8th Annual

Surgery, Intervention, and Engineering Symposium

DECEMBER 11TH, 2019

202 Light Hall

"End Game"

A surgeon's pespective on the future of technology and innovation in healthcare.

Louis Kavoussi, MD

Chairman, Department of Urology
Professor, Donald and Barbara Zucker School of Medicine at Hofstra Northwell University Medical School

VISE VANDERBILT INSTITUTE FOR SURGERY AND ENGINEERING

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.

"End Game"

A Surgeon's perspective on the future of technology and innovation in healthcare.

Presented by

Louis Kavoussi, MD

Chairman, Department of Urology
Professor, Donald and Barbara Zucker School of Medicine at Hofstra
Northwell University Medical School

Keynote Abstract

“End Game”

A surgeon’s perspective on the future of technology and innovation in healthcare

Louis Kavoussi, MD

Chairman of Urology for Northwell Health, and
Waldbaum Gardner Professor of Donald and Barbara Zucker
School of Medicine at Hofstra/Northwell

Surgery can be used to treat many pathological conditions; however, the price of cure includes potential convalescence, discomfort, impact on cosmesis, variable functional outcomes and complications. Improvements in techniques as well as technology have decreased morbidity and mortality once commonly associated with an operation. Currently there is still inconsistency in outcomes related to innate differences among surgeons as well as patients. Advances in technology will allow surgery to evolve into the ideal patients’ desire. A guaranteed perfect outcome absent of problems and disruption of individual normality. We rely upon our engineering colleagues to help deliver this reality.

Biography

Dr. Kavoussi completed his undergraduate degree at Columbia University and medical degree at the State University of New York at Buffalo. He obtained his urologic training at Washington University of St. Louis and directly following residency was named Chief of Urology at the Jewish Hospital of St. Louis. In 1991 he was appointed Assistant Professor at Harvard School of Medicine and Director of Endourology at the Brigham and Women's Hospital. In 1993 he joined the faculty of Johns Hopkins University School of Medicine where he was Vice Chairman of Urology and Patrick C. Walsh Distinguished Professor.

Dr. Kavoussi is currently the Chair of Urology for the Northwell Health (Formerly North Shore-LIJ Health System) and the Waldbaum-Gardner Distinguished Professor of Urology at the Donald and Barbara Zucker School of Medicine at Hofstra/ Northwell.

Dr. Kavoussi has made many important contributions to urology.He was part of several first teams that engendered many of the minimally invasive approaches we use today including the laparoscopic nephrectomy, laparoscopic donor nephrectomy and laparoscopic prostatectomy. His contributions have been documented in over 400 peer reviewed publications. He has edited multiple texts including his role as a co-editor of Campbell-Walsh Urology, Smith's Endourology, Atlas of Retroperitoneal Surgery and Handbook of Surgical Techniques.

He helped found the first robotics laboratory dedicated to urological applications and developed telerounding and teleinteraction with patients for which he was a Smithsonian Computerworld Medalist. His contributions to the field of urology earned him the Golden Cystoscope Award of the American Urological Association, The Lifetime Achievement Award from the American Kidney Foundation and the 2018 Distinguished Contribution Award from the American Urological Association.

Dr. Kavoussi has mentored over 35 fellows in minimally invasive surgery who are academic leaders around the world. This achievement was recognized through him being awarded the Endourology Society Mentoring Award in 2014. He has served the field of urology in many areas. He has been on the Board of the Endourology Society. He currently is treasurer of the New York Section of the American Urological Association (in line for Presidency coming year). He is also President elect of the Society for Academic Urologists.

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.come/user/ARMAVU/videos
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Participating Laboratories

Bai Lab

PI: Mingfeng Bai, Ph.D.
Assistant Professor
Radiology and Radiological Sciences,
Vanderbilt University

Our lab is focused on the development and in vivo evaluation of targeted molecular probes for fluorescence imaging-guided surgery and photodynamic therapy (PDT). We are also interested in investigating the effect of systemic anti-tumor immunity and overcoming chemoresistance caused by our PDT treatment.

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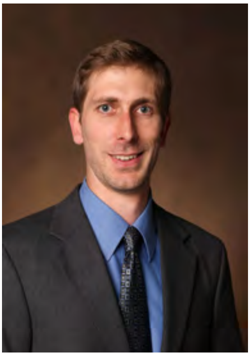
Participating Laboratories



Biomedical Elasticity and Acoustic Measurement (BEAM) Laboratory

PI: Brett Byram, Ph.D.
Assistant 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.

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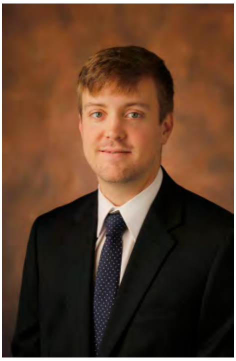

Biomedical Image Analysis for Image Guided Interventions (BAGL) Laboratory

PI: Prof. Jack H. Noble, Ph.D.
Assistant Professor of Electrical Engineering and Computer Science,
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.

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Participating Laboratories

Biomedical Modeling (BML) Laboratory

PI: Michael I. Miga, Ph.D.
Harvie Branscomb Professor, Professor of Biomedical Engineering, Radiology & Radiological Sciences, and Neurological Surgery, 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 deep brain stimulation, ablative therapies, neoadjuvant chemotherapy, and convective chemotherapy are also being investigated. With respect to diagnostic imaging, applications in elastography, strain imaging, model-based chemotherapeutic tumor response and radio-therapy 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 is present with a central focus at translating the information to directing therapy/intervention or characterizing tissue changes for diagnostic value.

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Participating Laboratories

Brain Imaging and Electrophysiology Network (BIEN) Laboratory

PI: Dario J. Englot, M.D., Ph.D.
Assistant Professor of Neurological Surgery, Radiology and Radiological Sciences, Electrical Engineering, and Biomedical Engineering,
Vanderbilt University Medical Center

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.

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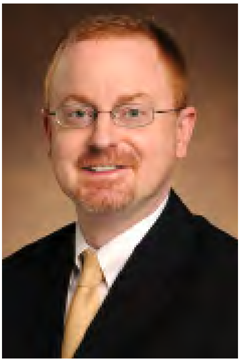
Participating Laboratories



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. wSome 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.

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Participating Laboratories

Computational Flow Physics and Engineering Lab

PI: Haoxiang Luo, Ph.D.
Associate Professor, 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. We use computational modeling and high-performance computing techniques to solve fluid (i.e., liquids or gases) flow problems and also problems involving interaction between fluids with solid structures. The current research thrusts in the lab include: 1) computational modeling vocal fold vibration and interaction with glottal aerodynamics for surgery planning of voice disorders and other airway diseases, 2) computational modeling the cardiovascular flows such as heart valves, 3) aerodynamics and aeroelasticity of biological wings (e.g., insects and birds), and hydrodynamics of fish, for applications in unmanned aerial and underwater vehicles, and 4) particle-laden flows in electrochemical systems for applications in energy storage and water deionization.

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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.

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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 imagining 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.

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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, and 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.

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Participating Laboratories

Laboratory for the Design and Control of Energetic Systems

PI: Eric Barth, Ph.D.
Associate 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.

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Participating Laboratories

Laboratory for Organ Recovery, Regeneration and Replacement (LOR3)

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

The LOR3 is focused on creating organ support systems that provide extended physiologic support for injured organs, bioengineering platforms for organ recovery and regeneration as well as developing artificial pulmonary assist devices. The lab maintains a full complement of devices for extracorporeal life support and has developed durable support systems for lung and liver with translational potential. It works in partnership with programs at VUMC, Carnegie Mellon University and Columbia University. The LOR3 is dedicated to translating basic science research into clinical platforms for patients with end organ failure.

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Participating Laboratories

MRI Methods Lab

PI: Saikat Sengupta, PhD,
Research Assistant Professor,
Vanderbilt University

The Magnetic Resonance Imaging Methods lab at the Vanderbilt University Institute of Imaging Science (VUIIS) is dedicated to the development of innovative methods for rapid and robust human Magnetic Resonance Imaging. Projects include developing better, artifact resistant probes for interventional MRI applications, real time MRI for dynamic anatomies, real time motion correction for high resolution neuroimaging and development of imaging sequences robust to motion and physiological influences. The lab is headed by Saikat Sengupta, Research Assistant Professor of Radiology.

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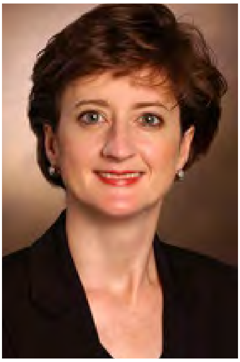
Participating Laboratories



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.

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Participating Laboratories

Medical-image Analysis and Statistical Interpretation (MASI) Laboratory

PI: Bennett Landman, Ph.D.
Associate Professor Electrical Engineering, Biomedical Engineering, Computer Science, Radiology and Image Science, and Chancellor Faculty Fellow
Vanderbilt University

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.

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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.

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Participating Laboratories

Medical Image Computing (MedICL) Laboratory

PI: Ipek Oguz, Ph.D.
Assistant Professor of Computer Science
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.

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Participating Laboratories

Medical Image Processing (MIP) Laboratory

PI: Benoit Dawant, Ph.D.,
Cornelius Vanderbilt Chair in Engineering
Professor of Electrical Engineering
Professor of Biomedical Engineering Professor of Radiology & Radiological Sciences
Vanderbilt University

The Medical Image Processing (MIP) laboratory of the Electrical Engineering and Computer Science (EECS) 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 (1) automatically localize radiosensitive structures to facilitate radiotherapy planning, (2) assist in the placement and programming of Deep Brain Stimulators used to treat Parkinson's disease, (3) localize automatically structures that need to be avoided while placing cochlear implants, (4) develop methods for cochlear implant programming or (5) track brain shift during surgery. 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.

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Participating Laboratories

Morgan Engineering and Imaging in Epilepsy Lab

PI: Vicky Morgan, Ph.D.,
Associate Professor, Radiology & Biomedical Engineering, Institute of Imagine Science (VUIIS), 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).

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Participating Laboratories

Neuroimaging and Brain Dynamics Lab

PI: Catie Chang, Ph.D.
Assistant Professor of Computer Science, Electrical Engineering, Computer Engineering, Vanderbilt University

The goal of our research is to advance understanding of human brain function in health and disease. We develop new approaches for studying human brain activity by integrating functional neuroimaging (fMRI, EEG) and computational analysis techniques. In one major avenue, we are examining the dynamics of large-scale brain networks across cognitive and physiological state changes and translating this information into novel fMRI biomarkers. To enable clearer inferences about brain function with fMRI, we also work toward resolving the complex neural and physiological underpinnings of fMRI signal fluctuations. A complementary branch of our research strives to improve neuroimaging data quality, such as through algorithms for reducing artifacts in fMRI and EEG signals. Our research is highly interdisciplinary and collaborative, bridging fields such as engineering, computer science, neuroscience, psychology, and medicine.

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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
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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. 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.

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. We are currently applying capsule robot technologies to early detection and treatment of gastrointestinal cancers (i.e. colorectal cancer, gastric cancer) and are developing a new generation of surgical robots that can enter the patient's abdomen by a single tiny incision. Building upon these competences, we are always ready to face new challenges by modifying our capsule robots to emerging medical needs.

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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.

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Participating Laboratories

Vanderbilt Biophotonics Center

PI: Anita Mahadevan-Jansen, Ph.D.
Orrin H. Ingram Professor of Biomedical Engineering,
Professor of Neurological Surgery,
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.

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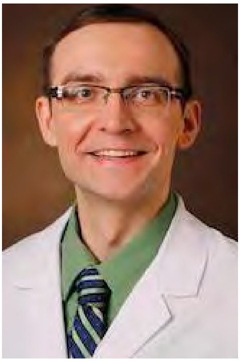
Participating Laboratories



Vanderbilt Dermatology Translational Research Clinic (VDTRC)

PI: Eric Tkaczyk, M.D., Ph.D., FAAD,
Assistant Professor, Dermatology, VUMC Assistant Professor, Biomedical Engineering,
Vanderbilt University,
Attending Dermatologist, Nashville VA Medical Center

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).

