patients, and supine MR breast imaging can more closely represent the tumor surgical presentation compared to conventional pendant positioning. Utilization of preoperative imaging for surgical guidance requires an accurate image-to-physical registration. Three registration techniques were investigated: (1) a point-based rigid registration using synthetic fiducials, (2) a non-rigid biomechanical model-based registration using sparse data, and (3) a data-dense 3D image-to-image-based registration used as a comparison metric. Registration accuracy significantly improved from (1) to (2) to (3), and this analysis may inform future development of image guidance systems for lumpectomy procedures.

## 9. Segmentation of kidney stones in endoscopic video feeds

Zachary A Stoebner, Daiwei Lu, Seok Hee Hong, Nicholas L Kavoussi, and Ipek Oguz

Vanderbilt University, Nashville, TN, USA (all)

Image segmentation has been increasingly applied in medical settings as the advent of AI has skyrocketed the application of deep learning. Urology, specifically, is one field of medicine that is primed for the adoption of a real-time image segmentation system with the aim of automating endoscopic stone treatment. In this project, we explored supervised deep learning models to annotate kidney stones in surgical endoscopic video feeds. In this paper, we describe how we built the dataset from the raw videos and how we developed a pipeline to automate as much of the process as possible. To maintain the project in the long term, we also began to engineer a utilities library to expedite data management at each endpoint of the model's use. Most importantly, we adapted and analyzed three baseline deep learning models - U-Net, U-Net++, and DenseNet - to predict annotations on the frames of the endoscopic videos with the highest accuracy above 90%. To show clinical promise, we also confirmed that our best trained model can accurately annotate new videos at 30 frames per second. Our results demonstrate that the proposed method justifies continued development and study of image segmentation to annotate utereroscopic video feeds.

## 10. Dense Multi-Object 3D Glomerular Reconstruction and Quantification on 2D Serial Section Whole Slide Images

Ruining Deng<sup>1</sup>, Haichun Yang<sup>2</sup>, Zuhayr Asad<sup>1</sup>, Zheyu Zhu<sup>1</sup>, Shiru Wang<sup>1</sup>, Lee E. Wheless<sup>3</sup>, Agnes B. Fogo<sup>2</sup>, and Yuankai Huo<sup>1</sup>

1. Department of Computer Science, Vanderbilt University, Nashville, TN, 37235 USA 2. Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, TN, 37232, USA 3. Department of Dermatology, Vanderbilt University Medical Center, Nashville TN 37232, USA

There has been a long pursuit for precise and reproducible glomerular quantification in the field of renal pathology in both research and clinical practice. Currently, 3D glomerular identification and reconstruction of large-scale glomeruli are labor-intensive tasks, and time-consuming by manual analysis on whole slide imaging (WSI) in 2D serial sectioning representation. The accuracy of serial section analysis is also limited in the 2D serial context. Moreover, there are no approaches to present 3D glomerular visualization for human examination (volume calculation, 3D phenotype analysis, etc.). In this paper, we introduce an end-to-end holistic deep-learning-based method that achieves automatic detection, segmentation and multi-object tracking (MOT) of individual glomeruli with large-scale glomerular-registered assessment in a 3D context on WSIs. The high-resolution WSIs are the inputs, while the outputs are the 3D glomerular reconstruction and volume estimation. This pipeline achieves 81.8 in IDF1 and 69.1 in MOTA as MOT performance, while the proposed volume estimation achieves 0.84 Spearman correlation coefficient with manual annotation. The end-to-end MAP3D+ pipeline provides an approach for extensive 3D glomerular reconstruction and volume quantification from 2D serial section WSIs.

# 11. Systemically Delivered Lipophilic MMP13 siRNA Conjugate binds Endogenous Albumin In Situ for Efficient Joint Drug Delivery and Therapeutic Knockdown in a Post-Traumatic Osteoarthritis Mouse Model

Juan M. Colazo<sup>1, #</sup>, Ella Hoogenboezem<sup>1</sup>, Fang Yu<sup>1</sup>, Veeraj Shah<sup>1</sup>, Justin Lo<sup>1</sup>, Hongsik Cho<sup>2</sup>, Karen A. Hasty<sup>2</sup>, and Craig L. Duvall<sup>1</sup> \*

1. Department of Biomedical Engineering, Vanderbilt University, Nashville, TN.

2. Department of Orthopaedic Surgery and Biomedical Engineering, Memphis VA Medical Center, Memphis, TN # Presenting author: [juan.m.colazo@vanderbilt.edu](mailto:juan.m.colazo@vanderbilt.edu);

\* Corresponding author; Disclosures: None

**Introduction:** Post-traumatic osteoarthritis (PTOA) is induced by mechanical injury to a joint, often affects younger, highly active individuals, and shows rapid onset. Multiple joint osteoarthritis (MJOA) occurs in over 50% of OA/PTOA cases. The high incidence of MJOA motivate the development of systemic therapies that can reach and treat multiple joints after systemic treatment. In OA, synoviocytes/chondrocytes produce inflammatory cytokines and matrix metalloproteinases (MMPs) that drive the joint degenerative process. We recently showed that intraarticular injections of siRNA nanoparticles against MMP13 can reduce PTOA joint structural changes in cartilage, synovium, and meniscus. Systemic delivery of small molecule MMP inhibitors has been tested clinically for cancer but was dose limited by toxicities caused by the lack of MMP selectivity. Herein, we characterize and test chemically stabilized siRNA molecules end-modified with a diacyl lipid (siRNA-L2), which spontaneously forms a molecular nanocomplex with endogenous in vivo albumin (alb-NC/siRNA-L2).

**Results:** Initial proof of concept studies showed that albumin-binding dye Evan's Blue and exogenously delivered, fluorescently labeled albumin both accumulated more in mechanically loaded than unloaded murine knee joints. Albumin "hitchhiking" siRNA-L2 provided preferential delivery to mechanically loaded knee joints over healthy knee joints and demonstrated greater pharmacokinetics than unmodified siRNA and cholesterol-conjugated siRNA (siChol). Albumin hitchhiking provided greater ex-vivo porcine cartilage explant depth penetration and in-vitro cellular delivery. MMP13-targeting siRNA-L2, siMMP13-L2, provided greater MMP13 gene expression and protein knockdown capacity (in-vitro and in-vivo).

**Conclusion:** siRNA-L2 was shown to be safe, provide effective cartilage penetration, and provide homing and sustained target gene silencing bioactivity in PTOA joints in vivo. This system shows promise as a systemic anti-MMP13-specific therapy and represents a platform technology that can be readily adapted for targeting of other OA/rheumatic disease-driver genes.

## 12. Patient-Specific Stereotactic Frame for Transcranial Ultrasound Therapy

Jiro Kusunose (1), William Rodriguez (2), Huiwen Luo (1,3), Thomas Manuel (1,3), M. Anthony Phipps (1), William Grissom (1,3), Peter E. Konrad (4), Benoit M. Dawant (2,5), Charles Caskey (1,3,6)

1 VUIHS 2 VISE 3 VU Biomedical Engineering 4 Rockefeller Neuroscience Institute, West Virginia University 5 VU Electrical and Computer Engineering 6 VU Radiology and Radiological Sciences

MR-guided transcranial focused ultrasound (FUS) is being explored for many neural applications, as it is non-invasive and can target the brain in mm-scale. However, performing procedures within the MRI is costly and challenging. Not all procedures require close monitoring, and the ability to repeatedly apply FUS to the same location may be desirable in applications such as neuromodulation or drug delivery. We designed, fabricated, and characterized a patient-specific, 3D-printed, stereotactic frame for repeated FUS neuromodulation. The frame is compact, with minimal footprint, and can be removed and re-secured between treatments. The use of small skull anchor screws allows for the precise and repeatable transcranial FUS treatment without the need for MR-guidance following the initial calibration scan. Focus localization and repeatability were assessed via MR-thermometry on a macaque skull-phantom model. Focal localization, registration, steering, and re-steering was accomplished during the initial MRI calibration scan session. Keeping the steering coordinate constant in subsequent therapy and imaging sessions, we found good agreement between the steered foci and intended target, with target registration error of  $0.7 \pm 0.3$  and  $0.7 \pm 0.6$ mm ( $n = 4$ ) in lateral and axial dimension, respectively. Focus position (steered and non-steered) was consistent, with sub-mm variation in each dimension between studies. Our preliminary studies show that our 3D printed, patient-specific stereotactic frame can reliably position and orient the ultrasound transducer for repeated targeting of brain regions without the need for MR-guidance. This compact frame will make continued transcranial FUS treatments financially and logistically more accessible to patients.

### **13. Local spread of resting-state fMRI activity in mesial temporal structures is related to surgical outcomes in mesial temporal lobe epilepsy**

**Lucas E Sainburg (1,2), Baxter P Rogers (1,2), Catic Chang (2,3), Dario J Englot (1,2,3,4), Victoria L Morgan (1,2,4)**

1 Department of Biomedical Engineering, Vanderbilt University 2 Vanderbilt University Institute of Imaging Science, Department of Radiology and Radiological Sciences, Vanderbilt University Medical Center 3 Department of Electrical Engineering and Computer Science, Vanderbilt University 4 Department of Neurological Surgery, Vanderbilt University Medical Center

Mesial temporal lobe epilepsy (mTLE) patients can be treated with surgical resection or ablation of their epileptogenic zone (EZ), which is typically the anterior hippocampus. However, many patients suffer from seizure recurrence after surgical treatment. Spread of the EZ is one potential cause for both poor surgical outcomes and presence of focal to bilateral tonic-clonic seizures (FBTCS) in mTLE patients. In this study, we quantified resting brain activity using amplitude of low frequency fluctuation (ALFF) analysis of resting-state functional MRI (fMRI) to reflect potential extent of the EZ in 47 unilateral mTLE patients along with 96 healthy controls. fMRI activity in the EZ (anterior hippocampus) as well as connected potential “spread” regions (entorhinal cortex and parahippocampal gyrus) were compared to surgical outcomes and presence of FBTCS. We hypothesized that increased fMRI activity of the spread regions would reflect spread of the EZ and would therefore relate to presence of FBTCS and poorer surgical outcomes. Increased fMRI activity was not related to presence of FBTCS, however, patients with less favorable surgical outcomes had increased fMRI activity in their EZ and spread regions ipsilateral to the epileptic side ( $p < 0.05$ ). These results imply that increased resting activity in the EZ and connected regions may indicate EZ spread, contributing to poorer surgical outcomes in mTLE. This suggests that an extended resection of the mesial temporal lobe may improve outcomes in patients with spread of fMRI activity. NIH T32EB021937 (LES), R01 NS075270 (VLM), R01 NS108445 (VLM), R01 NS110130 (VLM), and R00 NS097618 (DJE).

## 14. AUTOMATIC, DEEP-LEARNING-BASED SEGMENTATION OF THE AMYGDALOHIPPOCAMPECTOMY

Dingjie Su, Vanderbilt University Dario Englot, VUMC Benoit Dawant, Vanderbilt University

Selective amygdalohippocampectomy (SelAH) for mesial temporal lobe epilepsy (mTLE) involves the resection of the anterior hippocampus and of a portion of the amygdala. A recent study related to SelAH reports that among 168 patients for whom two-year Engel outcomes data were available, 73% had Engel 1 outcomes (free of disabling seizure); 16.6% had Engel II outcomes (rare disabling seizures; 4.7% had Engel III outcomes (worthwhile improvement); and 5.3% had Engel IV outcomes (no worthwhile improvement). Success rate among sites also varies greatly. Possible explanations for variability in outcomes are the resected volume and/or the subregion of the hippocampus and amygdala that have been resected. To explore this hypothesis, the accurate segmentation of the resected cavity needs to be performed on a large scale. This is, however, a difficult and time-consuming task that requires expertise. Here we explore using a nnUNET to perform the task. We show that, even with a modest-sized training set (25 volumes), the median DICE value between automated and manual segmentations is 0.89. Furthermore, when evaluated visually by a trained neurosurgeon on a randomly selected subset, the contours obtained automatically were judged to be equal or superior to the manual contours in the majority of the cases. These results suggest that the automatic and accurate segmentation of the resection cavity is achievable.

## 15. Analysis of Bystander Studies for Image-Guided Robotic Partial Nephrectomy

Jason Shrand | Mechanical Engineering | Vanderbilt University

Piper Cannon | Mechanical Engineering | Vanderbilt University

Robotic partial nephrectomy has gained widespread popularity as a minimally invasive procedure to remove smaller kidney tumors. In previous research, we proposed a novel system to provide image guidance to surgeons during the operation. We hypothesized that image guidance would lead to more accurate localization of critical structures, such as the lesion, renal vein, and renal artery. Our system integrates with Intuitive's Da Vinci Xi, displaying the instruments in real-time within a virtual scene implemented in Slicer3D. The instruments are shown interacting with a 3D model of the kidney that is segmented from a pre-operative scan. The model serves as a "map" for the surgeon, showing the points of interest on the kidney even when they are obscured by fat tissue within the endoscope view. In our ongoing research, we have collected real-time intraoperative data of our system during a series of human bystander studies. Preliminary results from these procedures have directly informed revisions of our system and our protocol. Recent improvements show promising results for registration accuracy of the kidney surface and lesion. However, there is still a challenge in quantifying deformation of certain structures, such as the renal vein and artery. Here we summarize the results of the partial nephrectomy bystander studies, the iterative development of our system, and the challenges involved with image-guided surgery.

## 16. Non contact digitization method for laparoscopic liver surgery

**Bowen Xiang, Michael I. Miga**

Vanderbilt University, Vanderbilt Institute of Surgery and Engineering

In select patients when transplant is not possible, open and laparoscopic liver surgery are preferred treatments for liver cancer and performed with curative intent. Currently, only about 20% patients are eligible for resection due to the complexity of the procedure. One possibility to increase eligibility is to assist surgical practices by augmenting standard resection with image-guided navigation technology. One confounding factor in this framework is the presence of soft-tissue deformations that compromise the fidelity of navigation systems based on preoperative computed tomographic imaging (CT) data taken prior to surgery. One possibility is to use computational models in conjunction with sparse localization data taken during surgery to compensate for misalignment due to deformation. To date, collecting data has been accomplished with an optically tracked stylus that requires physical contact with the liver. Contact pressure could be a source of registration error. In our study, we used a non-contact digitization method called conoprobe which is based on polarized light interference inside of a birefringent crystal. We combined the conoprobe with optical tracking system to collect point clouds describing liver surface. One major obstacle in this approach for use in laparoscopic surgery is that the conoprobe's straight-path sensing results in less surface coverage than its stylus counterpart. In this work, a novel approach that is amenable to sterilization needs and uses an optical reflector is proposed to increase surface coverage. In addition, a 3D Slicer extension named ConoprobeInterface has been developed to both calibrate and scan liver surfaces. Preliminary realizations and data are reported.

