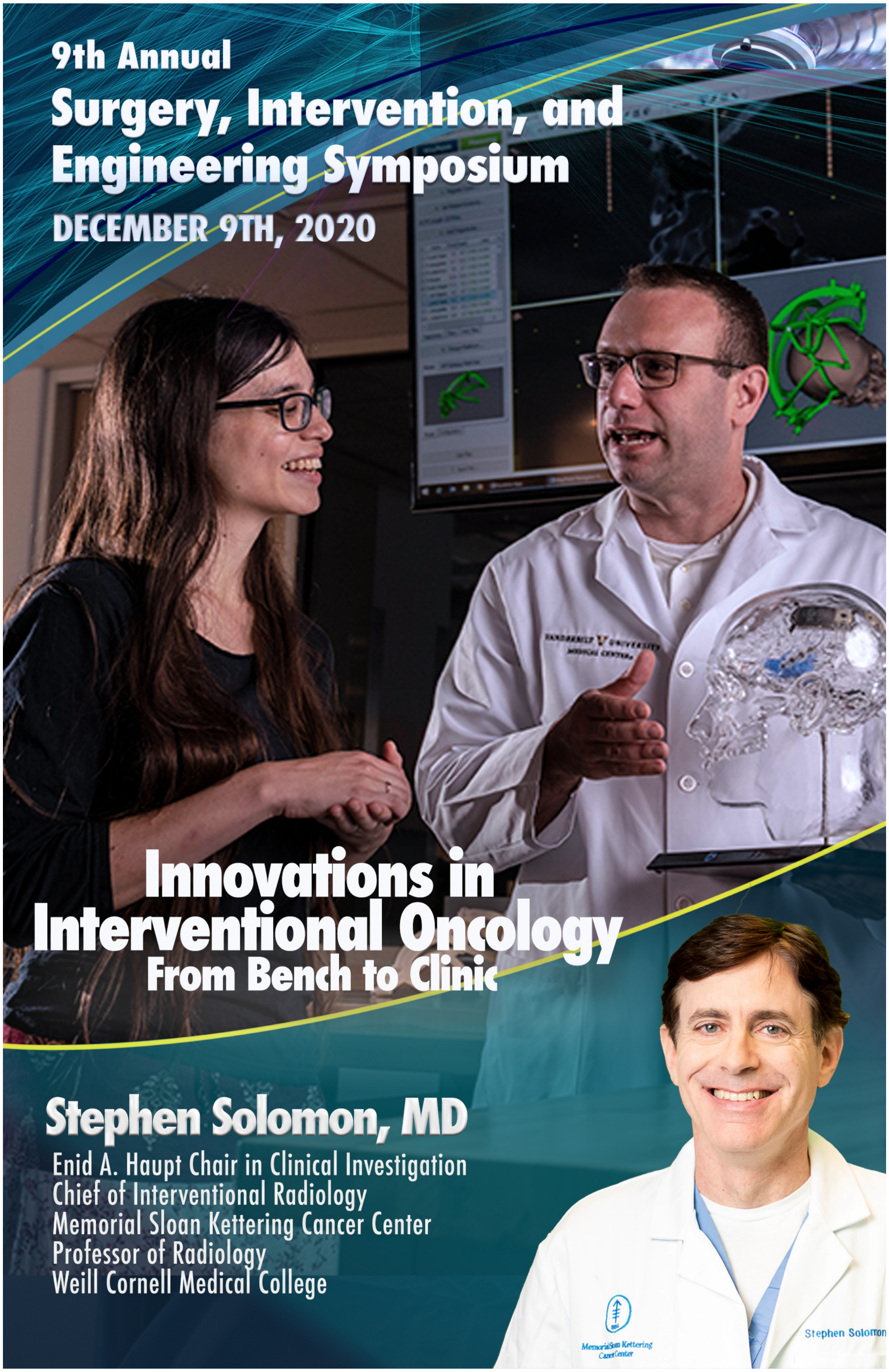
9th Annual
Surgery, Intervention, and
Engineering Symposium
DECEMBER 9TH, 2020
Innovations in
Interventional Oncology
From Bench to Clinic
Stephen Solomon, MD
Enid A. Haupt Chair in Clinical Investigation
Chief of Interventional Radiology
Memorial Sloan Kettering Cancer Center
Professor of Radiology
Weill Cornell Medical College

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 (MENG) in Engineering in Surgery and Intervention **(ESI)**

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.

IN FALL 2021, VANDERBILT UNIVERSITY WILL OFFER A NEW 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.

Innovations in Interventional Oncology:

From Bench to Clinic

Presented by

Stephen Solomon, M,D

Enid A. Haupt Chair in Clinical Investigation
Chief of Interventional Radiology
Memorial Sloan Kettering Cancer Center
Professor of Radiology
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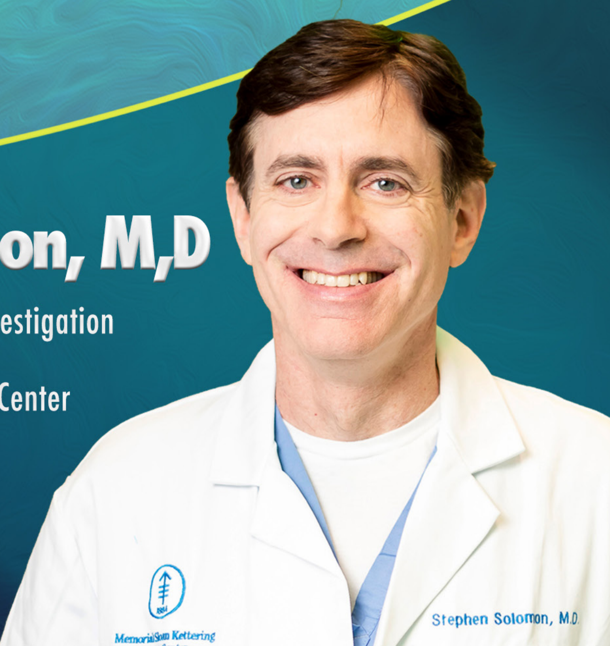

Keynote Abstract

Innovations in Interventional Oncology: From Bench to Clinic

Stephen Barnett Solomon, M,D.
Enid A. Haupt Chair in Clinical Investigation
Chief of Interventional Radiology
Memorial Sloan Kettering Cancer Center
Professor of Radiology
Weill Cornell Medical College

Advances in imaging and advances in engineering have enabled Interventional Oncology to become the fourth pillar of cancer care besides surgery, chemotherapy, and radiation therapy. The ability to have real-time imaging and customized devices integrated and incorporated into medical procedures has allowed for less invasive procedures with faster recoveries and fewer complications. These opportunities have exploded in oncology where the impact is felt in diagnosis, therapy, and palliation. At the heart of these innovations has been the close relationship between physicians and engineers. The current talk will review some of these advances and open our minds to future opportunities.

Biography

Stephen Solomon is a physician and scientist driven by innovation, strategic vision, and successful translation to improve clinical care. As Chief of Interventional Radiology over the last 12 years, he has transformed Memorial Sloan Kettering Cancer Center's (MSKCC's) Interventional Radiology (IR) Service from 6 faculty and 5,000 annual procedures to over 25 faculty performing 22,000 annual procedures. He has developed an internationally acclaimed Service by recruiting talented and diverse faculty to meet the Center's academic mission of delivering innovation to the clinical practice, research enterprise, and educational portfolio.

Dr. Solomon himself is regarded as a renowned innovator who holds many patents and has invented and developed several technologies that are being applied in clinical medicine today throughout the world. He has a creative mind that identifies solutions to unmet needs in medicine. He has done this through his own efforts and has instilled this same curiosity and creativity on his team in Interventional Radiology at Memorial Sloan Kettering.