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Participating Laboratories

Woodard Lab

PI: Lauren Woodard, PhD
Assistant Professor of Medicine,
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We engineer gene and cell therapies for kidney regeneration. We use mouse models and human 3D tissue culture systems, including kidney organoids. We focus on improving organ regeneration through transcription factor reprogramming and stem cells. We are studying the functional improvement and engraftment properties of stem cells for kidney repair following acute kidney injury. For example, using luciferase transposons together with advanced optimal tomography, we have found that human urine-derived stem cells home to the kidney and other organs after injury. We also investigate improvements to transposon systems and non-viral transfection techniques to further expand the available gene and cell therapy toolkit. Past and ongoing studies of transposase self-regulation continue to provide insights into how transposons function. Our expertise in recombinases, CRISPR/Cas systems, and transfection of cells and tissues allow exploration of regenerative gene therapies.

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Submitted Abstracts

1. Noninvasive Microscopic Imaging Reveals Increased Leukocyte Adhesion and Rolling in Skin of Acute Graft-Versus-Host Disease Patients Compared to Post-Transplant Controls

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Inflammatory tissue response is one of the first and most common manifestations of acute graft-versus-host disease (aGVHD), a potentially deadly immune-mediated disease that occurs in 30-60% of patients after hematopoietic cell transplantation (HCT). A fundamental challenge in developing effective treatment strategies for aGVHD is the lack of tools to study disease biology in real-time in post-transplant patients. In this cross-sectional pilot study, we tested the feasibility of parameters characteristic of leukocyte motion in skin capillaries as potential imaging biomarkers to detect aGVHD. We enrolled 10 patients with any organ aGVHD and 10 patients with no organ aGVHD on the day of the imaging. To noninvasively visualize leukocyte motion in the topmost capillaries of post-HCT patients' forearm and upper chest skin, we used a clinical reflectance confocal microscope (Vivascope 1500, Caliber I.D.). We found increased number of adherent and rolling leukocytes in the aGVHD group (median of 3 leukocytes per 10 minutes of videos per patient), compared to post-HCT controls (median of 0 leukocytes). Highest leukocyte rolling (>8 rolling leukocytes) was associated with increased all-cause mortality.
Interestingly, we observed 7 adherent leukocytes in one patient who had isolated gut aGVHD and no skin involvement. Our preliminary results show altered leukocyte-endothelial interactions in the skin capillaries of aGVHD patients, suggesting that confocal microscopy may be an important tool in augmenting the clinical diagnosis and managing post-HCT patients.

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2. Key Histopathology Features of Cutaneous Acute Graft-Versus-Host Disease Can Be Detected Noninvasively

Inga Saknite (1), Melissa Gill (2,3), Christi Alessi-Fox (4), Heidi Chen (5), Jeffrey P. Zwerner (6), Julia S. Lehman (7), Michi M. Shinohara (8), Roberto A. Novoa (9), Michael Byrne 10), Madan Jagasia (5,10), Salvador Gonzalez (11), Marco Ardigo (12), Eric R. Tkaczyk (1,13,14)

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Cutaneous erythema and histopathology features in patients post allogeneic hematopoietic cell transplantation (HCT) are nonspecific, making it difficult to accurately diagnose acute graft-versus-host disease (aGVHD), a potentially deadly immune-mediated disease. Proper biopsy site selection, timing, and serial noninvasive microscopic monitoring may improve our understanding and management of aGVHD. In this study, we tested the feasibility of noninvasive reflectance confocal microscopy (RCM) to detect key histopathology features of cutaneous aGVHD. In total, 16 lesions (11 patients) of cutaneous aGVHD-affected site were imaged by RCM (6x6 mm2 en face images at four different depths) and subsequently biopsied (4x4 mm punch biopsy). Four reflectance confocal microscopists blinded to histopathology independently evaluated the presence or absence of 18 RCM features. Concurrently, four dermatopathologists blinded to clinical and confocal information determined the presence or absence of 19 histopathology features. The reflectance confocal microscopist vote was then correlated to the dermatopathologist expert vote for 17 overlapping features. The main aGVHD features had > 88% correlation between RCM and histopathology. We found a similar interrater variability among RCM experts (70%) and dermatopathologists (68%). In this pilot study, we show that noninvasive label-free RCM of skin enables detection of the main features of cutaneous aGVHD. Future studies can build on this work to evaluate the feasibility of RCM to determine cutaneous aGVHD grade, as well as distinguish between rash due to aGVHD and drug reactions.

This work was partially supported by Career Development Award Number IK2 CX001785 from the United States Department of Veterans Affairs Clinical Sciences R&D (CSRD) Service, and the National Institutes of Health Grant K12 CA090625.

3. Infusensor: A “Smart” Catheter and Platform For Dynamic, “Closed-loop” Sedation And Anesthesia

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Background: Target-controlled infusion anesthesia (TCIA) has been used for decades to provide stable blood concentrations of propofol for clinical use. However, because the infusion microprocessor uses population-based pharmacokinetic data and biometrics to estimate the infusion rate, it has not been approved for use by the FDA. The objective of the project has been to quantify propofol levels in blood in real time and create a pathway for regulatory approval for TCIA. We have developed and patented a novel electrochemical biosensor for this purpose.
Results: We show that propofol concentration can be determined at sub-micromolar detection limit values even in the presence of clinical interfering agents. The dose-dependent signal for propofol is highly correlated with “gold standard” HP/LC methods in human serum and blood. Methods to rapidly detect and quantify propofol in flowing biofluids were developed using a benchtop automated flow analytical system to model blood flow and real time analysis of drug levels. The clinical platform includes the “smart” biosensor catheter, EC signal generation/detection and a readout display. An intuitive graphical user interface was developed to: 1) quantify the propofol signal, 2) determine the variance from targeted levels and communicate with the PID controller in real time, and 3) use the output modulate drug delivery in real time. Automated delivery and maintenance of propofol levels was demonstrated in a modeled “patient” using the known pharmacokinetics of the drug.
Conclusions: We present a successful proof of concept and validation of a “smart,” indwelling catheter-based propofol biosensor, able to deliver and monitor therapeutic levels of propofol in real time. The biosensor platform is also capable of precise continuous propofol delivery in an autonomous manner, a proof of principle for “closed-loop” anesthesia.

4. Active Shimming of Metallic Probes for Interventional MRI

Saikat Sengupta (Radiology) **Xinqiang Yan** (Radiology) **Robert Webster III** (Mechanical Engineering)

Artifacts caused by large magnetic susceptibility differences between metallic needles and tissue are a persistent problem in many interventional MRI applications. The signal void caused by the probe can obscure procedure targets and prevent accurate image-based monitoring. Here, we introduce a solution to this problem by designing, simulating, fabricating and testing an active shim insert inspired from degaussing coils used in ships and submarines for defense against sea mines, to correct the field disturbance ($\Delta B0$) caused by the needle. The field disturbance induced by a 6.35 mm hollow Titanium needle at 3 Tesla is modeled and an active 2 coil shim insert is designed, and shimming is simulated. Simulations are followed by experiments on a 3 Tesla MRI scanner. A shim insert is fabricated from a 4 mm cylindrical former with 26-gauge shim wire. The shim set is inserted into the titanium rod and placed in a water bottle phantom to match the simulation condition. 3D GRE imaging with field mapping is performed to assess shimming performance. Simulations predict significant reduction of the field disturbance outside the needle with active shimming. Experiments agreed with simulations and showed large reduction in the signal void and field inhomogeneity around the Titanium needle with active shimming. Around 58% of the lost signal around the needle was recovered. We demonstrate that it is possible to recover signal losses around metallic probes with active shim coils, which can have significant benefits in a variety of qualitative and quantitative IMRI applications.

5. Nucleus Basalis is a Central Network Structure of Perturbed Functional Connections in Temporal Lobe Epilepsy

Hernán F. J. González [1,4], Saramati Narasimhan [1,2,4], Graham W. Johnson [1,4], Kristin E. Wills [2,4], Peter E. Konrad [1,2], Catie Chang [1,4,5], Victoria L. Morgan [1,2,3,4], Mikail Rubinov [1], Dario J. Englot [1,2,3,4]

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Introduction: Temporal lobe epilepsy (TLE) patients exhibit aberrant connectivity of subcortical arousal structures like brainstem and thalamus. Further, prior rodent studies in TLE have demonstrated depressed nucleus basalis of Meynert (NBM) activity during seizures. However, interictal connectivity of NBM has not been examined in human TLE.

Objectives: We hypothesize recurrent seizures in TLE may beget interictal NBM abnormalities, which may be associated with neurocognitive deterioration.

Methods: We examined 40 TLE patients and 40 controls with functional MRI to calculate resting-state functional connectivity (FC) of NBM. We compared community structure in TLE patients vs. controls and examined relationships between FC, network-properties, and disease severity.

Results: FC between bilateral NBM and frontoparietal neocortex was lower in TLE patients vs. controls ($p<0.01$, paired t-test) and was more decreased in patients with higher seizure frequency ($r=-0.412$, $p<0.01$, Pearson correlation). Using community detection, we found that NBM functionally grouped with limbic system in healthy controls. However, in TLE patients NBM no longer clustered with limbic structures. Additionally, more abnormal community structure was associated with worse performance in multiple neurocognitive domains ($r=0.32$-0.53, $p<0.05$, Spearman's rho). Lastly, both ipsilateral and contralateral NBM displayed decreased clustering coefficient vs. controls ($p<0.01$, Mann-Whitney U-test), and ipsilateral NBM had the most decreased clustering coefficient of all 133 brain regions we examined.

Conclusions: NBM exhibits markedly disturbed connectivity and network properties in TLE and may be one of the most perturbed network hubs in TLE. Given its widespread excitatory projections NBM may be a novel network-based neuromodulation target to treat this devastating disorder.

6. A General Framework for Channel Domain SVD Clutter Filtering

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Clutter rejection is necessary for reliable visualization of blood flow, as clutter signals bias measures of velocity and power, and can exceed the magnitude of weak blood echoes by 40-100 dB. Prior studies have shown eigen-based clutter filters may offer greater clutter rejection performance than traditional filtering of Doppler data. However, practical translation of these eigen-based techniques to channel data filtering applications is limited by their high computational burden. To enable efficient eigen-based filtering of channel domain data, we propose a domain-adaptive methodology, in which a linear basis set derived from RF data is used to filter delayed channel data.
Preliminary efficacy is demonstrated using perfusion phantom data. Blood mimicking fluid was perfused at 5mm/sec through a 0.64mm vessel. Nine angled plane waves spanning -8° to 8° were collected using a Verasonics L12-5 probe with f_0 of 7.8MHz. The eigen-based filter threshold was defined using the gradient of eigenvalue energy and the mean temporal eigenvector frequency. The domain-adaptive filter was tested in CFPD and ppCFPD beamforming schemes, which rely on clutter rejection operations applied to channel data. Performance was assessed in comparison to a 6th order Chebyshev filter with a 20 Hz cutoff. The coherence beamformers (CFPD and ppCFPD) offered improved suppression of incoherent clutter compared to conventional power Doppler, producing contrast improvements up to 4.28 and 6.37 dB, respectively. Application of the domain-adaptive filter further improved clutter rejection, in comparison to the IIR filter, increasing contrast by 7.44 dB for ppCFPD and by 4.70 dB for CFPD.

