11th Annual

Surgery, Intervention, and Engineering Symposium

DECEMBER 7th, 2022

"Crossing the academia-industry bridge: Delivering a brain responsive neurostimulator for intractable epilepsy"

Martha J. Morrell MD

Clinical Professor of Neurology,
Stanford University
Chief Medical Officer, NeuroPace

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.

Visit our website.

Master of Engineering in Surgery and Intervention (ESI) Program

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

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

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

You can read all about the new degree in our program guide,
What is Innovation in Procedural Medicine? Getting an Engineering Degree in Surgery and Intervention.

"Crossing the academia-industry bridge: Delivering a brain responsive neurostimulator for intractable epilepsy"

Presented by

Martha Morrell MD

Clinical Professor of Neurology, Stanford University
Chief Medical Officer, NeuroPace

Keynote Speaker

Martha J. Morrell MD

Clinical Professor of Neurology, Stanford University
Chief Medical Officer, NeuroPace

Keynote Abstract

Relief of suffering from illness or disability is a primary motivation for many who have entered the broad field of medical/biomedical science. This may take the form of fundamental scientific discovery, direct patient care, or of discovery, development and delivery of new therapies that bring benefit. In some instances, therapies provide incremental benefit and less often, true innovation. The efforts to create better treatments for patients in need requires multi-disciplinary and multi-institutional collaboration. If the worlds of academia and industry are seen as separate in intent and motivation, and if these each views the other with distrust, then new therapies and solutions are at risk into falling in the "Valley of Death" between discovery and deliver. Creating obstacles rather than bridges between the 2 entities may deprive persons of therapies that offer relief.

The importance of collaboration between academia and industry will be discussed by sharing the story of a start-up company formed to develop of a responsive brain neurostimulator for persons with drug resistant epilepsy. The story is one of discovery, development and delivery of a novel therapy for a group of patients with a great clinical need. Emphasis will be given to the importance of a team with diverse expertise, the unexpectedly long path filled with accomplishments and disappointments, and the steps that led to eventual success.

Biography

Dr. Morrell has been Chief Medical Officer of NeuroPace, Inc. and a Clinical Professor of Neurology at Stanford University since July 2004. Before joining NeuroPace, she was the Caitlin Tynan Doyle Professor of Clinical Neurology at Columbia University and Director of the Columbia Comprehensive Epilepsy Center at New York Presbyterian Hospital in New York City. Previously she was on the faculty of the Stanford University School of Medicine where she served as Director of the Stanford Comprehensive Epilepsy Center. A graduate of Stanford Medical School, she completed residency training in Neurology at the University of Pennsylvania, as well as fellowship training in EEG and epilepsy.

Dr. Morrell has been actively involved in helping to bring new therapies to patients. Her responsibilities at NeuroPace include all clinical and pre-clinical research for a novel responsive neurostimulator for the treatment of medically uncontrolled epilepsy. She has been actively involved in investigational trials of new epilepsy therapies as an academic investigator, and has authored or coauthored more than 150 publications.

Service to professional societies includes member of the Board of Directors of the American Epilepsy Society, member and Chair of the Board of the Epilepsy Foundation, member of the Council of the American Neurological Association and Chair of the Epilepsy Section of the American Academy of Neurology. She is an elected Ambassador for Epilepsy of the International League Against Epilepsy and received the American Epilepsy Society's 2007 Service Award for outstanding leadership and service. She is the immediate past-Chair of the American Society for Experimental Neurotherapeutics.

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 and industrial 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 steerable micro-catheters for ischemic stroke treatment, OCT-guide robotics for retinal therapeutic delivery (NIH), In-Situ Collaborative Industrial Robotics for confined spaces (NSF), Transurethral bladder tumor 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 also collaborate closely with industry on translation of 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

The Bick Lab

PI: Sarah Bick, MD, Assistant Professor of Neurological Surgery, Vanderbilt University Medical Center

The Bick neurophysiology lab at Vanderbilt University Medical Center is led by neurosurgeon scientist Sarah Bick, MD. The focus of the lab is using human neurophysiology and imaging methods to understand the neural signaling underlying cognitive and psychiatric processes with the ultimate goal of developing novel neuromodulation techniques.

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Participating Laboratories

Biomedical Elasticity and Acoustic Measurement (BEAM) Laboratory

PI: Brett Byram, Ph.D.
Associate Professor of Biomedical Engineering, Vanderbilt University

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

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Participating Laboratories

Biomedical Image Analysis for Image Guided Interventions (BAGL) Laboratory

PI: Jack H. Noble, Ph.D.
Assistant Professor of Electrical & Computer Engineering
Director of Graduate Student Recruitment, ECE
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.

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Participating Laboratories

Biomedical Modeling (BML) Laboratory

PI: Michael I. Miga, Ph.D.
Harvie Branscomb Professor
Professor of Biomedical Engineering
Professor of Radiology and Radiological Sciences
Professor of Neurological Surgery
Professor of Otolaryngology
Vanderbilt University

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

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Participating Laboratories

Bowden Biomedical Optics (BBOL) Laboratory

PI: Audrey Bowden, Ph.D.
Dorothy J Wingfield Phillips Chancellor Faculty Fellow, Associate Professor, Biomedical Engineering, Associate Professor, Electrical and Computer Engineering

The primary aim of the Bowden Biomedical Optics Laboratory (BBOL) is to develop and deploy novel imaging and sensing technologies to address unmet clinical needs in medicine and biology.
We blend knowledge and experience from diverse fields such as optics, microfluidics, signal processing and computer science to develop software- and hardware-based tools for the healthcare provider that advance the state of the art and aid in scientific discovery. While the majority of our solutions are relevant to optics, as engineers, we are committed to taking a "whatever means necessary" approach to solving the clinical problem. We are also committed to developing novel solutions to improve delivery and affordability of healthcare in low-resource and resource-constrained environments. Our technologies and projects have found application in various clinical departments, including urology, dermatology, otolaryngology and women's health.

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Participating Laboratories

Brain Imaging and Electrophysiology Network (BIEN) Laboratory

PI: Dario J. Englot, M.D., Ph.D.
Associate Professor of Neurological Surgery, Neurology, Radiology and Radiological Sciences, Electrical and Computer Engineering, and Biomedical Engineering - Director of Functional NeurosurgeryVanderbilt University

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

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Participating Laboratories

Computational Flow Physics and Engineering (CFPE) Lab

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

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

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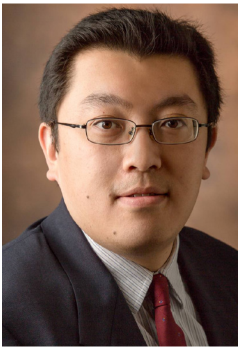
Participating Laboratories



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

tHe biomedical data Representation and Learning laB

PI: Yuankai Huo, Ph.D.
Assistant Professor of Computer Science
Assistant Professor of Computer Engineering
Vanderbilt University

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

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Participating Laboratories

Internet of Medical Things (IoMT) Lab

PI: James Weimer, Ph.D.
Assistant Professor of Computer Science
Vanderbilt University

The internet of medical things (IoMT) consists of devices, infrastructure, and software connected through communication networks (e.g., the internet or hospital intranet). Consequently, in the past decade, the IoMT has grown to incorporate most commercial medical devices and consumer health products. In the IoMT lab, we seek to push the boundaries of how the IoMT can impact clinical care and patient health. The IoMT lab connects clinicians and engineers with the IoMT to create new inter-operable learning-enabled medical systems. Through collaborative interdisciplinary use-inspired research, we seek to address three foundational challenges facing the IoMT. First, the IoMT requires systems and protocols for identifying and collecting the right data in a timely manner. Second, the IoMT data must be processed to provide actionable feedback to clinicians and caregivers. Third, the IoMT should safely automate some aspects of care to reduce clinician and caregiver workload. To maximize the real-world IoMT lab impact, we go beyond traditional academic research and innovate -- often developing intellectual property that is licensed to commercial entities. Through licensing and research, the IoMT lab has partnered with startup companies such as Neuralert and Vasowatch, as well as larger companies including Hill-Rom. Graduate and undergraduate students in the IoMT Lab have a unique educational experience that includes working side-by-side with clinicians. In the IoMT lab, students are encouraged to not only work on lab projects, but to pursue their own ideas as they learn to be both researchers and innovators in medical devices and health technologies.

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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,
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.
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,
Professor of Surgery,
Vanderbilt University Medical Center

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

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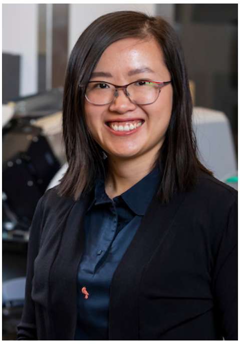
Participating Laboratories



Machine Automation, Perception, and Learning (MAPLE) Laboratory

PI: Jie Ying Wu, Ph.D.
Assistant Professor, Computer Science
Vanderbilt University

At the MAPLE lab, our goal is to build intelligent surgical robots that can assist surgeons in the operation room. While surgical robots have changed many procedures by providing higher dexterity, motion scaling, and other innovations, they are still only extensions of the surgeon's arms. By modeling different aspects of surgery and how they interact, we aim to make the robots more capable. We use machine learning to augment traditional modeling techniques, such as correcting physics-based soft-tissue models with observations of tissue interactions. We work with clinicians to use accurate soft-tissue models to provide guidance during surgeries based on preoperative imaging. Another project looks at modeling how expert surgeons move surgical instruments and the endoscope during procedures, which can help us develop better ways to train novice surgeons. At the same time, we are building models of the trainee's actions, eye-gaze, and pupillometry to obtain insight into their cognitive load. We use this to develop a personalized curriculum and feedback.

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Participating Laboratories

Machine Intelligence and Neural Technologies (MINT) Laboratory

PI: Soheil Kolouri,
Assistant Professor of Computer Science
Vanderbilt University

At the Machine Intelligence and Neural Technologies (MINT) Lab, we develop next-generation core Machine Learning (ML) solutions for practical problems in medicine and strive to advance healthcare. Our interdisciplinary team at MINT Lab uses biological inspirations together with mathematical and geometrical tools to innovate theoretically grounded algorithms that address the current deficiencies in ML technologies regarding lifelong/continual learning, sample/label efficiency, explainability, and brittleness. In one of our main research thrusts, we develop brain-inspired, robust machine intelligence that can continually learn and adapt to the input stream of nonstationary multimodal data. Continual learning is specifically relevant to medical applications where: 1) the data is continually accumulated from new patients, and 2) diseases constantly mutate and new variants emerge. We are developing next-generation computational models that adapt to these constant variations, learn from the past to solve future problems and leverage new knowledge to improve the previous solutions. Our research is highly interdisciplinary, and we have collaborations across fields including computer science, biomedical engineering, cognitive science, electrical engineering, and neuroscience.

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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. (he/him/his)
Professor and Department Chair
Electrical and Computer Engineering (primary), Computer Science, Biomedical Engineering, Vanderbilt University

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

Biomarker Core Co-Lead
Vanderbilt Alzheimer's Disease Research Center

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

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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, steerable needles in the lung, image guidance for surgical GPS on the da Vinci Surgical System, and MRI-guided robots aimed at curing epilepsy.

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Participating Laboratories

Medical Image Computing (MedICL) Laboratory

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

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

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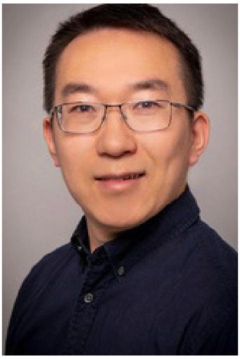
Participating Laboratories



Miniature Robotics Laboratory (Dong Lab)

PI: Xiaoguang Dong, Ph.D.
Assistant Professor of Mechanical Engineering
Vanderbilt University

Miniature Robotics Laboratory is focusing on the design and control of the shape-morphing behaviors (single-body deformation and collective formations) in various soft matter to create functional miniature soft machines and minimally invasive medical devices. These miniature soft machines and medical devices are further integrated with their wireless actuation (e.g. magnetic), control and sensing systems, to resolve challenging problems in minimally invasive medical procedures. Ongoing research highlight includes developing novel minimally invasive medical functions of soft miniature robots, such as biofluid pumping, local drug delivery, and targeted biopsy. The long-term research of Dong Lab focuses on three aspects: 1) The design, manufacture and control of miniature soft robots, and their applications in minimally invasive medicine, microfluidics and biomechanics. 2) The design, manufacture and control of miniature swarm robots, and their applications in biomedicine and biomechanics. 3) The modeling, design, manufacture and control of intelligent soft materials and devices based on mechanics model and machine learning.

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Participating Laboratories

Morgan Engineering and Imaging in Epilepsy Lab

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

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

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Participating Laboratories

Moyer Laboratory

PI: Daniel Moyer, Ph.D.
Assistant Professor, Computer Engineering
Vanderbilt University

Professor Moyer's group is working to bridge the gap between Machine Learning, and Medical Imaging. We work directly with clinicians and researchers to translate advances in computer vision to better outcomes for patients, and new discoveries in imaging-based scientific fields. While we're most used to MRI and CT, we're not afraid to look into new domains, and we're always happy to meet with new potential collaborators to discuss what might be possible

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Participating Laboratories

Neuroimaging and Brain Dynamics Lab

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

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

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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 Nutrition, VUMC;
Department of Mechanical Engineering,
Vanderbilt University

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

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

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

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

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Participating Laboratories

Surgical Analytics Lab

PI: Alexander Langerman, MD SM FACS
Associate Professor, Department of Otolaryngology, - Head and Neck Surgery, Associate Professor of Radiology and Radiological Sciences
Vanderbilt University Medical Center

The Surgical Analytics Lab focuses on novel methods of real-time surgical data collection and analysis. Our flagship projects are the Clearer Operative Analysis and Tracking ("CleOpATra") surgical video system - a wearable camera designed for open surgical procedures – and development of a deidentified surgical video library to enable downstream analytics.

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Participating Laboratories

Topf Lab

PI: Michael Topf, MD
Assistant Professor, Otolaryngology,
- Head and Neck Surgery

Our team is interested improving communication between oncologic surgeons and pathologists using 3D scanning of surgical specimens in real time. To date, we have scanned over 100 head and neck surgical specimens. We are now working on using mixed reality surgery in real time with 3D holograms via the Microsoft HoloLens. We are also interested in using a mixed reality environment for communication between surgeons / pathologists / radiation oncologists.