One of his most important contributions to Medicine has been the development of a navigational bronchoscope that has helped spawn the field of Interventional Pulmonary Medicine. Before this invention, bronchoscopy could only visualize structures within the airway. Dr. Solomon developed an electromagnetic position ("GPS") sensor that tracked the location of the bronchoscope as it moved in the airway. Marrying this location to a CT scan enabled visualization of structures in and out of the airway. This allowed biopsy and other interventions to be performed on structures outside of the airway and allowed guidance to abnormalities seen on a CT scan. This innovation was developed in the laboratory, evaluated in animal models, was translated into clinical trials, and is now a standard tool throughout the world.

Dr. Solomon similarly used this electromagnetic position sensor to track other devices in the body. Another significant success was applying this sensor to catheters in the heart that would track and treat electrical rhythm abnormalities. By combining CT and MR imaging of the heart to the electrical and temporal rhythm of the heart beat, Dr. Solomon helped improve the ability to guide therapy in heart beat dysfunction such as atrial fibrillation. This is also a system that is a standard across the world.

Dr. Solomon's clinical expertise is image-guided interventions and specifically destroying (i.e. ablating) cancers with heat or cold. He is one of the foremost experts in this field and has developed and translated many of these tools into daily clinical practice at MSKCC and around the world. This has enabled destroying cancer with a simple needle rather than having to undergo a major surgical resection. This technology is routinely applied in lung cancers, liver cancers, bone cancers, kidney cancers, and others.

Dr. Solomon has worked with Nobel Laureate Jim Allison to demonstrate how using thermal ablation in mice can create an immune response to the dead ablated tissue and how this immune response can be trained to fight cancer in other parts of the body, creating a "personalized cancer vaccine." Dr. Solomon has helped translate this work into ongoing clinical studies.

Dr. Solomon's laboratory has also experimented with a variety of energy sources to destroy cancer. One of the most interesting has been the application of electrical fields on cancer cells. The field of electroporation has been around for a while and has allowed a cell's membrane to be temporarily permeable. Dr. Solomon has experimented with irreversible electroporation which permanently destroys cells by irreversibly destroying their cell membranes. This has benefits of destroying cells but not the proteins that create the structure of an organ. This may allow preservation of the organ's function (e.g. bile ducts or bronchi) while still killing the cancer cells. With his engineering partner he developed a new method of killing cancer cells called "e-stress" which through continued cell membrane depolarizations, that the cell must use energy to correct, "exhausts" the cells of its energy supply and leads to cell death.

While CAR T-cells have made a significant impact on "liquid tumors" such as lymphoma, it still has not been very successful in solid tumors. Dr. Solomon has teamed up with colleagues at MSKCC to improve CAR T-cell delivery with image-guidance and to apply electrical fields to enhance CAR T-Cell delivery to solid tumors. This has led to receipt of an NIH R01 grant.

As Precision Medicine has become central to cancer care, so too has the image-guided biopsy to collect the tissue necessary for genetic analysis. One of the challenges of image-guided biopsy is knowing while the patient is in the biopsy suite that the appropriate amount of tissue has been collected. Without knowing this a patient may return for treatment 3 weeks later to be told that insufficient tissue was collected to perform molecular analysis. Dr. Solomon has led development of an optical spectroscopy device that analyzes the tissue at the time of biopsy to determine sufficient quantity for molecular studies.

Dr. Solomon has been instrumental in a number of additional advances in cancer care ranging from molecular-guided PET interventions to protective displacement of organs undergoing radiation therapy to intra-arterial delivery of chemotherapy for lung metastases. He has encouraged his team to think creatively and apply the tools of imaging to solve the unmet challenges in medicine. This has led the MSKCC IR team to be one of the most academically prolific and well-funded worldwide with research across multiple DMT disease states.

Dr. Solomon has over 250 peer-reviewed publications, chapters, and reviews. He is a graduate of Harvard College and Yale School of Medicine. He completed his radiology residency at Johns Hopkins and his fellowship at New York Presbyterian Hospital/Weill Cornell Medical Center. He was a faculty member at Johns Hopkins for 7 years before joining MSKCC as the Director of The Center for Image Guided Intervention and then Chief of Service. He has recently been granted the Enid A. Haupt Endowed Chair in Clinical Investigation at Memorial Sloan Kettering.

Participating Laboratories

Participating Laboratories

Advanced Robotics and Mechanism Applications (ARMA) Laboratory

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

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

Web site: http://arma.vuse.vanderbilt.edu
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Participating Laboratories

Bai Lab

PI: Mingfeng Bai, Ph.D.
Assistant Professor
Radiology and Radiological Sciences,
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Our lab is focused on the development and in vivo evaluation of targeted molecular probes for fluorescence imaging-guided surgery and photodynamic therapy (PDT). We are also interested in investigating the effect of systemic anti-tumor immunity and overcoming chemoresistance caused by our PDT treatment.

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Participating Laboratories

Biomedical Elasticity and Acoustic Measurement (BEAM) Laboratory

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

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

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Participating Laboratories

Biomedical Modeling (BML) Laboratory

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

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

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Participating Laboratories

Brain Imaging and Electrophysiology Network (BIEN) Laboratory

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

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

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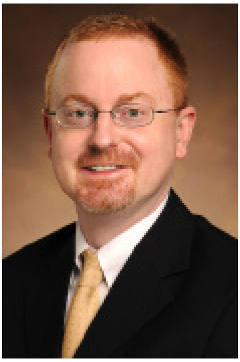
Participating Laboratories



Computer Assisted Otologic Surgery (CAOS) Laboratory

PI: Robert F Labadie, M.D., Ph.D.
Professor of Otolaryngology - Head and Neck Surgery,
Professor of Biomedical Engineering,
Vanderbilt University Medical Center

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

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Participating Laboratories

Computational Flow Physics and Engineering Lab

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

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

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Participating Laboratories

Diagnostic Imaging and Image-Guided Interventions (DIIGI) Laboratory

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

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

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Participating Laboratories

Grissom Laboratory: MRI-Guided Focused Ultrasound

PI: William Grissom, Ph.D.
Associate Professor Biomedical Engineering, Vanderbilt University

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

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Participating Laboratories

tHe biomedical data Representation and Learning laB

PI: Yuankai Huo, Ph.D.
Associate Professor in Computer Science,
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

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.
Associate Professor of Mechanical Engineering,
Vanderbilt University

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

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Participating Laboratories

Laboratory for Organ Recovery, Regeneration and Replacement (LOR3)

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

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

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Participating Laboratories

MRI Methods Lab

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

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

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Participating Laboratories

Mawn Laboratory

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

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

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Participating Laboratories

Medical-image Analysis and Statistical Interpretation (MASI) Laboratory

PI: Bennett Landman, Ph.D.
Professor, Chancellor Faculty Fellow,
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Vanderbilt Brain Institute, Psychiatry and Behavioral Sciences,
Biomedical Informatics,
Vanderbilt University
Director of the Center for Computational Imaging, Principal Scientist of ImageVU
Vanderbilt University Institute of Image Science,
Vanderbilt University Medical Center
Director of Graduate Studies, Electrical Engineering
Vanderbilt University

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

Participating Laboratories

Medical Engineering and Discovery (MED) Laboratory

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

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

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Participating Laboratories

Medical Image Computing (MedICL) Laboratory

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

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

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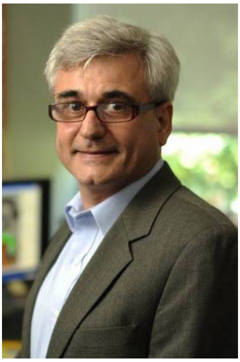
Participating Laboratories



Medical Image Processing (MIP) Laboratory

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

The Medical Image Processing (MIP) laboratory of the Electrical Engineering and Computer Science (EECS) Department conducts research in the area of medical image processing and analysis. The core algorithmic expertise of the laboratory is image segmentation and registration. The laboratory is involved in a number of collaborative projects both with others in the engineering school and with investigators in the medical school. Ongoing research projects include developing and testing image processing algorithms to (1) automatically localize radiosensitive structures to facilitate radiotherapy planning, (2) assist in the placement and programming of Deep Brain Stimulators used to treat Parkinson's disease, (3) localize automatically structures that need to be avoided while placing cochlear implants, (4) develop methods for cochlear implant programming or (5) track brain shift during surgery. The laboratory expertise spans the entire spectrum between algorithmic development and clinical deployment. Several projects that have been initiated in the laboratory have been translated to clinical use or have reached the stage of clinical prototype at Vanderbilt and at other collaborative institutions. Components of these systems have been commercialized.