7. OCT and fluorescence SLO for guided laser delivery and longitudinal imaging of targeted retinal injury

Joseph Malone (BME), **Edward Levine** (Cell and developmental biology), **Yuankai Tao** (BME)

Mice are commonly used to model human retinal disease and function because of similarities in ocular anatomy and function and availability of transgenic phenotypes. Focal laser injury has previously been demonstrated as a method to induce retinal regeneration and choroidal neovascularization in mice. Previous studies delivered lasers using slit-lamp or indirect ophthalmoscope systems that lacked precision aiming and control over retinal damage location and severity, and injury response was evaluated using histology, which limited tracking of longitudinal changes. Optical coherence tomography (OCT) overcomes this limitation by enabling visualization of three-dimensional microstructures in vivo. Similarly, scanning laser ophthalmoscopy (SLO) benefits ophthalmic imaging by leveraging fluorescent contrast and providing noninvasive en face fundus images with a cellular resolution. Recently, targeted delivery of photo-lesions has been demonstrated using either fundus or combined OCT and SLO imaging; however, these systems do not allow for simultaneous multimodality imaging and have limited frame-rates. Here, we present a system that combines multimodality OCT+SLO imaging with a photocoagulation laser and custom software that allows for targeted delivery of focal retinal laser injury using real-time en face OCT guidance. Targeted retinal laser injury titration experiments were performed in 5 transgenic mice (10 eyes) expressing tdTomato in Mueller cells under an IACUC-approved protocol. Longitudinal OCT+SLO imaging of injury response was performed weekly over 3 follow-up sessions. Imaging results showed lesions with varying degrees of retinal damage, injury response, and anatomic normalization.

8. Tensor-based grading: a novel patch-based grading approach for the analysis of deformation fields in Huntington's disease

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The improvements in magnetic resonance imaging have led to the development of numerous techniques to better detect structural alterations caused by neurodegenerative diseases. Among these, the patch-based grading framework has been proposed to model local patterns of anatomical changes. This approach is attractive because of its low computational cost and its competitive performance. Other studies have proposed to analyze the deformations of brain structures using tensor-based morphometry, which is a highly interpretable approach. In this work, we propose to combine the advantages of these two approaches by extending the patch-based grading framework with a new tensor-based grading method that enables us to model patterns of local deformation using a log-Euclidean metric. We evaluate our new method in a study of the putamen for the classification of patients with pre-manifest Huntington's disease and healthy controls. Our experiments show a substantial increase in classification accuracy (87.5 vs.81.3) compared to the existing patch-based grading methods, and a good complement to putamen volume, which is a primary imaging-based marker for the study of Huntington's disease.

9. Differential Effects of Temporal Lobe Epilepsy on the Functional Connectivity of Key Thalamic Arousal Nuclei

Kristin E. Wills [1,2], Hernán F.J. González [2,3], Graham W. Johnson [2,3], Victoria L. Morgan, PhD [2,3,4], Saramati Narasimhan, PhD [1,2], Dario J. Englot, MD, PhD [1,2,3,4,5]

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While temporal lobe epilepsy (TLE) is a focal epilepsy, it has been shown to cause widespread brain-network disruptions. Impaired visuospatial attention and learning in TLE may depend on connections between thalamic arousal nuclei and posterior quadrant. We have shown that TLE patients demonstrate loss of normal negative connectivity between central lateral (CL) thalamic nucleus and medial occipital-lobe, but CL connectivity may improve after epilepsy surgery. While others have shown pulvinar connectivity disturbances in TLE, it is incompletely understood how TLE affects pulvinar subnuclei, or postoperative functional connectivity. Now, we seek to differentiate effects of TLE on functional connectivity of two key thalamic arousal nuclei: lateral pulvinar (PuL) and CL. We evaluated resting-state functional connectivity of PuL and CL in 40 TLE patients and 40 controls using fMRI. In 25 patients, postoperative imaging (>1 year) was compared with preoperative images. TLE patients exhibited loss of normal positive connectivity between PuL and lateral occipital-lobe ($p<0.01$, paired t-test), compared to a loss of normal negative connectivity between CL and medial occipital-lobe ($p<0.01$, paired t-test). After surgery, patient's connectivity between PuL and lateral occipital-lobe remains abnormal ($p<0.01$, ANOVA). However, postoperative connectivity between CL and medial occipital-lobe improves towards controls ($p>0.05$, ANOVA, post-hoc Fischer's LSD). More abnormal connectivity between PuL and whole brain was associated with worse preoperative Continuous Visual Memory Test Learning scores ($p<0.05$, $r=0.44$, Pearson's r). Thalamic arousal nuclei exhibit abnormal connectivity with occipital-lobe in TLE; only some connections may improve after surgery. Studying thalamic arousal centers may help explain distal network disturbances in TLE.

10. Optimization of k-means clustering on quantitative susceptibility mapping images to validate automatic thalamic nuclei segmentation

Srijata Chakravorti (a), Paula Trujillo (b), Daniel O. Claassen (b) and Benoit M. Dawant (a)

(a) Electrical Engineering and Computer Science, Vanderbilt University (b) Neurology, Vanderbilt University Medical Center

Development of robust methods for intrathalamic nuclei segmentation is critical to support studies on neuropathology as well as for surgical planning. Recently, a shape model based method has been proposed to segment intrathalamic nuclei based on 7T MRI images. Current literature suggests that QSM, which is a relatively novel MRI technique, can be used to identify certain thalamic substructures as well. In this study, we use the heterogeneity in magnetic susceptibility values in QSM to identify natural intrathalamic structures and find the automatically segmented nuclei that most closely align with them - specifically the medial and the pulvinar groups. This provides a validation of our segmentation technique, as well as an insight into differential iron deposition in the thalamus. Our findings confirm that QSM image features can potentially guide automatic intrathalamic segmentation, and highlight the necessity for further studies on iron deposition in individual nuclei.

11. Identification of Epileptogenic Zones Using Directed Network Properties in Resting-State SEEG

Saramati Narasimhan [1,2,3], Keshav B. Kundassery [1], Kanupriya Gupta [1,2], Graham W. Johnson [2,3], Kristin E. Wills [1,2], John D. Rolston [4], Robert P. Naftel [1], Victoria L. Morgan [1,2,3,5], Benoit M. Dawant [3,6], Hernán F.J. González [2,3], Dario J. Englot [1,2,3,5,6]

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Introduction: In medically-refractory focal epilepsy patients, stereotactic-electroencephalography (SEEG) can aid in localizing epileptogenic regions for surgical treatment. However, SEEG requires long hospitalizations to record seizures. Our prior work showed that resting-state analyses may identify brain regions as epileptogenic or non-involved. Our objective is to distinguish between four categories of epileptogenicity using resting-state SEEG directional connectivity.

Methods: In 25 focal epilepsy patients who underwent SEEG, two-minutes of resting-state, artifact-free, SEEG data were selected per patient and functional connectivity was estimated. Using standard clinical interpretation, regions (14.3±4.7) were classified into one of four categories: ictogenic, early-propagation, irritative, or none. Three non-directional measures (between- and within-region imaginary coherence, and mutual information (MI)) and two directional measures (partial directed coherence (PDC) and directed transfer function (DTF)) were calculated. Linear regression was used to combine the five metrics into a predictive model of ictogenic regions.

Results: Ictogenic regions had the highest MI strength and uninvolved regions had the lowest. While both PDC and DTF inward strengths were highest in ictogenic regions, outward strengths did not differ among categories. Area under the curve (AUC) values of non-directional measures were 0.63-0.77. The AUC values for PDC and DTF were 0.84 and 0.73 respectively, and the model AUC was 0.88.

Conclusions: Our results are among the first demonstrating ictogenic regions having markedly increased inward directional connectivity relative to other regions during resting-state. These analyses were performed using resting-state SEEG data without ictal recordings. If validated, these methods may improve epileptogenic region identification and reduce patient length-of-stay for SEEG.

12. Visualization of changes in cutaneous microvasculature after hematopoietic cell transplantation by noninvasive reflectance confocal video microscopy

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Acute graft versus host disease (aGVHD), a common and potentially deadly complication after hematopoietic cell transplantation (HCT), is difficult to diagnose with traditional clinical and histopathologic examination. Through noninvasive imaging of immune cells of patients post-HCT, we characterized differences in microvasculature among patients with cutaneous acute graft-versus-host disease compared to post-HCT patients without any organ aGVHD. We present parameters characteristic of individual cell motion within upper dermal capillaries, which could enable noninvasive tracking of disease development. We used a clinical reflectance confocal microscope, the Vivascope 1500 (Caliber I.D., Rochester, NY), to image left volar forearm upper dermal capillaries of five cutaneous aGVHD patients and five post-HCT control patients. We analyzed capillary density and size, and the number and size of paused (temporarily stopping) leukocytes. Patients were similarly distributed in terms of gender, age, days post-HCT, and underlying disease. We found an increased number of paused (3 vs. 1) leukocytes in aGVHD patients compared to post-HCT controls. The average time of a leukocyte being paused was higher in aGVHD patients (6 ± 8 seconds) than post-HCT controls (2 ± 3 seconds). The size of paused leukocytes was greater in aGVHD patients (9 ± 2 μm) compared to controls (6 ± 4 μm). Capillary size (8 ± 2 vs. 8 ± 2 μm) and density (4 ± 1 vs. 3 ± 2 capillaries) were similar among both groups. We characterized human skin capillaries through six microvascular parameters. In similar sized capillaries, the size of paused leukocytes was larger in aGVHD patients.

13. Deep-Learning Based Automated Instument-Tracking and Adaptive-Sampling for 4D Ophthalmic Surgical Guidance

Eric M. Tang - BME **Mohamed T. El-Haddad** - BME **Joseph D. Malone** - BME
Yuankai K. Tao - BME

Intraoperative optical coherence tomography (iOCT) enables real-time visualization of ophthalmic surgical maneuvers and has been shown to guide decision-making in the operating room. Clinical adoption of iOCT is impeded by relatively slow imaging speeds over static field-of-views (FOVs). Alignment of OCT imaging to surgical regions-of-interest is complex and requires real-time tracking of instrument motions during surgery. Previous studies have demonstrated 3D instrument-tracking, but are limited to the anterior segment and by OCT acquisition speeds. Here, we demonstrate deep-learning based automated instrument-tracking and adaptive-sampling for 4D guidance of ophthalmic surgical maneuvers. Volumetric imaging is performed using spectrally encoded coherence tomography and reflectometry (SECTR), which provides simultaneous en face spectrally encoded reflectometry (SER) and cross-sectional OCT images. A GPU-accelerated convolutional neural network (CNN) was trained to detect and localize 25G internal limiting membrane forceps in SER images. Bounding box outputs produced by the CNN were used to track the surgical instrument and densely sample the instrument tip by dynamically modifying galvanometer scanning.

This work was partially supported by Career Development Award Number IK2 CX001785 from the United States Department of Veterans Affairs Clinical Sciences R&D (CSRD) Service, and the National Institutes of Health Grant K12 CA090625.

14. Eyes in Ears: A Miniature Steerable Digital Endoscope for Trans-Nasal Diagnosis of Middle Ear Disease

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We propose a new type of miniature steerable endoscope that is small enough to pass through the Eustachian tube to survey and diagnose middle ear disease. The distal section of the endoscope features a steerable tip that carries a complementary metal-oxide semiconductor (CMOS) image sensor and fiber-optic illumination to provide high-resolution visualization of critical middle ear structures with unprecedented quality. The motivation for this work comes from the high incidence of middle ear disease, and the current reliance on invasive surgery to diagnose these diseases which typically consists of the eardrum being lifted surgically to directly visualize the middle ear using a trans-canal approach. The miniature endoscope that we present in this paper would enable physicians to diagnose middle ear disease using a trans-nasal approach instead, enabling such procedures to be performed non-surgically in an office setting and greatly reducing the trauma endured by the patient. In this work we present a framework for computational design of the steerable tip based on computed tomography models of real human middle ear anatomy. We use this framework to design and fabricate the miniature steerable endoscope and an ergonomic user interface that allows a physician to control the insertion, rotation, and deflection of the steerable camera tip. We conclude with a pilot study of the steerable endoscope in three cadaveric temporal bone specimens, demonstrating that the scope can be used to survey critical features in the middle ear where disease is likely to occur.