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Participating Laboratories

Vanderbilt Biophotonics Center

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

The Vanderbilt Biophotonics Center is an interdisciplinary research center at the intersection of the College of Arts and Science, the School of Engineering and the School of Medicine that brings together faculty, post-doctoral fellows, graduate and undergraduate students dedicated to biophotonics research. VBC provides a state-of-the-art research facility and a collaborative environment and includes shared core facilities and resources for research that spans everything from fundamental discovery to clinical translation. Research is organized into 3 thrust areas: Clinical Photonics, Neurophotonics and Multi-scale biophotonics. Other research interests include application of optical techniques in a variety of other areas such as diabetes research, neonatology, ophthalmology, critical care, surgery, obstetrics, and orthopedics for clinical translation as well as fundamental research. Further, since many of our team are engineers and physicists, research is also focused on the discovery of new optical methodologies and the support needed to advance current technologies to new levels. Example projects include near-infrared fluorescence for real time guidance of endocrine surgery, intraoperative nerve imaging and monitoring as well as interventional diagnostic imaging for various diseases.

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Participating Laboratories

Vanderbilt Dermatology Translational Research Clinic (VDTRC)

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

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

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

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

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Submitted Abstracts

1. Quantification of Behavioral Changes in hand posture of non-human primates using 3D video-based analysis and machine learning

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Measures of behavioral deficits are essential for interpreting MR images of non-human primates following spinal cord injury. The objective of this study is to quantify hand grasping behaviors of monkeys before and after spinal cord injury. A total of twenty-four videos of three monkeys grabbing sugar pellets before and after suffering spinal cord injury were chosen to be analyzed. Quantitative analyses of hand and finger motions were implemented through machine learning with the open-source Deeplabcut software. A total of six markers are placed on the joints of the ring, index and middle fingers for tracking. After analysis, an excel spreadsheet containing all the coordinates of the markers at each frame are extracted and loaded into a MATLAB script. Here, a quantitative analysis is performed to determine behavioral and motor changes of each digit separately. This procedure is then repeated for each of the three cameras placed in the video recording system. Significant change in hand posture shape is reflected when comparing pre-lesion and post-lesion data. The trajectory over time plot presented in the post-lesion line graph contains multiple peaks. In contrast, the pre-lesion analysis shows a steady pattern of movement with small amplitudes throughout the analysis. Quantifying position and behavioral changes in hand grasping allows us to determine which digit undergoes the biggest difference and track the hand posture change after spinal cord injury. Further research will be geared towards creating a software package that will quantify behavioral changes and tremor in non-human primates and human patients with neurodegenerative disease.sional recording system, we can extract hand posture changes from different angles and increase the sensitivity and accuracy in digit tracking. Quantifying position and behavioral changes in hand grasping allows us to determine which digit undergoes the biggest difference and track the hand posture change after spinal cord injury. Further research will be geared towards creating a software package that will quantify behavioral changes and tremor in non-human primates and humanpatients with neurodegenerative disease.

2. Surface-based Laplacian cortical thickness

Kathleen E. Larson, BME, Vanderbilt University Saramati Narasimhan, VUMC
Ipek Oguz, CS, Vanderbilt University

Cortical thickness (CT) is an important image-based marker for both healthy aging and neurodegeneration. However, the most commonly used surface-based method for its measurement, the symmetric closest point (SCP) distance mapping, is prone to underestimation in curved regions and lacks the symmetry that its name suggests. Volumetric CT measurement techniques have provided alternative methods by employing PDEs to create a one-to-one, symmetric mapping between the GM and WM boundaries, but are prone to error from partial volume effects and susceptibility to noise. To address these shortcomings, we present a surface-based Laplacian (SBL) CT measurement technique that circumvents the pitfalls of both the SCP and volumetric methods. Our pipeline models the interior of the cortical ribbon with an irregular grid, solves the Laplacian equation over this grid, and measures thickness by numerically integrating along the normalized solution gradient. In this work, we validate our pipeline using both digital phantoms and cortical surfaces. We compare CT values between the SBL and SCP methods, and show that the SBL produces higher thickness values than the SCP in areas with higher curvature. We also show that the SBL can replicate previously observed CT patterns of a healthy brain.

3. Coded Excitation for Increased Sensitivity in Transcranial Power Doppler Imaging

Emelina Vienneau, Abbie Weeks, Brett Byram

Department of Biomedical Engineering Vanderbilt University

Functional ultrasound imaging (fUSI) is a promising new modality for neuroimaging that measures the power Doppler signal as a proxy for neural activation. However, clinical translation of noninvasive, transcranial fUSI (tfUSI) is hindered by the low signal-to-noise ratio (SNR) from the skull which greatly limits blood flow sensitivity. To overcome this issue, we demonstrate a coded excitation approach to increase SNR in transcranial power Doppler imaging and thereby increase blood flow sensitivity. In three healthy adult subjects we showed an average SNR gain of 17.77 ± 1.05 dB, contrast-to-noise ratio gain of 4.97 ± 4.18 dB, and contrast ratio gain of 22.53 ± 11.34 dB using a 65 bit code. These promising results indicate that tfUSI may be feasible using our coded excitation approach.

4. Time-distance vision transformers in lung cancer diagnosis from longitudinal computed tomography

Thomas Z. Li (a,b), Kaiwen Xu (c), Riqiang Gao (c), Yucheng Tang (d), Thomas A. Lasko (c,e), Fabien Maldonado (f), Kim Sandler (g), Bennett A. Landman (a,c,d,g)

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Background and Significance Features learned from single radiologic images are unable to provide information about whether and how much a lesion may be changing over time. Time-dependent features computed from repeated images can capture those changes and help identify malignant lesions by their temporal behavior. However, longitudinal medical imaging presents the unique challenge of sparse, irregular time intervals in data acquisition. While self-attention has been shown to be a versatile and efficient learning mechanism for time series and natural images, its potential for interpreting temporal distance between sparse, irregularly sampled spatial features has not been explored. Methods In this work, we propose two interpretations of a time-distance vision transformer (ViT) by using (1) vector embeddings of continuous time and (2) a temporal emphasis model to scale self-attention weights. The two algorithms are evaluated based on benign versus malignant lung cancer discrimination of synthetic pulmonary nodules and lung screening computed tomography studies from the National Lung Screening Trial (NLST). Results Experiments evaluating the time-distance ViTs on synthetic nodules show a fundamental improvement in classifying irregularly sampled longitudinal images when compared to standard ViTs. In cross-validation on screening chest CTs from the NLST, our methods (0.785 and 0.786 AUC respectively) significantly outperform a cross-sectional approach (0.734 AUC) and match the discriminative performance of the leading longitudinal medical imaging algorithm (0.779 AUC) on benign versus malignant classification. Conclusions This work represents the first self-attention-based framework for classifying longitudinal medical images. Our code is available at https://github.com/tom1193/time-distance-transformer.

5. Psychomotor and EEG-derived Measures of Vigilance in Patients with Epilepsy

Caroline Martin (Electrical & Computer Engineering) Kristin Wills (Department of Neurosurgery) Haateff Pourmotabbed (Biomedical Engineering) Jasmine Jiang (Department of Neurosurgery) Sarah Goodale (Biomedical Engineering) Sean Tuttle (Electrical & Computer Engineering) Shiyu Wang (Biomedical Engineering) Eric Feng (Electrical & Computer Engineering) Victoria Morgan (Department of Radiology) Dario Englot (Department of Neurosurgery) Catie Chang (Electrical & Computer Engineering)

Patients with temporal lobe epilepsy (TLE) tend to suffer from broad neurocognitive deficits extending beyond the seizure's focal region. Subcortical vigilance structures may be relevant in explaining the sleep-wake and attention deficits seen in patients. Here, we explored vigilance differences in patients and controls using EEG and the psychomotor vigilance task (PVT). We studied 39 participants (9 patients, 30 controls). For PVT, the outcome measures were response speed and the 10% slowest/fastest response times. For EEG, we evaluated: 1) EEG alpha-theta ratio, where a higher ratio equates to higher alertness and 2) VIGALL classification, which quantitatively stages EEG into discrete vigilance states: 1 (sleep), 2-3 (drowsy), and 4-6 (alert). Patients showed lower PVT scores (slower response speed) compared to controls. Though non-significant after a Bonferroni correction, the trend suggests a group difference in vigilance (p(uncorr) = 0.02). Similarly, patients showed higher, yet non-significant, self-reported drowsiness. For the EEG, alpha-theta showed a trend towards significance during scan two (p(uncorr)=0.04), suggesting greater vigilance differences over time. VIGALL is consistent with this effect and even outperforms alpha-theta (p(uncorr) = 0.02). We also plotted the average EEG time course, separated by scan number. Again, we see greater differences between the time courses for patients and controls, especially during scan two. Consistent with prior reports, PVT and EEG results showed a group difference. For EEG, this difference increased over time. This work is part of an ongoing EEG-fMRI study aiming to define the relationships between connectivity, vigilance, and cognition in epilepsy.

6. Cross-scale Attention Guided Multi-instance Learning for Crohn's Disease Diagnosis with Pathological Images

Ruining Deng(1), Can Cu(1), Lucas W. Remedios(1), Shunxing Bao(1), R. Michael Womick(2), Sophie Chiron(3), Jia Li(3), Joseph T. Roland(3), Ken S. Lau(1), Qi Liu(3), Keith T. Wilson(3,4), Yaohong Wang(3), Lori A. Coburn(3,4), Bennett A. Landman(1), Yuankai Huo(1)

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Multi-instance learning (MIL) is widely used in the computer-aided interpretation of pathological Whole Slide Images (WSIs) to solve the lack of pixel-wise or patch-wise annotations. Often, this approach directly applies "natural image driven" MIL algorithms which overlook the multi-scale (i.e. pyramidal) nature of WSIs. Off-the-shelf MIL algorithms are typically deployed on a single-scale of WSIs (e.g., 20 x magnification), while human pathologists usually aggregate the global and local patterns in a multi-scale manner (e.g., by zooming in and out between different magnifications). In this study, we propose a novel cross-scale attention mechanism to explicitly aggregate inter-scale interactions into a single MIL network for Crohn's Disease (CD), which is a form of inflammatory bowel disease. The contribution of this paper is two-fold: (1) a cross-scale attention mechanism is proposed to aggregate features from different resolutions with multi-scale interaction; and (2) differential multi-scale attention visualizations are generated to localize explainable lesion patterns. By training ~250,000 H&E-stained Ascending Colon (AC) patches from 20 CD patient and 30 healthy control samples at different scales, our approach achieved a superior Area under the Curve (AUC) score of 0.8924 compared with baseline models. The official implementation is publicly available at https://github.com/hrlblab/CS-MIL.

7. Automated instrument-tracking for video-rate 4D visualization of ophthalmic surgical maneuvers

Eric M. Tang, Department of Biomedical Engineering; Mohamed T. El-Haddad, Department of Biomedical Engineering; Shriji N. Patel, Vanderbilt Eye Institute, Vanderbilt University Medical Center; Yuankai K. Tao, Department of Biomedical Engineering

Intraoperative optical coherence tomography (iOCT) provides real-time visualization of ophthalmic microtissue that helps guide clinical decision-making. However, current commercial iOCT systems are limited to 2D cross-sectional imaging, which precludes 3D/4D imaging of surgical dynamics. Manual alignment of static iOCT imaging fields-of-view (FOVs) to regions-of-interest impacts surgical workflow and increases overall operation times. In order to address these limitations, our group had previously developed a deep-learning-based automated instrument-tracking method. In particular, we leverage our spectrally-encoded coherence tomography and reflectometry (SECTR) system that provides simultaneous en face and cross-sectional imaging via spectrally encoded reflectometry (SER) and OCT, respectively. Convolutional neural network (CNN) detection of instrument position from SER images enables real-time motion estimation that is used to dynamically update iOCT FOVs. Here, we demonstrate video-rate 4D imaging and automated instrument-tracking of multiple surgical instruments in ex vivo porcine eyes at 16 volumes/second. The presented methods will facilitate ophthalmic surgery by providing volumetric feedback on instrument-tissue interactions.

8. Leverage Supervised and Self-supervised Pretrain Models for Pathological Survival Analysis via a Simple and Low-cost Joint Representation Tuning

Quan Liu, Can Cui, Ruining Deng, Zuhayr Asad, Tianyuan Yao, Zheyu Zhu, Yuankai Huo

Vanderbilt University

The large-scale pretrained models from terabyte-level (TB) data are now broadly used in feature extraction, model initialization, and transfer learning in pathological image analyses. Most existing studies have focused on developing more powerful pretrained models, which are increasingly unscalable for academic institutes. Very few, if any, studies have investigated how to take advantage of existing, yet heterogeneous, pretrained models for downstream tasks. As an example, our experiments elucidated that self-supervised models (e.g., contrastive learning on the entire The Cancer Genome Atlas (TCGA) dataset) achieved a superior performance compared with supervised models (e.g., ImageNet pretraining) on a classification cohort. Surprisingly, it yielded an inferior performance when it was translated to a cancer prognosis task. Such a phenomenon inspired us to explore how to leverage the already trained supervised and self-supervised models for pathological survival analysis. In this paper, we present a simple and low-cost joint representation tuning (JRT) to aggregate task-agnostic vision representation (supervised ImageNet pretrained models) and pathological specific feature representation (self-supervised TCGA pretrained models) for downstream tasks. Our contribution is in three-fold: (1) we adapt and aggregate classification-based supervised and self-supervised representation to survival prediction via joint representation tuning, (2) comprehensive analyses on prevalent strategies of pretrained models are conducted, (3) the joint representation tuning provides a simple, yet computationally efficient, perspective to leverage large-scale pretrained models for both cancer diagnosis and prognosis. The proposed JRT method improved the c-index from 0.705 to 0.731 on the TCGA brain cancer survival dataset. The feature-direct JRT (f-JRT) method achieved 60 times training speedup while maintaining 0.707 c-index score.

9. Visualizing perfusion throughout the cardiac cycle using advanced power Doppler acquisition and filtering methods

Abbie Weeks, Emelina Vienneau, Brett Byram

Department of Biomedical Engineering , Vanderbilt University

Evaluating blood flow in the liver has clinical implications for functional and oncological assessment. Here, we explore visualization of temporally varying power Doppler signals in the 3 vasculature systems in the liver using coded excitation acquisitions and block-wise SVD filtering that mitigate the limitations of poor SNR, spectral overlap, and shorter ensembles. We acquired 2 seconds of data with matched ECG traces, and then evaluated 100 sample ensembles across the ECG trace to assess optimal cardiac phases for forming images. We show that while forming images throughout the cardiac cycle is important for visualizing various vasculature, the highest CNR and SNR values are obtained from images formed during diastole.