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Participating Laboratories

Morgan Engineering and Imaging in Epilepsy Lab

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

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

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Participating Laboratories

Neuroimaging and Brain Dynamics Lab

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

The goal of our research is to advance understanding of 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. To enable clearer inferences about brain function with fMRI, 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.
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Department of Mechanical Engineering,
Vanderbilt University

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

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

The continuous quest for miniaturization has made the science fiction vision of miniature capsule robots working inside the human body a reality. At the STORM Lab, we are designing and creating mechatronic and self-contained devices to be used inside specific districts of the human body to detect and cure diseases in a non-invasive and minimally invasive manner.

Capsule robots represent a challenging paradigm for both research and learning. They embed sensors, actuators, digital intelligence, miniature mechanisms, communication systems, and power supply, all in a very small volume. Capsule robots may be autonomous or teleoperated, they can work alone or as a team, and they can be customized to fulfill specific functions. We are currently applying capsule robot technologies to early detection and treatment of gastrointestinal cancers (i.e. colorectal cancer, gastric cancer) and are developing a new generation of surgical robots that can enter the patient's abdomen by a single tiny incision. Building upon these competences, we are always ready to face new challenges by modifying our capsule robots to emerging medical needs.

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Participating Laboratories

Surgical Analytics Lab

PI: Alexander Langerman, M.D.
Associate Professor, Department of Otolaryngology, Vanderbilt University Medical Center

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

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Participating Laboratories

Vanderbilt Biophotonics Center

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

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

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Participating Laboratories

Vanderbilt Dermatology Translational Research Clinic (VDTRC)

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

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

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

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

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Participating Laboratories

Woodard Lab

PI: Lauren Woodard, PhD
Assistant Professor of Medicine,
Vanderbilt University Medical Center

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

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Submitted Abstracts

1. CircleNet: Anchor-Free Glomerulus Detection with Circle Representation

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There has been a long pursuit for precise and reproducible glomerular quantification on renal pathology to leverage both research and practice. When digitizing the biopsy tissue samples using whole slide imaging (WSI), a set of serial sections from the same tissue can be acquired as a stack of images, similar to frames in a video. In radiology, the stack of images (e.g., computed tomography) is naturally used to provide 3D context for organs, tissues, and tumors. In pathology, it is appealing to do a similar 3D assessment for glomeruli using a stack of serial WSI sections. However, the 3D identification and association of large-scale glomeruli on renal pathology is challenging due to large tissue deformation, missing tissues, and artifacts from WSI. Therefore, existing 3D quantitative assessments of glomeruli are still largely operated by manual or semi-automated methods, leading to labor costs, low-throughput processing, and inter-observer variability. In this paper, we propose a novel Multi-Object Association for Pathology in 3D (Map3D) method for automatically identifying and associating large-scale crosssections of 3D objects from routine serial sectioning and WSI. The innovations of the Map3D method are three-fold: (1) the largescale glomerular association is principled from a new multi-object tracking (MOT) perspective; (2) the quality-aware whole series registration is proposed to not only provide affinity estimation but also offer automatic kidney-wise quality assurance (QA) for registration; (3) a dual-path association method is proposed to tackle the large deformation, missing tissues, and artifacts during tracking. To the best of our knowledge, the Map3D method is the first approach that enables automatic and large-scale glomerular association across 3D serial sectioning using WSI.

2. Improving Speed of Advanced Ultrasound Tissue Displacement Estimation Algorithm using a Bayesian Equation with Gradient Descent and Newton's Method

Kristy Walsh [1] and Brett Byram [1]

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CAcoustic radiation forced-based elasticity imaging can be used to displace tissue at a focused region and determine its mechanical properties by monitoring displacement. The quality of acoustic radiation force-based elastography greatly depends on the ability to measure tissue displacement, especially in high shearing, noisy environments, or other applications such as measuring displacement directly at the push location. We have developed an advanced Bayesian displacement estimator that introduces a small amount of bias that reduces displacement estimation variance and has a lower mean-square error than an unbiased estimator. We compare our estimator to a commonly used normalized cross-correlation that has low jitter for an unbiased estimator, but still cannot be used in those challenging cases. Also, normalized cross-correlation and the Bayesian displacement estimator have a high computational cost compared to simpler methods. Here, we explore optimizers and solutions to the Bayesian displacement estimator to speed up computation. Using the gradient of the Bayesian displacement estimator, we were able to find displacements 50 times faster and on the order of the speed of normalized cross-correlation. We can also find a solution similar to normalized cross-correlation using a gradient descent approach in half the time. Currently, we are investigating the Hessian matrix of the Bayesian equation to solve for displacements using Newton's method which would be an order of magnitude faster.

3. MK2 Inhibitory Nanopolyplexes Inhibit Vascular Graft Failure By Blocking Smooth Muscle Cell Phenotype Switch

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Saphenous vein grafts used to bypass complex arterial disease have a high rate of failure associated with intimal hyperplasia (IH). In IH, vascular smooth muscle cells (VSMCs) in the graft undergo a contractile-to-synthetic phenotype switch, leading to increased proliferation, migration, and neointima formation. We test the hypothesis that brief intra-operative graft treatment with MAPKAP kinase 2 inhibitory peptide nano-polyplexes (MK2i-NPs) reduces IH through a mechanism of action that involves blocking the VSMC phenotype switch. MK2i-NPs produced higher cellular delivery and more potent pharmacodynamic effects compared to free MK2i peptide using phosphorylated CREB as a biomarker of MK2 inhibition in VSMCs. MK2i-NP treatment also reduced proliferation and lowered vimentin levels (synthetic phenotype marker), while maintaining higher levels of alpha smooth muscle actin (a-SMA, contractile phenotype marker), in primary rat VSMCs cultured in serum-containing media for 7 passages. MK2i-NPs also decreased vimentin, increased a-SMA, and reduced IH, along with allowing effective graft endothelialization, in an in vivo rabbit vein graft model. MK2i-NP inhibition of VSMC phenotype switch was also validated in an ex vivo human saphenous vein model. Looking forward, this delivery system is being tested in an in vivo delivery system to prevent intimal hyperplasia and phenotype switching in arteries after angioplasty.