15. Metal Artifact Reduction And Intra Cochlear Anatomy Segmentation In CT Images Of The Ear With A Multi-Resolution Multi-Task 3d Network

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Segmenting the intra-cochlear anatomy structures (ICAs) in post-implantation CT (Post-CT) images of the cochlear implant (CI) recipients is challenging due to the strong artifacts produced by the metallic CI electrodes. We propose a multi-resolution multi-task deep network which synthesizes an artifact-free image and segments the ICAs in the Post-CT images simultaneously. The output size of the synthesis branch is 1/64 of that of the segmentation branch. This reduces the number of parameters of the model and the memory usage for training, while generate segmentation labels of high resolution. In this preliminary study, we use the segmentation results of an automatic method as the ground truth to provide supervision to train our model, and we achieve median Dice index value of 0.792. Our experiments also confirm the usefulness of the multi-task learning.

16. An Improved Training Scheme for Deep Neural Network Ultrasound Beamforming

Emelina Vienneau, Adam Luchies, Brett Byram

Department of Biomedical Engineering

Feed-forward neural networks can approximate any continuous function through nonlinear transformations, making them a powerful tool for image reconstruction tasks such as ultrasound beamforming that can be cast as such. Deep neural networks (DNNs) have shown great efficacy in adaptive beamforming by successfully suppressing sources of acoustic clutter such as off-axis scattering in challenging imaging scenarios. However, our previous work in this area has been limited by the difficulty of model selection. When training with traditional L1 or mean squared error (MSE) loss functions, we have observed a consistent trend that lower loss upon convergence does not necessarily lead to higher image quality metrics such as contrast-to-noise ratio (CNR), signal-to-noise ratio (SNR), and contrast ratio (CR) reconstruction accuracy. This phenomenon motivated the creation of a new ultrasound-specific loss function. Advanced optimization techniques were also utilized for increased robustness and more reliable convergence.

17. Overview of the Brain Imaging and Electrophysiology Network (BIEN) Lab

Keshav B. Kundassery [1], Hernán F.J. González [2,4], Graham W. Johnson [2,4], Kristin E. Wills [1,4], Saramati Narasimhan, PhD [1,4], Dario J. Englot, MD, PhD [1,2,3,4,5]

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Background: Epilepsy is a debilitating disorder, affecting over three-million individuals in the United States. Drugs can control seizure frequency, but some epilepsy is medically resistant. Surgery may be pursued if the epilepsy is localized to a focal region that can be resected. For these patients, which our lab focuses on, modalities like functional MRI (fMRI) and stereo-electroencephalography (SEEG) are used for surgical planning.
Objective: Our lab seeks to inform epilepsy treatment by understanding network perturbations. SEEG is used to localize epileptogenic brain regions during seizures. The objective of our SEEG work is to develop a model to glean such information from resting-state data. Our fMRI studies intend to develop an understanding of network abnormalities in focal epilepsy. Moreover, we investigate what network changes are associated with postoperative seizure outcomes.
Methods: Our lab uses two main modalities to study these objectives: fMRI and SEEG. Our fMRI studies evaluate undirected connectivity in patients, comparing regional connectivity measures to matched controls. We also compare patients before and after successful surgery to study how brain networks are modified. Our SEEG work utilizes segments of resting-state data from patients, analyzed with undirected and directed network measures.
Conclusions: Our fMRI research has elucidated aberrations in connectivity of subcortical arousal structures in focal epilepsy patients. This supports the extended network-inhibition hypothesis, which suggests that brainstem, diencephalic, and basal forebrain disruptions may contribute to broader negative network effects in epilepsy patients. Furthermore, our SEEG work has demonstrated a relationship between both undirected/directed connectivity and epileptogenicity of brain areas.

18. Optimal Bending Rigidity of Aortic Valve Based on Computational Fluid-Structure Interaction

Ye Chen, Department of Mechanical Engineering **Haoxiang Luo**, Department of Mechanical Engineering

Proper bending stiffness and the ability to quickly respond to the dynamic pressure load on their surfaces are critical for the heart valves to carry out their physiological functions. Studies on how the flexibility of the leaflets affects the fluid-structure interaction (FSI) of heart valves are still very limited. In this work, three-dimensional FSI simulations of a bioprosthetic aortic valve are performed using a parallelized immersed-boundary method. The pressure distribution over the leaflets and transient force on the valve are calculated. The thickness of the leaflets is varied from 0.1 mm to 0.8 mm, which covers a wide range of non-dimensional bending rigidity EB*, normalized by the transvalvular pressure gradient. For valves with low bending rigidity (EB* around 1.0E-2), the valve functions normally and produces physiological characteristics of healthy valves. However, exceedingly low rigidity (for example, EB* = 1.2E-3) leads to flapping motion of the leaflets and impairs the valve's performance. Stiffer valves (EB* greater than 0.2) are more difficult to open and slower to close, which leads to higher resistance and a reduced flow rate during systole. The results reveal the existence of an optimal range of bending rigidity for the valve, where EB* is roughly between 0.003 and 0.04. Effects of bending rigidity on valve deformation and flow characteristics will also be discussed.

19. Towards Semi-Automated Mechanical Thrombectomy: Path Planning Considerations for a Double Articulated Microcatheter

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Stroke is the third leading cause of death in the world. Recent studies have demonstrated that mechanical thrombectomy, the endovascular retrieval of blood clots with a stent retriever or aspiration force, achieves superior clinical outcome for patients with large vessel occlusions (LVOs). The recent awareness to the importance of early revascularization via mechanical thrombectomy stands in contrast to the current availability of this intervention. Widespread adoption is partly hindered by its technical complexity. Due to the lack of distal control in existing catheters, neurointerventionalists rely on the use of a passive guidewire and a complex combination of stacked catheters to navigate to the occlusion site. This preliminary work investigates the feasibility of using a 0.88 mm double articulated robotic microcatheter to navigate the Internal Carotid Artery, a common site of LVO. We derive the kinematics of this robotic microcatheter using image-based calibration. We propose the use of pre-operative CT scans for trajectory planning, and a least squares algorithm to minimize the shape error between the catheter and the vasculature. Finally, we evaluate the feasibility of using intraoperative imaging (bi-plane fluoroscopy) to update the pre-operative plan and track the pose of the microcatheter. This pipeline was evaluated in a simulation study and on a planar bifurcation model. The results from this investigation will be used to optimize the design of dexterous steerable catheters that eliminate the need for use of a guidewire and facilitate future robot-assisted thrombectomy.

20. Insertion Depth for Optimized Positioning of Pre-Curved Cochlear Implant Electrodes

Rueben Banalagay - EECS **Robert Labadie** - Otolaryngology **Srijata Chakravorti** - EECS **Jack Noble** - EECS

Hypothesis: Generic guidelines for insertion depth of pre-curved electrodes are sub-optimal for many individuals.
Background: Insertion depths that are too shallow result in decreased cochlear coverage, and ones that are too deep lift electrodes away from the modiolus and degrade the electro-neural interface. Guidelines for insertion depth are generically applied to all individuals using insertion depth markers on the array that can be referenced against anatomical landmarks.
Methods: To normalize our measurements, we determined the optimal position and insertion vector where a pre-curved array best fits the cochlea for each patient in an IRB approved, N=131 subject CT database. The distances from the most basal electrode on an optimally placed array to anatomical landmarks, including the round window (RW) and facial recess (FR), was measured for all patients.
Results: The standard deviations of the distance from the most basal electrode to the FR and RW are 0.65mm and 0.26 mm, respectively. Due to the high variability in FR distance, using the FR as a landmark to determine insertion depth results in 0.5mm difference with ideal depth in 44% of cases. Alignment of either of the two most proximal RW markers with the RW would result in over-insertion failures for 80% of cases, whereas the use of the third, most medial marker would result in under-insertion in only 19% of cases.
Conclusions: Normalized measurements using the optimized insertion vector show low variance in distance from the basal electrode position to the RW, thereby suggesting it as a better landmark for determining insertion depth than the FR.

21. Image Quality in Transcranial Ultrasound Imaging

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Temporal and spatial coherence are useful tools to isolate different signals of image degradation when imaging in the transcranial cavity. Acoustic clutter and thermal noise are major contributors to image degradation inside the transcranial cavity as the skull tissue both creates an environment that promote clutter and leads to a decreased signal strength, which causes the drowning out of tissue signals by thermal noise. As only certain signal types are coherent in the temporal and spatial domain, a system of equations was able to be derived to isolate out the signal power of tissue, acoustic clutter, and thermal noise individually. Through the application of these filters to ultrasound images of the transcranial cavity, there is shown to be high levels of acoustic clutter near the surface, which decreases in strength with depth; the noise is shown to act opposite, having a weaker signal near the surface but increasing with depth. Signal to noise, signal to clutter, and signal to interference ratios are able to be found while using these filters. Application of these metrics can be used to better modify transcranial imaging techniques to better isolate tissue signals.

22. Hybrid Control and Palpation Assistance for Situational Awareness in Telemanipulated Task Execution

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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.

23. Joint-Level Force Sensing for Indirect Force Control of Continuum Robots With Friction

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Continuum robots offer the dexterity and obstacle circumvention capabilities necessary to enable surgery in deep surgical sites. They also can enable joint-level ex-situ force sensing (JEFS), which provides an estimate of end-effector forces given joint-level forces. In this work, we overcome limitations in modeling assumptions of prior art by cancelling frictional losses with a feed-forward term based on support-vector regression in joint space with new hysteresis-capturing features. Residual joint-force errors are further minimized using a least-squares model parameter update. An indirect hybrid force/position controller using JEFS is presented with evaluation carried out on a realistic pre-clinically deployable insertable robotic effectors platform (IREP) for single port access surgery. Automated mock force-controlled ablation, exploration, and knot tightening are evaluated. A user study involving the daVinci Research Kit surgeon console and the IREP as a surgical slave is carried out to compare the performance of users with and without force feedback based on JEFS for force-controlled ablation and knot tightening. Results in automated experiments and a user study of telemanipulated experiments suggest that intrinsic force-sensing can achieve levels of force uncertainty and force regulation errors on the order of 0.2N. Using JEFS and automated task execution, repeatability and force regulation accuracy is shown to be comparable to using a commercial force sensor for human-in-the-loop feedback.

24. Cochlear implant electrode sequence optimization using patient specific neural stimulation models

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Cochlear implants (CIs) use an array of electrodes implanted in the cochlea to directly stimulate the auditory nerve. After surgery, CI recipients undergo many programming sessions with an audiologist who adjusts CI processor settings to improve performance. However, few tools exist to help audiologists know what settings will lead to better performance. In this paper, we propose a new method to assist audiologists by determining a customized firing order of the electrodes on the array using image-based models of patient specific neural stimulation patterns. Our models permit estimating the time delay needed after firing an electrode so that the nerve fibers they stimulate can recover from the refractory period. These predictions allow us to design an optimization algorithm that determines a customized electrode firing order that minimizes negative effects of overlapping stimulation between electrodes. The customized order reduces how often nerves that are in a refractory state from previous stimulation by one electrode are targeted for activation by a subsequent electrode in the sequence. Our experiments show that this method is able to reduce the theoretical stimulation overlap artifacts and could lead to improved hearing outcomes for CI recipients.