10. Temporal Bone CT Synthesis for MR-only Cochlear Implant Preoperative Planning

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Cochlear implant (CI) surgery requires manual or robotic insertion of an electrode array into the patient's cochlea. At the vast majority of institutions including ours, preoperative CT scans are acquired and used to plan the procedure because they permit to visualize the bony anatomy of the temporal bone. However, CT images involve ionizing radiation, and some institutions and surgeons prefer preoperative MRI, especially for children. To expand the number of patients who can benefit from a computer-assisted CT-based planning system we are developing without additional radiation exposure, we propose to use a conditional generative adversarial network (cGAN)-based method to generate synthetic CT (sCT) images from multi-sequence MR images. We use image quality-based, segmentation-based, and planning-based metrics to compare the sCTs with the corresponding real CTs (rCTs). Loss terms were used to improve the quality of the overall image and of the local regions containing critical structures used for planning. We found very good agreement between the segmentations of structures in the sCTs and the corresponding rCTs with Dice values equal to 0.94 for the labyrinth, 0.79 for the ossicles, and 0.81 for the facial nerve. Such a high Dice value for the ossicles is noteworthy because they cannot be seen in the MR images. Furthermore, we found that the mean errors for quantities used for preoperative insertion plans were smaller than what is humanly perceivable. Our results strongly suggest that potential CI recipients who only have MR scans can benefit from CT-based preoperative planning through sCT generation.

11. Predicting Crohn's disease severity in the colon using mixed cell nucleus density from pseudo labels

Lucas W. Remedios* (a), Shunxing Bao (b), Cailey I. Kerley (b), Leon Y. Cai (c), François Rheault (b,d), Ruining Deng (a), Can Cui (a), Sophie Chiron (i), Ken S. Lau (e,f,g), Joseph T. Roland (f), Mary K. Washington (h), Lori A. Coburn (i,j,k,l), Keith T. Wilson (h,i,j,k,l), Yuankai Huo (a,b), Bennett A. Landman (a,b,c)

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Crohn's disease (CD) is a debilitating inflammatory bowel disease with no known cure. Computational analysis of hematoxylin and eosin (H&E) stained colon biopsy whole slide images (WSIs) from CD patients provides the opportunity to discover unknown and complex relationships between tissue cellular features and disease severity. While there have been works using cell nuclei-derived features for predicting slide-level traits, this has not been performed on CD H&E WSIs for classifying normal tissue from CD patients vs active CD and assessing slide label-predictive performance while using both separate and combined information from pseudo-segmentation labels of nuclei from neutrophils, eosinophils, epithelial cells, lymphocytes, plasma cells, and connective cells. We used 413 WSIs of CD patient biopsies and calculated normalized histograms of nucleus density for the six cell classes for each WSI. We used a support vector machine to classify the truncated singular value decomposition representations of the normalized histograms as normal or active CD with four-fold cross-validation in rounds where nucleus types were first compared individually, the best was selected, and further types were added each round. We found that neutrophils were the most predictive individual nucleus type, with an AUC of 0.92 ± 0.0003 on the withheld test set. Adding information improved cross-validation performance for the first two rounds and on the withheld test set for the first three rounds, though performance metrics did not increase substantially beyond when neutrophils were used alone.

12. SynBOLD-DisCo: Synthetic BOLD images for distortion correction of fMRI without additional calibration scans

Tian Yu (a, *), Leon Y. Cai (b, *), Victoria L. Morgan (b,c,d,f), Sarah E. Goodale (b), Dario J. Englot (b,c,d,e,f), Catherine E. Chang (a,b,d,e), Bennett A. Landman (a,b,c,d,e), and Kurt G. Schilling (c,d)

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The blood oxygen level dependent (BOLD) signal from functional magnetic resonance imaging (fMRI) is a noninvasive technique that has been widely used in research to study brain function. However, fMRI suffers from susceptibility-induced off resonance fields which may cause geometric distortions and mismatches with anatomical images. State-of-the-art correction methods require acquiring reverse phase encoded images or additional field maps to enable distortion correction. However, not all imaging protocols include these additional scans and thus cannot take advantage of these susceptibility correction capabilities. As such, in this study we aim to enable state-of-the-art distortion correction with FSL's topup algorithm of historical and/or limited fMRI data that include only a structural image and single phase encoded fMRI. To do this, we use 3D U-net models to synthesize undistorted fMRI BOLD contrast images from the structural image and use this undistorted synthetic image as an anatomical target for distortion correction with topup. We evaluate the efficacy of this approach, named SynBOLD-DisCo (synthetic BOLD images for distortion correction), and show that BOLD images corrected using our approach are geometrically more similar to structural images than the distorted BOLD data and are practically equivalent to state-of-the-art correction methods which require reverse phase encoded data. Future directions include additional validation studies, integration with other preprocessing operations, retraining with broader pathologies, and investigating the effects of spin echo versus gradient echo images for training and distortion correction. In summary, we demonstrate SynBOLD-DisCo corrects distortion of fMRI when reverse phase encoding scans or field maps are not available.

13. Survival Prediction of Brain Cancer with Incomplete Radiology, Pathology, Genomic, and Demographic Data

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Integrating cross-department multi-modal data (e.g., radiology, pathology, genomic, and demographic data) is ubiquitous in brain cancer diagnosis and survival prediction. To date, such an integration is typically conducted by human physicians (and panels of experts), which can be subjective and semi-quantitative. Recent advances in multi-modal deep learning, however, have opened a door to leverage such a process in a more objective and quantitative manner. Unfortunately, the prior arts of using four modalities on brain cancer survival prediction are limited by a "complete modalities" setting (i.e., with all modalities available). Thus, there are still open questions on how to effectively predict brain cancer survival from incomplete radiology, pathology, genomic, and demographic data (e.g., one or more modalities might not be collected for a patient). For instance, should we use both complete and incomplete data, and more importantly, how do we use such data? To answer the preceding questions, we generalize the multimodal learning on cross-department multi-modal data to a missing data setting. Our contribution is three-fold: 1) We introduce a multimodal learning with missing data (MMD) pipeline with competitive performance and less hardware consumption; 2) We extend multi-modal learning on radiology, pathology, genomic, and demographic data into missing data scenarios; 3) A large-scale public dataset (with 962 patients) is collected to systematically evaluate glioma tumor survival prediction using four modalities. The proposed method improved the C-index of survival prediction from 0.7624 to 0.8053.

14.fMRI correlates of vigilance fluctuations in Temporal Lobe Epilepsy

Sarah Goodale1, Caroline Martin2, Jared Shless3, Hernan Gonzalez4, Victoria L. Morgan1,3,4, Dario Englot1,2,4, Catie Chang1,2

Departments of Biomedical1 and Electrical and Computer2 Engineering at Vanderbilt University. Department of Radiology3 and Neurological Surgery4 at Vanderbilt Medical Center.

While temporal lobe epilepsy (TLE) is a focal epilepsy, TLE is associated with widespread effects such as difficulty maintaining alertness, increased fatigue, and neurocognitive deficits that are unrelated to temporal lobe functions. Recent work suggests that interictal abnormalities in subcortical arousal structures may be related to these neurocognitive disturbances. Characterizing whole-brain fMRI vigilance signatures in TLE could improve the understanding of neurocognitive disturbances and enable new investigations of vigilance-related signals as potential biomarkers for epilepsy. Simultaneous eyes-closed, resting-state fMRI-EEG data was collected from 11 TLE patients (44.4yo+/-13.0) and 11 healthy subjects (43.1yo+/-13.6). EEG is the gold standard for monitoring vigilance; however, it is not always available during fMRI scans. Previously, we developed an approach that can map fMRI correlates of EEG-determined vigilance fluctuations resulting in fMRI-derived vigilance predictions. We used this method to extract vigilance predictions in TLE patients using a model trained on healthy controls and a model trained on TLE patients. Using cross-validation, these fMRI-derived vigilance estimates were evaluated via comparison to an EEG vigilance measure. Overall, these fMRI results demonstrate that fMRI patterns linked with EEG-vigilance are similar across TLE patients and healthy subjects. They also demonstrate that our previously established fMRI-based vigilance detection approach may be robust enough to predict vigilance fluctuations in epilepsy fMRI-only datasets. However, it is important to note this study was conducted with a sample size of N=11. Future studies are needed to understand the implications of how these vigilance patterns may be influencing epileptic fMRI data and clinical comparisons.

15. In vivo delivery of an MK2 inhibitory peptide to prevent restenosis after peripheral angioplasty

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Peripheral artery disease, characterized by a buildup of plaque in the peripheral arteries, can be treated with balloon angioplasty where a balloon is inflated at a high pressure to restore blood flow. However, these high-pressure inflations cause damage and stress to the arterial wall, leading to excessive proliferation of the smooth muscle cells and reocclusion, or restenosis, of the artery. Our lab has shown that treatment with an MK2 inhibitory peptide nanopolyplex (MK2i-NP) can prevent stress-induced smooth muscle cell phenotype switching and overproliferation. This project seeks to develop an in vivo delivery strategy to rapidly administer MK2i-NPs at the site of angioplasty. To accomplish this goal, two methods of delivery were compared: a standard coated balloon and a specialized occlusion perfusion catheter (OPC). The OPC uses a convection-based delivery approach to diffuse MK2i throughout the vascular wall, whereas coated angioplasty balloons directly transfer MK2i to the artery. The balloon coatings utilize a layer-by-layer approach, alternating positively charged MK2i with negatively charged poly(propyl acrylic acid) polymer to create a transferable coating of drug. Layering was verified with fluorescent imaging and balloons were stripped to measure loading and release. Rat aortas were treated ex vivo with either OPC or coated balloon delivery to measure MK2i transfer and penetration into the arterial wall. Smooth muscle cells were isolated from treated aortas and cell uptake of MK2i was measured by flow cytometry. Overall, this work shows the promise of in vivo OPC and coated balloon delivery of MK2i to peripheral arteries after angioplasty.

16. Structural disconnection relates to functional changes after temporal lobe epilepsy surgery

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Epilepsy surgery consists of surgical resection of the epileptic focus and is recommended for patients with drug-resistant temporal lobe epilepsy (TLE). However, the focal resection in TLE surgery leads to functional changes in brain regions distant from the resection. Here we hypothesize that these distant changes in brain function caused by TLE surgery are due to the structural disconnection from the resected epileptic focus. Changes in brain function from pre to post surgery were quantified in a group of TLE patients using a measure of functional magnetic resonance imaging (fMRI) activity. We identified regions with significant fMRI changes from pre to post surgery that had high structural connectivity to the resected region based on diffusion MRI (dMRI) from healthy controls. fMRI activity increased from pre to post surgery in TLE in the two regions most highly structurally connected to the resected region - the thalamus and the fusiform gyrus ipsilateral to the side of surgery ($p_{FWE} < 0.05$). The structural disconnection from the resected epileptic focus was then estimated using presurgical dMRI and correlated with the fMRI changes from pre to post surgery in the ipsilateral thalamus and fusiform gyrus. The magnitude of the fMRI activity changes in both the thalamus and fusiform gyrus increased with a higher structural disconnection from the resected epileptic focus ($p < 0.05$). These results suggest that the structural disconnection from the resected epileptic focus may contribute to the distant functional changes seen after epilepsy surgery. Funded by NIH T32EB021937, R01NS075270, R01NS108445, R01NS110130 and R00NS097618.

17. Handheld spectrally encoded coherence tomography and reflectometry improvements for clinical translation in point-of-care ophthalmic diagnostics

Jacob J. Watson, Department of Biomedical Engineering **Rachel Hecht**, Department of Biomedical Engineering **Eric M. Tang, PhD**, Department of Biomedical Engineering **Yuankai K. Tao, PhD**, Department of Biomedical Engineering

Ophthalmic imaging of mobility-impaired and pediatric patients is often impeded by traditional benchtop optical coherence tomography (OCT) systems, which require upright patient fixation for imaging. Here, we demonstrate our improved handheld spectrally encoded coherence tomography and reflectometry (HH-SECTR) system with increased optical throughput in a more clinically resilient form factor. The addition of mechanical focus-adjust allows for photographer-ergonomic correction of optical power between patient eyes for optimal imaging performance in all patients. We predict these improvements will allow for improved functionality and reproducibility for clinical translation of HH-SECTR in point-of-care ophthalmic imaging.

18. Improvements in intraoperative spectrally encoded coherence tomography and reflectometry (iSECTR) for ophthalmic surgery

Rachel Hecht, Department of Biomedical Engineering **Jake Watson,** Department of Biomedical Engineering **Eric Tang, PhD,** Department of Biomedical Engineering **Yuankai Tao, PhD,** Department of Biomedical Engineering

Visualization in ophthalmic surgery benefits from high-resolution, volumetric imaging provided by intraoperative optical coherence tomography (iOCT). Recent advancements have enabled video-rate iOCT imaging of surgical dynamics and en face retinal imaging, which enables robust visualization of surgical instruments for tool-tracking. Here, we demonstrate our improved intraoperative spectrally encoded coherence tomography and reflectometry imaging (iSECTR) system with increased optical throughput and a more clinically robust form factor. iSECTR uses spatiotemporally co-registered multimodal spectrally encoded reflectometry (SER) and OCT for automated en face instrument-tracking and volumetric visualization of surgical dynamics. We demonstrate several optical and optomechanical design improvements, including a modular aluminum skeleton to maintain system alignment and increased optical power throughput to improve imaging performance. The additional implementation of mechanical focus adjust allows independent focus correction of iSECTR from the surgical microscope binoculars for optimal imaging performance and concurrent ophthalmologist visualization of the surgical environment. We predict these improvements will allow reproducibility and functionality in iSECTR clinical translation during ophthalmic surgery.

19.Mapping the Impact of Nonlinear Gradient Fields with Noise on Diffusion MRI

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In diffusion MRI, gradient nonlinearities cause spatial variations in the magnitude and direction of diffusion gradients. Studies have shown artifacts from these distortions can results in biased diffusion tensor information and tractography. Here, we investigate the impact of gradient nonlinearity correction in the presence of noise. We introduced empirically derived gradient non-linear fields at different signal-to-noise ratio (SNR) levels in two experiments: tensor field simulation and simulation of the brain. For each experiment, this work compares two techniques empirically: voxel-wise gradient table correction and approximate correction by scaling the signal directly. The impact was assessed through diffusion metrics including mean diffusivity (MD), fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD), and principal eigen vector (V1). The study shows (1) the correction of gradient nonlinearities will not lead to substantively incorrect estimation of diffusion metrics in a linear system, (2) gradient nonlinearity correction does not interact adversely with noise, (3) nonlinearity correction suppresses the impact of nonlinearities in typical SNR data, (4) for SNR below 30, the performance of both the gradient nonlinearity correction techniques were similar, and (5) larger impacts are seen in regions where the gradient nonlinearities are distinct. Thus, this study suggests that there were greater beneficial effects than adverse effects due to the correction of nonlinearities. Additionally, correction of nonlinearities is recommended when region of interests are in areas with pronounced nonlinearities.