4. Joint cortical surface and structural connectivity analysis of Alzheimer's Disease

Leon Y. Cai (a), Cailey I. Kerley (b), Chang Yu (b), Katherine S. Aboud (c), Lori L. Beason-Held (d), Andrea T. Shafer (d), Susan M. Resnick (d), Lori C. Jordan (e), Adam W. Anderson (a,f,g), Kurt G. Schilling (f,g), Ilwoo Lyu (b), and Bennett A. Landman (a,b,f,g)

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Joint independent component analysis (jICA) is a common data-driven approach for integrating electroencephalography (EEG) and functional magnetic resonance imaging (MRI) data. It is often used for hypothesizing joint electrical and hemodynamic neurological phenomena. The applicability of this approach to other types of multimodal neuroimaging data remains largely underexplored. We present a preliminary study performed on T1 and diffusion weighted MRI data from the Baltimore Longitudinal Study of Aging to demonstrate that this approach can be applied to complex cortical surface metrics and structural connectivity metrics with regards to Alzheimer's Disease (AD). We calculate 588 region-based cortical metrics and 4,753 f ractional anisotropy-based connectivity metrics and project them into a low-dimensional manifold with principal component analysis. We perform jICA on the manifold and subsequently backproject the independent components to the original data space. We demonstrate component stability with 3-fold cross validation and find differential component loadings between 776 cognitively unimpaired control subjects and 23 with AD that generalizes across folds. In addition, we perform the same analysis on the surface and connectivity metrics separately and find that the joint approach identifies both novel and similar components to the separate approaches. To illustrate the joint approach's primary utility, we provide an example hypothesis for how surface and connectivity components may vary together with AD. These preliminary results suggest jointly varying independent cortical surface and structural connectivity components can be consistently extracted from MRI data and provide a data-driven way for generating novel hypotheses about AD that may not be captured by separate analyses.

5. Design and prototyping of a disposable transmission for concentric tube continuum robots

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Concentric tube robots (CTRs) are ideally suited for minimally-invasive surgical procedures through small orifices, and the small size and enhanced dexterity of CTRs, in comparison to standard, rigid endoscopic tools, enables these new surgical approaches. One important aspect of clinical feasibility of CTRs is sterility. Here, we propose a compact robot with a disposable transmission designed to meet sterilization requirements of the operating room. The design includes a disposable transmission with reusable, modular motor packs and proves feasibility of an additively manufactured CTR transmission unit. We also propose a novel technique for grasping CTR tubes within the transmission, based on compressed rubber rings. The actuation unit consists of a reusable, encapsulated motor pack and a disposable transmission mechanism. Each tube is mounted inside a bi-directional gear with each gear inserted into a cylindrical housing such that the gear can rotate and translate. The housing facilitates a spur gear interface for the motor packs to connect to, enabling simultaneous control of the axial tube translation and rotation. Each motor pack can be snapped onto the transmission body. The concentric tubes are clamped to the bi-directional gear using rubber O- rings, and the holding force of the O-ring mount was measured and compared to design requirements for CTRs. The functional prototype uses 8 brushless motors (Maxon) to enable independent, joint-level position control of two CTR arms. A backlash analysis and joint-level trajectory following experiments were conducted and compared to other surgical robots.

6. Joint analysis of structural connectivity and cortical surface features: correlates with mild traumatic brain injury

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Mild traumatic brain injury (mTBI) is a complex syndrome that affects up to 600 per 100,000 individuals, with a particular concentration among military personnel. About half of all mTBI patients experience a diverse array of chronic symptoms which persist long after the acute injury. Hence, there is an urgent need for better understanding of the white matter and gray matter pathologies associated with mTBI to map which specific brain systems are impacted and identify courses of intervention. Previous works have linked mTBI to disruptions in white matter pathways and cortical surface abnormalities. Herein, we examine these hypothesized links in an exploratory study of joint structural connectivity and cortical surface changes associated with mTBI and its chronic symptoms. Briefly, we consider a cohort of 12 mTBI and 26 control subjects. A set of 588 cortical surface metrics and 4,753 structural connectivity metrics were extracted from cortical surface regions and diffusion weighted magnetic resonance imaging in each subject. Principal component analysis (PCA) was used to reduce the dimensionality of each metric set. We then applied independent component analysis (ICA) both to each PCA space individually and together in a joint ICA approach. We identified a stable independent component across the connectivity-only and joint ICAs which presented significant group differences in subject loadings ($p<0.05$, corrected). Additionally, we found that two mTBI symptoms, slowed thinking and forgetfulness, were significantly correlated ($p<0.05$, corrected) with mTBI subject loadings in a surface-only ICA. These surface-only loadings captured an increase in bilateral cortical thickness.

7. Validation of a Hybrid Active Shape and Deep Learning Intracochlear Anatomy Segmentation Method for Image-guided Cochlear Implant Programming

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Cochlear implants (CIs) are neuroprosthetic devices that can improve hearing in patients with severe-to-profound hearing loss. Postoperatively, a CI device needs to be programmed by an audiologist to determine parameter settings that lead to the best outcomes. Our group has developed an image-guided cochlear implant programming (IGCIP) system to simplify this laborious post-programming procedure and improve hearing outcomes. IGCIP requires image processing techniques to analyze the location of the inserted electrode arrays (EAs) with respect to the intracochlear anatomy (ICA). An active shape model (ASM)-based method is currently in routine use in our IGCIP system for ICA segmentation. Recently, we have proposed a hybrid ASM/deep learning (DL) segmentation method that improves segmentation accuracy. In this work, we evaluate the effect of this method on so-called distance-vs.-frequency curves (DVFs), which permit to visualize electrode interaction and are used to provide programming guidance. Results we have obtained show that the hybrid ASM/DL segmentation technique tends to generate DVFs with smaller frequency error and distance error, and electrode configurations which are comparable to the existing ASM-based method.

8. Microsphere antioxidant and sustained erythropoietin-R76E release functions cooperate to reduce traumatic optic neuropathy

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Wild-type erythropoietin (EPO) is promising for neuroprotection, but its therapeutic use is limited because it causes a systemic rise in hematocrit. We have developed an EPO-R76E derivative that maintains neuroprotective function without effects on hematocrit, but this protein has a short half-life in vivo. Here, we compare the efficacy and carrier-induced inflammatory response of two polymeric microparticle (MP) EPO-R76E sustained release formulations based on conventional hydrolytically degradable poly(lactic-co-glycolic acid) (PLGA) and reactive oxygen species (ROS)-degradable poly(propylene sulfide) (PPS). Both MP types effectively loaded EPO-R76E and achieved sustained release, providing detectable levels of EPO-R76E at the injection site in the eye in vivo for at least 28 days. Testing in an in vitro oxidative stress assay and a mouse model of blast-induced indirect traumatic optic neuropathy (bITON) showed that PPS and PLGA MP-mediated delivery of EPO-R76E provided therapeutic protection. While unloaded PLGA MPs inherently increase levels of pro-inflammatory cytokines in the bITON model, drug-free PPS MPs have innate antioxidant properties that provide therapeutic benefit both in vitro and in vivo. Both PLGA and PPS MPs enabled sustained release of EPO-R76E, providing therapeutic benefits including reduction in inflammation and axon degeneration, and preservation of visual function as measured by electroretinogram. The PPS-based MP platform is especially promising for further development, as the delivery system provides inherent antioxidant benefits that can be harnessed to work in complement with EPO-R76E or other drugs for neuroprotection in the setting of traumatic eye injury.

9.Metal Artifact Reduction, Intracochlear Anatomy Segmentation, and Cochlear Implant Electrodes Localization in CT Images with a Multi-task 3D Network

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Cochlear implants (CIs) are surgically implanted neural prosthetic devices to treat severe-to-profound hearing loss. Accurately localizing the CI electrodes relative to the intracochlear anatomy structures (ICAS) in the post-implantation CT (Post-CT) images of the CI recipients can help audiologists with the post-programming of the CIs. Localizing the electrodes and segmenting the ICAS in the Post-CT images are challenging due to the limited image resolution and the strong artifacts produced by the metallic electrodes. Currently, the most accurate approach to determine the physical relationship between the electrodes and the ICAS is to localize the electrodes in the Post-CT image, segment the ICAS in the pre-implantation CT (Pre-CT) image of the CI recipient, and register the two images. Here we propose a 3D multi-task network to remove the artifacts, segment the ICAS, and localize the electrodes in the Post-CT images simultaneously. Our network is trained with a small image set and achieves comparable segmentation results and encouraging electrode localization results compared to the current state-of-the-art methods. As our method does not require the Pre-CT images, it provides the audiologist with information that guides the programming process even for patients for whom these images have not been acquired or are not accessible.