25. Resting State Functional Connectivity Between Hippocampi and Language Cortex Reveals Distinct Patterns in Temporal Lobe Epilepsy

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Language deficits are extremely common in temporal lobe epilepsy (TLE) patients due to repeated seizures that damage the language cortex, as well as surgical intervention that often causes further language impairments. Consequently, measures that could predict whether a patient will have a poor language outcome following surgery are urgently needed. The present study measured functional connectivity of the bilateral hippocampi to language cortex to noninvasively assess plasticity and reorganization of connectivity patterns, with the long-term goal to use this method to predict language deficits following surgery. Presurgical resting state 3T fMRI data (TR: 2 s, total duration: 10 mins, voxel size: 3 x 3 x 4 mm3) was acquired from 27 patients with right TLE (M: 39.44 years, SD: 10.52), 13 patients with left TLE (M: 37.2 years, SD: 15.23), and 54 healthy controls (M: 37.00 years, SD: 13.78). We found that unique functional connectivity patterns from anterior hippocampi to temporo-parietal language regions close to the seizure foci differentiated patients whose seizures originate in the left vs. right hippocampus, and these patterns showed significant associations with language abilities. This work suggests that functional connectivity from the bilateral hippocampi to language cortex can be used to understand presurgical organization and current language abilities, and these relationships may be robust enough to predict postsurgical outcomes using resting state presurgical scans. Work is currently ongoing to collect longitudinal data from these patients to assess the prediction of postsurgical language outcomes, and/or whether specific patterns of reorganization lead to better language outcomes.

26. Preoperative prediction of insertion depth of lateral wall cochlear implant electrode arrays

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Cochlear implants (CI) use an array of electrodes surgically threaded into the cochlea to restore hearing sensation. Techniques for predicting the insertion depth of the array into the cochlea could guide surgeons towards the more optimal placement of the array in order to reduce trauma and preserve the residual hearing. In addition to the electrode array geometry, the base insertion depth (BID) and the cochlear scale could impact the overall array insertion depth. In this paper, we investigated using these measurements to develop a model which can make preoperative or intraoperative predictions of insertion depth of lateral wall cochlear implant electrodes. CT images of 86 CI recipients were analyzed. Using previously developed automated algorithms, the relative electrode position inside the cochlea was measured from the CT images. A linear regression model is proposed for insertion depth prediction based on cochlear size, array geometry, and BID. The model is able to accurately predict angular insertion depths with a standard deviation of 41 degrees. Surgeons may use this model for the patient-customized selection of the electrode array and/or to plan a base insertion depth for a given array that minimizes the likelihood of causing trauma to regions of the cochlea where residual hearing exists.

27. Toward Clinical Deployment of Magnetically Steered Robotic Insertion of Cochlear-Implant Electrode Arrays

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Cochlear-implant electrode arrays (EAs) must be inserted accurately and precisely to avoid damaging the delicate anatomical structures of the inner ear. It has previously been shown on the benchtop that using magnetic fields to steer magnet-tipped EAs during insertion reduces insertion forces, which correlate with insertion errors and damage to internal cochlear structures. We present several advancements toward the goal of deploying magnetic steering of cochlear-implant EAs in the operating room. In particular, we integrate image guidance with patient-specific insertion vectors, we incorporate a new non-magnetic insertion tool, and we use an electromagnetic source, which provides programmable control over the generated field. The electromagnet is safer than prior permanent-magnet approaches in two ways: it eliminates motion of the field source relative to the patient's head and creates a field-free source in the power-off state. Using this system, we demonstrate system feasibility by magnetically steering EAs into cadaver cochleas for the first time. We show that magnetic steering decreases average insertion forces, in comparison to manual insertions and to image-guided robotic insertions alone.

28. Combining Model- and Deep-Learning-Based Methods for the Accurate and Robust Segmentation of the Intra-Cochlear Anatomy in Clinical Head CT Images

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Cochlear implants (CIs) are neuroprosthetic devices that can improve hearing in patients with severe-to-profound hearing loss. Postoperatively, a CI device needs to be programmed by an audiologist to determine parameter settings that lead to the best outcomes. Recently, our group has developed an image-guided cochlear implant programming (IGCIP) system to simplify the traditionally tedious post-programming procedure and improve hearing outcomes. IGCIP requires image processing techniques to analyze the location of inserted electrode arrays (EAs) with respect to the intra-cochlear anatomy (ICA), and robust and accurate segmentation methods for the ICA are a critical step in the process. We have proposed active shape model (ASM)-based method and deep learning (DL)-based method for this task, and we have observed that DL methods tend to be more accurate than ASM methods while ASM methods tend to be more robust. In this work, we propose a U-Net-like architecture that incorporates ASM segmentation into the network so that it can refine the provided ASM segmentation based on the CT intensity image. Results we have obtained show that the proposed method can achieve the same segmentation accuracy as that of the DL-based method and the same robustness as that of the ASM-based method.

29. Exceeding Traditional Curvature Limits of Concentric Tube Robots Through Redundancy Resolution

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Understanding elastic instability has been a recent focus of concentric tube robot research. Modeling advances have enabled prediction of when instabilities will occur and produced metrics for the stability of the robot during use. In this work, we show how these metrics can be used to resolve redundancy to avoid elastic instability, opening the door for the practical use of higher curvature designs than have previously been possible. We demonstrate the effectiveness of the approach using a three-tube robot that is stabilized by redundancy resolution when following trajectories that would otherwise result in elastic instabilities. We also show that it is stabilized when teleoperated in ways that otherwise produce elastic instabilities. Lastly, we show that the redundancy resolution framework presented here can be applied to other control objectives useful for surgical robots, such as maximizing or minimizing compliance in desired directions.

30. Continuum Robots with Equilibrium Modulation: Feasibility of High-Resolution 3D OCT Imaging

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Continuum Robots (CR) have enabled dexterous access for surgical interventions for tasks requiring dexterity at a macro-scale resolution, with the finest resolution in sub-millimetric motion. However, there are a host of tasks requiring micro-scale motion such as micro-vascular reconstruction and image-based biopsy or confocal endo-microscopic imaging. Recently, a new concept of micro/macro motion generation using CR with equilibrium modulation (CREM) was presented by our group. According to this design concept, macro-motion is achieved by pushing and pulling on tubular backbones. Micro-motion is achieved by sliding equilibrium modulation wires inside the backbones, thereby, shifting the static equilibrium pose of the robot (equilibrium modulation). In addition to modeling the micro-motion kinematics for these robots, we have integrated a custom B-mode optical coherence tomography (OCT) probe modified and demonstrated the ability of CREM to use micro-motion to construct high fidelity 3D OCT scans. This preliminary work has demonstrated the feasibility of 3D OCT using CREM and showed that 3D scans with a separation of 1 micron between scan planes are possible. We present a proof-of-concept system using an external OCT probe and the first attempt of an integrated OCT probe on the CR for closed-loop OCT-guided control.

31. Diagnostic Potential of Five Different Biomechanical Parameters to Detect Sclerotic Cutaneous Graft-Versus-Host Disease

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INTRODUCTION Skin sclerosis is a significant cause of morbidity in chronic graft-versus-host disease (cGVHD). There is an urgent need to develop objective measures of sclerosis to enable accurate monitoring of disease. The Myoton device can measure five biomechanical parameters in soft tissue: stiffness, relaxation time, oscillation frequency, logarithmic decrement, and creep. Here, we report the ability to differentiate sclerotic from unaffected post-transplant skin for all five available biomechanical parameters.

METHODS Sclerotic cGVHD patients (n=13), post-transplant controls (n=10), and healthy controls (n=14) were measured with the Myoton on 10 bilateral sites (shin, dorsal forearm, volar forearm, upper arm, shoulder, chest, abdomen, upper back, lower back, calf). For each parameter, the overall value per subject was calculated as the average over all 20 measurement sites. We performed receiver operating characteristic (ROC) and area under the curve (AUC) analyses to compare the diagnostic sensitivity of these parameters. **RESULTS** Sclerotic cGVHD patients showed significant increases ($p<0.05$) in stiffness and frequency and decreases ($p<0.05$) in relaxation time compared to controls. The ROC and AUC analyses revealed that the overall frequency (sensitivity: 91%; specificity: 93%; AUC: 0.92), stiffness (sensitivity: 91%; specificity: 93%; AUC: 0.92), and relaxation time (sensitivity: 100%; specificity: 82%; AUC: 0.85) allow for high accuracy in the differentiation of sclerotic patients from post-transplant controls.

CONCLUSIONS Frequency, stiffness and relaxation time of skin demonstrated high accuracy in the differentiation of sclerotic GVHD patients from post-transplant controls. Larger study is needed to develop a multivariate predictive model based on combinations of highly discriminatory sites and parameters.

32. Reproducibility of the Myoton and durometer devices to quantify skin stiffness and hardness in sclerotic chronic graft-versus-host disease

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INTRODUCTION Skin is the most commonly involved organ in chronic graft-versus-host disease (cGVHD). Sclerosis is a common manifestation associated with significant morbidity, but there is an unmet need for quantitatively measuring sclerosis to track the progression of disease. Myoton and durometer are two candidate technologies to measure skin biomechanical properties. However, the reproducibility of these devices in sclerotic cGVHD is critical missing information in designing longitudinal studies measuring sclerosis in cGVHD patients.

METHODS Seven sclerotic cGVHD patients were measured by three observers with the Myoton and durometer on 10 body sites. Intraclass correlation coefficients (ICC) and minimal detectable change (MDC95) were used to estimate clinical repeatability to differentiate amongst patients. Mean coefficient of variation was calculated to estimate device repeatability within patients.

RESULTS Patient overall hardness/stiffness interobserver ICCs were 0.92 [95% confidence interval 0.82 - 1.00] for Myoton and 0.82 [0.61 - 1.00] for durometry. The Myoton had superior reproducibility to durometry in calves and upper arms, but was inferior in the dorsal forearms. Coefficients of variation across observers were under 10% and the overall normalized MDC95 was 22 to 23% for both devices.

CONCLUSION Both devices exhibit high reproducibility in sclerotic cutaneous cGVHD, and the Myoton trended towards higher reproducibility when compared to the durometer. The interobserver ICCs of both devices is significantly higher than the typical range of ICCs (0.21-0.60) associated with clinical exam-based measurement of moveable sclerosis. Prospective longitudinal study is warranted to validate the use of skin stiffness measurements to monitor disease progression and treatment response.

33. Improving Non-Contrast Perfusion Ultrasound Imaging for Early Assessment of Trans-arterial Chemoembolization

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Transarterial chemoembolization (TACE) is an important yet variably effective treatment for management of hepatic malignancies. Lack of response can be in part due to inability to assess treatment adequacy in real-time. Gold-standard contrast enhanced computed tomography and magnetic resonance imaging, although effective, suffer from treatment-induced artifacts that prevent early treatment evaluation. Non-contrast ultrasound is a potential solution but has historically been ineffective at detecting treatment response. Here, we propose non-contrast ultrasound with recent perfusion-focused advancements as a tool for immediate evaluation of TACE. We demonstrate initial feasibility in an 11-subject pilot study. Treatment-induced changes in tumor perfusion are detected best when combining adaptive demodulation (AD) and singular value decomposition (SVD) techniques. Using a 0.5s (300-sample) ensemble size, AD+SVD resulted in a 7.42dB median decrease in tumor power after TACE compared to only a 0.06dB median decrease with conventional methods.

34. Input Domain Comparison for Deep Neural Network Ultrasound Beamforming

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Ultrasound B-mode imaging remains an invaluable tool for clinicians because it is real-time, cost-effective, and portable. However, poor image quality can make diagnostic and guidance tasks with ultrasound unreliable. We previously showed that deep neural network (DNN) ultrasound beamforming can improve image quality compared to conventional delay-and-sum (DAS). Our DNN implementation operates on raw channel data in the frequency domain. Although time domain implementations have been pursued by others, it is assumed that networks trained on individual frequencies, albeit more computationally complex, will be more robust to varying pulse shapes due to phenomena like depth dependent attenuation. However, this assumption has not been thoroughly investigated nor have frequency and time domain implementations been directly compared. We address this by comparing our frequency domain implementation to different time domain implementations, namely in-phase quadrature (IQ), analytic, and radio frequency (RF). Training data were generated from simulated anechoic cysts. Test data were generated from simulated a nechoic cysts with fixed SNR, varied SNR, and varied pulse shapes in addition to physical phantom data. Although more variable, optimal IQ and analytic time domain networks demonstrate comparable performance to optimal frequency domain networks across all test cases. Additionally, analytic, RF, and frequency domain implementations achieve overall higher image quality metrics when multiple depths or frequencies are used as input to a single network. Our findings suggest that time domain and multiple input implementations are more robust than previously assumed and, as they are less computationally complex, could be better suited for real-time clinical or commercial applications.