## **17. Automated Instrument-Tracking for Video-Rate 4D Intraoperative OCT Imaging of Ophthalmic Surgical Dynamics**

**Eric M. Tang**, Department of Biomedical Engineering

**Mohamed T. El-Haddad**, Department of Biomedical Engineering

**Shriji N. Patel**, Vanderbilt Eye Institute

**Yuankai K. Tao**, Department of Biomedical Engineering

Intraoperative OCT (iOCT) provides real-time imaging data that can be used to aid clinical decision-making and verify completion of surgical goals. However, video-rate 4D iOCT imaging of surgical dynamics is limited by the need to manually align the OCT field-of-view (FOV) to the region-of-interest, thus significantly impacting surgical workflow. Our group previously demonstrated a deep-learning based approach for automated instrument-tracking and adaptive sampling. The method takes advantage of our spectrally encoded coherence tomography and reflectometry (SECTR) system, which provides simultaneous high-speed en face spectrally encoded reflectometry (SER) and cross-sectional OCT imaging. Convolutional neural network (CNN) detection of instrument position from SER images enables real-time motion estimation. In addition, CNN bounding box position outputs allow for dynamic modification of scan waveforms to center the iOCT FOV on the surgical instrument without the need for manual realignment. Adaptive-sampling by densely-sampling the instrument tip and sparsely-sampling the periphery provides additional widefield fiducials without sacrificing speed or sampling density. However, previous implementations of our automated instrument tracking platform were limited by slow tracking update rates and poor tracking accuracy. Here, we demonstrate an updated and simplified framework for automated instrument-tracking that is capable of generating instrument position outputs at over 120 Hz. We present video-rate 4D imaging and tracking of 25G internal limiting membrane forceps in a retinal phantom at 16 volumes/second. The proposed method and improvements will facilitate the broad adoption of iOCT technology by providing real-time volumetric feedback on surgical dynamics and instrument-tissue interactions.

## 18. SimTriplet: Simple Triplet Representation Learning with a Single GPU

Quan Liu<sup>1</sup> Peter C. Louis<sup>2</sup> Yuzhe Lu<sup>1</sup> Aadarsh Jha<sup>1</sup> Mengyang Zhao<sup>1</sup> Ruining Deng<sup>1</sup> Tianyuan Yao<sup>1</sup> Joseph T. Roland<sup>2</sup> Haichun Yang<sup>2</sup> Shilin Zhao<sup>2</sup> Lee E. Wheless<sup>2</sup> Yuankai Huo<sup>1</sup>

1. Vanderbilt University, Nashville TN 37215, USA 2. Vanderbilt University Medical Center, Nashville TN 37215, USA

Contrastive learning is a key technique of modern self-supervised learning. The broader accessibility of earlier approaches is hindered by the need of heavy computational resources (e.g., at least 8 GPUs or 32 TPU cores), which accommodate for large-scale negative samples or momentum. The more recent SimSiam approach addresses such key limitations via stop-gradient without momentum encoders. In medical image analysis, multiple instances can be achieved from the same patient or tissue. Inspired by these advances, we propose a simple triplet representation learning (SimTriplet) approach on pathological images. The contribution of the paper is three-fold: (1) The proposed SimTriplet method takes advantage of the multi-view nature of medical images beyond self-augmentation; (2) The method maximizes both intra-sample and inter-sample similarities via triplets from positive pairs, without using negative samples; and (3) The recent mix precision training is employed to advance the training by only using a single GPU with 16GB memory. By learning from 79,000 unlabeled pathological patch images, SimTriplet achieved 10.58% better performance compared with supervised learning. It also achieved 2.13% better performance compared with SimSiam. Our proposed SimTriplet can achieve decent performance using only 1% labeled data. The code and data are available at <https://github.com/hrlblab/SimTriplet>.

## 19. Ultra-high-resolution Mapping of Cortical Layers 3T-Guided 7T MRI

**Karthik Ramadass<sup>a</sup>, Francois Rheaultc, Leon Y. Caib, Lucas W. Remediosa, Micah DArchangele, Ilwoo Lyuc,d, Laura A. Barqueroe, Allen T. Newtonb,f, Laurie E. Cuttinge, Yuankai Huoa,c, Bennett A. Landmana,b,c,e,f**

<sup>a</sup>Department of Computer Science, Vanderbilt University, Nashville, TN, USA;

<sup>b</sup>Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA;

<sup>c</sup>Department of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA;

<sup>d</sup>Department of Computer Science and Engineering, Ulsan National Institute of Science and Technology, Ulsan, South Korea; <sup>e</sup>Vanderbilt Brain Institute, Vanderbilt University, Nashville, TN, USA; <sup>f</sup>Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, USA.

<sup>f</sup>Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, USA.

7T MRI provides unprecedented resolution for examining human brain anatomy in vivo. For example, 7T MRI enables deep thickness measurement of laminar subdivisions in the right fusiform area. Existing laminar thickness measurement on 7T is labor intensive, and error prone since the visual inspection of the image is typically along one of the three orthogonal planes (axial, coronal, or sagittal view). To overcome this, we propose a new analytics tool that allows flexible quantification of cortical thickness on a 2D plane that is orthogonal to the cortical surface (beyond axial, coronal, and sagittal views) based on the 3D computational surface reconstruction. The proposed method further distinguishes high quality 2D planes and the low-quality ones by automatically inspecting the angles between the surface normals and slice direction. In our approach, we acquired a pair of 3T and 7T scans (same subject). We extracted the brain surfaces from the 3T scan using MaCRUISE and projected the surface to the 7T scan's space. After computing the angles between the surface normals and axial direction vector, we found that 18.58% of surface points were angled at more than 80 degrees with the axial direction vector and had 2D axial planes with visually distinguishable cortical layers. 15.12% of the surface points with normal vectors angled at 30 degrees or lesser with the axial direction, had poor 2D axial slices for visual inspection of the cortical layers. This effort promises to dramatically extend the area of cortex that can be quantified with ultra-high resolution in-plane imaging methods.

## 20. Physiologic and hemodynamic consequences of extracorporeal circuit configuration for pulmonary hypertension and right ventricular failure in a novel ovine model

**Authors:** Rei Ukita, John W. Stokes, W. Kelly Wu, Yatrik Patel, J. R. Talackine, Nancy Cardwell, Clayne Benson, Ryan LeFevre, Susan Eagle, Caitlin Demarest, Yuliya Tipograf, Elizabeth Simonds, Michael Cortelli, William Grogan, Emily Tsai, David Skoog, Keith Cook, Erika B. Rosenzweig, Matthew Bacchetta

**Affiliations:** Ukita, Stokes, Wu, Patel, Talackine, Cardwell, Demarest, Tipograf, Bacchetta: Vanderbilt University Medical Center (VUMC), Department of Thoracic Surgery  
Eagle, Benson, Lefevre: VUMC, Department of Anesthesiology -  
Skoog, Cook, Bacchetta: Advanced Respiratory Technologies LLC -  
Cook: Department of Biomedical Engineering, Carnegie Mellon University -  
Simonds: Vanderbilt University School of Medicine -  
Rosenzweig: Department of Pediatrics, Columbia University Medical Center

**Introduction:** Right ventricular failure (RVF) is a major cause of mortality in pulmonary hypertension (PH). Mechanical cardiopulmonary support (MCS) holds promise for this population, but there are currently no clinical devices for long-term support. Investigations into optimal MCS cannulation configurations for PH-induced RVF are needed.

**Methods:** We evaluated a low-profile, ventricular assist device (VAD) pump combined with a low-resistance gas exchanger, the Pulmonary Assist Device (PAD), for acute RV support in 11 chronic PH sheep. Four cannulation configurations were evaluated: (1) right atrium-to-left atrium (RA-LA, N=3), (2) RA-to-pulmonary artery (RA-PA, N=3), (3) pumpless PA-to-LA (PA-LA, N=2), and (4) RA-ascending aorta (RA-Ao, N=3). Acute RVF was induced, and MCS was provided for up to 6 hours with blood flow rates of 1-3 L/min. Circuit, hemodynamic and echocardiographic data were collected.

**Results:** RA-LA easily achieved blood flow of 3 L/min, while RA-PA and RA-Ao were flow-limited due to their higher pump afterload. Pumpless PA-LA could not consistently achieve flow above 1 L/min. The PAD maintained a low resistance of <4 mmHg/L/min and transferred 114 mL O<sub>2</sub>/min. RA-LA demonstrated RV unloading and lower inotropic dependence with increasing flow. RA-Ao unloaded the RV, but less so than RA-LA. Meanwhile, RA-PA did not appreciably unload the RV. One trial of RA-PA support elicited severe pulmonary hemorrhage. Based on echocardiograms, only RA-LA restored physiologic ventricular geometry.

**Conclusion:** RA-LA successfully unloads the RV at a lower pump speed, lower inotrope requirement, and improved ventricular geometry compared to RA-Ao. RA-PA and pumpless PA-LA were less viable as RV support in this study.

## 21. Acoustic neuroma segmentation using ensembled convolutional neural networks

Qibang Zhu<sup>1</sup>, Hao Li<sup>2</sup>, Nathan D. Cass<sup>3</sup>, Nathan R. Lindquist<sup>3</sup>, Kareem O. Tawfik<sup>3</sup>, and Ipek Oguz<sup>1</sup>

<sup>1</sup>Department of Computer Science, Vanderbilt University <sup>2</sup>Department of Electrical Engineering, Vanderbilt University <sup>3</sup>Department of Otolaryngology-Head & Neck Surgery, Vanderbilt University Medical Center

Acoustic neuroma (AN) is a noncancerous and slow-growing tumor that influences the human hearing system. Magnetic resonance images (MRIs) are routinely utilized to monitor tumor progression. Quantifying tumor growth in an automated manner would allow more precise studies, both at the population level as well as for clinical management of individual patients. Deep learning methods have shown excellent performance for many medical image segmentation tasks in recent years. However, most current methods do not work well on heterogeneous datasets where MRIs are acquired with vastly different protocols. In this paper, we propose a deep learning framework with ensembled convolutional neural networks (CNNs) to segment acoustic neuromas even in heterogeneous datasets. We ensemble a 2.5D CNN model and a 3D CNN model together along with augmentations added to the model for better inter-dataset segmentation performance. We test our methods on 2 datasets: the publicly available dataset from the crossMoDA challenge and an in-house dataset. We examine our method with supervised learning on the crossMoDA dataset and directly apply the trained model to the in-house dataset. The Dice score, average surface distance (ASD), and 95-percent Hausdorff distance (95HD) are used as evaluation metrics. Our method has better performance than the baseline methods, not only on intra-dataset segmentation accuracy but also on inter-dataset generalizability.

## 22. Mapping the Impact of Non-Linear Gradient Fields on Diffusion MRI Tensor Estimations

Praitayini Kanakaraja, Colin B. Hansena, Francois Rheaulta,c, Leon Y. Cai\* b, Karthik Ramadassa, Baxter P. Rogers b, Kurt G. Schillingb, Bennett A. Landmana,d,e

aDepartment of Computer Science, Vanderbilt University, Nashville, TN, USA;

bVanderbilt University Institute for Imaging Science, Vanderbilt University Medical Center, Nashville, TN, USA; cDepartment of Radiology and Radiological Services, Vanderbilt University Medical Center, Vanderbilt University Medical, Nashville, TN, USA;

dDepartment of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA; eDepartment of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA University Medical Center

Non-linear gradients impact diffusion weighted MRI by corrupting the experimental setup and lead to complication in the interpretation of results and conclusions while studying tractography and tissue microstructure. To interpret the degree of consequences of gradient non-linearities (denoted  $L(r)$  fields), we introduced empirically derived  $L(r)$  fields on ground truth tensors at different orientations and anisotropies. The impact is assessed through mean diffusivity (MD), fractional anisotropy (FA) and principal eigen vector (PEV). Lower FA are more susceptible to  $L(r)$  fields and  $L(r)$  fields with greater absolute Jacobian determinants corrupt tensors more. MD corruption is dependent upon the magnitude of the field.  $L(r)$  fields have a larger impact on PEV when FA value is small. The results are dependent on the underlying orientation. This work provides insight into characterizing the non-linear gradient error and aids in selecting correction techniques to address the inaccuracies b-value.

## **23. Acoustic Signature: a therapeutic ultrasound guidance technique with submillimeter accuracy**

**Thomas J. Manuel<sup>1,3</sup>, Aparna Singh<sup>1,3</sup>, Jiro Kusunose<sup>2,3</sup>, Adrienne Hawkes<sup>2</sup>, William Rodriguez<sup>4,5</sup>, Benoit M. Dawant<sup>4,5</sup>, Charles F. Caskey<sup>1,2,3</sup>**

<sup>1</sup>Vanderbilt University, Department of Biomedical Engineering, Nashville, USA.

<sup>2</sup>Vanderbilt University Medical Center, Department of Radiology, Nashville, USA

<sup>3</sup>Vanderbilt University Institute of Imaging Science, Nashville, USA <sup>4</sup>Vanderbilt Institute for Surgery and Engineering, Nashville, USA <sup>5</sup>Vanderbilt University, Department of Electrical and Computer Engineering, Nashville, USA

Accurate targeting is paramount for transcranial ultrasound procedures. Here we describe a new method for targeting transcranial ultrasound dubbed acoustic signature which uses acoustic feedback from a target's unique reflection patterns to guide the transducer to a previously defined orientation. We characterize the uniqueness and convergence of acoustic signatures on a macaque head phantom. Using feedback from the acoustic signature to inform a gradient descent algorithm which drives positioning motors, we demonstrate submillimeter targeting accuracy. This method provides an accurate and repeatable method for therapeutic transducer array placement.

## 24. Efficient Quality Control with Mixed CT and CTA Datasets

Lucas W. Remedios\* [a], Leon Y. Cai [b], Colin B. Hansen [a], Samuel W. Remedios [c,d], Bennett A. Landman [a,b,e,f]

[a] Department of Computer Science, Vanderbilt University, Nashville, TN, USA;

[b] Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA;

[c] Department of Computer Science, Johns Hopkins University, Baltimore, MD, USA;

[d] Department of Radiology and Imaging Sciences, National Institutes of Health, Bethesda, MD, USA; [e] Department of Radiology and Radiological Sciences,

Vanderbilt University Medical Center, Nashville, TN, USA;

[f] Department of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA;

Deep learning promises the extraction of valuable information from traumatic brain injury (TBI) datasets and depends on efficient navigation when using large-scale mixed computed tomography (CT) datasets from clinical systems. To ensure a cleaner signal while training deep learning models, removal of computed tomography angiography (CTA) and scans with streaking artifacts is sensible. On massive datasets of heterogeneously sized scans, time-consuming manual quality assurance (QA) by visual inspection is still often necessary, despite the expectation of CTA annotation (artifact annotation is not expected). We propose an automatic QA approach for retrieving CT scans without artifacts by representing 3D scans as 2D axial slice montages and using a multi-headed convolutional neural network to detect CT vs CTA and artifact vs no artifact. We sampled 848 scans from a mixed CT dataset of TBI patients and performed 4-fold stratified cross-validation on 698 montages followed by an ablation experiment-150 stratified montages were withheld for external validation evaluation. Aggregate AUC for our main model was 0.978 for CT detection, 0.675 for artifact detection during crossvalidation and 0.965 for CT detection, 0.698 for artifact detection on the external validation set, while the ablated model showed 0.946 for CT detection, 0.735 for artifact detection during cross-validation and 0.937 for CT detection, 0.708 for artifact detection on the external validation set. While our approach is successful for CT detection, artifact detection performance is potentially depressed due to the heterogeneity of present streaking artifacts and a suboptimal number of artifact scans in our training data.