10. Automatic detection of surgical AOI using Mask-RCNN

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Open surgery represents a dominant proportion of procedures performed, but has lagged behind endoscopic surgery in video-based insights due to the difficulty obtaining high-quality open surgical video. Automated detection of the open surgical wound would enhance tracking and stabilization of body-worn cameras to optimize video capture for these procedures. We present results using a mask R-CNN to identify the surgical wound (the "area of interest", AOI) in image sets derived from 23 open neck procedures (a 2273-image training/validation set and a 400-image testing set). Bounding box application to the surgical wound was reliable (F-1 > 0.88) in the testing sets with a 5% false positive rate (recognizing non-wound areas as the AOI). Mask application to greater than 50% of the wound area had modest success (F-1 = 0.769) under parameters set for high specificity. When applied to short video clips as proof-of-principle, the model performed well both with emerging AOI (i.e., identifying the wound as incisions were developed) and with recapture of the AOI following obstruction). Overall, we identified image lighting quality and the presence of distractors (e.g., bloody sponges) as the primary sources of model errors on visual review, and are continuing to tune the model to address these errors. These data serve as a first demonstration of open surgical wound detection using first-person video footage, and sets the stage for further work in this area.

11. PRAGMA: Interactively Constructing Functional Brain Parcellations

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A prominent goal of neuroimaging studies is mapping the human brain, in order to identify and delineate functionally-meaningful regions and elucidate their roles in cognitive behaviors. These brain regions are typically represented by atlases that capture general trends over large populations. Despite being indispensable to neuroimaging experts, population-level atlases do not capture individual differences in functional organization. In this work, we present an interactive visualization method, PRAGMA, that allows domain experts to derive scan-specific parcellations from established atlases. PRAGMA features a user-driven, hierarchical clustering scheme for defining temporally correlated parcels in varying granularity. The visualization design supports the user in making decisions on how to perform clustering, namely when to expand, collapse, or merge parcels. This is accomplished through a set of linked and coordinated views for understanding the user's current hierarchy, assessing intra-cluster variation, and relating parcellations to an established atlas. We assess the effectiveness of PRAGMA through a user study with four neuroimaging domain experts, where our results show that PRAGMA shows the potential to enable exploration of individualized and state-specific brain parcellations and to offer interesting insights into functional brain networks.

12. Large Vessel Occlusion (LVO) Identification Using Machine Learning on Computed Tomography Angiography (CTA)

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Large Vessel Occlusion (LVO) Identification Using Machine Learning on Computed Tomography Angiography (CTA)

PURPOSE: Patients with acute ischemic stroke due to LVO are at high risk for severe outcomes and benefit from early identification. Machine learning may help, yet studies are limited on automated LVO identification using CTA. We aimed to train a convolutional neural network (CNN) to identify LVO using CTA.

METHODS: Stroke-alerted patients at Vanderbilt University Medical Center between November 2017-May 2019 were included. Exclusion criteria were missing or poor-quality images, intracranial hemorrhage or implant, or rare pathology including posterior circulation LVO. Images were processed with registration, skull removal, manual intensity adjustment, and generation of 40mm axial maximum intensity projections (MIP) to optimally depict anterior circulation. Phi-Net, a deep CNN implemented using Keras and TensorFlow, was trained with 10-fold cross-validation for binary classification of LVO or no LVO. Dataset was balanced, though not necessarily in each fold, and 20% was held out for future test set use.

RESULTS: Training included 240 patients. Mean metrics as 95% confidence intervals for test sets across 10 folds are precision-recall area under the curve (AUC) 0.868±0.095, F1 score 0.856±0.04, and receiver operating characteristic (ROC) AUC 0.919±0.048. At threshold 0.5, accuracy 85%±4%, precision 82.8%±8.1%, recall 90.9%±5.3%, and specificity 81.4%±8.7% were calculated.

CONCLUSION: We successfully classified LVO presence with high performance. Current work includes comparison of other networks on the same dataset and automation of intensity adjustment. With improved performance and full automation, future translation into clinical practice may accelerate stroke triage decisions.

13. Brain Vessel Segmentation in Contrast-enhanced T1-weighted MR Images for Deep Brain Stimulation of the Anterior Thalamus Using a Deep Convolutional Neural Network.

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Deep brain stimulation (DBS) has been recently approved by the FDA to treat epilepsy patients with refractory seizures, i.e., patients for whom medications are not effective. It involves stimulating the anterior nucleus of the thalamus (ANT) with electric impulses using permanently placed electrodes. One main challenge with the procedure is to determine a trajectory to place the implant at the proper location while avoiding sensitive structures. In this work, we focus on one category of sensitive structures, i.e., brain vessels, and we propose a method to segment them in clinically acquired contrast-enhanced T1-weighted (T1CE) MRI images. We propose a deep-learning based method that we train/test on a set of images for which we have created the ground truth. We compare this approach to a traditional vesselness-based technique and we show that our method produces significantly better results, especially for small vessels.

14. Increasing Signal-to-Noise Ratio in Transcranial Ultrasound Imaging with Coded Excitation

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Clinical translation of transcranial ultrasound imaging has been challenging due to extremely poor image quality in the vast majority of non-neonatal patients. The high acoustic impedance mismatch between the skull and surrounding tissue greatly reduces acoustic penetration and therefore the signal-to-noise ratio (SNR). Reduced SNR also leads to a reduction in sensitivity to blood flow, making cerebrovascular imaging virtually impossible without the use of microbubble contrast agents which increase scan time, complexity, cost, and invasiveness. Alternatively, coded excitation can be used to increase SNR within FDA safety limits and without requiring the use of contrast agents, thereby enabling noninvasive ultrasound neuroimaging. This work encompasses a method to design long binary coded pulses along with a pulse compression technique to completely suppress range lobes, thereby recovering axial resolution and improving SNR by as much as a factor of 10log10(code length). This coded excitation framework simultaneously optimizes for SNR gain, image quality, frame rate, and hardware complexity, unlike any previous coded excitation approach. Moreover, it was shown to be highly effective in increasing the SNR in transcranial imaging of five healthy adult subjects. These results pave the way for further advancements to ultimately enable completely noninvasive functional neuroimaging with ultrasound.

15. Needle Steering Through Flexible Endoscopes in Lung: Needle Pose Estimation in the Presence of Torsional Windup

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A very promising application for steerable needles is to use them for reaching lesions in the lung via bronchoscopy. However, for this application, the needles have to be much longer than regular steerable needles in order to pass through the flexible endoscope, which makes them torsionally more flexible. Combined with the friction interaction between the needle and the working channel of the endoscope, this significantly amplifies the torsional windup behavior for these steerable needles, which is a known problem for steerable needles in general. The torsional windup behavior can be summarized as the lag in the roll angle about needle axis at the needle tip with respect to the needle base, and it needs to be accounted for accurate control of the needle steering. Unlike their larger 6-DOF (Degrees of Freedom) alternatives, the roll angle at the needle tip cannot be sensed directly with the small 5-DOF magnetic tracking coils which enable us to use smaller and less invasive needles. In this work, we developed a torsional windup aware kinematic needle model and implemented it to an Extended Kalman Filter in order to accurately estimate the needle pose during steering. A 5-DOF magnetic coil is embedded in the needle and used to provide feedback for the Kalman filter. Using this method, we performed several needle steering experiments in gelatin phantoms and ex-vivo porcine lungs. We showed that the needle was able to follow the desired trajectories accurately in both tissues with errors mostly less than 2 mm.