35. A Weakly Supervised Approach for the Segmentation of Skin Lesions in Chronic Graft Versus Host Disease

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Chronic graft-versus-host-disease (cGVHD) is a common occurrence after hematopoietic stem cell transplantation (HCT). The symptoms typically occur 100 days after the transplant and the primary affected organ is skin. The common forms of skin cGVHD are erythema, hyperpigmentation and hypopigmentation. The extent of the disease is measured in terms of affected body surface area (BSA) by an expert dermatologist. An automatic image segmentation algorithm would allow a convenient assessment of the BSA in clinics where there is a scarcity of expert dermatologists. However, the current deep learning algorithms which are dominating the field of semantic segmentation requires a large amount of annotated data. It is difficult to collect pixel-level annotations from experts for two reasons, 1) it is time-consuming, 2) there is inter-rater variability in the case of pixel-level annotations. An image could be cropped into patches and a patch level annotation scheme would significantly reduce annotation time. We propose a weakly supervised segmentation (WSS) approach which can perform image segmentation using the patch level information. The solution involves training a convolutional neural network classifier and extracting the class activation maps (CAM) of the trained network using Gradient-weighted Class Activation Mapping (Grad-CAM). We test our algorithm on images of skin cGVHD acquired from patients using a commercial stereoscopic Vectra H1 camera. The camera captures 3D cross-polarized photos which are exported to 2D images. The experiment shows that the class activation maps focus on the affected body surface area.

36. An Integrated Multi-Physics Finite Element Modeling Framework for Deep Brain Stimulation: Preliminary Study on Impact of Brain Shift on Neuronal Pathways

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Deep brain stimulation (DBS) is an effective therapy for movement disorders. The efficacy of DBS depends on electrode placement accuracy and programming parameter optimization to modulate desired neuron groups and pathways. Compounding the challenge of surgical targeting and therapy delivery is brain shift during DBS burr hole surgery. Brain shift introduces potentially significant misalignment between intraoperative anatomy and preoperative imaging data used for surgical planning and targeting. Brain shift may also impact the volume of tissue activation (VTA) and consequently neuronal pathway recruitment for modulation. This work introduces an integrated framework of patient specific biomechanical and bioelectric models to account for brain shift and examines its impact on DBS delivery. Specifically, the biomechanical model was employed to predict brain shift via an inverse problem approach, which was driven by sparse data derived from interventional magnetic resonance (iMR) imaging data. A bioelectric model consisting of standard conductive physics was employed to predict electric potential maps in the presence of the deformed patient anatomy. The electrode leads for creating the potential maps were reconstructed from iMR visualized trajectory and a known lead model geometry. From the electric potential distribution, the VTA was estimated. In an effort to understand changes to neuronal pathway recruitment, the model displacement field was used to estimate shift impact on the VTA intraoperatively. Finally, VTAs in patient space with and without shift consideration were transformed to an atlas available via the Human Connectome Project where tractography was performed. This enabled the observation and comparison of neuronal pathway recruitment due to VTA distributions with and without shift considerations. Preliminary results using this framework in 2 patients indicate that brain shift impacts the extent, number, and volume of neuronal pathways affected by DBS. Hence consideration of brain shift in DBS burr hole surgery is desired to optimize outcome.

37. Engineering in Surgery an Intervention: A Novel Program in Clinical Immersion for Procedural Medicine

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Over the past 4 decades at Vanderbilt, research among the domains of surgery, intervention, and engineering has generated novel surgical/interventional technologies to improve treatment and advance discovery. From the development of the theory of error associated with image guided surgery, to the invention of new approaches to cochlear implant and programming, or to novel non-contrast interventional ultrasound imaging advances, a multitude of research programs at Vanderbilt targeted at clinical translational engineering/science has developed over this period. Recently, a novel NIH-funded training program (T32EB021937) has been created to codify this past training framework of clinical exposure into an educational paradigm emphasizing 'real domain experiences'. The hypothesis of this work is that highly trained engineers intimately familiar with human disease and treatment, and trained in the inception of novel technology-based platforms, are required for resolving the bottlenecks in clinical research. It is further hypothesized that continued scientific discoveries within the human environment as well as the future of novel treatment approaches are highly dependent on these technology-based instrumentation platforms. To begin to answer this hypothesis, a self-reporting survey was developed to assess the value of this novel immersion program. Three years of trainees (n=13) have completed the core training and results are reported. Perceived improvement in twelve areas before and after core course completion was determined. Some of the more salient foci surveyed were: (1) understanding of procedural medicine, (2) education level in surgical technologies, (3) education in translational clinical research, (4) understanding of clinical specialty, (5) perceived importance of procedural observation to your research, (6) ability to pose questions that affect human health, and (7) perception of the need for research in procedural medicine. Based on self-reporting, the student evaluation of the program is that it is of high learning value. The two largest changes assessed by students were the understanding of the clinical specialty they observed, and the perceived importance of procedural observation to their research.

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38. Block-wise Independent Component Analysis for Slow Flow Non-Contrast Ultrasound Imaging

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Slow blood flow imaging has proven to be a difficult clinical problem. Imaging modalities, such as MR Angiography and Contrast-Enhanced Ultrasound, attempting to solve this problem are expensive and time-consuming. Both eigen-based filters and spatial filters have been proposed to improve ultrasound power Doppler blood flow images. Block-wise methods and Independent Component Analysis (ICA) filters have each individually been previously shown to improve tissue clutter and noise s uppression. Here, we aim to develop a Block-wise implementation of ICA to evaluate blood flow in ultrasound blood flow imaging. We show through phantom studies that by applying ICA in a block-wise manner, we see qualitative improvements as compared to other eigen-based filters applied in global and block-wise manners.

39. On-axis acoustic radiation force-based elasticity measurement in homogeneous and layered, skin-mimicking phantoms

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Shear wave elasticity imaging has been difficult in inhomogeneous tissue, such as skin, where thin layers cause bias in shear wave speed estimates. Instead, we propose an FEM-based look-up table to estimate shear modulus at the on-axis location rather than at lateral locations. We estimate the time-to-peak on-axis displacement at each depth and use a look-up table to estimate shear modulus. We generated a stiffness look-up table using a 3D FEM model coupled to Field-II simulations. We simulated shear moduli of 1-13kPa using a CL15-7 transducer, 1.1cm axial push focus, 8.9MHz push frequency, push F/3, 10.4MHz tracking frequency, and plane wave tracking. The displacements were estimated using an advanced Bayesian displacement estimator. Here we test the on-axis stiffness estimates in homogeneous and layered polyvinylalcohol (PVA) phantoms. Before the phantoms were sliced into thin layers, we computed five independent shear wave speeds at the same depth that would be sliced and took the median. After slicing and layering the phantoms, we tested the on-axis method and compared it to shear wave speed-derived shear modulus estimates. The presliced homogeneous PVA phantoms had a mean shear modulus of 5.56+/-0.76kPa and 5.46+1.06kPa for the on-axis method and shear wave speed-derived moduli, respectively. The mean shear moduli for the on-axis method and shear wave speed-derived estimates in the thin layer were 5.92+/- 1.15kPa and 6.50+/-0.31kPa, respectively. The shear wave speed-derived estimates had a bias of -1.04kPa and the on-axis method had a bias of -0.46kPa. The on-axis method had a larger variance in shear modulus estimates, but a smaller bias than shear wave speed-derived estimates.

40. Group discussion improves the inter-rater reliability of adherent and rolling leukocyte assessment via in vivo reflectance confocal video microscopy

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Reflectance confocal microscopy (RCM) enables noninvasive, real-time visualization of human upper dermal microvasculature. We previously described a method to evaluate the number of adherent and rolling leukocytes in human skin via RCM, but the inter-rater reliability remains to be investigated. We used a clinical reflectance confocal microscope (Vivascope 1500) to acquire 88 videos of cutaneous microcirculation at 9 frames per second. Three raters independently determined the number of adherent and rolling leukocytes per video by using previously developed video analysis guidelines. After completing their initial assessments, the raters discussed their discrepancies, updated the guidelines, and independently re-assessed the same 88 videos. We calculated the intraclass correlation coefficient (ICC) for the number of adherent and rolling leukocytes pre- and post-group discussion using the SPSS Statistics software based on a single-rating, absolute-agreement, 2-way random effects model. For the number of adherent leukocytes, inter-rater reliability was higher post-discussion (ICC: 0.705, confidence interval, CI: 0.613, 0.784) than pre-discussion (ICC: 0.003, CI: -0.093, 0.122). Similarly, inter-rater reliability for the number of rolling leukocytes increased post-discussion (ICC: 0.859, CI: 0.807, 0.901), compared to pre-discussion (ICC: 0.516, CI: 0.394, 0.630). As expected, ICC values significantly increased after the group discussion. Given that the post-discussion ICC values are indicative of excellent but not perfect agreement, this suggests that there is inherent ambiguity associated with identification of adherent and rolling leukocytes. The updated guidelines will aid future studies in the evaluation of adherent and rolling leukocytes in human skin vasculature.

41. Influence of physiology and vigilance on fMRI signal fluctuations

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Resting-state functional magnetic resonance imaging (rs-fMRI) provides insight into brain functional organization and the identification of biomarkers in the diagnosis of multiple neurological disorders. Recent research reveals that physiological factors (e.g., respiration) and vigilance states can influence rs-fMRI signals. However, the exact relationship between physiological changes, vigilance, and fMRI signals remains largely unknown. Here, we investigate the contribution of physiological effects to rs-fMRI variations in eye-closed settings across vigilance states, as defined by scalp EEG. We also added pulse wave amplitude (PWA), which quantifies fingertip blood volume, to the (more standard) respiration and cardiac rate factors in our analysis. To test how vigilance states might modulate the relationship between physiological and fMRI signals, we first verified a previously reported effect that fMRI fluctuation amplitude is negatively correlated with levels of EEG alpha-band power, a common indicator of vigilance state. Second, we observed that the introduction of PWA greatly increases the variance explained by physiological factors in multiple fMRI-defined brain networks, particularly the default mode network, the basal ganglia, and the salience network, during states of low vigilance. This finding suggests that the covariation of physiological and fMRI signals is dependent on vigilance state.

42. Multiple Sclerosis Lesion Segmentation with Tiramisu and 2.5D Stacked Slices

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We present a fully convolutional densely connected network (Tiramisu) for multiple sclerosis (MS) lesion segmentation. Different from existing methods, we use stacked slices from all three anatomical planes to achieve a 2.5D method. Individual slices from a given orientation provide global context along the plane and the stack of adjacent slices adds local context. By taking stacked data from three orientations, the network has access to more samples for training and can make more accurate segmentation by combining information of different forms. The conducted experiments demonstrated the competitive performance of our method. For an ablation study, we simulated lesions on healthy controls to generate images with ground truth lesion masks. This experiment confirmed that the use of 2.5D patches, stacked data and the Tiramisu model improve the MS lesion segmentation performance. In addition, we evaluated our approach on the Longitudinal MS Lesion Segmentation Challenge. The overall score of 93.1 placed the L2-loss variant of our method in the first position on the leaderboard, while the focal-loss variant had obtained the best Dice coefficient and lesion-wise true positive rate with 69.3% and 60.2%, respectively.

43. Iterative model-based beamforming for high dynamic range applications

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Adaptive beamforming methods in ultrasound have become increasingly popular in recent years due to increased performance over traditional methods. However, these methods can be subject to sidelobe and dark region artifacts that can hurt performance or create misleading results. These artifacts are especially common in high dynamic range scenarios where acoustically strong targets may obscure nearby weaker targets. Iterative ADMIRE is a model-based adaptive beamformer designed to mitigate both the sidelobe and dark region artifacts, resulting in improved dynamic range. It seeks to iteratively fit sources of clutter and remove them from the input signal, allowing for the weaker acoustic signals to be progressively fit. This results in a more accurate estimate of those weaker signals, mitigating the dark region artifact and providing a more true measure of contrast. Compared to the standard delay-and-sum method as well as several other adaptive beamformers, iterative ADMIRE provides a solution to the dark region artifact problem, as well as improved dynamic range due to sidelobe clutter suppression.