## **25. Electrical stimulation overlap visualization for image-guided cochlear implant programming**

**Erin L. Bratu (1), Linsey W. Sunderhaus (2), Katelyn A. Berg (2), Robert T. Dwyer (2), Robert F. Labadie (3), Rene H. Gifford (2), Jack H. Noble (1, 2, 3)**

(1) VU Dept. of Electrical & Computer Engineering (2) VUMC Dept. of Hearing & Speech Sciences (3) VUMC Dept. of Otolaryngology - Head & Neck Surgery

The cochlear implant is neural prosthesis consisting of an external sound processor and implanted receiver/stimulator with an attached electrode array. It is designed to directly stimulate auditory nerve fibers to induce the sensation of hearing in those who have experienced severe-to-profound hearing loss. After surgical implantation, audiologists program the processor with settings intended to produce optimal hearing outcomes. The likelihood of achieving optimal outcomes increases when audiologists are provided with tools that assist them in making objective decisions based on the patient's own anatomy and the surgical placement of the array. A visualization tool currently in use, called distance-vs.-frequency (DVF) curves, can be used to estimate channel interactions between electrodes. Although the information presented in this visualization is objective, an audiologist's decisions are subject to their own subjective interpretation of these curves. In this paper, we present a new visualization technique we call the Activation Region Overlap (ARO) image. The activation region overlap image is designed to remove the subjectivity of visually assessing channel interactions between electrodes. A multi-reviewer study of 15 cases shows that plans created using this new visualization are more consistent, are created more efficiently, and are rated as optimal more frequently than plans generated using the DVF curves.

## 26. Improving Slow Blood Flow Ultrasound Imaging with Coded Excitation and Block-wise SVD+ICA Filtering

Abbie Weeks, Biomedical Engineering Dr. Brett Byram, Biomedical Engineering

Slow blood flow imaging with ultrasound Doppler methods is difficult due to spectral overlap with tissue clutter induced by physiological and sonographer-hand motion as well as the low signal power inherent to slow blood flows less than 1 cm/s. We can improve separation of blood and clutter Doppler signals with advanced filtering methods such as Singular Value Decomposition and Independent Component Analysis. These two methods exhibit different strengths; SVD methods can delineate well between tissue and blood signals but struggle to differentiate blood and noise. Independent Component Analysis relies heavily on spatial characteristics to separate linearly mixed signals into independent components; thus, ICA improves separation between blood and noise signals. Both methods, used independently and in concert, perform even better when applied in a block-wise fashion by dividing the dataset into smaller overlapping blocks of data, processing these blocks independently, then reconstructing the full filtered dataset. Block-wise methods improve noise stationarity in a local region leading to improved filtering Signal-to-Noise ratio. The inherent SNR of the data can be improved by transmitting a longer pulse on acquisition; to do this without sacrificing axial resolution, we employ a coded excitation approach that allows compression and recovery of the longer transmission pulse to maintain axial resolution and improve SNR, which ultimately leads to improved filtering outcomes. Combining these acquisition and filtering methods resulted in an average 12.45 dB increase in SNR for in vivo images of a healthy liver.

## 27. Acquisition and Processing of Simultaneous EEG-fMRI

**Caroline Martin** (Electrical Engineering and Computer Science) **Sarah Goodale** (Biomedical Engineering) **Sean Tuttle** (VU Computer Science and Mathematics student) **Eric Feng** (VU Computer Science and Economics student) **Shiyu Wang** (Electrical Engineering and Computer Science) **Haatef Pourmotabbed** (Electrical Engineering and Computer Science) **Jasmine Jiang** (Neurological Surgery) **Jackson P. Rusch** (VU Computer Science student) **Dario Englot** (Neurological Surgery) **Victoria Morgan** (Radiology and Radiological Sciences) **Catie Chang** (Electrical Engineering and Computer Science)

Simultaneous EEG-fMRI leverages the complementary spatial and temporal resolution of these two modalities, providing supplementary information on brain function and dysfunction. Since EEG data must undergo extensive processing to remove artifacts induced by the MR environment and cardio-ballistic effects (related to heartbeat), appropriate practices for data acquisition and artifact reduction are critical for data quality. Here, we outline important considerations for EEG-fMRI setup and EEG artifact processing to optimize signal quality. We also demonstrate the simultaneous EEG-fMRI data that we have acquired at VUIIS (28 subjects). Supplied by Brain Products, our MR-compatible EEG system includes a 32-electrode cap with carbon-wire loops (CWL). These insulated loops provide a reference signal that is useful for correcting residual motion and vibration artifacts (e.g., cardio-ballistic, MRI helium pump). Our analysis compares EEG artifact correction performed by conventional template-based correction software (Brain Vision Analyzer 2.0) to CWL-based correction in MATLAB (EEGLAB algorithm). The cleaned data are represented as a spectrogram, which can indicate an individual's vigilance state. While results can vary across subjects, we expect that the CWL-based artifact correction will outperform the template-based EEG correction, especially in participants with motion artifacts. These considerations for EEG-fMRI setup and cleaning are important for reproducible research and should improve our integration of these modalities. One of our main goals is to link physiological measures of EEG-fMRI with each other and uncover associations between vigilance and cognition in epilepsy patients.

## 28. CATS: Complementary CNN and Transformer Encoders for Segmentation

Hao Li, Ipek Oguz

Department of Electrical Engineering and Computer Science, Vanderbilt University

Recently, deep learning methods have achieved state-of-the-art performance in many medical image segmentation tasks. Many of these are based on convolutional neural networks (CNNs). For such methods, the encoder is the key part for global and local information extraction from input images; the extracted features are then passed to the decoder for predicting the segmentations. In contrast, several recent works show a superior performance with the use of transformers, which can better model long-range spatial dependencies and capture low-level details. However, transformer as sole encoder underperforms for some tasks where it cannot efficiently replace the convolution-based encoder. In this paper, we propose a model with double encoders for 3D biomedical image segmentation. Our model is a U-shaped CNN augmented with an independent transformer encoder. We fuse the information from the convolutional encoder and the transformer, and pass it to the decoder to obtain the results. We evaluate our methods on three public datasets from three different challenges: BTCV, MoDA and Decathlon. Compared to the state-of-the-art models with and without transformers, our proposed method obtains higher Dice scores across the board.

## 29. Uncovering BOLD fMRI signals linked with breathing

**Kimberly Rogge-Obando**, Graduate Student in the Quantitative Chemical Biology Program. **Catie Chang**- Electrical Engineering, Assistant Professor

fMRI signals are sensitive to respiration. A mere change of breathing rate can lead to a false positive that indicates significant neural activity. Furthermore, it is imperative to uncover which fMRI signals are closely related to breathing to accurately infer neuronal activity. Our ongoing studies use a pneumatic belt to acquire respiration data to enable correlating respiration features to fMRI signals. However, in recent scans, the pneumatic belt from the scanner's built-in monitoring system would abruptly stop tracking breathing at intermediate points during collection. These transient artifacts impacting respiration data need to be corrected before we can effectively use these signals in our studies. Here we investigate methods for correcting this systematic error using MATLAB's outlier and filler functions, after calculating the respiration volume per time. We also investigate whether we can reproduce known patterns of correlation between respiration and fMRI in our dataset. From the results of previous studies, we hypothesis that large vessels, the posterior cingulate, and the inferior occipital cortex will positively correlate with respiration volume fluctuations.

## 30. Repairing transient artifacts in PPG signals acquired during fMRI

**Bohan Jiang, S.E. Goodale, C. Chan**

Department of Electrical Engineering and Computer Science and Biomedical Engineering, Vanderbilt University, Vanderbilt University Institute of Imaging Science, Vanderbilt University Medical Center

Photoplethysmography (PPG) is a fast and noninvasive way of measuring pulse rate and other valuable physiological variables during functional magnetic resonance imaging (fMRI) scans. However, large chunks of noise in the waveform can result from slight subject movement and interfere with the data, undermining its utility in data processing such as its use in fMRI denoising. Oftentimes, to correct for the noisy region, pulse intervals will have to be manually calculated and filled in. Since the PPG waveform can have large variations in amplitude over time, generating reasonable waveforms to replace such regions can be challenging. To tackle this issue, a convenient and simple algorithm is developed to correct transient artifacts in the PPG waveform. This algorithm can automatically detect outliers in the data and interpolate with precision close to a manual fix. This saves a significant amount of repetitive work in the preprocessing stage and allows for better and more extensive use of the data in preprocessing of fMRI data. Over the past year, the validation for the correctness of the algorithm is furthered in two major directions. The algorithm is tested on a wider range of different types and formats of PPG data, namely the LEMON data set. The output of the algorithm is also tested against several online toolkits that focus on PPG waveform correction/enhancement and peak detection. The results confirm that the algorithm is robust in comparison to outputs of other toolkits and that the PPG interpolation functionality the algorithm provides is unique.

## 31. Unfolding Model-Based Beamforming for High Quality Ultrasound Imaging

**Christopher Khan** (Department of Biomedical Engineering, Vanderbilt University), **Ruud J.G. van Sloun** (Department of Electrical Engineering, Eindhoven University of Technology), and **Brett Byram** (Department of Biomedical Engineering, Vanderbilt University)

Aperture Domain Model Image REconstruction (ADMIRE) is an advanced ultrasound beamforming method that uses a model-based approach to suppress sources of acoustic clutter and improve ultrasound image quality. However, although effective, ADMIRE requires solving an inverse problem that is ill-posed, which means that there are infinitely many solutions that can have different impacts on image quality. Currently, linear regression with elastic-net regularization is used to obtain a solution, but there are potentially better methods for performing model fitting. Therefore, in this work, we propose using a deep neural network sparse encoder for performing the model fits of ADMIRE. In particular, we unfold the iterations of the iterative shrinkage and thresholding algorithm (ISTA) as a feedforward neural network and train it using different training schemes to perform sparse coding. Test results using both simulated and in vivo data demonstrate that ADMIRE using a deep neural network sparse encoder has the potential to outperform conventional ADMIRE in terms of ultrasound image quality while still preserving the model based intuition of ADMIRE.

## 32. Finite difference modelling of the Laplacian on irregular grids for surface-based cortical thickness measurement

Kathleen Larson, VU Saramati Narasimhan, PhD, VUMC Ipek Oguz, PhD, VU

Cortical thickness (CT), the thickness of the cortical gray matter (GM) layer of the brain, is an important image-based marker for neurodegeneration. Surface-based measurements are obtained by reconstructing mesh representations of GM and white matter (WM) surfaces that enclose the cortical ribbon and measuring the distance between these at each point. This distance is generally defined using the symmetric closest point (SCP) distance formula, which is prone to underestimation in high curvature sulci and gyri. Further, this formula is not one-to-one between surfaces, nor is it truly symmetric-measuring distance from the GM surface to WM yields a different value than from WM to GM. Thus, we propose an alternative method-the surface-based Laplacian (SBL) distance mapping-that addresses both the shortcomings of the SCP and those of the volumetric Laplacian method upon which it is based, such as poor resolution or high computation cost. In the SBL method, we model the cortical ribbon as a non-uniform grid, and numerically solve for the Laplacian field within this domain using finite volume techniques. We define neighbors for interpolation within this model by employing the concept of “natural neighbors” obtained from the Voronoi diagram of the node set within the domain; this allows for generalization to any irregular grid. Finally, we calculate CT by integrating along this field from one boundary to the other. In this poster, we explain our method using a spherical model as an example and present developing research questions as we expand our method to the cortex.

### 33. Abnormalities in Voxel-Wise Thalamic Connectivity in Patients with Temporal Lobe Epilepsy

Saramati Narasimhan \* Ph.D. 1,2,3,4, Aarushi S. Negi \* 3, Hernán F. J. González, Ph.D. 2,3,4, Graham W. Johnson, B.S. 2,3,4, Jasmine W. Jiang, B.E. 1,2,3, Derek Doss B.S. 2,3,4, Danika Paulo, M.D. 1, Catic Chang, Ph.D. 2,3,4,5, Benoit Dawant Ph.D. 2,3,5, Victoria L. Morgan, Ph.D. 1,2,3,4, Dario J. Englot, M.D., Ph.D. 1,2,3,4,5

\* Authors contributed equally Department of 1Neurological Surgery; 2Vanderbilt University Institute of Imaging Science; at Vanderbilt University Medical Center; 3Vanderbilt Institute for Surgery and Engineering; Department of 4Biomedical Engineering; Department of 5Electrical Engineering and Computer Science at Vanderbilt University, Nashville, Tennessee, USA.

**Introduction:** Patients with temporal lobe epilepsy (TLE) experience broad deleterious changes in brain structural and function which cannot be explained by their focal disease alone. The thalamus, located in the midbrain, has reciprocal projections throughout the cortex and serves as a relay hub. Based on its central role, we hypothesize that we will detect abnormalities in thalamic connectivity with the cortex and arousal regions in patients compared to controls.

**Methods:** We collected resting-state fMRI for 50 patients with TLE and matched controls and 26 postoperative patients. We calculated correlations between patient-specific thalamic voxels and cortical regions of interest, including premotor cortex, mesial temporal structures, limbic cortex, prefrontal association cortex, somatosensory association cortex, superior frontal cortex, visual association cortex, primary visual cortex, primary somatosensory cortex, primary motor cortex, temporal neocortex. Using winner-takes-all analysis and voxel-wise comparisons, we quantified differences between preoperative patients and controls and changes in thalamic connectivity after surgery. We also applied Louvain community detection algorithm to the time series data to detect clusters of thalamic voxels. We elucidated the ideal gamma for Louvain-assigned communities and generated voxel clusters for preoperative, postoperative, and control subjects.

**Results:** We observed differences between our subject groups using winner-takes-all analysis and statistical analysis ( $p < 0.05$ ). Also, the optimal gamma across subjects was  $\sim 0.25$  on both left and right side of the brain, yielding 2-3 clusters of thalamic voxels per subject.

**Conclusions:** Differences between patients with TLE and controls can help explain global deficits seen in TLE patients and possibly identify new targets for neuromodulation-based treatments.