16. Transurethral Anastomosis after Radical Prostatectomy with Concentric Tube Robots

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Current surgical approaches to radical prostatectomy are associated with high rates of erectile dysfunction and incontinence due to the invasive approach with access through the abdominal space. These complications occur secondary to the disruption of surrounding healthy tissue, which is required to expose the prostate. The urethra offers the least invasive access to the prostate, and feasibility has been demonstrated of enucleating the prostate with an endoscope using Holmium laser, which can itself be aimed by concentric tube robots. However, the transurethral approach to radical prostatectomy has thus far been limited by the lack of a suitable means to perform an anastomosis of the urethra to the bladder after prostate removal. Only a few intraluminal anastomotic devices currently exist, and none are small enough to pass through the urethra. In our research, we propose to utilize concentric tube robots to perform the anastomosis transurethrally by harnessing their enhanced dexterity. Due to their miniaturization potential (diameters < 2mm) two robots at a time can be deployed through a conventional endoscope into the urethra. A novel suturing technique and customized end effectors enable the anastomosis in this challenging approach. In the initial investigations, we successfully demonstrate proof-of-concept on an anatomical silicone phantom model revealing the potential of our method.

17. Validation of active shape model techniques for intra-cochlear anatomy segmentation in CT images

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Cochlear implants (CIs) have been shown to be effective restorative devices for patients suffering from severe-to-profound hearing loss. Hearing outcomes with CIs are dependent on the positions of the electrodes with respect to intra-cochlear anatomy. However, intra-cochlear anatomy can only be directly visualized using high resolution modalities such as μCT, which cannot be used in vivo. Despite this limitation, we have developed an active shape model approach for segmenting the intra-cochlear anatomy by leveraging the visible structures of landmarks. In this study, we validate the ASM performance with an expanded dataset of 16 samples and provide a more comprehensive validation of the method's performance with respect to model parameters and training set size. We found parameters that optimize mean surface segmentation performance to 0.11mm. Parameters that corresponded to tighter constraints generally led to smaller errors, and returns on segmentation performance begin diminishing after 11 samples, thus suggesting that the main performance bottleneck is due to the searching scheme rather than a limited training set size. These results are critical to understand the limitations of the method for clinical use and for future development.

18. Changes in resting-state frequency dynamics in mesial temporal lobe epilepsy

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Resting-state functional magnetic resonance imaging (rsfMRI) is often used to distinguish the resting brain activity between healthy and diseased populations. rsfMRI measures fluctuations in blood oxygenation to infer neural activity. One commonly used metric in rsfMRI is the fractional amplitude of low frequency fluctuations (fALFF), i.e. the fraction of summed signal amplitudes in a low frequency band, which reflects the strength of slow neural activity in different brain regions. Changes in fALFF have been demonstrated in mesial temporal lobe epilepsy (mTLE), where the mesial temporal lobe is the seizure focus. However, this technique is constrained to the conventional frequency band of ~0.01-0.08 Hz, leaving out the majority of the full recoverable frequency range (~0-0.25 Hz). Contrary to prior studies, we investigated fALFF across the full frequency range and found widespread cortical differences between patients and controls in two frequency bands (~0.021-0.047 Hz and ~0.168-0.198 Hz, both $p < 0.05$). We also found differences in the total amplitude across the full frequency spectrum between patients and controls in structures previously identified to be altered in mTLE ($p < 0.05$). These results indicate specific frequency bands that may be altered across the cortex in mTLE as well as a new metric, i.e. the total amplitude across the full frequency spectrum, that may identify altered regions in mTLE. These novel analyses utilizing the full frequency band of rsfMRI signals can be applied further to mTLE to elucidate the frequency abnormalities over time and during clinical intervention.

19. Predicting Temporal Lobe Epilepsy Laterality and Surgical Outcome with Interpretable Diffusion Imaging Features

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Predicting Temporal Lobe Epilepsy Laterality and Surgical Outcome with Interpretable Diffusion Imaging Features

Introduction: Pre-surgical workup of medically-refractory temporal lobe epilepsy (TLE) relies on determining seizure onset laterality and excluding the possibility of bilateral seizure onset. Of further interest is surgical outcome because up to 40% of patients will continue to have seizures post-operatively. Diffusion MRI has been used to study the white-matter structure of the brain in TLE, but diagnostic and prognostic abilities have been limited.

Objectives: Our objective was to extract interpretable features from diffusion imaging to predict seizure onset laterality and surgical outcome. Methods: Probabilistic tractography was conducted on 155 subjects using MRTrix3 to obtain structural connectivity and mean fractional anisotropy within the Desikan-Killiany parcellation. Bayesian optimization was used to extract features with reconstruction-ICA and fit an elastic net regression to predict the following binary decision tree: controls (n=89) vs TLE (n=66), unilateral (n=37) vs bilateral TLE (n=7), unilateral right (n=22) vs left TLE (n=13), Engel1a (right=16, left=10) vs Engel1b+ (right=18, left=8) outcome. Each branch used 5-fold cross-validation with training (70%), validation (20%), and testing set (10%).

Results: Cross-fold average testing area under the receiver operating characteristic curve (AUCROC) for each branch was as follows: controls vs TLE (0.745), unilateral vs bilateral TLE (1.000), unilateral right vs left TLE (0.662), Engel1a vs Engel1b+ surgical outcome (right: 0.549, left: 0.800).

Conclusions: Of potential clinical significance this approach effectively stratified most decision branches. Furthermore, interpretable features were obtained that can be used for future hypothesis-driven analyses.

20. OCT denoising with pseudo-multimodal fusion network

Dewei Hu, Joseph D. Malone, Yigit Atay, Yuankai K. Tao, Ipek Oguz

Optical coherence tomography (OCT) is a prevalent imaging technique for the retina. However, it is affected by multiplicative speckle noise that can degrade the visibility of essential anatomical structures, including blood vessels and tissue layers. Although averaging repeated B-scan frames can significantly improve the signal-to-noise-ratio (SNR), this requires longer acquisition time, which can introduce motion artifacts and cause discomfort to patients. In this study, we propose a learning-based method that exploits information from the single-frame noisy B-scan and a pseudo-modality. The pseudo-modality is created by a network that can mimic the self-fusion algorithm with boosted processing speed. The pseudo-modality provides good SNR for layers that are barely perceptible in the noisy B-scan, but it can over-smooth fine features such as small vessels. By using a fusion network, we can combine desired features from each modality, and the weight of their contribution is adjustable. Evaluated by intensity-based and structural metrics, the result shows that our method can effectively suppress the speckle noise and enhance the contrast between retina layers while preserving the overall structure and small blood vessels. Compared to the single modality network, our method improves the structural similarity with low noise B-scan from 0.559 ± 0.033 to 0.576 ± 0.031. The denoised OCT volume by the proposed method is available for angiography.