20. Self-supervised Registration and Segmentation on Ossicles with A Single Ground Truth Label

Yike Zhang Department of Computer Science **Jack H. Noble** Department of EECE

For image-guided surgeries, such as Cochlear Implants (CIs), accurate object segmentation can provide useful information before an operation. Recently published image segmentation methods that leverage machine learning usually rely on a large number of manually predefined ground truth labels. However, it is a laborious and time-consuming task to prepare the dataset. This paper presents a novel technique using a self-supervised 3D-UNet that produces a dense deformation field between an atlas and target image that can be used for atlas-based segmentation of the ossicles. Our results show that our method outperforms traditional image segmentation methods and generates a more accurate boundary around the ossicles based on Dice similarity coefficient and point-to-point error comparison. The mean Dice coefficient is improved by 8.51% with our proposed method.

21. Comparing Techniques for Multi-Site Harmonization of Structural Connectivity

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Diffusion weighted imaging (DWI) is a non-invasive, in-vivo imaging modality. Tractography is a method to reconstruct white matter microstructure from DWI information and connectomics maps this reconstruction to a graph representation. Complex graph theory measures (GTMs) of brain structural connectomes provide insight into the network structure of the brain. We compute modularity, assortativity, global efficiency, and average betweenness centrality on this graph. We model changes in these measures with age and sex using DWI for 212 healthy patients from the Baltimore Longitudinal Study of Aging (BLSA) with 1:1 sex, age, and ApoE4 status matched participants from the Vanderbilt Memory and Aging Project (VMAP). Data from different sites requires harmonization to remove site-effects. We compare performances of ComBat and LinearRISH harmonization techniques at reducing CoV and removing confounding site-effects from associated linear models. We find that ComBat is effective for all measures, and LinearRISH combined with ComBat performs better for global efficiency and average betweenness centrality. Second, we analyze the change in site, age, and sex effect-size and significance between harmonization techniques. ComBat eliminated significant site effects for all GTMs, LinearRISH removed significant site effects for assortativity only.

22. Extending the Value of Routine Lung Screening CT with Quantitative Body Composition Assessment

Kaiwen Xu, Riqiang Gao, Yucheng Tang, Steve A. Deppen, Kim L. Sandler, Michael N. Kammer, Sanja L. Antic, Fabien Maldonado, Yuankai Huo, Mirza S. Khan, Bennett A. Landman

Certain body composition phenotypes, like sarcopenia, are well established as predictive markers for post-surgery complications and overall survival of lung cancer patients. However, their association with incidental lung cancer risk in the screening population is still unclear.We study the feasibility of body composition analysis using chest low dose computed tomography (LDCT). A two-stage fully automatic pipeline is developed to assess the cross-sectional area of body composition components including subcutaneous adipose tissue (SAT), muscle, visceral adipose tissue (VAT),and bone on T5, T8 and T10 vertebral levels.Time-to-event analysis for lung cancer incidence indicates inverse association between measured muscle cross-sectional area and incidental lung cancer risks ($p < 0.001$female, $p < 0.001$male). In conclusion, automatic body composition analysis using routine lung screening LDCT is feasible.

23. Automatic, Deep-Learning-Based Segmentation of the Amygdalohippocampectomy Resection Cavity in MR Images

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Resection of parts of the hippocampus and the amygdala is done to treat refractory mesial temporal lobe epilepsy but outcomes associated with the procedure vary. Large-scale studies exploring relations between extent and location of the resection are needed. Manual segmentation of the cavity is time-consuming, requires expertise, and is prone to errors thus hampering such studies. To address this issue, we propose the first fully automatic method to segment the resection cavity in MR images. Results show that using a deep-learning approach we have obtained expert-level contours of the resection cavity.

24. Min-Max Similarity: A Contrastive Semi-Supervised Deep Learning Network for Surgical Tools Segmentation

Ange Lou, Electrical Engineering **Kareem Tawfik,** VUMC **Xing Yao,** Computer Science **Ziteng Liu,** Computer Science **Jack Noble,** Electrical Engineering

A common problem with segmentation of medical images using medical neural networks. This is mainly due to is the difficulty to obtain a significant number of pixel-level annotated data for training. To address this issue, we proposed a semi-supervised segmentation network based on contrastive learning. In contrast to the previous state-of-the-art, we introduce Min-Max Similarity (MMS), a contrastive learning form of dual-view training by employing classifiers and projectors to build all-negative, and positive and negative feature pairs, respectively, to formulate the learning as MMS problem. The all-negative pairs are used to supervise the networks learning from different views and to capture general features, and the consistency of unlabeled predictions is measured by pixel-wise contrastive loss between positive and negative pairs. To quantitatively and qualitatively evaluate our proposed method, we test it on four public endoscopy surgical tool segmentation datasets and one cochlear implant surgery dataset, which we manually annotated. Results indicate that our proposed method consistently outperforms state-of-the-art semi-supervised and fully supervised segmentation algorithms. And our semi-supervised segmentation algorithm can successfully recognize unknown surgical tools and provide good predictions. Also, our MMS approach could achieve inference speeds of about 40 frames per second (fps) and is suitable to deal with the real-time video segmentation.

25. Unsupervised Registration Refinement for Generating Unbiased Eye Atlas

Ho Hin Lee, Department of Computer Science **Yucheng Tang,** Department of Electrical and Computer Engineering **Shunxing Bao,** Department of Computer Science **Qi Yang,** Department of Computer Science **Xin Yu,** Department of Computer Science **Kevin L. Schey,** Department of Biochemistry **Jeffrey M. Spraggins,** Department of Cell and Development Biology **Yuankai Huo,** Department of Electrical and Computer Engineering **Bennett A. Landman,** Department of Electrical and Computer Engineering

With the confounding effects of demographics across large-scale imaging surveys, substantial variation is demonstrated with the volumetric structure of orbit and eye anthropometry. Such variability increases the level of difficulty to localize the anatomical features of the eye organs for populational analysis. To adapt the variability of eye organs with stable registration transfer, we propose an unbiased eye atlas template followed by a hierarchical coarse-to-fine approach to provide generalized eye organ context across populations. Furthermore, we retrieved volumetric scans from 1842 healthy patients for generating an eye atlas template with minimal biases. Briefly, we select 20 subject scans and use an iterative approach to generate an initial unbiased template. We then perform metric-based registration to the remaining samples with the unbiased template and generate coarse registered outputs. The coarse registered outputs are further leveraged to train a deep probabilistic network, which aims to refine the organ deformation in unsupervised setting. Computed tomography (CT) scans of 100 de-identified subjects are used to generate and evaluate the unbiased atlas template with the hierarchical pipeline. The refined registration shows the stable transfer of the eye organs, which were well-localized in the high-resolution (0.5 mm^3) atlas space and demonstrated a significant improvement of 2.37% Dice for inverse label transfer performance. The subject-wise qualitative representations with surface rendering successfully demonstrate the transfer details of the organ context and showed the applicability of generalizing the morphological variation across patients.

26. Deep Constrained Spherical Deconvolution for Robust Harmonization

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Diffusion-weighted magnetic resonance imaging (DW-MRI) captures tissue microarchitectures at a millimeter scale. With the recent advantages in data sharing, large-scale multi-site DW-MRI datasets can be made available for multi-site studies. However, DW-MRI suffers from measurement variability (e.g., inter- and intra-site variability, hardware performance, and sequence design), which yields inferior performance on multi-site and/or longitudinal diffusion studies. In this study, we propose a novel deep learning-based method to harmonize DW-MRI signals for a more reproducible and robust estimation of microstructure. Our method introduces a scanner-invariant regularization from a data-driven scheme to model a more robust fiber orientation distribution function (FODF) estimation. In empirical validation, the Human connectome Project (HCP) young adults test-retest group and the MASIVar dataset (with inter- and intra-site scan/rescan data) are involved. The 8th order spherical harmonics coefficients are employed as data representation. The results show that the proposed harmonization approach achieves a higher consistency of FODF signals while maintaining higher angular correlation coefficients (ACC) with the ground truth signal, compared with the baseline supervised deep learning scheme. Furthermore, the proposed data-driven framework is flexible and potentially applicable to a wider range of data harmonization problems in neuroimaging.

27. Automated Detection of Temporal Encephaloceles Using Voxel-based Morphometry

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Temporal encephaloceles (TEs) are herniations of cerebral parenchyma through structural defects in the floor of the middle cranial fossa. They are a known cause of refractory temporal lobe epilepsy (RTLE). Approximately one-third of epilepsy patients do not have an adequate response to anti-seizure medications and in these cases, surgical options need to be considered. Uncontrolled epilepsy is associated with many negative longterm health consequences including risk of death. One of the most predictive factors associated with successful surgery is identification of an abnormality on imaging. However, TEs are often overlooked on neuroimaging studies and likely underdiagnosed on patients' initial assessments. The goal of this project is to improve detection of TEs on MRI through automated identification using voxel-based morphometry (VBM). VBM is a technique that measures local differences in brain tissue by voxel-wise comparison with a control dataset using statistical parametric mapping. It allows for detection of subtle changes in brain parenchyma such as protrusions of gray matter into white matter. We have developed a VBM algorithm based on the Morphometric Analysis Program (MAP18) to automate TE detection. On initial evaluation, our program identified TEs in MRIs of 4 out of 5 patients with RTLE. We plan to test our algorithm more rigorously on a dataset of ~80 patients composed of MRIs with confirmed TEs, unconfirmed TEs, and normal controls. Given the difficulty associated with detection of TEs, our study has the potential to significantly improve the diagnosis and treatment of an underrecognized cause of RTLE.

28. Widespread Cortical Thickness Changes After Mesial Temporal Resection in Temporal Lobe Epilepsy

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Temporal lobe epilepsy (TLE) and surgical interventions cause widespread changes in the brain, which may be quantified by cortical thickness measurements. TLE patients are known to experience cortical thinning at a rate greater than normal thinning attributed to aging, and surgical resection of the epileptic focus may slow this progression. We hypothesized that surgery has varied effects on cortical thickness trajectories with age in TLE patients. This analysis examined cortical thickness changes presurgically to postsurgically and cortical thickness changes postsurgically over time. Age corrected cortical thickness was assigned for all patients (n=25) using controls (n=98) to account for normal cortical thinning with age. We identified regions in which cortical thickness changed most significantly between pre and postsurgical scans, as well as pre and postsurgical regions that differed from age-matched controls. Ipsilateral temporal gyri, many of which were in close proximity to the region of surgical resection, experienced thinning pre to postsurgically and all of these regions were thinner than age-matched controls after surgery. We then generated a linear mixed effects model to examine the trajectory of cortical thickness changes with time after surgery (n=8 patients). Cortical thinning of occipital gyri slowed as time after surgery increased and eventually these regions demonstrated less thinning than age-matched controls as time progressed, which may be attributed to connectivity between temporal and occipital regions. Funded by R01NS075270, R01NS108445, R01NS110130, and R00NS097618.

29. Indirect Structural Changes Lead to Changes in Function After Temporal Lobe Epilepsy Resection

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Temporal lobe epilepsy (TLE) is a neurological disorder characterized by recurrent and unpredictable seizures, typically arising from small, focal regions in the hippocampus. Evidence shows that brain regions are impaired beyond the seizure focus and that regions remote to the focus may be affected by surgery and may contribute to seizure recurrence after surgery. Typical analysis methods utilizing structural connectivity are limited because we lack robust methods that allow us to probe the indirect effects of the seizure focus and its resection on all nodes of the network. The objective of this study was to investigate network-wide alterations in brain dynamics of TLE patients before and after surgical resection of the seizure focus using average regional controllability (ARC). ARC is a measure of the ability for each node to steer the network into different states with little effort. We acquired diffusion weighted imaging in 27 TLE patients, who underwent selective amygdalohippocampectomy. Edge-wise strength, node strength and node ARC were compared before and after surgery in each TLE patient using paired t-tests ($p<0.05$, FDR-adjusted $q=0.05$). We found indirect ARC changes outside the resection zone within the ipsilateral occipital lobe. We then identified a set of hub nodes that form a link between direct node effects of the resection detected mostly with strength changes and indirect effects detected only with controllability. This relationship between indirect structural network changes and brain function may be useful to understanding seizure recurrence after surgery. Funded by NIH NS075270, NS110130, NS108445, R00 NS097618, and T32 EB001628.

30. The relationship between postsurgical MRI connectivity and seizure outcome in temporal lobe epilepsy

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In patients with drug resistant temporal lobe epilepsy (TLE) resection of the seizure focus is a potential treatment. However, seizure recurrence can result from inaccurate localization, incomplete resection, development of new epileptogenic zones, and widespread effect of resection on the brain. We hypothesized that functional (FC) and structural (SC) connections that become or remain different from healthy control after surgery contribute to seizure recurrence. We divided patients into two groups, seizure-free (Engel Ia) and non-seizure-free (Engel Ib+). Then, the absolute value of the postsurgical FC or SC (in units of standard deviation from age-matched controls) was averaged within and between various brain lobes. An ANOVA was used to evaluate the relationship between lobe connections and surgical outcomes. Our findings show that ipsilateral parietal-temporal and parietal-subcortical lobe connections are altered in the non-seizure-free group, suggesting a relationship to seizure recurrence. Moreover, the ipsilateral parietal-prefrontal/subcortical connections are altered in both patient groups, suggesting these changes are related to epilepsy or surgery in all TLE patients. According to the SC results, the lobe connections relating to the temporal lobe are altered in both TLE groups. These lobe connections are directly related to surgery. In order to leverage the potential heterogeneity in the patient groups, we next plan to use the geodesic distance as a metric to determine the relationship between the postsurgical FC and SC networks and surgical outcomes. Funded by NIH R01NS075270, R01NS110130, R01NS108445, and R00NS097618.