## 34. Multimodal neuroimaging in pediatric type 1 diabetes: a pilot multisite feasibility study of acquisition quality, motion, and variability

Leon Y. Cai (a), Costin Tanase (b), Adam W. Anderson (a,c), Karthik Ramadass (d), Francois Rheault (d), Chelsea A. Lee (c,f), Niral J. Patel (c,f), Sky Jones (c,f), Lauren M. LeSturgeon (g), Alix Mahon (h), Sumit Pruthi (i), Kriti Gwal (j), Arzu Ozturk (j), Hakmook Kang (k), Nicole Glaser (l), Simona Ghetti (h), Sarah S. Jaser (e), Lori C. Jordan (c,f), and Bennett A. Landman (a,c,d,i)

(a) Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA; (b) Department of Psychiatry, University of California, Davis, Davis, CA, USA; (c) Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, USA; (d) Department of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA; (e) Department of Pediatrics, Vanderbilt University Medical Center, Nashville, TN, USA; (f) Department of Neurology, Vanderbilt University Medical Center, Nashville, TN, USA; (g) Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA; (h) Department of Psychology, University of California, Davis, Davis, CA, USA; (i) Department of Radiology and Radiological Sciences, Vanderbilt University Medical Center, Nashville, TN, USA; (j) Department of Radiology, UC Davis Health, UC Davis School of Medicine, Sacramento, CA, USA; (k) Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA; (l) Department of Pediatrics, UC Davis Health, UC Davis School of Medicine, Sacramento, CA, USA

Type 1 diabetes (T1D) affects over 200,000 children and is associated with an increased risk of cognitive dysfunction. Prior imaging studies suggest the neurological changes underlying this risk are multifactorial, including macrostructural, microstructural, and inflammatory changes. However, these studies have yet to be integrated, limiting investigation into how these phenomena interact. To better understand these complex mechanisms of brain injury, a well-powered, prospective, multisite, and multimodal neuroimaging study is needed. We take the first step in accomplishing this with a preliminary characterization of multisite, multimodal MRI quality, motion, and variability in pediatric T1D. We acquire structural T1 weighted (T1w) MRI, diffusion tensor MRI (DTI), functional MRI (fMRI), and magnetic resonance spectroscopy (MRS) of 5-7 participants from each of two sites. First, we assess the contrast-to-noise ratio of the T1w MRI and find no differences between sites. Second, we characterize intervolumetric motion in DTI and fMRI and find it to be on the subvoxel level. Third, we investigate variability in regional gray matter volumes and local gyrification indices, bundle-wise DTI microstructural measures, and N-acetylaspartate to creatine ratios. We find the T1-based measures to be comparable between sites before harmonization and the DTI and MRS-based measures to be comparable after. We find a 5-15% coefficient of variation for most measures, suggesting ~150-200 participants per group on average are needed to detect a 5% difference across these modalities at 0.9 power. We conclude that multisite, multimodal neuroimaging of pediatric T1D is feasible with low motion artifact after harmonization of DTI and MRS.

## 35. Combining ADMIRE and MV to improve image quality

**Siegfried Schlunk, Bretty Byram.**

Department of Biomedical Engineering, Vanderbilt University.

Aperture domain model image reconstruction (ADMIRE) is a model-based beamformer able to remove noise and clutter sources while also keeping the input data in a format to allow additional post-processing beamformers to be applied. For example, minimum variance (MV) is a beamformer able to reduce off-axis interference and improve lateral resolution, but is known to struggle in high noise scenarios. By implementing these methods in sequence, we expect to achieve the benefits of both these beamformers in high noise situations. We demonstrate the use of ADMIRE as a pre-processing step to suppress noise from simulations and in vivo data before applying MV. We use histogram matching to show that ADMIRE+MV can achieve the performance improvements of both ADMIRE and MV simultaneously, and in some cases improve upon either method alone.

## **36. Development of Intraoperative Fiber-based Handheld Laser Speckle Imaging for Parathyroid Glands**

**Han Dong and Bio-Photonics Center**

Post-surgical hypoparathyroidism occurs in nearly 50% of all thyroid surgeries that the blood supply to healthy parathyroid glands is accidentally disrupted. With the existing method of using the Laser Speckle Contrasting Imaging (LSCI) method to detect blood flow in the current clinical setting, our group proceeds to develop a fiber-based handheld Laser Speckle device that is more suitable and easier to operate in the operating room. Here we present how LSCI can be used to distinguish between parathyroid vascularity and how a fiber-based handheld LSCI was developed and can be beneficial in comparison to the original device. The ability to detect vascular compromise with fiber-based handheld LSCI was validated in the muscle tissue of mice comparing alive and 3 min after death. The difference between alive and dead was noted, yet more processing optimization is needed for more stable output and statistical significance.

## **37. Antioxidant Microparticle Technology for Sustained Delivery of EPO in Glaucoma**

**Carlisle DeJulius**, Biomedical Engineering **Sarah Naguib**, Ophthalmology & Visual Sciences **Tonia Rex**, Ophthalmology & Visual Sciences; Vanderbilt Eye Institute **Craig Duvall**, Biomedical Engineering; Ophthalmology & Visual Sciences

Glaucoma is a degenerative disease of the optic nerve and a leading cause of blindness worldwide, with a major driver being reactive oxygen species (ROS). Erythropoietin (EPO) is a pleiotropic cytokine with neuroprotective effects due to its ability to activate antioxidant Nrf2 signaling. Intravitreal injection of EPO can be promising for glaucoma treatment; however, EPO is cleared quickly from the vitreal space. Packaging of therapeutic biomolecules like EPO into polymeric microparticles (MPs) is an established technique for improving local retention and efficacy of these drugs. Here, we utilize an antioxidant copolymer for microparticle formulation which can chemically scavenge excess ROS within the vitreal space, complimenting the antioxidant effects of EPO signaling. Through sustained release of EPO and elimination of ROS, we show that our microparticle system significantly improves outcomes in a mouse model of glaucoma. At 6 weeks, MPs +/- EPO significantly reduced retinal ROS levels. This scavenging led to improved retinal and optic nerve function, as measured by electroretinograms and visual evoked potential tests. We are currently working to evaluate the effect on the optic nerve histologically. This system is also being tested in non-human primates for translational potential.

### **38. Neural network trained on distant cortico-cortical evoked potentials can localize ictal onset in temporal lobe epilepsy**

**Graham W. Johnson,1,2 Leon Y. Cai,1 Aarushi S. Negi,3 Jasmine W. Jiang,2,3 Saramati Narasimhan,1,2,3 Danika L. Paulo,3 Hernán F. J. González,1,2 Victoria L. Morgan,1,2,3,4 Dario J. Englot1,2,3,4,5**

Department of 1Biomedical Engineering at Vanderbilt University; 2Vanderbilt University Institute of Imaging Science at Vanderbilt University Medical Center; Departments of 3Neurological Surgery, Neurology4, 5Radiology and Radiological Sciences at Vanderbilt University Medical Center

**INTRODUCTION** Patients with medically refractory temporal lobe epilepsy often undergo extensive diagnostic workups to localize areas of ictal onset. A few groups have used single pulse electrical stimulation (SPES) to create cortico-cortical evoked potentials (CCEP) in distant gray matter regions to localize ictal onset. However, the important localizing features of CCEPs remain unclear - a potential reason could be that important CCEP features could be complex and non-linear. Thus, we aimed to leverage a neural network's ability to extract non-linear features to identify the ictal onset zone.

**METHODS** We included ten patients with medically refractory focal epilepsy admitted to the hospital for intracranial monitoring. We conducted SPES and then used a one-dimensional convolutional neural network to categorize whether signals were generated from stimulation of an ictogenic or non-ictogenic region (labeled by attending epileptologist). To assess generalization, we implemented a leave-one-out testing across all ten patients.

**RESULTS** Distant CCEPs can classify ictogenic regions with the most informative period being 0-350 ms post-stimulation. Testing sensitivity of 78.1% and specificity of 74.6%. The 0-350 ms period cannot be split any further without significant decrease in model accuracy.

**CONCLUSION** This work serves as evidence that a neural network can be trained with multi-channel SPES data to categorize ictogenic versus non-ictogenic regions. This work is significant because it outlines the possibility that a neural network trained on a larger dataset could be used during intracranial monitoring in real time at the bedside or in the operating room to categorize brain regions as ictogenic.

## 39. Image-Guided Optimization of Robotic Catheters for Patient-Specific Endovascular Intervention

Colette Abah (1), Jared P. Lawson (1), Rohan Chitale (2), Nabil Simaan (1)

1) Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37235, USA - (c.abah, jared.p.lawson, nabil.simaan)@vanderbilt.edu 2) Department of Neurological Surgery, Vanderbilt University Medical Center, Nashville, TN 37232, USA - rohan.chitale@vumc.org

Endovascular intervention for ischemic stroke requires dexterous manipulation of catheters and guidewires. Robot-assisted steerable microcatheters can facilitate navigation along tortuous vasculature and bifurcation selection, thereby reducing the surgical skill demands. To achieve effective catheter deployment, the kinematic parameters of the catheter should ideally be selected to minimize the passive deflection of a given catheter. This paper presents a first-step towards automated selection of catheter parameters for traversal of a target anatomical vessel. The image-segmentation and vessel skeletonisation are presented along with a kinematic model of an antagonistic pair two-segment continuum robot. The nonlinear kinematic model is captured using a sparse representation achieved via a Kronecker product solution to a least-squares formulation of a matrix equation. The path planning is cast as a nonlinear parameter optimization that includes the lengths of the segments and their relative angles. This approach was used to determine the optimal catheter parameters for a specific anatomical model. The initial results suggest the possible utility of this approach for the development of a library of catheters that may be designed a-priori for anatomical regions while taking into account across-patient anatomical variabilities. Using a custom robotic milling process, a two-segment continuum robot was fabricated with the optimized design parameters, and this prototype will be used for future experimental evaluation. For clinical-deployment, the same optimization methods can be used to select the best catheter candidate from a library of catheters.

## 40. Abnormal Resting-State fMRI Connectivity of Hypothalamic Subregions in Patients with Mesial Temporal Lobe Epilepsy

Jasmine W. Jiang, B.E. 1,2,3, Saramati Narasimhan, Ph.D. 1,2,3,4, Graham W. Johnson, B.S. 2,3,4, Hernán F. J. González, Ph.D. 2,3,4, Danika Paulo, M.D. 1, Aarushi S. Negi 3, Catic Chang, Ph.D. 2,3,4,5, Victoria L. Morgan, Ph.D. 1,2,3,4, Dario J. Englot, M.D., Ph.D. 1,2,3,4,5

Department of 1 Neurological Surgery; 2 Vanderbilt University Institute of Imaging Science; at Vanderbilt University Medical Center; 3 Vanderbilt Institute for Surgery and Engineering; Department of 4 Biomedical Engineering; Department of 5 Electrical Engineering and Computer Science at Vanderbilt University, Nashville, Tennessee, USA.

**Introduction:** Mesial temporal lobe epilepsy (mTLE) is the most common form of focal epilepsy, with patients experiencing seizures originating from the hippocampus and/or amygdala. These patients exhibit impaired vigilance and cognitive processing, problems which cannot be explained by temporal lobe abnormalities alone. While the hypothalamus, particularly the posterior hypothalamus, has been shown to have a role in regulation of vigilance states, hypothalamic connectivity in mTLE patients has rarely been studied.

**Methods:** For 56 preoperative mTLE patients and 95 healthy controls, we acquired two 10-minute recordings of resting-state fMRI. Hypothalamic subregions (anterior, tuberal, and posterior) were segmented using an automated, patient-specific method (FreeSurfer). Selected cortical regions related to vigilance (prefrontal cortex, anterior/posterior cingulate, inferior parietal lobule) were designated (Desikan-Killiany atlas). Functional connectivity between hypothalamic subregions to regions of interest were calculated using Pearson correlations and Fisher z-transformed. Linear age regression was performed on the z-scores using healthy control connectivity and divided by RMSE. Finally, one-sample t-tests with Bonferroni-Holm correction ( $p < 0.05$ ) were performed on these residuals.

**Results:** Patients exhibited abnormal functional connectivity between all three hypothalamic subregions and both the ipsilateral/contralateral anterior cingulate ( $p < 0.01$ , t-test, corrected) compared to controls. Additionally, patients exhibited abnormal functional connectivity between the posterior and tuberal hypothalamus and regions of the prefrontal cortex (ipsilateral/contralateral superiorfrontal gyrus ( $p < 0.05$ ), orbitofrontal cortex ( $p < 0.01$ )) as well as between the posterior hypothalamus and ipsilateral/contralateral inferior parietal ( $p < 0.01$ ).

**Conclusions:** Individual hypothalamic subunits may have different roles in mTLE patients in our preliminary observations. These hypothalamic connectivity abnormalities may contribute to widespread vigilance impairments in mTLE patients.

## 41. Inpainting Missing Tissue in Multiplexed Immunofluorescence Imaging

**Shunxing Bao(a,b), Yucheng Tang(b), Ho Hin Lee(a), Riqiang Gao(a), Qi Yang(b), Xin Yu(b), Sophie Chiron(c), Lori A. Coburn(c,d,e,g), Keith T. Wilson(c,d,e,f,g), Joseph T. Roland(h), Bennett A. Landman(a,b), Yuankai Huo(a,b)**

a Dept. of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA  
b Dept. of Computer Science, Vanderbilt University, Nashville, TN, USA  
c Division of Gastroenterology, Hepatology, and Nutrition, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA  
d Vanderbilt Center for Mucosal Inflammation and Cancer, Nashville, TN, USA  
e Program in Cancer Biology, Vanderbilt University School of Medicine, Nashville, TN, USA  
f Dept. of Pathology, Microbiology, and Immunology, Vanderbilt University Medical Center, Nashville, TN, USA  
g Veterans Affairs Tennessee Valley Healthcare System, Nashville, TN, USA  
h Epithelial Biology Center, Vanderbilt University Medical Center, Nashville, TN, USA

Multiplex immunofluorescence (MxIF) is an emerging technique that allows for staining multiple cellular and histological markers to stain simultaneously on a single tissue section. However, with multiple rounds of staining and bleaching, it is inevitable that the scarce tissue may be physically depleted. Thus, a digital way of synthesizing such missing tissue would be appealing since it would increase the useable areas for the downstream single-cell analysis. In this work, we investigate the feasibility of employing generative adversarial network (GAN) approaches to synthesize missing tissues using 11 MxIF structural molecular markers (i.e., epithelial and stromal). Briefly, we integrate a multi-channel high-resolution image synthesis approach to synthesize the missing tissue from the remaining markers. The performance of different methods is quantitatively evaluated via the downstream cell membrane segmentation task. Our contribution is that we, for the first time, assess the feasibility of synthesizing missing tissues in MxIF via quantitative segmentation. The proposed synthesis method has comparable reproducibility with the baseline method on performance for the missing tissue region reconstruction only, but it improves 40% on whole tissue synthesis that is crucial for practical application. We conclude that GANs are a promising direction of advancing MxIF imaging with deep image synthesis.