21. Effects of Cochlear Implant Position on Open-set Word Recognition Outcomes

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Cochlear implants (CIs) are standard-of-care neuroprosthetics for moderate to profound sensory hearing loss. Despite their success in a large part of the population, there is considerable unexplained variance in the hearing outcomes. Previously, we have demonstrated how the final positions of the different CI arrays influence outcomes by supervised automatic feature selection to construct general linear models. However, while such models provide maximum interpretability, the effects of some aspects of positioning could not be adequately captured. In this current work, we aim to improve our ability to predict patient-specific outcomes by rigorously exploring the relationship between position and outcome. On our enhanced dataset, preliminary investigations reveal that the descriptors of electrode location are nonlinearly correlated with each other, and electrode positioning in the inner segments of the cochlea are strongly correlated with better outcomes. A comprehensive understanding of these associations can better guide patient counseling and surgical techniques. Our future work involves integrating these insights into appropriate predictive models.

22. Synthetic atrophy for longitudinal surface-based cortical thickness measurement

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Difficulty in validating accuracy remains a substantial setback in the field of surface-based cortical thickness (CT) measurement due to the lack of experimental validation against ground truth. Although methods have been developed to create synthetic datasets for this purpose, none provide a robust mechanism for measuring exact thickness changes with surface-based approaches. This work presents a registration-based technique for inducing synthetic cortical atrophy to create a longitudinal, ground truth dataset specifically designed for accuracy validation of surface-based CT measurements. Across the entire brain, we show our method can induce up to between 0.6 and 2.6 mm of localized cortical atrophy in a given gyrus depending on the region's original thickness. By calculating the image deformation to induce this atrophy at 400% of the original resolution in each direction, we can induce a sub-voxel resolution amount of atrophy while minimizing partial volume effects. We also show that our method can be extended beyond application to CT measurements for the accuracy validation of longitudinal cortical segmentation and surface reconstruction pipelines when measuring accuracy against cortical landmarks. Importantly, our method relies exclusively on publicly available software and datasets.

23. Robust Multiple Sclerosis Lesion Inpainting with Edge Prior

Huahong Zhang (EECS, VU); **Rohit Bakshi** (Brigham and Women's Hospital); **Francesca Bagnato** (VUMC); **Ipek Oguz** (EECS, VU).

Inpainting lesions is an important preprocessing task for algorithms analyzing brain MRIs of multiple sclerosis (MS) patients, such as tissue segmentation and cortical surface reconstruction. We propose a new deep learning approach for this task. Unlike existing inpainting approaches which ignore the lesion areas of the input image, we leverage the edge information around the lesions as a prior to help the inpainting process. Thus, the input of this network includes the T1-w image, lesion mask and the edge map computed from the T1-w image, and the output is the lesion-free image. The introduction of the edge prior is based on our observation that the edge detection results of the MRI scans will usually contain the contour of white matter (WM) and grey matter (GM), even though some undesired edges appear near the lesions. Instead of losing all the information around the neighborhood of lesions, our approach preserves the local tissue shape (brain/WM/GM) with the guidance of the input edges. The qualitative results show that our pipeline inpaints the lesion areas in a realistic and shape-consistent way. Our quantitative evaluation shows that our approach outperforms the existing state-of-the-art inpainting methods in both image-based metrics and in FreeSurfer segmentation accuracy. Furthermore, our approach demonstrates robustness to inaccurate lesion mask inputs. This is important for practical usability, because it allows for a generous over-segmentation of lesions instead of requiring precise boundaries, while still yielding accurate results.

24. Training Deep Network Ultrasound Beamformers with Unlabeled In Vivo Data

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Conventional ultrasound beamforming is highly efficient but also suffers from various sources of image degradation. Several adaptive beamformers have been proposed to address this problem, including more recently proposed deep learning methods. With deep learning, adaptive beamforming is typically framed as a regression problem, where clean, ground-truth physical information is used for training. Because it is difficult to know ground truth information in vivo, training data are usually simulated. However, deep networks trained on simulated data underperform when applied to in vivo data, due to domain shift between simulated and in vivo data. In this work, we show how to correct for domain shift by learning deep network beamformers that leverage both simulated data and unlabeled in vivo data via a novel domain adaptation (DA) scheme. A challenge in our scenario is that domain shift exists both for noisy input and clean ground truth target data. We address this challenge by extending cycle-consistent generative adversarial networks, where we leverage maps between synthetic simulation and real in vivo domains to ensure that the learned beamformers capture the distribution of both noisy input and clean target data. Using various types of training data, we explore the limitations and underlying functionality of the proposed DA approach. Additionally, we compare our proposed approach to several other adaptive beamformers and demonstrate consistent in vivo image quality improvements.

25. Uncertainty Estimation in Medical Image Localization: Towards Robust Anterior Thalamus Targeting for Deep Brain Stimulation

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Atlas-based methods are the standard approaches for automatic targeting of the Anterior Nucleus of the Thalamus (ANT) for Deep Brain Stimulation (DBS), but these are known to lack robustness when anatomic differences between atlases and subjects are large. To improve the localization robustness, we propose a novel two-stage deep learning (DL) framework, where the first stage identifies and crops the thalamus regions from the whole brain MRI and the second stage performs per-voxel regression on the cropped volume to localize the targets at the finest resolution scale. To address the issue of data scarcity, we train the models with the pseudo labels which are created based on the available labeled data using multi-atlas registration. To assess the performance of the proposed framework, we validate two sampling- based uncertainty estimation techniques namely Monte Carlo Dropout (MCDO) and Test-Time Augmentation (TTA) on the second-stage localization network. Moreover, we propose a novel uncertainty estimation metric called maximum activation dispersion (MAD) to estimate the image-wise uncertainty for localization tasks. Our results show that the proposed method achieved more robust localization performance than the traditional multi-atlas method and TTA could further improve the robustness. Moreover, the epistemic and hybrid uncertainty estimated by MAD could be used to detect the unreliable localizations and the magnitude of the uncertainty estimated by MAD could reflect the degree of unreliability for the rejected predictions.

26. Toward a Data-Driven Predictive Modeling Framework for Guiding Locoregional Microwave Ablation Therapy

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In this work, a data-driven predictive modeling framework is described that combines computational modeling with data from pre- and post-procedural imaging, and intra-procedural therapeutic delivery. The result of the work is to improve localization and predict thermal dose extent during microwave ablation. With respect to the computational model, soft-tissue biomechanics and bioelectric/bioheat transport are used to create a patient-specific scaffold that embodies therapy delivery. Once established, pre-, intra-, and post- procedural data allow the tuning of data-driven predictive dielectric and thermal material models to be used on novel patients. This framework in interventional data science reflects the use of computational models as a biophysical filter to large-scale data sets such that therapeutic predictors can be distilled and used for the delivery of locoregional therapy. Results indicate superior localization and accurate prediction of lesion formation using our data-driven approach to ablation forecasting. Results also provide insight on the impact that localization and material property inaccuracies contribute to the degradation of lesion-to-target overlap.

27. ASIST: Annotation-free synthetic instance segmentation and tracking for microscope video analysis

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Instance object segmentation and tracking provide comprehensive quantification of objects across microscope videos. The recent single-stage pixel-embedding based deep learning approach has shown its superior performance compared with "segment-then-associate" two-stage solutions. However, one major limitation of applying a supervised pixel-embedding based method to microscope videos is the resource-intensive manual labeling, which involves tracing hundreds of overlapped objects with their temporal associations across video frames. Inspired by the recent generative adversarial network (GAN) based annotation-free image segmentation, we propose a novel annotation-free synthetic instance segmentation and tracking (ASIST) algorithm for analyzing microscope videos of sub-cellular microvilli. The contributions of this paper are three-fold: (1) proposing a new annotation-free video analysis paradigm is proposed. (2) aggregating the embedding based instance segmentation and tracking with annotation-free synthetic learning as a holistic framework; and (3) to the best of our knowledge, this is first study to investigate microvilli instance segmentation and tracking using embedding based deep learning. From the experimental results, the proposed annotation-free method achieved superior performance compared with supervised learning.