31. Digital Twin Forecasting of Microwave Ablation via Fat Quantification Image-to-Grid Computational Methods

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Computational tools, such as “digital twin” modeling, are beginning to enable patient-specific surgical planning of ablative therapies to treat hepatocellular carcinoma. Digital twins models use patient functional data and biomarker imaging to build anatomically accurate models to forecast therapeutic outcomes through simulation, i.e., providing accurate information for guiding clinical decision-making. In the context of microwave ablation (MWA), tissue-specific factors (e.g., tissue perfusion, material properties, disease state, etc.) can affect ablative therapies, but current thermal dosing guidelines do not account for these differences. This study establishes an imaging-data-driven framework to construct digital twin biophysical models to predict ablation extents in livers with varying fat content in MWA. Patient anatomic scans were segmented to develop customized three-dimensional computational biophysical models, and fat-quantification images were acquired to reconstruct spatially accurate biophysical material properties. Simulated patient-specific microwave ablations of the digital twin models and the homogenous control models were performed at four levels of fatty liver disease (low, mild, moderate, and high). When comparing both models, there was a non-significant difference in the short-axis, long-axis, and ablation trajectory between both models. Because of this similarity of the results, the entire patients’ livers were resampled again, and it was discovered that all patients had evenly distributed liver-fat -explaining the similarities in ablation margins. In future work it would be advantageous to simulate ablation in livers with focal fat distributions. Overall, the results suggest that modeling heterogeneous clinical fatty liver disease using fat-quantitative imaging data can improve patient specificity for this treatment modality.

32. VesselMorph: Domain Generalized Retinal Vessel Segmentation via Shape-aware Causal Representation

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Due to the absence of a single standardized imaging protocol, the distribution shift between datasets is an inherent property of medical images and has become a major obstacle for large-scale deployment of learning-based algorithms. Although the domain shift can cause the variation of intensity, contrast and resolution of the image, the anatomy remains unaffected. Specifically, for segmentation tasks, the anatomy can be regarded as a causal feature that is invariant across domains. Thus, forming a good representation for the anatomical structure could allow aligning these domains for generalization purposes. In this study, we propose a method called \textit{VesselMorph} which generalizes the 2D retinal vessel segmentation task by synthesising a shape-aware causal representation. Inspired by the traditional Frangi filter and the diffusion tensor imaging literature, we introduce a Hessian-based bipolar tensor field to depict the morphology of the vessels so that the shape information can also be taken into account. We map both the intensity image and the tensor field to a causal latent feature space via a variational auto-encoder for domain alignment. This unified representation turns out to provide a synthetic angiogram with well-enhanced vasculature that boosts the generalizability. We evaluate the proposed method on public datasets of diverse modalities including fundus and OCT angiography. The results suggest that the VesselMorph achieves superior performance compared with competing methods in both cross-site and cross-modality scenarios.

33. Frequency band specific directed connectivity patterns in focal epilepsy: a single pulse electrical stimulation study

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Rationale: While previous studies have found that seizure-generating regions ("seizure onset zones" or SOZs) and propagation zones (PZs) exhibit high directed connectivity to rest of the brain during single pulse electrical stimulation (SPES), frequency-specific components of network connectivity have not been well-characterized. Our investigation assesses SOZ, PZ, and non-involved zone (NIZ) frequency-band-specific directed connectivity with SPES to elucidate electrographic "signatures" of each zone for improved SOZ localization and better understanding of epileptogenic network.

Methods: We included 23 patients who underwent stereotactic electroencephalography (SEEG) in pre-surgical workup of drug-resistant focal epilepsy and were consented for SPES. Directed connectivity of SOZs, PZs, and NIZs was analyzed in theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (31-80 Hz) frequency bands. Band-specific connectivity was measured by relative band power change from pre-stimulation baseline over 5-300 millisecond post-stimulation time window.

Results: In theta band, SOZs demonstrated strong inward connectivity through high theta band attenuation relative to NIZs and pre-stimulation baseline. SOZs also showed high inward connectivity in beta band through increased excitation of beta power relative to NIZs and pre-stimulation baseline. In gamma band, SOZs exhibited greater inward excitation than PZs.

Conclusion: Our work provides evidence that SOZs, PZs, and NIZs exhibit distinguishable frequency-band-specific directed connectivity patterns, and that inward connectivity characteristics of SOZ seemingly flip from attenuation to excitation in lower (theta) to higher (beta, gamma) frequency bands. This work may help us better understand spectral electrographic signatures of SOZs, PZs, and NIZs to aid in more accurate localization of epileptogenic zones in focal epilepsy.

34. Low-cost fabrication of well-of-the-well (WOW) dishes with arbitrary 3D microwell shapes for improved embryo culture

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The well-of-the-well (WOW) culture system is a platform for in-vitro mammalian embryo culture that has been shown to enhance the developmental competence of embryos and clinical pregnancy rates in humans compared to traditional in in-vitro fertilization (IVF) dishes. As such, use of WOW dishes is a potentially promising advance to improve IVF outcomes. However, systematic studies to investigate why WOW dishes work and which WOW dish design is best are hindered by the difficulty in fabricating WOW dishes with arbitrary shapes and dimensions. In this manuscript, we propose a low-cost and simple method to fabricate WOW dishes with microwells of arbitrary shapes and dimensions. Our strategy involves use of a low-cost 3D printing service to fabricate a poly(dimethylsiloxane) (PDMS)-based WOW insert that can be paired with a standard IVF dish to create a novel WOW dish. This strategy also makes it possible to fabricate WOW dishes at lower cost than commercially available dishes, which could encourage adoption of this promising technology. We validate the quality of the WOW inserts fabricated with this strategy and demonstrate the utility of the assembled WOW dishes for observation and grading of mouse embryo quality. We also report the first use of pyramidal and hemispherical WOW dishes for embryo culture. Our results indicate that hemispherical microwells may offer better culture outcomes than both traditional IVF dishes and the truncated cone microwell shapes used in commercial WOW dishes, suggesting that translation of our technology to IVF clinics may provide new tools to bolster IVF success rates.

35. Comparison Study of Intraoperative Surface Acquisition Methods for Surgical Navigation

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In select patients when transplant is not possible, liver surgery are preferred treatments for liver cancer and performed with curative intent. Currently, only about 20% patients are eligible for resection due to the complexity of the procedure. One confounding factor in this framework is the presence of soft-tissue deformations that compromise the fidelity of navigation systems based on preoperative computed tomographic imaging (CT) data taken prior to surgery. To date, collecting data has been accomplished with an optically tracked stylus that requires physical contact with the liver. Contact pressure could be a source of registration error. In our study, we used a non-contact digitization method called Conoprobe. A novel device attachment is developed to enable operating room use. The goal of this work is to study the difference between the rigid registration and non rigid registration method with respect to two forms of digitization (contact and non contact). For this study n=15 subjects were enrolled in an IRB approved study at Memorial Sloan Kettering Cancer Center. The organ surface coverage of the two digitization methods are compared. Rigid registration and model-based deformation correction was performed and evaluated for 6 of the 15 surgeries with a total of 18 evaluations performed (in each case, three subsurface targets are evaluated). The segmented contour of the target on the intraoperative ultrasound image are used for registration accuracy validation. In conclusion, the surface coverage of Conoprobe is less than that of stylus. Previous study has demonstrated that surface extent could affect the registration results. Therefore, even though the evaluation results of Conoprobe did not outperform that of stylus, it is reasonable to expect that designing new attachment to increase the surface extent could make Conoprobe a useful tool for acquiring surface data.

36. Longitudinal Variability Analysis on Low-dose Abdominal CT with Deep Learning-based Segmentation

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Metabolic health is increasingly implicated as a risk factor across conditions from cardiology to neurology, and efficiency assessment of body composition is critical to quantitatively characterizing these relationships. 2D low dose single slice computed tomography (CT) provides a high resolution, quantitative tissue map, albeit with a limited field of view. Although numerous potential analyses have been proposed in quantifying image context, there has been no comprehensive study for low-dose single slice CT longitudinal variability with automated segmentation. We studied a total of 1816 slices from 1469 subjects of Baltimore Longitudinal Study on Aging (BLSA) abdominal dataset using supervised deep learning-based segmentation and unsupervised clustering method. 300 out of 1469 subjects that have two year gap in their first two scans were pick out to evaluate longitudinal variability with measurements including intraclass correlation coefficient (ICC) and coefficient of variation (CV) in terms of tissues/organs size and mean intensity. We showed that our segmentation methods are stable in longitudinal settings with Dice ranged from 0.821 to 0.962 for thirteen target abdominal tissues structures. We observed high variability in most organ with ICC<0.5, low variability in the area of muscle, abdominal wall, fat and body mask with average ICC≥0.8. We found that the variability in organ is highly related to the cross-sectional position of the 2D slice. Our efforts pave quantitative exploration and quality control to reduce uncertainties in longitudinal analysis.

37. Reducing Positional Variance in Cross-sectional Abdominal CT Slices with Deep Conditional Generative Models

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2D low-dose single-slice abdominal computed tomography (CT) slice enables direct measurements of body composition, which are critical to quantitatively characterizing health relationships on aging. However, longitudinal analysis of body composition changes using 2D abdominal slices is challenging due to positional variance between longitudinal slices acquired in different years. To reduce the positional variance, we extend the conditional generative models to our C-SliceGen that takes an arbitrary axial slice in the abdominal region as the condition and generates a defined vertebral level slice by estimating the structural changes in the latent space. Experiments on 1170 subjects from an in-house dataset and 50 subjects from BTCV MICCAI Challenge 2015 show that our model can generate high quality images in terms of realism and similarity. External experiments on 20 subjects from the Baltimore Longitudinal Study of Aging (BLSA) dataset that contains longitudinal single abdominal slices validate that our method can harmonize the slice positional variance in terms of muscle and visceral fat area. Our approach provides a promising direction of mapping slices from different vertebral levels to a target slice to reduce positional variance for single slice longitudinal analysis. The source code is available at: https://github.com/MASILab/C-SliceGen

38. An Empirical Assessment of ComBat's Assumptions

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Diffusion weighted imaging (DWI) is a subset of magnetic resonance imaging (MRI) that provides useful information about white matter microstructure in the brain. However, it is a well-established issue that different scanners and acquisition parameters introduce confounding effects in the data. In order to perform effective multi-site data analysis studies, these scanner biases must first be removed in a process called harmonization. One harmonization technique that is widely applied is a statistical tool known as ComBat, used for post-processing of features that have already been extracted from the data. Originally an algorithm designed for removing batch effects in gene expression studies, it has been applied to neuroimaging data in recent years for removing scanner biases. ComBat assumes that the data can be attributed both a site-specific shift and scaling of the true mean and iteratively determines and removes them. While widely used, ComBat's assumptions have not yet been validated for DWI metrics in terms of the situations in which it can effectively identify these shift and scaling effects. We plan to vary experimental parameters based on ComBat's assumptions and compare the results to a 'silver-standard' result from an ideal dataset. As past studies have found significant correlations in DWI metrics and age, we expect successfully harmonized data to reproduce the trend we calculate for the silver-standard result. Additionally, ComBat assumes prior distributions for these shift and scaling factors, so comparison of the distributions to those of the silver standard can help determine effectiveness of harmonization as well.

39. 3D scanning and specimen mapping: innovations in intraoperative communication of frozen section results

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Background: For head and neck cancer patients, a positive surgical margin results in treatment intensification, increased cost, and an increased risk of recurrence and death. To address positive margins during surgery, surgeons rely on communication with pathologists by telephone without any visual aid to relocate the positive margin and resect additional tissue. Relocating the positive margin site using current protocols is difficult in the head and neck due to complex 3D anatomy. To address this unmet need, our team developed a protocol termed CAD margin analysis which utilizes ex vivo optical 3D scanning and specimen mapping to enhance intraoperative communication.

Methods: Resected tumor specimens were 3D scanned and margins annotated using computer assisted design (CAD) software. The virtual 3D specimen map was displayed on overhead operative room monitors via teleconferencing to facilitate communication between surgeon and pathologist surrounding frozen section results.

Results: We performed our protocol for twelve surgical cases. In eight patients, actionable information (close or focally positive margin) was delivered to the OR using anatomic visual guidance. Seven of the cases resulted in negative margins on re-resection. Final negative margin rate was 91.6% (11 of 12 cases). In the one case with a final positive margin, the surgeon determined it was not feasible to resect further based on the 3D scan.

Conclusion: 3D scanning and specimen mapping allows for enhanced intraoperative communication between surgeon and pathologist during oncologic surgery. Future prospective studies are required to determine if this protocol results in fewer positive margins.

40. Influence of auditory nerve fiber model parameters on electrical stimulus thresholds

Erin L. Bratu - Electrical & Computer Engineering **Ziteng Liu -** Computer Science
Jack H. Noble - Electrical & Computer Engineering

The standard-of-care treatment to restore sound perception for individuals with severe-to-profound sensorineural hearing loss is the cochlear implant (CI) - a small, surgically-inserted electronic device that bypasses most of the mechanism of unaided acoustic hearing to directly stimulate auditory nerve fibers (ANFs). Although many individuals experience success with these devices, a significant portion of recipients receive only marginal benefits. Biophysical models of ANFs have been developed that could be used in an image-guided treatment pipeline for patient-customized CI interventions. However, due to the difficult nature of determining neuron properties in humans, existing models rely on parameters derived from animal studies that were subsequently adapted to human models. Additionally, it is well-established that individual neurons of a single type can be non-homogeneous. In this research, we present a sensitivity analysis of a set of parameters used in one existing fiber model to (1) establish the influence of these parameters on predicted neural activity and (2) explore whether incorporation of these properties as patient-specific tunable parameters in a neural health optimization algorithm can produce a more comprehensive picture of ANF health when used in an image-guided treatment pipeline.

41. Local Structure-Function Coupling of Seizure Onset and Propagation Zones: A Combined Diffusion MRI and SEEG Study

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INTRODUCTION Increasing evidence has suggested that identification of regions involved in early seizure propagation (“Propagation Zones”, PZ) is important to predict seizure freedom after epilepsy surgery. Resting-state connectivity analyses using stereo-electroencephalography (SEEG) have shown promise in efficiently characterizing seizure onset zones (SOZ) but have found difficulty in distinguishing both SOZs and PZs from non-involved brain regions. Thus, we investigated if resting-state structure-function coupling differed between SOZs, PZs, and non-involved regions and could be used to efficaciously characterize the ictal onset and early propagative epileptic network without ictal recordings.

METHODS We calculated the SEEG partial directed coherence of 26 consented patients with focal epilepsy undergoing presurgical evaluation. Using preoperative diffusion MRI, we calculated the structural connectivity of SOZs, PZ, and non-involved regions over a range of Euclidean distances from 5 to 80 mm. We then generated models using a support vector machine to classify SOZs, PZs, and non-involved regions.