## **42. Supervised Deep Generation of High-Resolution Arterial Phase Computed Tomography Kidney Substructure Atlas**

**Ho Hin Lee, Yucheng Tang, Shunxing Bao, Qi Yang, Xin Yu, Agnes B. Fogo, Raymond Harris, Mark P. de Caestecker, Jeffrey M. Spraggins, Mattias Heinrich, Yuankai Huo, Bennett A. Landman**

The Human BioMolecular Atlas Program (HuBMAP) provides an opportunity to contextualize findings across cellular to organ systems levels. Constructing an atlas target is the primary endpoint for generalizing anatomical information across scales and populations. An initial target of HuBMAP is the kidney organ and arterial phase contrast-enhanced computed tomography (CT) provides distinctive appearance and anatomical context on the internal substructure of kidney organs such as renal context, medulla, and pelvicalyceal system. With the confounding effects of demographics and morphological characteristics of the kidney across large-scale imaging surveys, substantial variation is demonstrated with the internal substructure morphometry and the intensity contrast due to the variance of imaging protocols. Such variability increases the level of difficulty to localize the anatomical features of the kidney substructure in a well-defined spatial reference for clinical analysis. In order to stabilize the localization of kidney substructures in the context of this variability, we propose a high-resolution CT kidney substructure atlas template. Briefly, we introduce a deep learning preprocessing technique to extract the volumetric interest of the abdominal regions and further perform a deep supervised registration pipeline to stably adapt the anatomical context of the kidney internal substructure. To generate and evaluate the atlas template, arterial phase CT scans of 500 control subjects are de-identified and registered to the atlas template with a complete end-to-end pipeline. With stable registration to the abdominal wall and kidney organs, the internal substructure of both left and right kidneys are substantially localized in the high-resolution atlas space. The atlas average template successfully demonstrated the contextual details of the internal structure and was applicable to generalize the morphological variation of internal substructure across patients.

### 43. Intermittent Stimulation of the Nucleus Basalis Improves Working Memory Performance in Aged Monkeys

Zhengyang Wang<sup>1</sup>, Janki Bava<sup>2</sup>, Clement Garin<sup>2</sup>, Katelyn Clemencich<sup>2</sup>, Kendyl Pennington<sup>4</sup>, Sarah K. Bick<sup>3</sup>, Dario J. Englot<sup>2,3</sup>, David T. Blake<sup>4</sup>, Christos Constantinidis<sup>1, 2, 5</sup>

1. Neuroscience Program, Vanderbilt University 2. Department of Biomedical Engineering, Vanderbilt University 3. Department of Neurological Surgery, Vanderbilt University Medical Center 4. Brain and Behavior Discovery Institute, Department of Neurology, Medical College of Georgia, Augusta University 5. Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center

Degeneration of the forebrain cholinergic system is a key component in age-related cognitive decline and cholinesterase inhibitors are frontline medications in Alzheimer's disease. Improvement in cognitive functions may alternatively be achieved by Deep Brain Stimulation targeting the Nucleus Basalis (NB) of Meynert, the source of neocortical cholinergic activation in humans and non-human primates. Here we tested whether NB stimulation improves working memory function in aged monkeys. Seven rhesus monkeys (*Macaca mulatta*) 24-30 years of age were trained on a delayed-match-to-sample task and tested after reaching asymptotic performance. Adaptive control of delay durations allowed tracking of threshold delays corresponding to 79% correct choices in each session. Two female animals (age 24 and 28 years) were implanted with electrodes targeting the NB. Daily, the subjects received unilateral 60-Hz stimulation, lasting 20 seconds every minute, in a 1-hour window. Significant increases of 3.51 seconds (permutation test,  $p = 7.0E-4$ ) and 3.70 seconds (permutation test,  $p = 4.0E-4$ ) in the average threshold delay durations were observed during 4 and 5 weeks of stimulation respectively. A generalized linear mixed-effect model showed that this change in performance was significantly larger (interaction effect = 3.66 seconds, 95% CI [1.92, 5.40],  $p = 4.30E-5$ ,  $df = 381$ ) than what was expected from the unstimulated counterparts ( $n = 5$ ) across the same time frame. The current results show that intermittent stimulation of NB is effective in improving working memory in a non-human primate model of aging.

## 44. Domain Adaptive Deep Neural Network for Echocardiography

Preston Pan, Jaime Tierney, Brett Byram

Transthoracic echocardiography is the first-line imaging modality for the heart. However, sources of image degradation, including off-axis scattering, phase aberration, and reverberation limit the diagnostic value of TTE images. Our lab had previously designed a framework to address off-axis scattering and reverberation with the use of a deep neural network. Leveraging existing ultrasound simulation software, we curated a simulated dataset of anechoic cysts. Signals originating from within the cyst are zeroed out to reflect the absence of scatterers, while those generated from the surrounding are kept the same. Furthermore, we incorporated in-vivo data into model training with a domain adaptation scheme to improve model generalizability to unseen in-vivo data. While some neural networks successfully suppress off-axis scattering, others introduce artifacts into the image. In this work, we analyzed the network output in the aperture domain (before image formation) and report shortcomings of our current approach. These include 1) the reduction in axial resolution, 2) the presence of a default state, and 3) the tendency to over correlate signals in space. We connect these observations to network artifacts and propose correction methods. By investigating the network output in the aperture domain, we gain valuable insight into the models' performance and robustness.

## 45. Active Shape Models with Locally Weighted Components

Rueben Banalagay -- EECE Jack Noble PhD -- EECE

While state-of-the-art deep learning methods consistently provide the most accurate image segmentation results when sufficient training datasets are available, in some applications large datasets are difficult to acquire. For example, a model for inner ear structures can only be constructed by ex vivo specimen imaging modalities such as  $\mu$ CT. Constructing such datasets is costly and time consuming. Active shape models (ASM) have been a successful technique in medical image segmentation and require less extensive datasets for training. However, the ability of the ASM framework to capture complex shape variation is limited by representing variations across all global-pose-normalized training exemplars in a single, linear vector space. In this work, we describe a novel non-linear extension to the ASM in the form of a multi-component mixture of landmark weighted ASMs. Unlike the original ASM formulation, which modelled shape from a single global pose, our model accounts for differences in regional pose, by allowing each component in our proposed model to utilize a unique set of landmark importance weights during the shape registration and model fitting process. Landmark weights are optimized to minimize the overall ASM-mixture's fitting error on the training set shapes. We demonstrate the advantage of this approach in segmenting the labyrinth structure in the inner ear. We find that the ASM-mixture consistently outperforms a traditional ASM on similar sample sizes, and ASM-mixtures trained on 10 samples outperform traditional ASMs trained with 15 samples. These results show the method's potential advantages in applications that are limited by small shape libraries.

## 46. Handheld Device and Admittance Controlled Robot for Manipulating OCT-Monitored Retinal Gene Therapy Injections

**Elan Ahronovich, Neel Shihora, Giuseppe Del Giudice:** Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37235 **Jin Shen:** Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, TN 37232 **Karen Joos:** Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, TN 37232. Department of Biomedical Engineering, Vanderbilt University, Nashville, TN 37235 **Nabil Simaan:** Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37235. Corresponding Author

Vitreoretinal surgery presents challenges to surgeons in terms of precision, perception, and manipulation dexterity. Vitreoretinal surgeries are commonly conducted through sclerotomies using long rigid surgical tools with limited distal dexterity offering four degrees of freedom. The delicate anatomy of the retina stunts tactile sensation and surgeons also only have limited stereo vision offered by surgical microscopes. Retinal gene therapy is an emerging approach to addressing retinal degenerative diseases and delivery of these therapies using subretinal drug injections require fine control of needle depth. This work proposes a two-mode robotic system that will control subretinal drug injections under Optical Coherence Tomography (OCT) guidance. Mode 1 is a handheld device with user-controlled needle depth and scleral stabilization tip. The user controls needle depth via analog foot pedals that provide variable axial tool tip velocity. Mode 2 is a cooperative hand-on-hand robotic system that drives the needle advancement manipulator (Mode 1 device) enabling semi-autonomous assisted retinal gene therapy injections. The robot is built using the Meca500 6-axis industrial robot and an ATI Mini 40 6-axis load cell used to inform an admittance controller to drive the robot. A variable admittance control algorithm is implemented to provide natural tool motions from the robot in certain motion regimes (i.e. acceleration). Force information from an additional load cell and feedback from the OCT are used to establish virtual fixtures limiting interaction forces between the robot and eyeball and limiting injection depth to distinct subretinal tissue layers.

## 47. Volume of tissue activation assessment during DBS in a coupled finite element and neuron model: effect of different model parameters

**Kyvia Pereira** Department of Biomedical Engineering, Vanderbilt University **Ma Luo** Department of Biomedical Engineering, Vanderbilt University **Michael I. Miga**, Professor of Biomedical Engineering, Vanderbilt University Professor of Radiology, Neurosurgery, & Otolaryngology - Head and Neck Surgery, Vanderbilt University Medical Center

Deep brain stimulation treatment response and adverse side effects are directly correlated to the accurate electrode location and stimulus parameters. However, electrodes' precise placement can be significantly affected by brain shift associated with burr hole and dura opening in DBS procedures. In this regard, patient-specific DBS computation models can be constructed from medical imaging data and provide a non-invasive way to assess the impact of shift on neuron recruitment and allow the analysis of various stimulation parameters. To achieve this, finite element biomechanical models that estimate shift are coupled to bioelectric tissue models that include both field and neuron activation capabilities. By understanding detailed neuroanatomy within the context of these comprehensive models, it may allow for enhanced interpretation of clinical outcomes as well as optimization. In this work, the last component, neuron activation, is investigated. More specifically, tractography data and bioelectric stimulus models are employed to estimate extracellular potentials along axonal distributions. This distribution is then employed within the context of separate computational models of neurons to determine activation status. The outcome is a volume of tissue activation. By coupling these simulations to a structural connectome analysis, it is possible to get an insight into the neuromodulation impact on brain connectivity and clinical outcomes. In this work, we present a patient-specific DBS bioelectric model coupled with VTA estimation, obtained via neuron recruitment analysis in NEURON 8.0 software. An analysis of modeling parameters that have an impact on the VTA was performed and results are presented here.

## 48. Improved correspondence of simultaneous fMRI/EEG vigilance measures using multi-echo ICA

**Sarah Goodale** (BME), **Bohan Jiang** (EECE), **Difan Yang** (EECE), **Vicky Morgan** (VUMC depts of Radiology, Neurology, and Neurological Surgery, VU dept of BME), **Dario Englot** (VUMC depts of neurological surgery, radiology, and VU dept of BME), **Catie Chang** (VU dept of EECE, CS, and BME)

Despite the rapid growing use of fMRI in neuroscience research, there are still unexplained sources of variability that compromise its potential for studying brain function. Multi-echo independent component analysis (ME-ICA) is a recently developed preprocessing tool that denoises fMRI-BOLD data using an echo-time dependence to separate the data into BOLD and non-BOLD components. This method and the benefits of ME-ICA processing could help to explain these sources of variability. Our work has been investigating its effects in correspondence between BOLD signal and true neuronal signal, such as assessed from simultaneous EEG. My current work investigates the effects of BOLD pre-processing on the correspondence between fMRI and EEG vigilance-related measures. Further, we examine whether ME-ICA can improve the prediction of behavioral performance from fMRI data, based on an established fMRI vigilance metric. We used simultaneous fMRI-EEG data acquired from 14 healthy adult subjects who underwent both a resting-state and auditory tone task scan. Preliminary results demonstrated significantly stronger correlations with EEG vigilance for the ME-ICA processed fMRI data compared to conventional pre-processing methods. We have also found improved distinction between behavioral states in the ME-ICA processed data, allowing us to better predict whether a subject responded to an upcoming task stimulus. Ongoing work expands our pre-processing methods to ensure the robustness of our findings for ME-ICA, as well as digging further into whether ME-ICA can enhance detection of activation in various regions associated with vigilance in the sub-cortical and brainstem areas.

## 49. DBS Electrode Positioning with Multisite Microelectrode Recordings, Macrostimulation, and Atlas-Based Prediction Maps

Danika L Paulo \* MD (1), Saramati Narasimhan \* PhD (1-4), Hernan FJ Gonzalez PhD (2-4), Graham W Johnson (2-4), Derek Doss (2-4), Jasmine Jiang (1), Aarushi Negi (1), Tyler Ball MD (1), Rui Li MS (3), William Rodriguez MS (3), Peter E Konrad MD PhD (5), Joseph S Neimat MD (6), Hamid M Shah MD (1), Sarah K Bick MD (1), Benoit Dawant \* PhD (2-4), Dario J Englot \* MD PhD (1-4)

(1)Department of Neurological Surgery, Vanderbilt University Medical Center (2)Vanderbilt University Institute of Imaging Science (3)Vanderbilt Institute for Surgery and Engineering (4)Department of Biomedical Engineering, Vanderbilt University (5)Department of Neurological Surgery, West Virginia University (6)Department of Neurological Surgery, University of Louisville

**Introduction:** Deep brain stimulation (DBS) at VUMC is performed with custom-made miniature stereotactic frame (STarFix, FHC) and patients awake during electrode implantation to perform microelectrode recordings (MER) and macrostimulation testing. Pre-operative targets are selected with guidance of atlas-based efficacy prediction maps. Multisite intraoperative microelectrode recordings (MER) and macrostimulation data are collected and integrated into final target selection. We are aiming to quantify value of intraoperative testing to support its use by evaluating how often it changes final electrode position (FEP).

**Methods:** A heuristic sample of 490 patients treated with 892 individual DBS leads at VUMC (2011-2021) were included. Per surgery, FHC microelectrodes are implanted in 2-3 test tracks per side and microelectrode recordings are collected per tract. Atlas-based prediction maps help guide targeting. Macrostimulation data is collected on the same tracks, with symptom improvement quantified and side effects notated. Preoperative maps and intraoperative data are visualized and integrated real-time to guide optimal FEP selection.

**Results:** Of 892 individual leads, 489(55%) had FEP in the center track. MER was collected in 435(49%) of test tracks with 380(43%) recordings being collected in the FEP track. Stimulation data was collected for all leads and 867(97%) of FEP tracks.

**Conclusion:** Although planned targets were carefully selected preoperatively based on anatomy and guidance from atlas-based efficacy maps, the FEP differed from anticipated targets in multiple cases. Multisite intraoperative microelectrode recordings, macrostimulation, and prediction maps during DBS surgery provide valuable information about maximization of efficacy and minimization of side effects leading to optimization of FEP.