44. A GPU-Based Implementation of ADMIRE

Christopher Khan (Biomedical Engineering), **Kazuyuki Dei** (Biomedical Engineering), **and Brett Byram** (Biomedical Engineering)

Multipath and off-axis scattering are two of the primary mechanisms for ultrasound image degradation. To address their impact, we have proposed Aperture Domain Model Image REconstruction (ADMIRE). This algorithm utilizes a model-based approach in order to identify and suppress sources of acoustic clutter. The ability of ADMIRE to suppress clutter and improve image quality has been demonstrated in previous works, but its use for real-time imaging has been infeasible due to its significant computational requirements. However, in recent years, the use of GPUs for general-purpose computing has enabled significant acceleration of compute-intensive algorithms. This is due to the fact that many modern GPUs have thousands of computational cores that can be utilized to perform massively parallel processing. Therefore, in this work, we have developed a GPU-based implementation of ADMIRE. The computations were distributed across two GPUs, and speedups of almost three orders of magnitude were achieved when compared to a serial CPU implementation. The frame rate depends upon various imaging parameters, and we demonstrate this using a small cyst simulation dataset and a large in-vivo kidney dataset. However, even for the large dataset, the implementation still provides the ability to process multiple frames of data per second. Due to this, it has the capability to serve as a real-time imaging framework.

45. Assessment of Antioxidant Copolymers for Improved Superoxide Scavenging in PTOA

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Post-traumatic osteoarthritis (PTOA) is a degenerative joint disease in joints which have experienced a traumatic injury. As cartilage destruction propagates, the inflammatory environment is exacerbated by high levels of reactive oxygen species (ROS). ROS contribute to disease progression by promoting cellular dysfunction, inflammatory signaling, and biomolecule damage. The goal of this project is to optimize an injectable, ROS-scavenging polymer for intra-articular PTOA therapy. The hydrophobic drug TEMPO is co-polymerized with the hydrophilic spacer molecule, dimethylacrylamide (DMA) at various ratios to tune water solubility and scavenging potential. Characterization by electron spin resonance (ESR) and high-performance liquid chromatography (HPLC) have demonstrated an increase in free radical signal and hydrophobicity as a higher percentage of TEMPO is grafted onto the polymer backbone. In cell-free systems, general antioxidant activity and superoxide scavenging have been optimized at a ratio of 60% DMA and 40% TEMPO. This lead candidate protects ATDC5 chondrocyte-like cells from exogenous superoxide. Additionally, polymerization improves uptake of the drug over the free TEMPO molecule. Future experiments will test the ability of the lead candidate copolymer to suppress oxidative stress and inflammatory markers in a mouse model of localized inflammation. The result of this project will be the production of an optimized drugamer for ROS scavenging in vivo which will be tested for PTOA therapy. The copolymer will be incorporated into advanced drug delivery systems for long-term joint retention upon intra-articular injection.

46. Network-Based Analysis of EEG-fMRI temporal relationship

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The hemodynamic response function (HRF) models blood oxygen level dependent (BOLD) signals in functional magnetic resonance imaging (fMRI) by describing local changes in cerebral blood flow, volume, and oxygenation associated with neuronal activity. Most EEG-fMRI studies, including those of the alpha band power (an 8-12 Hz oscillation linked with relaxed wakefulness), assume a pre-defined relation between BOLD signal changes and alpha power, which is described typically as the sum of two gamma functions. However, HRF variability has been noted across brain regions, physiological modulations, and subjects. Here, we investigate the degree to which alpha-BOLD coupling differs across brain networks and vigilance states. Data was collected using simultaneous fMRI-EEG recordings on ten healthy adult subjects while they either rested passively with eyes closed or listened to auditory tones. Using the EEG data, a time course representing vigilance levels was calculated as the ratio between alpha and theta power fluctuations, sampled at each time-point in the fMRI scan (every 2.1s). During each condition, time courses of EEG power fluctuation were convolved with an HRF basis set (canonical HRF, and canonical plus time and dispersion derivatives) in order to determine the variability of the impulse response shapes, and of the model fit, across key resting-state networks. Preliminary results demonstrate the importance of accounting for HRF variability across brain networks when mapping between EEG and fMRI signals.

47. Automatic Segmentation of Brain Tumor in Intraoperative Ultrasound Images using 3D U-Net-based Deep Learning

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Because of the deformation of the brain during neurosurgery, intraoperative imaging is used to visualize the actual location of the brain structures. These images are used for image-guided navigation as well as determining whether the resection is complete and localizing the remaining tumor tissue. Intraoperative ultrasound (iUS) is a convenient modality with short acquisition times. However, iUS images are difficult to interpret because of the noise and artifacts. In particular, tumor tissue is difficult to distinguish from healthy tissue and it is very difficult to delimit tumors in iUS images. In this work, we propose an automatic method to segment brain tumors in iUS images using a 3D U-Net. We trained the network with twelve cases and evaluated the results on three folds with five cases each. The obtained results are promising, with a median Dice score of 0.72. The volume differences between the estimated and ground truth segmentations were similar to the intra-rater volume differences.

48. Identifying Open Surgical Fields Using Surgeon-Worn “Cleopatra” Video Camera

Gianna Riccardi, Danny Levy, Rachel Broadway, Alex Quinones, William Rodriguez, Alexander Langerman

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Surgery requires expert performance of critical, intricate tasks, yet surgery has lagged behind other industries in adopting video technology for performance assessment. Ubiquitous acquisition of high-quality video would allow surgeons to review their procedures, disseminate best practices for educational purposes, and provide clarity for medical records. One of the primary challenges to widespread adoption is difficulty in capturing consistent, high-quality video in “open” (as opposed to endoscopic) surgical procedures. We have developed a novel, lightweight camera system, “Cleopatra”, designed specifically for use in open surgical procedures.
We are presently using Cleopatra footage to identify the open surgical field (Area of Interest, “AOI”). The goals of identifying the AOI are to enable tracking mechanisms for consistent high-resolution image capture and to focus computer vision analysis on the most important in-frame elements.
In this poster we demonstrate our progress identifying the AOI through light, color, and content cues in the surgical field.

49. Improving accuracy of image-guided liver surgery via sparse feature constraints from tracked intraoperative ultrasound

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Although the safety of hepatic surgery depends on accurate knowledge of the subsurface anatomy, intraoperative localization of deep structures remains challenging due to organ deformation. To compensate, many liver registration techniques rely on the shape of the organ surface to predict the underlying state of deformation. However, the visible extent of surface coverage is often limited and can be insufficient for achieving accurate registrations throughout the depth of the liver. We propose applying tracked intraoperative ultrasound (iUS) to extend the coverage of intraoperative data available for registration. To streamline procedural workflow, we aim to maximize registration accuracy throughout the organ while minimizing the number of iUS planes collected for registration. In this work, we identify how registration performance changes when features from iUS are incorporated in various ways. From an initial error of 10.4±8.2 mm after surface registration, incorporating features from one well-positioned iUS plane decreased error to 5.4±2.8 mm throughout the liver.

50. Localization of urine derived stem cells in kidney organoids derived from human induced pluripotent stem cells

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There is a lack of efficient non-invasive therapies available to treat individuals with renal diseases. This has led to the use of donor-derived somatic cells or stem cells for differentiation into renal cell types for drug screening or therapeutic studies. Modeling of kidney disease with normal or CRISPR-mutant kidney organoids derived from human induced pluripotent stem cells (hiPSCs) has been termed a 'disease in a dish' model. For this project, we developed kidney organoids from fibroblast-derived human iPS cells using the established protocol from Takasato and Little, following optimization. We found that applying a longer phase of Wnt signaling activation using CHIR99021 on iPSCs during the intermediate mesoderm stage resulted in the induction of posterior intermediate mesoderm. The resulting organoids express the expected markers at 28 days, including ECAD,GATA3,PAX2,LTL. Since iPSCs can be made in a patient-specific manner, deriving kidney organoids from iPSCs for therapeutic screening for kidney diseases may be possible. In the second part of this project, we studied the incorporation of urine-derived stem cells (USCs) into kidney organoid models. Viable cells from urine were first successfully isolated from newborn infants by Sutherland and Bain. Multiple groups have reproduced the procedure to isolate USCs, including Zhang and colleagues, which can be expanded in vitro for more than ten passages. Even though there is evidence suggesting that USCs are most likely from glomerular parietal epithelial cells, the studies thus far have not able to identify the exact origin of USCs. Identifying the origin of USCs will lead to a better understanding of the potential impact of this population in the urinary tract system following cell therapy for the treatment of kidney injury. We incorporated the USCs into the organoids to understand the localization. The results will provide more insight into the localization of USCs in kidney which can be utilized for drug discovery and therapeutic interventions for renal diseases. In future studies, we will induce kidney injury on the organoids to evaluate how the colocalized USCs behave following kidney injury.

51. Deep Learning Approach to Optical Coherence Tomography Vessel Segmentation

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Retinal vasculature is of great importance in clinical diagnosis, so we are interested in extracting vessel structure from optical coherence tomography (OCT) images. Due to imaging technique, OCT is often degraded by speckle noise which may severely obscure fine morphological details especially vessels. Average of repeated OCT B-scans can certainly improve SNR, but more times of imaging at the same location are required to give a higher quality denoised output. The long acquisition time makes the approach impractical. Other denoising techniques, Although other denoising techniques can produce promising results, they cannot guarantee to preserve the tiny vessel features. We are trying to setup a deep learning based approach to skip the denoising step and get the vessel segmentation directly. The major obstacle is the lack of ground truth on OCT B-scans which makes it impossible to train on real OCT images. So we used a phantom, namely, a simple tube with liquid flowing through to mimic a single vessel. When the phantom is imaged, each slice in this volume can be regarded as an analogy of a retinal OCT B-scan. The phantom OCT B-scans only include an ellipse which is the intersection with the tube as a target to detect. By applying basic image processing techniques including: smoothing, thresholding and ellipse Hough transform, we can get the ground truth for the Phantom data.
U-net, the classic deep learning model on medical image segmentation is then trained on this dataset. Then the problem we need to address is the dissimilarity between the training data and OCT. Although a simple 2D U-net can give a promising performance on the Phantom data, the neural network tends to get overfitted and loses the ability to work on other datasets. Currently I am working on a 3D multi-channel U-net in seeking to learn the intrinsic property of vessel features.

52. Association between fMRI brain entropy features and behavioral measures

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An important goal in neuroscience is to understand the relationship between brain activity features and cognitive traits. Here, we investigate brain fMRI features based upon Sample Entropy (SampEn), a nonlinear signal processing measure that captures the complexity of a time series. Using 90 selected regions of interest (ROIs) across 96 unrelated subjects from the Human Connectome Project (HCP) we found that SampEn-based features generated reproducible patterns of correlation with 19 selected cognition-related behavioral measures. We further applied a multiple linear regression model relating SampEn-based brain features to cognitive measures, and verified the consistency of this brain-behavior relationship across repeated scans of the same individual. To further probe the relationships between specific ROIs and each of the behavioral labels, the LASSO regression model was incorporated into the process of Monte Carlo cross validation over 5000 iterations. Our results indicate that the SampEn in certain brain areas may be associated with specific behavioral measures. Together with the within-subject consistency of SampEn, these results contribute further evidence that SampEn of resting-state fMRI time series may form a stable and relevant marker of cognitive traits.