RESULTS PZs exhibit significantly higher local structure-function coupling to that of non-involved regions, with SOZs exhibiting the highest local structure-function coupling. A support vector machine to classify SOZs, PZs, and non-involved regions at the SEEG contact level was able to significantly increase model accuracy by incorporating local structure-function coupling.

CONCLUSIONS SOZs and PZs demonstrate a distinct local structure-function coupling to that of non-involved regions and each other. This distinct coupling profile can be used to accurately classify SOZs, PZs and non-involved regions. These findings could be used clinically to efficiently characterize the epileptic network using only brief resting-state recordings.

42. Electrographically Characterizing Seizure Onset Zones in Focal Epilepsy with Stereotactic-Electroencephalography

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Rationale Successful epilepsy surgery requires localization of seizure onset zone(s) (SOZ). Previous work has shown that SOZs can be classified with resting-state stereo-electroencephalography (SEEG) connectivity patterns (Goodale et al., 2020). This work further characterizes these connectivity patterns by outlining the inward vs. outward connectivity of SOZs to localize SOZs more accurately in the presurgical workup.

Methods 81 patients with medically refractory epilepsy underwent SEEG recordings obtained at the Vanderbilt University Medical Center. SEEG data was obtained for a 20-minute epoch in the resting state and was filtered with passbands of 1-59 Hz and 61-119 Hz. SOZs, non-SOZs, and early propagation zones (PZ: ictal activity spread within 10 seconds) were assigned by an epileptologist. Across patients, we evaluated undirected functional connectivity (alpha-band imaginary coherence), as well as inward and outward connectivity (alpha-band partial directed coherence).

Results We observed that alpha-band inward connectivity (Figure 1B) for SOZs is greater than that of non-SOZs ($p < 5E-6$) and PZs ($p < 5E-3$). Further, we observed that outward connectivity (Figure 1C) behaves in an inverse relationship to inward connectivity; outward connectivity is substantially decreased in SOZs compared to non-SOZs ($p < 5E-6$) and PZs ($p < 5E-3$). Finally, by computing reciprocal connectivity (Figure 1D), we observed an increased group difference between SOZs compared to non-SOZs ($p < 5E-6$), and PZ ($p < 5E-3$), measured by ANOVA ($p = 3.13E-13$). ANOVA was also used to identify differences between these regions with respect to inward ($p = 1.75E-12$) and outward ($p = 4.95E-10$) functional connectivity.

43. Widespread Ictal Connectivity Abnormalities in Focal Impaired Awareness Seizures

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Introduction Epilepsy is a common neurological disorder of recurrent seizures. Both focal aware seizures (FAS) and focal impaired awareness seizures (FIAS) drastically impact patients' lives. The loss of consciousness in FIAS can be particularly devastating and is hypothesized to arise from widespread network dysfunction. Evaluation of widespread brain network functional connectivity in FAS vs. FIAS may provide insight into the neurostimulation targets strategies to prevent loss of consciousness in FIAS.

Methods Stereotactic electroencephalography recordings of 34 patients were obtained. All FAS and FIAS were extracted and divided into 20 second sliding windows across the entire seizure. Relative bandpower and connectivity were computed on seizure epochs. Metrics were z-scored to a patient's 20-minute resting state. Variability of relative bandpower and connectivity was calculated as the standard deviation of the metric across all windows. Regions sampled were parcellated into the ipsilateral and contralateral mesial temporal, lateral temporal, and frontoparietal association cortex.

Results FIAS were associated with greater bandpower and connectivity variability while FAS demonstrated increased outward connectivity. FIAS were associated with significantly greater relative bandpower variability in the contralateral mesial and lateral temporal lobes (2-sample t-test, $p<0.001$). Additionally, FIAS demonstrated greater inward connectivity variability to the contralateral mesial temporal region from all other regions ($p<0.05$). Finally, FAS showed increased connectivity from the contralateral mesial temporal region to all other contralateral regions ($p<0.05$).

Conclusion This work shows that FIAS exhibit more connectivity and bandpower changes ictally, perhaps contributing to ictal loss of consciousness. This work could lead to the identification of neuromodulation strategies to preserve consciousness.

44. Heterogeneous Anisotropic Biomechanical Modeling to Predict Breast Deformations for Surgical Guidance

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1 in 8 women will be diagnosed with breast cancer in their lifetime, and breast conserving surgery (BCS) is a common treatment option for women with early-stage breast cancer. However, reoperation rates for BCS procedures are high with approximately 17% of patients having to return to the operating room for a second surgery because of recurrence due to incomplete excisions. Currently available tumor localization technologies do not provide surgeons with enough information to excise lesions accurately and completely in all cases. This clinical need presents an opportunity to develop an image-guidance navigation platform system specifically for BCS that can aid surgeons in accurately locating the tumor during surgery. Previously developed image-guided surgery systems for BCS have failed to account for nonrigid deformations that occur in the breast, which compromises the accuracy of these systems. In this work, three biomechanical modeling approaches are investigated to better predict nonrigid breast deformations: a homogeneous isotropic model, a heterogeneous isotropic model, and a heterogeneous anisotropic model. To simulate surgical deformations, MR imaging datasets of healthy volunteers were acquired with volunteers laying supine in arm-down and arm-up positions. The average target registration errors of anatomical features for the three model implementations were 5.4 ± 1.5 mm for the homogeneous isotropic model, 5.3 ± 1.5 mm for the heterogeneous isotropic model, and 4.7 ± 1.4 mm for the heterogeneous anisotropic model. Although more investigation is needed, these preliminary results show that a heterogeneous anisotropic model offers significant improvement for potential applications in real-time surgical guidance.

45. Atlas-Based Automatic Internal Auditory Canal Localization with a Weakly-Supervised 3D U-Net

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

Cochlear implants (CIs) are neural prosthetics which use an array of implanted electrodes to improve hearing in patients with severe-to-profound hearing loss. After implantation, the CI is programmed by audiologists who adjust various parameters to optimize hearing performance for the patient. Without knowing which auditory nerve fibers (ANFs) are being stimulated by each electrode, this process can require dozens of programming sessions and often does not lead to optimal programming. The internal auditory canal (IAC) houses the ANFs as they travel from the implantation site, the cochlea, to the brain. In this paper, we present a method for localizing the IAC in a CT image by deforming an atlas IAC mesh to a CT image using a 3D U-Net. Our results suggest this method is more accurate than an active shape model-based method when tested on a small set of images with known ground truth. This IAC segmentation can be used to infer the position of the invisible ANFs to assist with patient-specific CI programming.

46. Model-Based Pose Estimation of Steerable Catheters under Bi-Plane Image Feedback

Jared Lawson (VU Department of Mechanical Engineering) **Rohan Chitale, MD** (VUMC Department of Neurological Surgery) **Nabil Simaan, PhD** (VU Department of Mechanical Engineering)

Small catheters undergo significant torsional deflections during endovascular interventions. A key challenge in enabling robot control of these catheters is the estimation of their bending planes. This paper considers approaches for estimating these bending planes based on bi-plane image feedback. The proposed approaches attempt to minimize error between either the direct (position-based) or instantaneous (velocity-based) kinematics with the reconstructed kinematics from bi-plane image feedback. A comparison between these methods is carried out on a setup using two cameras in lieu of a bi-plane fluoroscopy setup. The results show that the position-based approach is less susceptible to segmentation noise and works best when the segment is in a non-straight configuration. These results suggest that estimation of the bending planes can be accompanied with errors under 30°. Considering that the torsional buildup of these catheters can be more than 180°, we believe that this method can be used for catheter control with improved safety due to the reduction of this uncertainty.

47. Robust generalized contrast-to-noise ratio

Siegfried Schlunk, Brett Byram

Biomedical Engineering, Vanderbilt University

The generalized contrast-to-noise ratio (gCNR) is a new but increasingly popular metric for measuring lesion detectability due to its robustness against transformations and dynamic range alterations, as well as its ease of implementation. The value of these kinds of metrics has become increasingly important as it becomes clear that traditional metrics can be arbitrarily boosted with the right kinds of processing. However, the standard implementation of gCNR using histograms can potentially be manipulated by altering the ratio of the number of pixels to the number of bins. This is demonstrated with simulated lesions by altering the number of pixels and bins used in the calculation, as well as by introducing some extreme transformations that produce better or worse gCNR as desired. In this work, the viability of a parametric gCNR implementation is tested, more robust methods for implementing histograms are considered, and an empirical gCNR estimate is shown. The most consistent methods found were to use histograms on rank-ordered data or histograms with variable bin widths, or to use empirical CDFs to estimate the gCNR.

48. Autonomous Needle Steering: A Minimally Invasive Surgical Solution In Vivo

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With lung cancer accounting for over 22% of cancer-related deaths in US, advancing the technologies surrounding the diagnosis and treatment of suspicious nodules within the lung is crucial. Reaching these nodules can be risky due to the risk of pneumothorax with percutaneous methods, and the minimally invasive interventions via bronchoscopy are limited to nodules near the bronchial tree. To overcome these challenges, we propose deploying a robotic system consisting of a clinical bronchoscope, notched aiming device, and laser-patterned, bevel tip needle to decrease risk and increase yield during diagnosis. In this work we present a semi-autonomous robotic system capable of navigating the tortuous airways to steer to nodules located in the periphery of the lung. This work describes, for the first time, the use of a robotic steerable needle in an in vivo animal model in a lung application. This work supports the clinical feasibility of the robotic steering system by showing its success in the presence of respiratory motion, cardiac motion, and other in vivo risks. Three steers were performed in an in vivo porcine model with an average targeting error of 2.63 mm. In addition, we conducted ex vivo experiments to compare our system to manual bronchoscopy, which showed that the robotic system was able to reduce the targeting error by an average of 11.35 mm. The successful in vivo, autonomous steers presented in this work coupled with the ability to outperform manual bronchoscopy ex vivo, highlights a promising solution for difficult-to-reach nodules in the lung.

49. ROI-free Assessment of In-vivo Image Quality with Feature Extraction and the Earth Mover's Distance

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Conventional image quality metrics require manual selection of regions of interest and can lead to a subjective, myopic, and inefficient image assessment. We propose an automated, image-based metric that compares a test image to a reference distribution composed of Field II simulations free of phase aberration, reverberation, and off-axis scattering. By training an autoencoder on channel data of in-vivo and simulated images, we extracted a 64-dimensional feature vector for each pixel. We aggregated all pixels of an image into a 64-dimensional distribution and compressed it with K-means clustering. Lastly, we computed the similarity between test and reference distributions with the earth mover's distance (EMD). Simulation experiments demonstrate that EMD decreases monotonically as signal to clutter ratio increases. In-vivo experiments on cardiac cineloops suggest that EMD is relatively consistent across frames, and appears to correlate with human perception of image quality.

50. ASSIST-U: A System for Segmentation and Image Style Transfer for Ureteroscopy

Daiwei Lu[1] *, Yifan Wu[1], Ayberk Acar[1], Xing Yao[1], Jie Ying Wu[1], Nicholas Kavoussi[2], and Ipek Oguz[1]

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Purpose: Kidney stones require surgical removal when they grow too large to be broken up externally or to pass on their own. These surgeries are difficult, particularly for trainees who often miss stone fragments, requiring reoperation. One cause of difficulty is the high cognitive strain surgeons experience in creating accurate mental models during the operation. There are currently no commonly used tools to visualize kidney structure to help surgical planning. We propose ASSIST-U, a system to automatically create realistic ureteroscopy images and videos solely using preoperative CT images to address this unmet need.

Methods: We train a 3D UNet model to automatically segment CT images and construct 3D surfaces. These surfaces are then skeletonized for rendering and camera position tracking. Finally, we train a style transfer model using CycleGAN to synthesize realistic ureteroscopy images.

Results: Cross validation on the UNet model achieved a mean Dice score of 0.853 $\pm$ 0.084. CycleGAN style transfer produced visually plausible images; the Frechet Inception Distance to real ureteroscopy images was reduced from 357 (rendered images) to 212 (synthesized ureteroscopy images). We also qualitatively demonstrate the entire pipeline from CT to synthesized ureteroscopy.

Conclusion: The proposed ASSIST-U system shows promise for aiding surgeons in preoperative visualization of kidney ureteroscopy.

51. Novel application of the attention mechanism on medical image harmonization

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Medical image harmonization aims to transform the image 'style' among heterogeneous datasets while preserving the anatomical content. It enables data-sensitive learning-based approaches to fully leverage the data-power of large multi-site datasets with different image acquisitions. Recently, the attention mechanism has achieved excellent performance on the image-to-image (I2I) translation of natural images. In this work, we further explore the potential of leveraging the attention mechanism to improve the performance of medical image harmonization. Here, we introduce two attention-based frameworks with outstanding performance in the natural I2I scenario into the context of cross-scanner MRI harmonization for the first time. We compare them with the existing commonly used harmonization frameworks by evaluating their ability to enhance the performance of the downstream subcortical segmentation task on T1w MRI datasets from 1.5T vs. 3T scanners. Both qualitative and quantitative results prove that the attention-mechanism contributes to a noticeable improvement in harmonization ability.

52. SSL^2: Self-Supervised Learning meets Semi-Supervised Learning: Multiple Sclerosis Segmentation in 7T-MRI from large-scale 3T-MRI

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Automated segmentation of multiple sclerosis (MS) lesions from MRI scans is important to quantify disease progression. In recent years, convolutional neural networks (CNNs) have shown top performance for this task when a large amount of labeled data is available. However, the accuracy of CNNs suffers when dealing with a small in-house dataset with limited manual labeling availability. A potential solution is to leverage the information available in public datasets as well as the unlabeled target dataset. In this paper, we propose a training framework, SSL^2 (self-supervised-semi-supervised), for multi-modality MS lesion segmentation with limited supervision. We adapt self-supervised learning to leverage the knowledge from large public 3T datasets to tackle the limitations of a small in-house 7T target dataset. To leverage the information from unlabeled 7T data, we also evaluate state-of-the-art semi-supervised methods for limited annotation settings such as small training size and sparse annotations. We use the shifted-window (Swin) transformer as our backbone network. The effectiveness of self-supervised and semi-supervised training is evaluated on our in-house 7T MRI dataset. The results indicate that each approach improves lesion segmentation for both limited training data size and for sparse labeling scenarios. The overall framework further improves the performance substantially compared to each of its components alone. Our proposed framework thus provides a promising solution for future data/label-hungry 7T MS studies.