## 50. Feasibility of Remote Robotic Palpation in Identifying the Landmark for Cricothyrotomy

Neel Shihora\*, Rashid Yasin\*, Ryan Walsh\*\*, Nabil Simaan\*

\* Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37235, USA (email: neel.shihora@vanderbilt.edu; rashid.m.yasin@vanderbilt.edu; nabil.simaan@vanderbilt.edu) \*\* Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN 37232, USA (email: ryan.walsh@vumc.org)

Cricothyrotomy is a life-saving emergency procedure that secures an alternate airway route through an incision in the cricothyroid membrane. Identifying the location of the cricothyroid membrane for incision is the most critical step of this procedure and is conventionally determined using a combination of visual and palpation cues. Enabling robot-assisted remote Cricothyrotomy may extend this life-saving procedure to injured soldiers or patients who may not be readily accessible for on-site intervention during search-and-rescue scenarios. As a first step towards achieving this goal, our effort explores the feasibility of palpation-assisted landmark identification for Cricothyrotomy. Using a cricothyrotomy training simulator, we explore several alternatives for in-situ remote localization of the incision site, which include: a) Unaided telemanipulation. b) Telemanipulation with direct force feedback. c) Telemanipulation with superimposed motion excitation for online stiffness estimation and display. d) Fully autonomous palpation scan initialized based on the user's understanding of key anatomical landmarks. Using the manually digitized incision location as ground truth, we compare these four methods for accuracy and repeatability of identifying the landmark for Cricothyrotomy, completion time, and ease of use. The results suggest that relying on visual feedback alone can be associated with unacceptably significant errors. Providing an online updating stiffness map and force feedback (method c) and automating the scanning task (method d) are less probable in damaging the anatomy around the cricothyroid membrane. The results also confirm that the landmark identification with remote palpation is feasible, satisfying an essential prerequisite for future robotic solutions for remote Cricothyrotomy.

## 51. Evaluating fMRI vigilance signals in relation to early-stage Alzheimer's Disease

Kate Wang<sup>1</sup>, Sarah Goodale<sup>2</sup>, Catic Chang<sup>1,2,3</sup>

Departments of Computer Science<sup>1</sup>, Biomedical Engineering<sup>2</sup>, Electrical and Computer Engineering<sup>3</sup> at Vanderbilt University

More than 6 million Americans aged 65 and older currently live with Alzheimer's Disease. Insomnia and changes in sleep pattern have been found to be early symptoms that contribute to cognitive decline. In functional magnetic resonance imaging (fMRI) studies, the global signal is thought to be a marker of vigilance (i.e., levels of alertness), and may therefore be a relevant neuroimaging marker of Alzheimer's Disease. This project investigates the relationship between the global signal and a template-based predictor of vigilance (an alternate method for extracting fMRI vigilance information) and examines the correlations between each of these signals and various clinical measures in aging. fMRI and structural brain scans for 135 subjects (aged healthy controls and patients with mild cognitive impairment (MCI)) were obtained from our collaborators at the Vanderbilt Memory and Alzheimer's Center (VMAC). Cross-correlations between the global signal and vigilance prediction signals were computed for each subject. A maximum cross-correlation, as well as an absolute value of the maximum cross-correlation, were determined for each subject. Preliminary analyses reveal that the global signal and vigilance time courses have moderate cross-correlations, suggesting that these signals may be capturing largely distinct activation in the brain. Future work will look into whether the template-based vigilance prediction is more indicative of a subject's alertness level than the global signal. This work will also be extended to relating vigilance and global signal to several clinical variables.

## 52. Voxel-based Analysis of MRI images to detect Focal Cortical Dysplasia

**Ethan Sheppard, Caitlin Grogan, Jarrod Eisma, Jonah Fox, M.D., , Dario Englot, M.D., Ph.D, Victoria Morgan, Ph.D.**

Focal cortical dysplasia (FCD), a region of brain cell malformation and disorganization, is a common cause of drug-resistant focal epilepsy, therefore requiring surgical treatment in most cases. FCDs can be difficult to visually detect in pre-surgical magnetic resonance images (MRI). Without localization on MRI, they may not be detectable at all or will require more invasive testing prior to surgery. Our project will use voxel-based MRI processing and analysis to enhance the detection of the abnormalities associated with FCD on MRI. Our project seeks to increase rates of FCD detection, allowing more patients to undergo surgery and improve overall patient outcomes. This will be a retrospective study using MRI images with clear contrast between gray and white matter from patients with pathology confirmed FCD. The processing of these images will involve creating two different mask images: the junction image and the extension image. These masks will each quantify abnormalities that are associated with FCD. The junction image will highlight areas of blurred gray-white junctions and the extension image will highlight areas where the gray matter abnormally extends into the white matter. These two mask images of an individual patient will be compared to a population of control images to increase diagnostic detection. This algorithm will be optimized to increase the sensitivity and specificity of FCD detection, and will eventually be utilized to improve detection of FCDs on MRI to allow more patients to undergo surgical treatment.

### **53. ROS Degradable Polythioketal Urethane Foam Dressings Promote Porcine Ischemic Wound Repair**

**Prarthana Patil<sup>1</sup>, Joshua T. McCune<sup>1</sup>, Alonda C. Pollins<sup>2</sup>, Jeffery M. Davidson<sup>3</sup>, Scott Guelcher<sup>1,4</sup>, Craig L. Duvall<sup>1</sup>**

<sup>1</sup>Department of Biomedical Engineering, Vanderbilt University, Nashville, Tennessee

<sup>2</sup>Department of Plastic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee

<sup>3</sup>Pathology, Microbiology, and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee

<sup>4</sup>Department of Chemical and Biomolecular Engineering, Vanderbilt University, Nashville, Tennessee

We have previously developed a class of reactive oxygen species (ROS) responsive polythioketal urethane (PTK-UR) foam dressings that promote wound healing. These foams overcome limitations associated with hydrolytically-degradable wound dressings, which are susceptible to autocatalytic degradation and biomaterial-associated inflammation. We hypothesize that treating ischemic excisional wounds with PTK-UR dressings will promote scaffold resorption by scavenging ROS while minimizing material-associated inflammation to promote improved tissue repair in a challenged wound model. EG7 PTK-UR scaffolds were evaluated *in vivo* in an ischemic full-thickness porcine wound model compared to NovoSorb BTM, an FDA-approved dermal substitute. Wound area was tracked throughout the study, and the quality of wound healing was evaluated blindly by a histopathologist. Additionally, immunohistochemistry was conducted to evaluate re-epithelialization and the biomaterial-associated immune response 17 days post-implantation. Within 17 days, ischemic wounds treated with EG7 PTK-UR achieved 76.1% closure, while NovoSorb treated wounds achieved 8.3% closure. EG7 PTK-UR treated wounds also achieved nearly complete re-epithelialization, while NovoSorb treated wounds achieved less than 40% re-epithelialization. Histological analysis of the treated wounds illustrated decreased inflammation and improved collagen deposition associated with EG7 PTK-UR, resulting in a greater wound healing score. Analysis of the inflammatory response associated with EG7 and NovoSorb via IHC indicated an increase in both macrophages and neutrophils associated with NovoSorb compared to EG7 PTK-UR. Ultimately, EG7 PTK-UR foam dressings have demonstrated improved wound healing in comparison to NovoSorb in a challenged wound model, decreasing the material-associated inflammatory response while promoting re-epithelialization and improved overall wound repair.

## 54. Multimodal Multiple Sclerosis segmentation using label-efficient deep neural network

Jiacheng Wang, Ipek Oguz

In this project, we introduce a novel semi-supervised learning method which takes multimodal medical images for detecting Multiple Sclerosis (MS) lesions in high resolution 3T, 7T 3D MRI images. Given the increasing demand of automated lesion segmentation in clinical diagnosis, monitoring and treatment planning for MS, we proposed an encoder-decoder deep neural network to achieve expert-level accuracy that can be adapted to different datasets. By integrating data from different modalities (MPRAGE, FLAIR, and T2) and comparing the similarity of latent space generated from encoder, the model can obtain more robust segmentation by combining information of different forms and regularizing the encoder in a contrastive learning framework. For the network structure, we proposed to let our model not only segment the lesion but also learn to synthesize the original images from an intermediate representation by using a conditional variational autoencoder. Previous studies have shown this structure can achieve state-of-the-art results in brain tumor segmentation competition (BraTs). Additionally, deep neural networks are known to be annotation-hungry. However, it is extremely expensive and time-consuming to label medical imaging data with high-quality annotations. Therefore, we leverage the model's generalization ability in a semi-supervised manner which takes partial labels for training; several self-supervised methods are considered. Beyond our in-house dataset, we also test our model's generalization ability in public datasets (ISBI2015, MICCAI2021) and competitions with different modalities (T1, FLAIR, PD).

## 55. Quantifying Sources of Image Degradation in Ultrasound Imaging

Emelina Vienneau and Brett Byram

Department of Biomedical Engineering

Thermal noise and acoustic clutter signals degrade ultrasonic image quality and contribute to unreliable clinical assessment. When both noise and clutter are prevalent, it is difficult to determine which one is a more significant contributor to image degradation because there is no way to separately measure their contributions in vivo. Efforts to improve image quality often rely on knowledge of the type of image degradation at play. To address this, we derived and validated a method to quantify the individual contributions of thermal noise and acoustic clutter to image degradation by leveraging spatial and temporal coherence characteristics. Using simulations in Field II, we validated the assumptions of our method, explored strategies for robust implementation, and investigated its accuracy and dynamic range. We determined that our method can estimate the signal-to-thermal noise ratio (SNR) and signal-to-clutter ratio (SCR) with high accuracy between SNR levels of -30 to 40 dB and SCR levels of -20 to 15 dB. We further determined that SNR and SCR can be estimated accurately with as little as ten frames and half of the available channels and demonstrated that it is possible to overcome in vivo motion using high-frame rate M-Mode imaging and adaptive ensemble selection.

## 56. Patient-specific modeling of Implant Design for Type I Thyroplasty Surgery

**Zheng Li**, Mechanical Engineering Department **Amit Avhad**, Mechanical Engineering Department **Haoxiang Luo**, Mechanical Engineering Department **Azure Wilson**, **Lea Sayce**, **Bernard Rousseau**, Department of Communication Science and Disorders, University of Pittsburgh

In this work, we aim to develop a patient-specific modeling tool to improve outcome of the Type I Thyroplasty, the surgical procedure to restore voice for unilateral vocal fold paralysis (UVFP) patients. Collaborating with a group at University of Pittsburgh who use rabbits as the animal model for phonation experiment, we develop computational models to evaluate the effect of the implant on the vocal fold function. In this integrated study, the rabbit larynx was first harvested for MRI scans as the baseline condition. The images were then imported to ITK Snap for segmentation to generate the surface meshes for different tissue components. The smoothed surface meshes were imported to COMSOL Multiphysics and create the FEM model . An implant of various shape parameters was inserted in the computational model to evaluate the vocal fold adduction due to the implant. The best implant option from modeling is then produced in the experiment to test its actual effect. The comparison of the post MRI scan with the simulation confirms that the adduction was achieved and the computer model was effective in the prediction. Therefore, this study shows a promising step toward computational modeling to improve the implant design.

## 57. Label-free parathyroid identification during pediatric neck surgeries with near infrared autofluorescence detection

**Parker Willmon** - Vanderbilt Biophotonics Center, Vanderbilt University **Giju Thomas** - Vanderbilt Biophotonics Center, Vanderbilt University **Ryan Belcher** - Vanderbilt University Medical Center **Monica Lopez** - Vanderbilt University Medical Center **Harold N. Lovvorn III** - Vanderbilt University Medical Center **Naira Baregamian** - Vanderbilt University Medical Center **Carmen C. Solórzano** - Vanderbilt University Medical Center **Anita Mahadevan-Jansen** - Vanderbilt Biophotonics Center, Vanderbilt University

Children are at a higher risk than adults for more severe postoperative complications like permanent hypoparathyroidism from accidental parathyroid gland (PG) damage/excision following neck surgeries. Earlier studies have demonstrated that near infrared autofluorescence (NIRAF) detection can be used reliably for label-free intraoperative PG identification. Nonetheless all prior studies have been investigated only in adults. In our study, we investigated the scope of NIRAF detection for PG identification in the pediatric population using a fiber-optic probe-based system for the first time. The probe-based approach was found to be more compatible for smaller neck incisions typically used in the pediatric population. By illuminating tissues with a wavelength of 785 nm, NIRAF intensities were measured from different neck structures using the fiber-optic probe. The surgeon's visual assessment of tissues was noted and the surgeon's confidence level in tissue identification was recorded as high, medium or low. Tissues identified with low confidence were excluded from analysis, if corresponding histological validation was not performed. NIRAF intensities were measured across 7 pediatric patients (Ages: 6 - 16 years) who underwent thyroidectomies. Normalized NIRAF intensity (expressed as Mean  $\pm$  Standard Deviation) for PGs ( $3.3 \pm 1.7$ ) was significantly higher than that of thyroid ( $1.2 \pm 0.5$ ,  $p=5.4 \times 10^{-5}$ ) and other soft tissues ( $0.7 \pm 0.3$ ,  $p=5.2 \times 10^{-6}$ ). Keeping an arbitrary threshold of 1.3, this technique yielded a PG detection rate of 94.4 (17/18 PGs). Our preliminary findings indicate that NIRAF detection can potentially be a valuable and non-invasive technique to identify PGs during neck surgeries in the pediatric population as well.

## 58. Segmentation of the nucleus basalis of Meynert in MRI using deep learning

Derek J. Doss,<sup>1,2</sup> Graham W. Johnson,<sup>1,2</sup> Saramati Narasimhan,<sup>1,2,3</sup> Jasmine W. Jiang,<sup>2,3</sup> Hernán F. J. González,<sup>1,2</sup> Danika L. Paulo,<sup>3</sup> Aarushi S. Negi,<sup>3</sup> Benoit M. Dawant,<sup>2,6,7</sup> Catic Chang,<sup>1,2,6,7</sup> Victoria L. Morgan,<sup>1,2,3,4</sup> Dario J. Englot<sup>1,2,3,4,5,6,7</sup>

Department of <sup>1</sup>Biomedical Engineering at Vanderbilt University; <sup>2</sup>Vanderbilt University Institute of Imaging Science at Vanderbilt University Medical Center; Departments of <sup>3</sup>Neurological Surgery, Neurology<sup>4</sup>, <sup>5</sup>Radiology and Radiological Sciences at Vanderbilt University Medical Center, Department of <sup>6</sup>Electrical and Computer Engineering at Vanderbilt University, <sup>7</sup>Vanderbilt Institute for Surgery and Engineering

**Introduction:** The nucleus basalis of Meynert (NBM) is a subcortical structure that has been implicated in several diseases, including temporal lobe epilepsy (TLE), Alzheimer's disease (AD) and Parkinson's disease dementia (PDD). However, there are two major challenges with studying the NBM. Accurate manual segmentation needs to be performed on 7T MRI scan rather than the more commonly used 3T MRI scans. Second, there is no method to segment NBM in a patient specific manner. Deep convolutional neural networks (CNNs) have been successfully used for segmentation of medical imaging data. Therefore, we propose a method of patient specific segmentation of the NBM using a CNN.

**Methods:** We obtained 19 paired 7T and 3T T1-weighted MRI scans of healthy subjects. The NBM was expertly segmented on the high-resolution 7T images with verification from a board-certified neurosurgeon. The 3T images were rigidly registered to the paired 7T image resulting in an accurate NBM segmentation on the 3T images. Data augmentation was performed, consisting of random rotations, elastic deformations, and bias field addition, resulting in 440 sets of data. The data was normalized to uniform intensity distributions between subjects and cropped to be a uniform size of 64x64x-64mm. A 5-layer CNN was created based on 3D-Unet architecture.