53. Predictive neural processing in the pleasure of music

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Music ranks among the greatest human pleasures, consistently engaging the brain's reward system as its structure unfolds over time. Converging evidence indicates that making and evaluating predictions is central to music's appeal and its recruitment of this system, including the nucleus accumbens (NAc). In a previous fMRI experiment with a music-based learning task, we showed that the NAc reflected formally modeled musical surprises, with activity increasing for surprises considered positive and decreasing for those considered negative. Moreover, the strength of these responses predicted performance in the learning task, and was enhanced in listeners with greater sensitivity to musical reward. These effects suggest that musical prediction errors might elicit reward by facilitating learning, which offers intrinsic, adaptive value. Yet confirming predictions is also informative, and excessive surprise impedes learning. The present study thus employs a well-validated information-theoretic model of musical expectation to systematically vary and measure the effects of musical predictability and predictive uncertainty. Participants rated their enjoyment of 50 musical excerpts with a joystick during fMRI scanning, followed by resting-state scans to explore the underlying effects of musical reward sensitivity and background. We observed reliable preferences for music that optimizes learning by balancing intermediate uncertainty with high predictability, and an interaction between surprise and liking in the NAc that corroborates our previous finding in a more naturalistic setting. Resting-state scans reveal a diffuse network of connections associated with musical reward processing and experience, underscoring the widespread networks involved in predictive neural processing and the pleasure of music listening.

54. A deep learning approach for MRI subcortical segmentation in neurodegeneration

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Huntington's disease(HD) effects the subcortical structures of brain, especially the caudate and the putamen. To better understand the HD, quantitative segmentation of subcortical structures in the MRI is important in clinical and research studies In this work, we adopted the LIVIANET (Dolz et al., 2017), which is the state-of-the-art deep learning approach for subcortical segmentation. We used patch-based input and employed larger patch sizes to obtain more contextual information.Additionally, we used a large enough number of patches that try to cover the whole image information. 9 convolution layers with kernel size 3 are used in our convolutional neural network. Furthermore, the spatial coordinates of subcortical structures are used as additional feature channels in our method to improve the results by suppressing false positive voxels in unlikely locations. We tested our method on the PREDICT-HD dataset, which includes control and HD subjects. We trained on 40 control subjects and test on 15 control subjects and 20 HD subjects. The Dice score is used as our metric. Compared to LIVIANet, we improved the accuracy of most structures, both for controls (8 structures out of 8) and HD patients (7 structures out of 8). The largest improvement of our method was on the caudate segmentation of the HD patients (mean Dice scores of 82.4 with LIVIANet vs. 89.1 with proposed), which is noteworthy since caudate is known to be severely atrophied in HD. This suggests our approach may be more generalizable to cohorts where significant neurodegeneration is present, without needing to be retrained.

55. MRI correlates of chronic symptoms in mild traumatic brain injury

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Some veterans with a history of mild traumatic brain injury (mTBI) have reported experiencing auditory and visual dysfunction that persist beyond the acute phase of the incident. The etiology behind these symptoms is difficult to characterize, since mTBI is defined by negative imaging findings on current clinical imaging. There are several competing hypotheses that could explain functional deficits; one example is shear injury, which may manifest in diffusion-weighted magnetic resonance (MR) imaging (DWI). Herein, we explore this alternative hypothesis in a pilot study of multi-parametric MR imaging. Briefly, we consider a cohort of 8 mTBI patients relative to 22 control subjects using structural T1-weighted imaging (T1w) and connectivity with DWI. 1,344 metrics were extracted per subject from whole brain regions and connectivity patterns in sensory networks. For each set of imaging-derived metrics, the control subject metrics were embedded in a low-dimensional manifold with principal component analysis, after which mTBI subject metrics were projected into the same space. These manifolds were employed to train support vector machines (SVM) to classify subjects as controls or mTBI. Two of the SVMs trained achieved near-perfect accuracy averaged across four-fold cross-validation. Additionally, we present correlations between manifold dimensions and 22 self-reported mTBI symptoms and find that five principal components from the manifolds (one component from the T1w manifold and four components from the DWI manifold) are significantly correlated with symptoms ($p<0.05$, uncorrected). The novelty of this work is that the DWI and T1w imaging metrics seem to contain information critical for distinguishing between mTBI and control subjects. This work presents an analysis of the pilot phase of data collection of the Quantitative Evaluation of Visual and Auditory Dysfunction and Multi-Sensory Integration in Complex TBI Patients study and defines specific hypotheses to be tested in the full sample.

56. Imaging-guided Surgery improves visualization of tumors by using TSPO-specific Biophotonic Intervention

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Background and Significance Significant advances have achieved in treating cancers recent years though; there isn't an ideal therapeutic approach for most of the malignance diseases. The most preferred initial treatment is surgical debulking, but it still has many limitations. Usually, it's hard to identify the tumor margin by the surgeons' naked eyes. If the tumor cannot be removed completely, the left tumor can lead to recurrence eventually. The fluorescence imaging-guided surgery (FIGS) can significantly improve surgical outcomes by helping surgeons identify tumor margin and macroscopic tumors. Here we choose the 18 kDa mitochondrial translocator protein (TSPO) as a specific target to develop fluorescent molecular probes used in imaging-guided surgery. TSPO is a target often upregulated in many types of cancer. Our innovative approach significantly improved the visualization of tumors in the removal surgery. Methods and Results Building upon our lead compound, we have developed TSPO-targeted probes, which showed a high binding affinity to TSPO protein. We conducted a FIGS study using the Curadel RP-1 optical surgery navigation system. A 2F8 tumor with similar color to the normal peritoneal tissues was labeled by fluorescence imaging and subsequently removed by surgery. When used in the pancreatic cancer mouse model, it also very helpful in visualizing the tumor margin under the optical surgical navigation system. Conclusions TSPO-targeted probes greatly improved visualization of tumor tissues. Which provided novel strategy that may have the potential to greatly improve the survival of cancer patients.

57. Longitudinal Graph-Based Cortical Segmentation and Thickness Analysis

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Longitudinal MRI is a powerful tool for measuring structural brain changes, specifically gray matter cortical atrophy, caused by neuropathologies. However, the complex geometry of the cortical surfaces renders such quantifications difficult - this elicits the need for robust segmentation and reconstruction techniques to both accurately and precisely measure cortical thickness. We propose a novel 4D graph segmentation approach, LOGISMOS-B (Layered Optimal Graph Image Segmentation of Multiple Objects and Surfaces for the Brain), for joint reconstruction of white and gray matter surfaces from longitudinal MRI datasets that guarantees an optimal solution. Precision is assessed by applying the segmentation pipeline to the publicly available Kirby dataset (n=21, 2 same-session repeat scans, Landman et al.) of healthy patients with no significant intrasubject structural changes between repeat scans. Accuracy is tested by performing joint segmentation on artificially deformed brain images with the goal of recovering the known degree of cortical atrophy synthetically introduced within a localized ROI. Both precision and accuracy are compared between 3D and 4D LOGISMOS-B, where the main difference is that unlike 3D (cross-sectional), 4D (longitudinal) employs temporal regularization in addition to spatial to jointly reconstruct cortical surfaces. Additionally, these techniques are also compared to the popular FreeSurfer segmentation pipeline, which utilizes longitudinal methods without any joint reconstruction. We hypothesize that 4D LOGISMOS-B will provide more accurate and more precise results than its 3D counterpart, and that both will outperform FreeSurfer.

58. Device and method of ascertaining volume status to allow early intervention to prevent/mitigate congestive heart failure exacerbations

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Background Chronic heart failure (CHF) affects 6 million Americans and has a projected cost of $53 billion in 2030. Hospital readmission rates due to CHF exacerbations contribute to this high cost. Approximately 25% of CHF patients are readmitted within 30 days. Therefore, interventions that reduce readmission can be effective in reducing costs. Patient volume status is an important factor in exacerbations. Existing methods to assess volume status including pulmonary capillary wedge pressure and echocardiogram are expensive, invasive, and/or must be done in the hospital. We propose an inexpensive "heart kit", a tool to monitor CHF patients' volume status and responsiveness at home and enable interventions to prevent exacerbations and subsequent readmission.   Methods Upon hospital admission, patients will have multiple parameters measured, including weight, BP, bioimpedence, peak expiratory flow, fluid intake, SpO2, and ring/finger size ("parameters"). These parameters will be measured daily during the hospitalization and correlated to standard clinical measurements. Upon discharge, patients will be given a kit allowing at-home measurements of the parameters. Daily measurements of the parameters will be submitted via a smartphone app or reported to a health coach calling. After sufficient data are collected demonstrating the utility of these parameters as surrogates for volume status and responsiveness, they can be used to inform clinical decision making, including increasing oral diuretic use and fluid restriction.   Plan We plan to conduct a pilot study of 50 CHF patients to test the relationships between the parameters measured by 'heart kit' and the clinically-defined volume status.

59. Image Guidance for the da Vinci Robot

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Our goal is to facilitate wider adoption of partial nephrectomy through image guidance. Partial nephrectomy involves removing a tumor while sparing surrounding healthy kidney tissue. It improves outcomes for patients but is underutilized because it is challenging to accomplish minimally invasively, requiring accurate spatial awareness of unseen subsurface anatomy. Image guidance can enhance spatial awareness by displaying 3D anatomical models derived from medical imaging information relative to a surgeon's tools. We present a clinically practical system for image guidance with the da Vinci robot that uses the robotic instruments themselves as localizers for tracing the kidney surface to perform a "touch-based" surface registration.

60. Textual fiducial detection in breast conserving surgery for a near-real time image guidance system

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Breast cancer is the most common cancer in American women, and is the second most deadly. Current guidance approaches for breast cancer surgery provide distance to a seed implanted near the tumor centroid. However, large deformations between preoperative imaging and surgical presentation, coupled with the lack of tumor extent information leads to difficulty in ensuring complete tumor resection. We propose a novel image guidance platform that is work-flow friendly, and near-real time with use of stereo cameras for surface acquisition. Surface acquisition must be robust to occlusion, as often not all fiducials are visible throughout a surgery. In order to provide updates throughout a procedure, it is also ideal to have a fiducial localization algorithm that does not rely on video history, but rather continuously updates with the most recent information. Using simple image processing techniques, the proposed technique can localize fiducials and character labels. Character based fiducial labels can be recognized and used to determine correspondence between left and right images in a pair of stereo cameras, and frame to frame in a real time sequence of images during a procedure. The stereo camera system can determine surface points with accuracy below 2mm when compared to optically tracked stylus points. These surface points are incorporated in 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.

61. A Cannabinoid CB2 receptors (CB2Rs)-targeted molecular agent for imaging-guided surgery in pancreatic and ovarian cancer mice models.

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Fluorescence imaging-guided surgery (FIGS) is emerging as a new interventional approach for cancer, which can greatly improve surgical outcomes by helping surgeons identify tumor margin and macroscopic tumors. In the current study, we chose the cannabinoid CB2 receptor (CB2R) as a new target and used a CB2R -targeted photosensitizer, NIR760-xlp6, for imaging-guided surgery. CB2R belongs to the G protein-coupled receptors (GPCRs, plasma membrane receptors) family and many types of cancers, including prostate, skin, liver, brain, thyroid, lymphoma, lung, colon, ovarian and breast cancers, up-regulate CB2R expression. An association between CB2R levels and tumor aggressiveness has also been identified. In the present study, we set out to investigate the potential of CB2R targeted imaging-guided surgery in pancreatic and ovarian cancer mice models. As expected, imaging-guided surgery with NIR760-xlp6 greatly improved visualization of pancreatic tumors and delineated the tumor boundaries during real-time surgery using a mouse pancreatic tumor model. In a mouse ovary cancer peritoneal metastasis model, the fluorescence signal from NIR760-xlp6 highlighted the metastasized tumors from the surrounding healthy tissue. In conclusion, this is the first study demonstrating intraoperative detection of pancreatic tumors and ovarian cancer metastases using CB2R-targeted NIR FIGS. Our results suggest that CB2R-targeted FIGS may have great potential in improving surgical outcomes in the clinic.

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