53. Super-resolution inner-ear tissue segmentation

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Cochlear implants (CIs) are considered the standard-of-care treatment for profound sensory-based hearing loss. In previous research, our group has developed methods that rely on atlas-based segmentation to improve CI hearing outcomes. Although the atlas-based method which uses scalae meshes and labels from μCTs results in accurate segmentation of scalae substructures, it is less accurate for tissue that is distant from the meshes. And the anatomical differences between ex-vivo μCTs and in-vivo patient CTs were not considered in that approach. Thus, we propose to use a deep learning-based method to obtain μCT level tissue labels using patient CT images. Experiments show that the proposed architecture outperforms the atlas-based method and produces comparable results to other deep learning architectures using only low-resolution input and fewer parameters.

54. A Virtual Reality Framework for Evaluating Concentric Tube Surgical Robot Designs

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Concentric tube robots (CTRs) are devices made from nesting pre-curved superelastic tubes, typically made from Nitinol. By twisting and bending the tubes within one another, CTRs are able to achieve tentacle-like motion that enables them to reach anatomical targets that are difficult to reach with conventional transendoscopic instruments. These robots have many design parameters that affect their shape, dexterity, and surgical workspace. Computational models have been developed to optimize tube parameters for a desired workspace. However, a purely numerical approach is not sufficient to guarantee the best manipulability across the range of surgical gestures needed by the surgeon. Human testing is required, to ensure that a tube design satisfies the desired "feel" for the intended tasks in the workspace. We have developed a virtual reality framework in Unity® for evaluating tube parameters in simulation. The virtual environment enables surgeons to test CTR parameters without the need for manufacturing physical tubes, saving time and material costs. Our simulator was designed to be easily adaptable to any physical user interface, so that surgeons may test CTR configurations with an interface of their choice. Touchpad and joystick controllers, a Phantom Omni®, and motion-tracked Oculus Quest® controllers have all been demonstrated successfully with the simulator so far. The virtual environment is also able to load user-defined exercises, so that different tasks can be simulated. Here we present the initial design for our virtual reality framework.

55. ASSIST-U: A System for Segmentation and Image Style Transfer for Ureteroscopy

Daiwei Lu 1 *, Yifan Wu 1, Ayberk Acar 1, Xing Yao 1, Jie Ying Wu 1, Nicholas Kavoussi 2 and Ipek Oguz 1

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Purpose: Kidney stones require surgical removal when they grow too large to be broken up externally or to pass on their own. These surgeries are difficult, particularly for trainees who often miss stone fragments, requiring reoperation. One cause of difficulty is the high cognitive strain surgeons experience in creating accurate mental models during the operation. There are currently no commonly used tools to visualize kidney structure to help surgical planning. We propose ASSIST-U, a system to automatically create realistic ureteroscopy images and videos solely using preoperative CT images to address this unmet need.

Methods: We train a 3D UNet model to automatically segment CT images and construct 3D surfaces. These surfaces are then skeletonized for rendering and camera position tracking. Finally, we train a style transfer model using CycleGAN to synthesize realistic ureteroscopy images.

Results: Cross validation on the UNet model achieved a mean Dice score of 0.853 $\pm$ 0.084. CycleGAN style transfer produced visually plausible images; the Frechet Inception Distance to real ureteroscopy images was reduced from 357 (rendered images) to 212 (synthesized ureteroscopy images). We also qualitatively demonstrate the entire pipeline from CT to synthesized ureteroscopy.

56. Deep whole brain segmentation of 7T structural MRI

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7T magnetic resonance imaging (MRI) has the potential to drive our understanding of human brain function through new contrast and enhanced resolution. Whole brain segmentation is a key neuroimaging technique that allows for region-by- region analysis of the brain. Segmentation is also an important preliminary step that provides spatial and volumetric information for running other neuroimaging pipelines. Spatially localized atlas network tiles (SLANT) is a popular 3D convolutional neural network (CNN) tool that breaks the whole brain segmentation task into localized sub-tasks. Each sub- task involves a specific spatial location handled by an independent 3D convolutional network to provide high resolution whole brain segmentation results. SLANT has been widely used to generate whole brain segmentations from structural scans acquired on 3T MRI. However, the use of SLANT for whole brain segmentation from structural 7T MRI scans has not been successful due to the inhomogeneous image contrast usually seen across the brain in 7T MRI. For instance, we demonstrate the mean percent difference of SLANT label volumes between a 3T scan-rescan is approximately 1.73%, whereas its 3T-7T scan-rescan counterpart has higher differences around 15.13%. Our approach to address this problem is to register the whole brain segmentation performed on 3T MRI to 7T MRI and use this information to finetune SLANT for structural 7T MRI. With the finetuned SLANT pipeline, we observe a lower mean relative difference in the label volumes of ~8.43% acquired from structural 7T MRI data. Dice similarity coefficient between SLANT segmentation on the 3T MRI scan and the after finetuning SLANT segmentation on the 7T MRI increased from 0.79 to 0.83 with $p<0.01$. These results suggest finetuning of SLANT is a viable solution for improving whole brain segmentation on high resolution 7T structural imaging.

57. Evaluation of the Myoton Illustrated Skin Manual in Training New Users

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The Myoton is a handheld device for rapid, non-invasive assessment of skin biomechanical properties. It has been proposed as a candidate technology for quantitatively evaluating cutaneous sclerosis by non-experts in diseases such as chronic graft-versus-host disease and scleroderma. The current gold standard for assessing skin sclerosis consists of semi-qualitative scales based on manual palpation of the skin by physicians. Future widespread usage of the Myoton, especially in large multi-center trials or for at-home use, requires the creation and evaluation of training materials for new users. In this study, we examined the efficacy of training materials consisting of an illustrated manual for new users of the device. The Myoton Illustrated Skin Manual aims to guide users through the data collection and storage procedure. It helps users to correctly identify anatomical sites to be measured with the device through extensive illustrations and practical tips. For this study, a novice user was provided with the Myoton device and a copy of the illustrated manual. The novice user studied the manual in their own time and further used it for real-time guidance during data collection. The performance of the novice user was compared to that of an experienced and an expert user. We find that after only one measurement session, the performance of the novice user compared favorably against the experienced and expert users. The data shows that the Myoton device can be used to collect reliable skin measurements by non-expert users with minimal training.

58. Exploring timing patterns around the phase transition of the brain system using resting-state fMRI

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A brain avalanche can be described as when the whole brain shows large-scale co-activation in the cortex. As many studies focus on exploring the brain behaviors around criticality, we introduced two approaches to explore the timing patterns in brain regions around the avalanche peaks of the signal. The first approach measures relative peaking time to the avalanche peak, while the second applies modified Principal component analysis for the sliding window to extract components and analyze the resulting coefficients. In both cases, we found trajectories across brain regions that could possibly show how a brain is working.

59. Neural Network Based Approach for Intraoperative Cochlear Implant Tip Fold-Over Detection Using a Dataset of Synthetic CT Images

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In cochlear implant (CI) procedure, an electrode array is surgically inserted into the cochlea that stimulates the auditory nerves in order of restoring the hearing sensation of the patient. During this surgical procedure the tip of the electrode array could curl in an irregular manner inside the cochlear volume resulting tip fold-over condition. This might lead to trauma, damage to the residual hearing and poor hearing restoration. Intraoperative detection of such a case can allow a surgeon to pull back the array and reinsert it into the cochlea. However, this intraoperative detection requires experience and audiological tests sometimes fail to detect a tip fold-over situation. Furthermore, tip fold-over cases being very rare, it is difficult to accumulate a balance dataset to train a neural network-based model for tip fold-over detection. Therefore, in this study we generated a dataset of synthetic CT images demonstrating tip fold-over conditions with realistic metal artifact. The dataset was used to train a modified multitasking 3D-UNet model for tip fold-over detection. We tested the trained model on 7 real tip fold-over CTs and the model could correctly classify all of them. Therefore, the model can be used as an intraoperative detection tool for tip fold-over cases and thus help the surgeon to avoid such abnormal curling of the electrode array during the CI surgical procedure.

60. Evaluating fMRI vigilance signals in relation to age-related cognitive changes

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The onset of Alzheimer's Disease (AD) has been linked to insomnia and changes in sleep patterns. Further, brain regions that show early degeneration in AD include subcortical regions involved in vigilance regulation, such as the basal forebrain. We hypothesize that the basal forebrain plays a key role in mediating the connection between vigilance-related brain activity and cognition in older adults. To test our hypothesis, we used fMRI data from the Vanderbilt Memory and Aging Project dataset, consisting of 49 mild cognitively impaired (MCI) patients (age = 75.1 ± 7.14) and 75 healthy controls (age = 74.4 ± 7.03). Since measures of vigilance (such as EEG) are not present during fMRI, here we used a data-driven technique for extracting vigilance information directly from fMRI data. With this approach, we derived subject-specific spatial maps reflecting a whole-brain activity pattern that is correlated with vigilance. Mediation analysis was performed to evaluate how basal forebrain volume (defined with multi-atlas parcellation) may mediate fMRI-derived vigilance effects on executive function. Significant clusters involved in the association between fMRI vigilance patterns and basal forebrain volume, and between basal forebrain volume and executive function, were found (FDR threshold; $q < 0.05$). The total and direct effects of vigilance patterns on executive function were also significant in regions including the occipital cortex at an FDR threshold of 0.05. These results suggest that cognitive decline in AD may be linked with both subcortical structural changes and full-brain vigilance patterns, which future work will explore.

61. Counting Monkeypox Lesions in Patient Photographs: Limits of Agreement of Manual Counts and Artificial Intelligence

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Monkeypox is considered the most important orthopox virus in humans, with new cases in Europe and North America in 2022 leading to the World Health Organization declaring a public health emergency of international concern. WHO guidelines assign monkeypox severity by the number of skin lesions. Daily lesion counts are an important monitoring parameter in imminent clinical trials but are labor intensive and logistically challenging. To determine the limits of agreement between automated photo analysis and manual lesion counts we used a set of 66 photographs of 18 patients from an observational study in the Democratic Republic of Congo. A team member marked borders of every lesion on each image. These annotations were used to train a U-net-based algorithm to recognize and count lesions. The algorithm was prospectively tested against the manual counts of three human raters. Ground truth lesions per image (rater 1 manual counts) ranged from 7 to 304 with a mean of 63.97 (standard deviation 58.84). The algorithm bias, calculated as mean difference from ground truth, was -5.86 (limits of agreement width 68.85). The remaining two human raters had biases of -3.24 (38.44) for rater 2, 9.68 (76.74) for rater 3, and 12.92 (81.91) between raters 3 and 2. The algorithm was also successful in counting lesions from publicly available images. With only limited training data, our method produced comparable performance to human raters for lesion counting. Automated photograph analysis may offer a scalable solution to stage and study monkeypox disease in observational and therapeutic studies.

62. Robotic Mediation Interface for Colonoscopy: a Combined Skill Assessment and Training Tool

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Colorectal Cancer is the second leading cause of cancer death in the United States.Periodic endoscopic screening(colonoscopy)is akey tool to reducing-deaths due to this disease.There is a growing world population in need of colonoscopies but an insufficient number of endoscopists to meet this demand. Despite the lengthy endoscopy training process that requires several years of precepted learning, there is still great variabilityin the quality of colonoscopy among endoscopists. This work presents a robotic system as a foundational tool for establishing objective and quantifiable metrics for the technical skill level of an endoscopist to ensure high level performance. The presented system is a two degrees-of-freedom cable-driven series-elastic actuator attachment for the OlympusEvis Exera IIColonoscope. We present our approach for obtaining quantifiableskill assessment data comprised of an estimate of the trainee's effort(motion and torque applied to the control wheels of the colonoscope). An initial design is presented with preliminary results of feasibility for using this device in admittance control mode and for estimatingthe user's effort.

63. Quantification of age-related changes in skin biomechanics through dynamic indentation

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Background: Quantitative comparison between biomechanical properties of healthy and diseased skin can help clinicians diagnose, track, and manage diseases with cutaneous manifestations such as chronic graft-versus-host disease and scleroderma. The biomechanical properties of healthy skin depend on several factors including age, sex, and body mass index. The Myoton is a handheld dynamic indentation device that characterizes the skin's biomechanical properties.

Methods: We examined five Myoton parameters (frequency, stiffness, relaxation time, creep, and decrement) at 14 anatomic sites in 55 healthy subjects. Pearson correlation coefficients were calculated for age and average measurement for each of the Myoton parameters. Five linear models were developed to examine the association of age, sex, race, and BMI with each Myoton parameter.

Results: Age and decrement were strongly correlated ($r = 0.89$ [0.82-0.93]). We found statistically significant positive associations between age and Myoton parameters decrement ($p < 0.001$), stiffness ($p < 0.001$), and creep ($p < 0.001$). Sex was also significantly associated with creep, with the average creep for males being 0.44 [0.33-0.56] less than females.

Conclusion: These results provide important information for the design of future studies evaluating skin biomechanics via the Myoton. Specifically, our data suggest age matching of control participants is necessary. When studying skin conditions that may alter the stiffness, creep, or decrement parameters of the skin, age matching to within a decade is important, however frequency and relaxation may be parameters less affected by age. Further studies are needed to validate these associations.

64. A Five Degree of Freedom (DoF) Remote Center of Motion (RCM) Device for Stable Optical Coherence Tomography (OCT) Imaging

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Jin Shen, Karen Joos: Vanderbilt Eye Institute, Vanderbilt University Medical Center

Clinical optical coherence tomography (OCT) enables high-definition images of intraocular tissues for disease diagnosis and monitoring. Handheld OCT has the potential for diagnosing diseases such as retinopathy of prematurity in patients unable to be imaged with standard clinical devices. However, high-fidelity images are difficult to acquire due to the awkward ergonomics of positioning the OCT probe even for highly skilled personnel. Further, acquiring accurate 3-dimensional images for lesion examination or volume estimation requires maintaining a fixed position for prolonged periods of time. The accuracy of reconstructed images can be significantly diminished by motions as small as a user's physiological tremor. This work presents a statically balanced five degree of freedom (DoF) Remote Center of Motion (RCM) device that carries an OCT probe used for 3D reconstruction. Improved image quality offered by the device over a traditional manual handheld approach is demonstrated by comparing 3D reconstructed OCT images of metal spheres in a phantom eye. A decrease in the OCT probe's positional variance throughout the imaging time period is also quantified.