**Results:** Data augmentation resulted in preservation of the spatial features of the NBM, maintaining an anatomically markers of the NBM. Preliminary observational results show anatomically correct identification of the NBM on 3T testing images.

**Conclusions:** A CNN based segmentation strategy could help further research on the NBM.

## 59. Domain generalization for retinal vessel segmentation with vector field transformer

Dewei Hu, Ipek Oguz

Electrical and Computer Engineering

Although deep learning has become a prevalent method in medical image analyzing tasks, lack of generalizability caused by the divergence of data distribution is one of its main drawbacks. For most of the medical data modalities, the inconsistency of distribution exists due to the imaging techniques. Hence, finding a method that enables the deep learning model to work on different domains/modalities is a heated research topic. Our specific task is retinal vessel segmentation. There are 2 types of 2D data modalities, projected OCT angiography (OCT-A) and fundus images which characterize the retinal vasculature in different ways. Based upon the fact that the human perception of vesselness depends heavily on the local contrast instead of absolute intensity value, we hypothesize that the eigenvector of the Hessian matrix can sufficiently represent the vessel by vector flow. This vector field can be regarded as a common domain for different modalities as it is very similar even for data that follows completely different distribution. We propose a vector field transformer (VFT) network which provides a strong sense of local vector homogeneity. In exhaustive experiments, we show that the model can work in both cross-domain and cross-modality fashion.

## 60. Automatic Internal Auditory Canal Segmentation Using a Weakly Supervised 3D U-Net

**Hannah G. Mason** (Dept. of Computer Science, Vanderbilt University) **Jack H. Noble** (Dept. of Computer Science, Vanderbilt University) (Dept. of Electrical and Computer Engineering, Vanderbilt University)

Cochlear implants (CIs) are neural prosthetics used to improve hearing in patients with severe-to profound hearing loss. After implantation, the process of fine-tuning the implant for a specific patient is expedited if the audiologist has tools to approximate which auditory nerve fiber regions are being stimulated by the implant's electrode array. Auditory nerves travel from the cochlea where the prosthetic is implanted to the brain via the internal auditory canal (IAC). In this paper, we present a method for segmenting the IAC in a CT image using weakly supervised 3D U-Nets. Our approach is to train a U-Net with a custom loss function to refine a localization provided by a previously proposed active-shape-model-based IAC segmentation method. Preliminary results indicate that our proposed approach is successful in refining IAC localization.

## **61. Touchpad with Haptic Force Feedback: A Novel User Interface For A Hand-Held Surgical Robot**

**Jesse F d'Almeida [1], Tayfun Efe Ertop [1], Jason Shrand [1], Naren Nimmagadda [2], Shaan Setia [2], Nicholas L Kavouss [2], Duke S Herell III [2], and Robert J. Webster III [1]**

[1] Department of Mechanical Engineering, Vanderbilt University [2] Department of Urology, Vanderbilt University Medical Center

Recent advances in medical technology have made robotic surgery the state-of-the-art for many surgical procedures. This, combined with the emerging trend towards minimally invasive surgeries through natural orifices with endoscopes, has resulted in several hand-held, small-footprint robotic systems to be proposed in the literature. The teleoperation accuracy desired with these systems depends highly on the performance of the user interfaces that are utilized, which must be intuitive to surgeons and small enough to fit onboard. We propose a novel onboard touchpad-based 3D user interface that tracks the fingertip of the surgeon directly in 3D position and maps it robot tip to solve this problem. Our design utilizes a familiar touchpad interface (to control the x- and y-position) mounted on a spring with loadcell (to control the z-position). This design provides the user with compliance normal to touchpad plane so that the users can move their fingertips in this direction as well. Most other controllers proposed before in literature have at least one axis that is controlled independently (i.e., uncoupled), and we hypothesize that this hurts the intuitiveness of these interfaces. We tested this hypothesis and the user interface design against others established in the literature, including a joystick and a 3D spacemouse. Each user interface was evaluated by tasking surgeons with virtual path-following and point-touching activities. This study summarizes our findings from these experiments, comparing the quantitative data from each simulated task as well as the qualitative feedback from the surgeons according to the NASA Task Load Index method.

## 62. Implementing Machine learning Techniques to provide Sensitive and Non-biased Data Quantification of non-human primate behavior

Daniela Hernandez Duque, Zou Yue, Pai-Feng Yang, John Gore, LiMin Chen

**Background and Significance** The objective of this study is to quantify hand grasping behavior obtained from (NHP) before and after spinal cord injury. The goal is to identify sensitive and specific sensory and motor indices for monitoring behavior recovery after injury, evaluating behavioral relevance for noninvasive MRI biomarkers, and in future assessing therapeutic outcomes. The motivation behind this research relies on the need to obtain results that would not only determine the monkey's capability to grasp sugar pellets, but also separately analyze the change in their motor versus sensory behavior. This can be obtained through neural network analysis implementation focusing on the primate's hand movement.

**Methods** Data from six monkeys were studied. Videos of multiple monkeys grabbing sugar pellets before and after suffering spinal cord injury are chosen to be analyzed. This analysis is implemented through machine learning with the open-source Deeplabcut software.

**Results** After extracting the hand movement behavior of six different primates, a significant change was reflected between the pre-lesion and post-lesion data. The plots were separated into 3 different subplots with the range of movement of each finger. A constant pattern was detected on the post-lesion behavior of the six primates. The movement overtime plot presented in the post-lesion line graph contains multiple peaks with significant amplitudes. In contrast, the pre-lesion analysis shows a steady pattern of movement with small amplitudes throughout the analysis. The scatter plots help us identify the positions at which digit position is clustered.

### **63. Evaluation of Hybrid Control and Palpation Assistance for Situational Awareness in Telemanipulated Task Execution**

**Rashid Yasin(1), Preetham Chalasani(3), Nicolas Zevallos(2), Mahya Shabazi(3), Zhaoxhuo Li(3), Anton Deugnet(3), Peter Kazantzides(3), Howie Choset(2), Russell H. Taylor(3), Nabil Simaan(1)**

(1) Department of Mechanical Engineering, Vanderbilt University (2) The Robotics Institute, Carnegie Mellon University (3) Department of Computer Science, Johns Hopkins University

The use of intelligent feedback modalities to control and react to interaction forces during surgical procedures is an important factor in enabling safe and precise surgery. We explore the use of a model-mediated telemanipulation framework to enhance a user's situational awareness using assistive virtual fixtures and semi-automated task execution for safe and intuitive environment interaction during robotic laparoscopic surgery. The framework allows stiffness mapping with semi-autonomous excitation, hybrid position-force control, and model updates during soft geometry contact. A 24-person study was carried out at 3 sites in simulated ablation and palpation of phantom anatomy. Compared to methods lacking intelligent feedback and guidance, the proposed framework improved task execution metrics (force regulation, completion time, path-following error) and reduced user effort. The work presents a new framework for situational awareness augmentation and shared control for force-controlled ablation and for palpation-assisted localization of mock tumors. The performance of users using the da-Vinci research kit in uni-lateral telemanipulation with/without force feedback and with/without assistive virtual fixtures and stiffness information overlay is evaluated. Assistive control is implemented to test the utility of regulating the normal force while applying an assistive control law (virtual fixture) to follow a path on the surface of an organ. The user effort and accuracy in performing each ablation and tumor localization are compared in several modes of assistive sensing and control. We believe that this work is a key step towards situational awareness augmentation and seamless integration of assistive behaviors for sensory acquisition and for regulated interaction with the anatomy.

## 64. Quantification of muscle, bones and fat on single slice thigh CT

Qi Yang\*<sup>a</sup>, Xin Yua, Ho Hin Leea, Yucheng Tang<sup>b</sup>, Shunxing Baoa, Kris S Gravensteinc, Ann Zenobia Moorec, Sokratis Makrogiannisd, Luigi Ferrucci<sup>c</sup>, Bennett A Landmana,<sup>b</sup>

<sup>a</sup>Computer Science, Vanderbilt University, TN; <sup>b</sup>Electrical and Computer Engineering, Vanderbilt University, TN; <sup>c</sup>Longitudinal Study Section, National Institute On Aging, MD; <sup>d</sup>Division of Physics, Engineering, Mathematics and Computer Science, Delaware State University, DE

Muscle, bone, and fat segmentation of CT thigh slice is essential for body composition research. Voxel-wise image segmentation enables quantification of tissue properties including area, intensity and texture. Deep learning approaches have had substantial success in medical image segmentation, but they typically require substantial data. Due to high cost of manual annotation, training deep learning models with limited human labelled data is desirable but also a challenging problem. Inspired by transfer learning, we proposed a two-stage deep learning pipeline to address this issue in thigh segmentation. We study 2836 slices from Baltimore Longitudinal Study of Aging (BLSA) and 121 slices from Gestalt studies. First, we generated pseudo-labels based on approximate hand-crafted approaches using CT intensity and anatomical morphology. Then, those pseudo labels are fed into deep neural networks to train models from scratch. Finally, the first stage model is loaded as initialization and fine-tuned with a more limited set of expert human labels. We evaluate the performance of this framework on 56 thigh CT scans and obtained average Dice of 0.979, 0.969, 0.953, 0.980 and 0.800 for five tissues: muscle, cortical bone, internal bone, subcutaneous fat and intermuscular fat respectively. We evaluated generalizability by manually reviewing external 3504 BLSA single thighs from 1752 thigh slices. The result is consistent and passed human review with 5 failed thigh images, which demonstrates that the proposed method has strong generalizability.

## 65. The fMRI signal exhibits more autonomic variance in drowsiness

Benjamin P. Gold (1,2), Sarah E. Goodale (3), Chong Zhao (1), Catic Chang (1,2,3)

1) Department of Electrical Engineering and Computer Science, Vanderbilt University

2) Vanderbilt University Institute of Imaging Science, Vanderbilt University Medical

Center 3) Department of Biomedical Engineering, Vanderbilt University

fMRI measures changes in blood oxygen levels as a proxy for neural activity, but is also influenced by autonomic fluctuations such as changing heart beats or breathing rates. Separate lines of research have associated the variability of both autonomic and fMRI signals to drowsiness, suggesting that these phenomena may be linked. The present study therefore examines the extent to which the fMRI signal exhibits systemic autonomic influence across drowsiness levels, and where in the brain this effect is most pronounced. To do so, we collected simultaneous autonomic, fMRI, and EEG data (for an electrophysiological measure of drowsiness) during two 24-min conditions: a sparse auditory task ( $n = 12$ ) in which participants pressed a button upon hearing rare and unpredictably spaced tones (mean interval  $\pm$  S.D. =  $38.84 \pm 14.69$  s), and rest ( $n = 11$ ), i.e. no task. Dividing each session into 11 non-overlapping windows, we then evaluated the average drowsiness level and the extent of autonomic-fMRI covariance in each one. We found that drowsiness was associated with slower responses and more variable autonomic activity in task participants, but with less variable autonomic activity in resting participants. Yet in both conditions, participants evinced greater autonomic contributions to fMRI signals during drowsiness. These effects were widespread, but especially prominent in cerebrospinal fluid, the default mode network, and the salience/ventral attention network. The relationship between autonomic and fMRI activity therefore seems to vary over time, state, and space, with important implications for the distinction of local neural activity from systemic autonomic influences.

## 66. Deep harmonization for multi-site 1.5T/3T sMRI studies of Huntington's Disease

Authors: Xing Yao, Ipek Oguz

Departmental affiliation: Computer Science Department

Huntington's disease (HD) is a rare dominantly-inherited neurodegenerative disease. Its main clinical symptoms usually include motor symptoms, cognitive dysfunction, and mental disorders, which are closely related to the impairment of brain function during disease. To get novel insight into the cognitive and motor function domains of the HD, large-scale multi-site MRI studies such as PREDICT-HD (NS040068) have been implemented by NIH to generate rich datasets of the HD. However, these multi-site datasets are highly heterogeneous due to the inter-site scanner differences as well as intra-site changes that occurred during the decade of image acquisition. For example, the scanner strength in each site has been upgraded from 1.5T to 3T over the course of the study to obtain higher quality data. Recently, data-driven approaches such as deep learning dramatically improved the performance of image segmentation and quantification in different medical scenarios, and reach a prominent position in the medical image analysis field. Nevertheless, these inter-site and intra-site heterogeneities dramatically impact the utility of highly data-sensitive learning-based approaches on the existing large multi-site datasets. Under this circumstance, harmonization of multi-site MRI data becomes crucial for maintaining statistical power for the current multi-site dataset and enabling deep learning techniques to be fully leveraged in large multi-site studies of HD. In this work, we aim to develop deep learning approaches for the 1.5T/3T harmonization of the existing multi-site scanning sMRI data. Multiple harmonization approaches including domain adaptation and content/style disentanglement will be considered. We will also develop the corresponding quantitative analysis methods to evaluate the harmonization results. Furthermore, we will try to leverage the large harmonized dataset to improve the performance of biomarker segmentation or the prediction of subject-specific disease trajectories.

## 67. Relationships of Connectivity between Arousal Structures and Intrinsic Connectivity Networks with Neurocognition and Alertness in Temporal Lobe Epilepsy

Hernán F. J. González, Ph.D.<sup>2,3,4</sup>, Saramati Narasimhan, Ph.D.<sup>1,2,3,4</sup>, Sarah E. Goodale, B.E.,<sup>2,4</sup>, Graham W. Johnson, B.S.<sup>2,3,4</sup>, Derek Doss B.S.<sup>2,3,4</sup>, Jasmine W. Jiang, B.E.<sup>1,2,3</sup>, Danika Paulo, M.D.<sup>1</sup>, Monica L. Jacobs, PsyD<sup>1</sup>, Peter. E. Konrad, M.D., Ph.D.<sup>1</sup>, Victoria L. Morgan, Ph.D.<sup>1,2,3,4</sup>, Catie E. Chang, Ph.D.<sup>5</sup>, Dario J. Englot, M.D., Ph.D.<sup>1,2,3,4,5</sup>

Department of 1Neurological Surgery; 2Vanderbilt University Institute of Imaging Science; at Vanderbilt University Medical Center; 3Vanderbilt Institute for Surgery and Engineering; Department of 4Biomedical Engineering; Department of 5Electrical Engineering and Computer Science at Vanderbilt University, Nashville, Tennessee, USA.

**Introduction**-Temporal lobe epilepsy (TLE) is a focal syndrome; however, patients experience widespread deficits. Others found abnormal intrinsic connectivity networks (ICNs) in epilepsy. We showed perturbed arousal structure connectivity in TLE. Notably, arousal structures may modulate ICNs. Here, we investigate if TLE patients have disturbed functional connectivity (FC) between arousal structures and ICNs.

**Methods**-We acquired resting-state fMRI in 50 TLE patients and 50 controls. We calculated non-directed FC (ndFC, correlation) and directed-FC (Granger causality laterality index=GCLI) within ICNs (default mode network=DMN, salience network=SN) and between arousal structures and ICNs. We compared FC in patients vs. controls and associated FC with neurocognition. Finally, we used an fMRI-based alertness measure to relate alertness to FC.

**Results**-We noted decreased ndFC within DMN in patients( $5.73 \pm 1.44$ , mean $\pm$ SD) vs. controls( $6.75 \pm 1.38$ ,  $p=0.0008$ ) and within SN in patients( $9.27 \pm 2.19$ ) vs. controls( $10.40 \pm 2.33$ ,  $p=0.0008$ ). We found decreased ndFC between arousal network and SN in patients( $1.12 \pm 1.03$ ) vs. controls( $2.04 \pm 1.27$ ,  $p=0.0001$ ).

Lower ndFC between nucleus basalis of Meynert (NBM) and SN associated with worse processing speed index( $r=0.251$ ,  $p=0.033$ ). Lower ndFC between pedunclopontine nucleus and SN associated with worse verbal comprehension index( $r=0.350$ ,  $p=0.015$ ) and full-scale IQ( $r=0.296$ ,  $p=0.043$ ). We noted abnormal GCLI between arousal network and SN in patients( $-0.095 \pm 0.21$ ) vs. controls( $-0.26 \pm 0.24$ ,  $p=0.0012$ ), meaning SN influences arousal structures in controls, but not patients. Using an fMRI-based alertness template, we found patients, but not controls, may exhibit decreased alertness, but FC remained unaffected by alertness.

**Conclusions**-These results suggest abnormal FC between arousal structures and ICNs may underlie neurocognitive deficits seen in TLE, and these networks may represent neuromodulation targets for neurocognitive comorbidities in TLE.

## 68. Fat Quantification Imaging and Biophysical Modeling for Patient-Specific Forecasting of Microwave Ablation Therapy

Frankangel Servin<sup>1,2</sup> Jarrod A. Collins<sup>3</sup>, Jon S. Heiselman<sup>1,2</sup>, Katherine C. Frederick-Dyer<sup>4</sup> Virginia B. Planz<sup>4</sup> Sunil K. Geevarghese<sup>7</sup> Michael I. Miga<sup>1,2,4,5,6\*</sup>

1 Department of Biomedical Engineering, Vanderbilt University, Nashville, TN USA

2 Vanderbilt Institute for Surgery and Engineering, Vanderbilt University, Nashville, TN USA

3 Siemens Healthineers, Siemens Medical Solutions USA, Inc., Houston, TX USA

4 Department of Radiology, Vanderbilt University Medical Center, Nashville, TN USA

5 Department of Neurosurgery, Vanderbilt University Medical Center, Nashville, TN USA

6 Department of Otolaryngology-Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, TN USA

7 Department of Surgery, Vanderbilt University Medical Center, Nashville, Tennessee.

**Introduction:** Hepatocellular carcinoma (HCC) accounts for 65% of all primary liver cancer, with 500 thousand new cases worldwide. Microwave Ablative Therapy (MWAT), is regarded as the best interventional therapy for early-stage HCC patients who cannot undergo resection. Within the literature, data suggests that patient-specific factors (e.g. tissue perfusion, material properties, disease state, etc.) may affect ablative therapies and current guidance practices for thermal dosing do not account for these. One possible strategy is to perform patient-specific modeling of MWAT procedures prior to and during a procedure to compensate for these factors.

**Methods:** This study establishes a patient-specific biophysical modeling framework to calculate ablation margins in livers with varying fat content. Patient anatomic scans were segmented to develop liver meshes and mDIXON fat-quantification images were sampled to calculate fat content. HCC microwave tumor ablations were simulated in COMSOL with varying properties according to fat content. The volume, long-diameter, short-diameter, and probe temperature were recorded.

**Results:** The fat data sampled from patients showed distributions that were significantly heterogeneous, even within their respective disease classifications, especially in patients with higher fat content. Models with high-fat livers had significantly larger ablation volumes compared to all other models ( $p < .01$ ). Final probe temperatures also ranged from 95-118 C based only on changes to liver fat.

**Discussion:** From the imaging, the data suggests that within typical disease states (e.g. low, mild, moderate, high fat), liver fat is multi-valued and quite spatially distributed. In addition, it is evident that liver fat significantly affects ablation volume. Interestingly, the common material assumptions regarding the presence of HCC had considerable less impact than underlying liver parenchyma. Overall, these results show the importance of modeling the material changes in fat content.

## 69. Accelerating 2D Abdominal Organ Segmentation with Active Learning

Xin Yu <sup>a</sup>, Yucheng Tang <sup>b</sup>, Qi Yang <sup>a</sup>, Ho Hin Lee <sup>a</sup>, Shunxing Bao <sup>b</sup>, Ann Zenobia Moore <sup>c</sup>, Luigi Ferrucci <sup>c</sup>, Bennett A. Landman <sup>a, b</sup>

<sup>a</sup>Computer Science, Vanderbilt University, Nashville, TN; <sup>b</sup>Electrical and Computer Engineering, Vanderbilt University, Nashville, TN; <sup>c</sup>National Institute on Aging, Baltimore, MD

Abdominal computed tomography CT imaging enables assessment of body habitus and organ health. Quantification of these health factors necessitates semantic segmentation of key structures. Deep learning efforts have shown remarkable success in automating segmentation of abdominal CT, but these methods largely rely on 3D volumes. Current approaches are not applicable when single slice imaging is used to minimize radiation dose. For 2D abdominal organ segmentation, lack of 3D context and variety in acquired image levels are major challenges. Deep learning approaches for 2D abdominal organ segmentation benefit by adding more images with manual annotation, but annotation is resource intensive to acquire given the large quantity and the requirement of expertise. Herein, we designed a gradient based active learning annotation framework by meta-parameterizing and optimizing the exemplars to dynamically select the ‘hard cases’ to achieve better results with fewer annotated slices to reduce the annotation effort. With the Baltimore Longitudinal Study on Aging (BLSA) cohort, we evaluated the performance with starting from 286 subjects and added 50 more subjects iteratively to 586 subjects in total. We compared the amount of data required to add to achieve the same Dice score between using our proposed method and the random selection in terms of Dice. When achieving 0.97 of the maximum Dice, the random selection needed 4.4 times more data compared with our active learning framework. The proposed framework maximizes the efficacy of manual efforts and accelerates learning.

## **70. Real-time assessment of frame quality to guide frame reacquisition for improved 3D reconstructions of cystoscopies**

**Rachel Eimen** - Vanderbilt Biophotonics Center and Department of Biomedical Engineering Vanderbilt University, Nashville, TN 37232 **Mayaank Pillai** - Department of Biomedical Engineering Vanderbilt University, Nashville, TN 37232 **Kristen Scarpato** - Department of Urology Vanderbilt University Medical Center, Nashville, TN 37232 **Audrey K. Bowden** - Vanderbilt Biophotonics Center and Department of Biomedical Engineering Vanderbilt University

White-light cystoscopy is the standard of care to diagnose and monitor bladder cancer. In the current standard of care, clinicians only save a few image frames and notes and typically discard the cystoscopy video, as the cystoscopy video is too cumbersome to review and annotate. The data lost by discarding the video could improve patient medical records, which may improve patient treatment and allow for longitudinal studies. Three-dimensional (3D) reconstructions of the bladder present the cystoscopy data in a form that is easy to review and preserves the appearances and 3D locations of features in the bladder. However, reconstruction performance is inherently limited by low-quality cystoscopy frames, particularly cystoscopy frames with motion blur, inconsistent lighting, bladder debris or a lack of vessel contrast. To increase the likelihood for successful reconstruction, we propose an Assessment and Guidance Pipeline that runs in real-time during the cystoscopy, assesses the quality of incoming frames, and alerts the clinician when low-quality frames are detected so they can be recollected. We hypothesize that the quality of 3D reconstructions will improve if we replace low-quality frames with recollected frames.

## 71. Automated, Contactless Skin Surface Measurements with Stereo Cameras in Image Guided Surgery

**Winona Richey**, Biomedical Engineering, Vanderbilt University **Jon Heiselman**, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, New York, USA **Ingrid Meszoely**, Surgical Oncology, Vanderbilt University Medical Center **Michael Miga**, Biomedical Engineering, Vanderbilt University

Breast cancer is the most common cancer in American women, and over 2/3rds of these patients will undergo breast conserving surgery as part of their treatment. Unfortunately, large deformations between preoperative imaging and surgical presentation and a difficulty understanding intraoperative tumor extent leads to unsuccessful resection for many patients. To provide tumor boundary localization in the operating room, we propose a novel image guidance platform that utilizes small fiducial points for precise and accurate localization with character-based labels for easy automated detection. Our system is work-flow friendly, and near-real time with use of stereo cameras for surface acquisition. Using simple image processing techniques, the proposed technique can localize fiducials and character labels, providing updates without relying on video history. The method is contactless, automated, and measures all surface fiducials simultaneously, which reduces breathing motion artifacts. Character based fiducial labels provide a feature rich environment which can be used to determine correspondence between left and right stereo camera images, and frame to frame in a sequence of images during a procedure. The stereo camera system can determine surface points with accuracy below 2 mm when compared to optically tracked stylus points. These surface points are incorporated into a four-panel guidance display that includes preoperative supine MR, tracked ultrasound, and a model view of the breast and tumor with respect to optically tracked instrumentation.

## 72. Patient-specific electro-anatomical modeling of cochlear implants using deep neural networks

**Ziteng Liu:** Dept. of Computer Science, Vanderbilt University **Jack H. Noble:** Dept. of Computer Science, Dept. of Electrical and Computer Engineering, Vanderbilt University

Cochlear implants (CIs) are considered the standard-of-care treatment for profound sensory-based hearing loss. After CI surgery, an audiologist will adjust the CI processor settings for CI recipients to improve overall hearing performance. However, this programming procedure can be long and may lead to suboptimal outcomes due to the lack of objective information. In previous research, our group has developed methods that use patient-specific electrical characteristics to simulate the activation pattern of auditory nerves when they are stimulated by CI electrodes. However, estimating those electrical characteristics require extensive computation time and resources. In this paper, we proposed a deep-learning-based method to coarsely estimate the patient-specific electrical characteristics using a cycle-consistent network architecture. These estimates can then be further optimized using a limited range conventional searching strategy. Our network is trained with a dataset generated by solving physics-based models. The results show that our proposed method can generate high-quality predictions that can be used in the patient-specific model and largely improve the speed of constructing models.

### 73. On-Axis Acoustic Radiation Force-based Quantitative Elasticity in Gelatin Phantoms of Varying Stiffness

Kristy Walsh [1], Mark Palmeri [2], and Brett Byram [1]

[1] Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA [2] Department of Biomedical Engineering, Duke University, Durham, NC, USA

Acoustic radiation forced (ARF)-based elasticity imaging can displace tissue at a focused region and determine its mechanical properties by monitoring displacement. Shear wave elastography imaging (SWEI) is a quantitative ARF-based method which derives shear modulus from the speed of shear wave displacements arriving at lateral locations from the ARF push. Instead of measuring laterally off-axis, we measure displacements directly at the push location. This can reduce data and hardware requirements and improve accuracy of estimates in an inhomogeneous media, such as skin. We use an FEM-based look-up table to estimate shear modulus that models the on-axis response of known simulated elasticities to a specific transducer push and tracking configuration. The quality of ARF-based elastography greatly depends on the ability to measure tissue displacement, especially in high shearing, noisy environments, such as the push location. We developed an advanced Bayesian displacement estimator that introduces a small amount of bias that reduces displacement estimation variance and has a lower mean-square error than an unbiased estimator. We compare our estimator to commonly used normalized cross-correlation that has low jitter for an unbiased estimator, but still fails in some challenging cases, such as on-axis. We tested our on-axis elasticity method in simulations and tissue-mimicking phantoms made of 2, 3, 4, and 5% gelatin (shear moduli of 2.7-14.4kPa, or shear wave speed 1.6-3.8m/s). The error in the homogeneous phantom results was computed between the shear wave speed-derived estimates and the on-axis estimates using the simulated look-up table. We show the on-axis elasticity method is made feasible by using an advanced Bayesian displacement estimator and can be applied to a range of elasticities.

# Registrants

Aarushi Negi	Frankangel Servin	Lucas Sainburg
Abbie Weeks	Gordon Bernard	Margaret Rox
Adam Yock	Graham Johnson	Matthew Bacchetta
Amanda Buck	Han Liu	Michael Miga
Andrew McNeil	Han Dong	Mikail Rubinov
Ange Lou	Hannah Mason	Morgan Ringel
Anirban Sengupta	Hao Li	Ms Choi
Ankush Ratwani	Hernan Gonzalez	Nabil Simaan
Behnaz Akbarian	Ho Hin Lee	Neel Shihora
Benjamin Gold	Ipek Oguz	Nicholas Kavoussi
Benoit Dawant	Jack Noble	Olina Wu
Bill Rodriguez	Jake Watson	Olivia Wright
Bohan Jiang	James Metz	Parker Willmon
Bowen Xiang	Jasmine Jiang	Philip Swaney
Brett Byram	Jason Shrand	Piper Cannon
Caitlin Grogan	Jesse d'Almeida	Praitayini Kanakaraj
Can Cui	Jiacheng Wang	Preston Pan
Carli DeJulius	Jiro Kusunose	Qi Yang
Caroline Martin	Jody Smith	Qibang Zhu
Catie Chang	Jon Heiselman	Quan Liu
Christopher Khan	Jorge Salas	Rachel Eimen
Christos Constantinidis	Jose Rico Jimenez	Rachel Hecht
Colette Abah	Joshua McCune	Rebecca Conley
Daniela Hernandez-	Juan Colazo	Rei Ukita
Duque	Karen Joos	Robert Webster
Danika Paulo	Karthik Ramadass	Rueben Banalagay
Dann Martin	Kate Wang	Ruining Deng
Dario Englot	Katelyn Clemencich	Ryan Hsi
David Armstrong	Kathleen Larson	Saikat Sengupta
Derek Doss	Keith Obstein	Sarah Goodale
Dewei Hu	Kenneth Lewis	Saramati Narasimhan
Diana Carver	Kenny Tao	Sheldon Ratnofsky
Dingjie Su	Kimberly Rogge-Obando	Shiyu Wang
Duke Herrell	Kristopher Castillo	Shunxing Bao
Duryodhan Prusty	Kristy Walsh	Siddharth Shah
Elan Ahronovich	Kush Hari	Siegfried Schlunk
Emelina Vienneau	Kyvia Pereira	Soheil Kolouri
Eric Tang	Laura Paulsen	Thomas Manuel
Erin Bratu	Leon Cai	Tingyan Deng
Ethan Sheppard	Lucas Remedios	Victoria Morgan

William Stevenson  
William Tierney  
Winona Richey  
Xin Yu  
Xing Yao  
Yike Zhang  
Yuankai Huo  
Yubo Fan  
Zachary Stoebner  
Zheng Li  
Zhengyang Wang  
Ziteng Liu

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Every effort was made to ensure all registrations, laboratory descriptions and abstracts were captured in this program.  
Please forgive any accidental omissions.



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