65. High Throughput QA and Tabulation of Measurements From Longitudinal Diffusion MRI

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Measures such as fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD)can be extracted from diffusion MRI to quantify the diffusivity in the brain.Together with other measures from longitudinal datasuch as volume of regions of brain, we can perform statistical analysis toshow the relationship between the variancesof these values and aging, so that understanding the development of the brain during normal aging. However, one vital thing to accomplish first is qualityassurance (QA), a necessary processto makesure thatthe data is reliable for future studies.In this work, we performed a high-throughput QA onthemicrostructural and macrostructural features measuredfrom scan and re-scan diffusion MRIsacquired during2742 sessionsof 1035 subjects ofthe Baltimore Longitudinal Study of Aging (BLSA), whose age ranges from 22.4 to 103 years old. In the end, we generated a spreadsheet with 2742 rows and 13900 columnsto share with our collaborators for studying aging.

66. Exploring An External Approach to Subretinal Drug Delivery via Robot Assistance and B-Mode OCT

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Injections into specific retinal layers of the eye present a serious challenge to surgeons in terms of accuracy and perception. The emergence of new gene therapies further emphasizes the need for effective tools for localized drug delivery. Unlike the dominant approach of delivering drugs via a transvitreal intraocular pathway, this work demonstrates the feasibility of delivering injections into the space between the choroid and the retina using an external injection approach. The design of a cooperative robotic system for robot-assisted extraocular subretinal injections is presented. The system uses a distal micromanipulator that can serve as a hand-held tool for Optical Coherence Tomography (OCT)-aided injection or attach to a six degree of freedom (DOF) serial robot arm for cooperative manipulation. The kinematics and control of the robot for constrained cooperative control motions to enable safe needle injection is presented and experimentally evaluated. These results suggest that the proposed external drug delivery approach is feasible, thereby enabling the advantages of preserving the integrity of the retina and omitting the necessity for resource-heavy procedures such as vitrectomy.

67. Registration of Surgical Video to Preoperative Imaging for Navigation in Endoscopic Kidney Surgery

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Purpose: Endoscopic renal surgeries have high re-operation rates, particularly for lower volume surgeons. Due to the limited field and depth of view of current endoscopes, mentally mapping preoperative computed tomography (CT) images of patient anatomy to the surgical field is challenging. The inability to completely navigate the intrarenal collecting system, moreover, leads to missed kidney stones and tumors, subsequently arising recurrence rates. We hereby propose a guidance system to estimate the endoscope positions within the CT to reduce re-operation rates.

Methods: We use a Structure-from-Motion algorithm to reconstruct the kidney from the endoscope videos. In addition, we manually segment the kidney from CT scans to create a 3D model of the kidney. We can then register the two kidney representations to provide information on the relative endoscope position.

Results: We demonstrate correct reconstruction and localization of intrarenal anatomy and endoscope position. Furthermore, we create a 3D map supported with the RGB endoscope images to reduce the burden of mental mapping during surgery.

Conclusion: The proposed reconstruction pipeline has been validated for guidance. It can reduce the mental burden for surgeons and is a step towards our long-term goal of reducing re-operation rates in kidney stone surgery.

68. Development of a Mixed Reality Application to Simulate Neurosurgical Procedures

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Conventional image guidance systems have become the standard for planning in neurosurgical procedures. While these systems have been shown to increase accuracy and precision for a variety of cases, there are still drawbacks. Such limitations revolve around the use of multiple physical components to separately display the information and the substantial amount of training time required for residents to become familiar with these systems. These disadvantages can increase the difficulty of the surgery unnecessarily, and thus affect quality. To address these concerns, a mixed reality application was developed on the Microsoft HoloLens as a surgical planning and teaching tool. The developed software was able to render 3D holograms of the patient's head on a simulated bed, and their MRI information along the axial, coronal and sagittal planes. From there, neurosurgeons could create a virtual craniotomy plan on the provided case through hologram interaction. These interactions included the ability to rotate the head to its desired location, perform an image-to-physical registration that could be compared with the HoloLens' own algorithm, and utilize the user's finger as a virtual stylus to collect points for the surgical plan. To evaluate the application prototype, practicing neurosurgeons were provided a demonstration and then promptly interviewed to assess design and efficacy. Initial responses indicate that the prototype could be an effective surgical teaching and planning tool for less-experienced neurosurgeons, and it could potentially be used to target and display tumor models on the patient's physical head.

69. Sources of Disagreement in Chronic Graft Versus Host Disease Skin Demarcations

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Erythema is a primary disease morphology of chronic graft-versus-host disease (cGVHD) and is used to identify the extent of the disease and its severity. A previous study by Mitchell et al. (American Society for Blood and Marrow Transplantation, 2011) reported a mean error of 4% (95% confidence interval width of 28%) between clinicians when visually assessing body surface area of erythema. The role of the visual system in this observed variability is unknown. The goal of our study was to investigate how color perception and inherent biases in the visual system may affect manual demarcations of cGVHD in patient photos. We analyzed biases in color perception using the a* value from CIELAB color space, which measures the intensity of redness. We assessed the variability of the demarcated areas using two measures: percent of skin area demarcated and dice coefficient, a spatial metric that measures the overlap of demarcations. We found a mean bias of 3.5% (95% CI width 63%), in erythema surface area demarcated by the two raters across the photoset, indicating high variability in demarcated areas. The median Dice coefficient was 0.64 (interquartile range 0.44-0.82), showing good overall agreement with position overlap. However, the mean bias for redness (a*) was close to zero, showing no consistent bias in the raters' perception of erythema across the photoset. As such, biases in human color vision alone do not explain the difference in clinician measurement of erythematous skin previously reported in the literature and observed in our study.

70. Predictive Characterization of Uncertainty in Deformable Image Registration: Novel Strategies for Assuring Registration Accuracy during Image-Guided Procedures

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Successful estimation of target registration error (TRE) would provide immense opportunities for controlling risks associated with navigation during image-guided surgery. While developed theories exist for predicting spatial distributions of TRE for rigid point-based registration, similar capabilities in the domain of deformable registration are still needed to develop truly reliable image guidance systems for navigation in soft tissue organs. Recently, breakthrough work derived two analytic uncertainty metrics based on the dissipation of constraint energy over distance to measure the susceptibility of elastic deformable registration to errors originating from unknown effects that occur where registration constraints are missing. In this work, these registration uncertainties are leveraged to classify error thresholds for detecting spatial regions that become vulnerable to inaccuracy in sparse data driven elastic registrations. With a large dataset of over 6000 registrations, receiver operating characteristic (ROC) analysis was performed to assess discriminatory performance of these uncertainty metrics to clinically relevant levels of registration error and to identify optimal binary cutoffs for their prediction. Both uncertainty metrics were capable of detecting regions of the organ where deformable registration accuracy exceeded the average magnitude of rigid registration error with AUC above 0.87. Furthermore, both metrics detected regions of the organ with TRE greater than 10 mm with AUC of approximately 0.8. These new capabilities will enhance clinical confidence in image-guided technologies in deforming organs through enabling immediate quantification and communication of navigational reliability and system accuracy during soft tissue surgery.

71. Vigilance-dependent connectivity of arousal and autonomic structures in healthy controls and temporal lobe epilepsy

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Patients with temporal lobe epilepsy (TLE) suffer from vigilance impairments seemingly unexplained by temporal lobe dysfunction. Previous studies have shown that TLE disease severity is associated with reduced structural and functional connectivity (FC) of arousal centers in the thalamus, basal forebrain (BF), and brainstem. Further insight may be gained by examining vigilance-related FC alterations in these subcortical structures. Multi-echo and 7T fMRI paradigms may improve the ability to characterize small and heterogeneous nuclei of the brainstem and BF prone to physiological contamination. This study included 3T and 7T fMRI from the Human Connectome Project (375 and 176 controls, respectively) and EEG-fMRI (3T multi-echo) collected at Vanderbilt (27 controls; 9 left or bilateral TLE patients). The whole-brain correlation pattern of 9 brainstem and 4 BF regions was computed for the entire scan and for alert and drowsy epochs identified from the EEG. The FC was compared between fMRI modalities, between alert and drowsy epochs in controls, and between controls and patients in the drowsy state. The cross-modality spatial overlap of the FC of the entire scan was moderate to strong (Dice coefficient > 0.4) for 11 subcortical regions. The regions with the greatest FC alterations (t-test; $p < 0.05$, FDR-corrected) between alert and drowsy included the locus coeruleus, cuneiform/subcuneiform nucleus, parabrachial nuclear complex, and right diagonal band of Broca and septal nuclei. Compared to controls in the drowsy state, TLE patients had nonsignificant FC reductions for most subcortical regions, particularly the periaqueductal gray and right nucleus basalis of Meynert.

72. Analyzing the extent of activation of vagus nerve stimulation - an optimization framework

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Vagus nerve stimulation (VNS) is an alternative therapy for drug-resistant epilepsy and refractory depression and a potential treatment option for various medical conditions such as bladder dysfunction, heart failure, and rheumatoid arthritis. Research findings indicate that the efficacy and range of applicability of VNS therapy can be improved by selectively modulating only nerve regions associated with a given function. In this regard, the variability in nerve anatomy among individuals poses a challenge when optimizing intervention stimulus delivery at the patient level. Thus, one may leverage patient-specific computational models to optimize electrical stimulation parameters based on the anatomy of the nerve and its neuro response. In this work, we use an optimization methodology to study the extent of activation of the vagus nerve by varying stimulation levels applied at the electrode and electrode array spatial configurations. Our results suggest that designs of multi-contact electrode arrangement may be beneficial to target specific nerve regions, as, in this scenario, the electric field originated at the cathodes and anodes interfere with each other, changing the neural activation pattern. In addition, specific regions of the vagus nerve are activated by optimizing the electrode array positioning and its electrical input, indicating that selective modulation may be achievable at a patient level.

73. A Method for Denoising Chest and Abdominal CT Scans Using Diffusion Probabilistic Models

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Computed Tomography (CT) is an essential part of modern medical practices, lending valuable information for diagnostic purposes, surgical planning and guidance, however, such technology has inherent limitations. Restrictions to contrast medium or dosage lead to degraded image quality occluding tissue structures necessary for clinical and research purposes. Such degraded images, however, often contain information that can be used to reconstruct the original clean image, and thus multiple signal processing approaches have been proposed to reconstruct noisy CT scans. Many approaches involve black box based models, such as generative adversarial networks (GAN) or variational autoencoders (VAE), which have shown promise in removing CT artifacts while producing photo-realistic reconstructions of CT frames. Diffusion Probabilistic Models, a recent advancement in computer image generation, have shown superior performance to GANs and VAEs on a number of tasks. However, these models are challenging to apply to medical data as they are sample inefficient. This project presents preliminary results of using diffusion probabilistic models to denoise CT scans, leveraging data augmentation and a previously proposed training routine to accommodate the small amount of available data. The diffusion model was trained using a combination of the LiTS17 and CHAOS datasets, which contain abdominal and chest CT scans. These clean images were degraded through a custom process and then passed to the model which learned to reconstruct the original image from the degraded sample. The resulting network shows comparable results to previous approaches and is able to reconstruct structures from the original image.

74. Induced Vertex Motion As a Performance Measure for Surgery in Confined Spaces

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While in the designing phase of a surgical robotic system for the procedures performed in surgical confined spaces or hard-to-reach-deep surgical fields, designers can leverage a systematic method to quantitatively compare the design alternatives for tele-surgical manipulators. Unlike most of the work in the literature, we propose an approach for comparing design alternatives by considering the spurious motions along the length of the manipulators in lieu of existing approaches looking at only the end-effector dexterity measures. We propose a performance measure quantifying these spurious motions, while end-effector is executing the application-critical tasks such as suturing and tying a knot. A good manipulator design should yield minimal swept volume along its length portions within the confined space. If informed about these spurious motions, that design would lead to reduced force on the internal organs which in turn reduces the pain and discomfort as well as occurrences of the extra-corporeal inter-manipulator collisions. For validating the proposed approach, we present two illustrative simulation case studies: (1) two planar rigid link serial robots performing the task of following the desired trajectory and (2) two different architectures of tele-surgical manipulators performing the task of passing a circular suture needle under the fulcrum constraints. The results show the applicability of the proposed performance measure in determining the suitability of a particular design alternative for a given task. Although results are promising, using this measure alone for design optimization may compromise overall device dexterity. Therefore, this measure needs to be incorporated into a weighted optimization framework for robot design optimization.

75. Designing a De-Identified Surgical Video Database

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The use of video recording in the operating room is becoming an increasingly accepted path for innovation in surgery. Video data is already being used for education, quality improvement, skills assessment and device development, yet there are significant medico-legal and ethical barriers to routine recording. To address these challenges our team has created a de-identified surgical video database that protects the privacy and interests of patients, surgical teams, and institutions. The de-identification process is carried out by removing identifiable footage of the video (e.g., faces, tattoos), stripping metadata, and categorizing videos by general features only (e.g., case type). Once de-identified, the videos cannot be re-associated with an individual patient, but this also means that patients will not have access to "their" videos. Recognizing the importance of patient agency in the use of their data, this database includes indicators for which uses are permissible for a given, individual video. Based on our prior research, patients have differing opinions on what a video of their body may be used for; during the consent process patients opt in/out for each of the following four uses: "medical teaching and education", "medical research", "public knowledge and education", device or product development", and "other purposes" (blanket permission). Since this is a new endeavor, we are currently piloting patient receptiveness to this protocol. In addition to qualitative feedback, we are also collecting demographic information to compare with granted permissions. At this symposium, we will present the database structure, patient feedback, and additional strategies for database implementation.

76. Intravendor CT reconstruction kernel conversion using Generative Adversarial Networks

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In CT imaging, the reconstruction kernel determines the image quality. Hard kernels tend to be noisier while soft kernels tend to be smoother. For different clinical applications and quantitative analysis, we require an appropriate choice of a reconstruction kernel. For example, the standard reconstruction kernel used for lung nodule detection in NLST CT images is the soft tissue kernel. However, it could be the case that only hard kernel images exist for a particular scan but soft kernel images are preferred for quantitative image analysis. Conversion of reconstruction kernel is an effective solution in such situations. Furthermore, kernel conversion has also been shown to improve the reproducibility of radiomic features between different kernels in CT images consisting of Pulmonary Nodules or Masses. We propose an intravendor kernel conversion solution using deep learning. A pix2pix Generative Adversarial Network (GAN) was trained on 100 aligned image pairs sampled from the NLST cohort to perform image translation of lung screening low-dose CT from a hard kernel (Siemens B50) to a soft kernel (Siemens B30). Using the proposed method, we test the model on 100 withheld pairs to understand the quality of the image generated. Moreover, we analyze percent emphysema correction between the converted image, source, and target images along with an analysis of image-based metrics such as RMSE, SSIM, and PSNR.

Registrants

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