28. Non-contrast power Doppler with higher-order SVD filtering for small vessel ultrasound imaging

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Department of Biomedical Engineering

Small vessel power Doppler (PD) imaging has been facilitated by the development of plane wave transmissions, high frame rate acquisitions, and advanced filters. Conventionally, clutter rejection is achieved using IIR, FIR, or regression filters, which operate along temporal series of Doppler data. More recently, adaptive filters that employ singular value decomposition (SVD) have emerged as a robust alternative to conventional methods. In this work, we present a higher-order singular value decomposition (HOSVD) filtering framework. Signal classification was performed by analyzing (1) the mean frequency of temporal singular vectors, (2) the coherence of channel singular vectors, and (3) the amplitude characteristics spatial singular vectors. Validation was performed using 5 single vessel datasets simulated in Field II and preliminary efficacy is shown using in vivo liver data collected on a Verasonics scanner. In simulation, HOSVD filtering resulted in a higher contrast (19.99 ± 1.97 dB) compared to 'gold standard' SVD (14.48 ± 3.13 dB) and SVD-A (19.54 ± 2.21 dB). Similarly, HOSVD produced a higher maximum CNR (22.11 ± 1.72 dB versus 15.59 ± 3.7 dB for SVD and 21.88 ± 1.81 dB for SVD-A). We demonstrate that HOSVD filtering can achieve greater suppression of clutter and noise without loss of blood flow sensitivity.

29. Cochlear Implant Electric Field Estimation Using 3D Neural Networks

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Cochlear implants (CIs) use an array of electrodes implanted in the cochlea to directly stimulate the auditory nerve. After surgery, CI recipients undergo many programming sessions with an audiologist who adjusts CI processor settings to improve performance. However, few tools exist to help audiologists know what settings will lead to better performance. In order to provide objective information to the audiologist for programming, our group has developed a system to permit estimating which auditory neural sites are stimulated by which CI electrodes. To do this, we have proposed physics-based models to calculate the electric field in the cochlea generated by electrical stimulation. However, solving these models require days of computation time and substantial computational resources. In this paper, we proposed a deep-learning-based method to estimate the patient-specific electric fields using a U-Net-like architecture with physics-based loss function. Our network is trained with a dataset generated by solving physics-based models and the results show that the proposed method can achieve similar accuracy with traditional method and largely improves the speed of estimating the intra-cochlear electric field.

30. A Graph-Based Method for Optimal Active Electrode Selection in Cochlear Implants

Erin Bratu (Department of Electrical Engineering and Computer Science), **Robert Dwyer** (Department of Hearing and Speech Sciences, VUMC), **Jack Noble** (Department of Electrical Engineering and Computer Science)

The cochlear implant (CI) is a neural prosthetic that is the standard-of-care treatment for severe-to-profound hearing loss. CIs consist of an electrode array inserted into the cochlea that electrically stimulates auditory nerve fibers to induce the sensation of hearing. Competing stimuli occur when multiple electrodes stimulate the same neural pathways. This is known to negatively impact hearing outcomes. Previous research has shown that image-processing techniques can be used to analyze the CI position in CT scans to estimate the degree of competition between electrodes based on the CI user's unique anatomy and electrode placement. The resulting data permits an algorithm or expert to select a subset of electrodes to keep active to alleviate competition. Expert selection of electrodes using this data has been shown in clinical studies to lead to significantly improved hearing outcomes for CI users. Currently, we aim to translate these techniques to a system designed for worldwide clinical use, which mandates that the selection of active electrodes be automated by robust algorithms. Previously proposed techniques produce optimal plans with only 48% success rate. In this work, we propose a new graph-based approach. We design a graph with nodes that represent electrodes and edge weights that encode competition between electrode pairs. We then find an optimal path through this graph to determine the active electrode set. Our method produces results judged by an expert to be optimal in over 95% of cases. This technique could facilitate widespread clinical translation of image-guided cochlear implant programming methods.

31. Sensitivity and Specificity Analysis for Power Doppler Clutter Filter Evaluation

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Non-contrast ultrasound blood flow imaging is difficult at slow blood flow rates. For slow flow rates, there is greater spectral overlap between tissue signal and blood signal than at faster velocities, which masks blood flow and results in low CR and SNR values. Singular value decomposition (SVD) and independent component analysis (ICA) are useful for separating tissue, blood, and noise sources for Doppler filtering. In addition, it has been shown that applying SVD and ICA in a block-wise manner further improves source separation; noise within a small block is theoretically more stationary, and thus easier to separate. However, there has been much discussion on how to properly sort and select appropriate singular values and independent components. Theoretically, ICA is more adept at source separation as it can remove higher-order dependencies that SVD cannot, ideally leading to better-separable components. Here, we evaluate and compare the efficacy of SVD and ICA component sorting and classification methods by analyzing the sensitivity and specificity of each method, as an adjunct to traditional image quality metrics. Additionally, we introduce a novel Hierarchical Clustering method for component sorting and classification. We found that ICA is capable of more complete delineation between tissue and blood signals than SVD, as expected. Also, we found that ICA is nearly perfectly specific, yet only marginally more sensitive than SVD. Even with this low sensitivity, the higher specificity of ICA leads to higher-quality images than SVD, with an average 13 dB improvement in SNR for 1 mm/s flow phantom datasets.

32. Expanded beamforming models for high dynamic range scenarios

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Department of Biomedical Engineering

Aperture domain model image reconstruction (ADMIRE) and its iterative variant (iADMIRE) were designed to suppress off-axis and reverberation clutter while avoiding the dark region artifact. However, for off-axis sources that originate near, but not in the region of interest, they are sometimes misclassified as region of interest (ROI) signals, resulting in an increase in sidelobe levels. As a result, we propose a modification to the standard ADMIRE model that helps to mitigate these particularly difficult signals. We show that this alternative model allows for improved lateral resolution, which can lead to improved sizing accuracy compared to standard and even advanced beamforming methods.

33. Retinal Gene Therapy Injection Admittance Controlled Robot with OCT Feedback.

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Jin-Hui Shen - Ophthalmology, VUMC **Karen Joos -** Ophthalmology and Biomedical Engineering, VUMC **Nabil Simaan -** Mechanical Engineering, Computer Science and Otolaryngology - Head & Neck Surgery

Vitreoretinal surgery presents challenges to surgeons in terms of precision, perception, and manipulation dexterity. Retinal surgeries are conducted through sclerotomies with long rigid surgical tools without distal dexterity offering only four degrees of motion. Surgeons are also hampered by the limited stereo vision offered by surgical microscopes and other sensory deficits owing to the delicate anatomy of the retina. Retinal gene therapy is an emerging approach addressing retinal degenerative diseases. Delivery of these therapies require high precision subretinal drug injections. We present a cooperative hand-on-hand robotic system for retinal gene therapy injections using a commercial 6-axis industrial robot with admittance control and Optical Coherence Tomography (OCT) as a feedback modality to establish virtual fixtures. A custom-built OCT probe enables imaging of the distinct subretinal tissue layers guiding robot manipulation and establishing needle penetration boundaries to maximize therapy application precision. The control loop runs on Matlab Simulink Realtime and communication to the robot is through EtherCAT at 500 Hz. Admittance control is accomplished by commanding new end effector positions by scaling a force input from the user through an ATI Mini40 Force Torque sensor. Additionally, the design of a custom Remote Center of Motion (RCM) apparatus is presented, designed to enable volumetric measurement of experimental injections using OCT. OCT requires stable perpendicular alignment to a surface to achieve accurate volumetric estimates. We achieve steady alignment with a statically balanced RCM arm allowing two degrees of OCT probe motion without disrupting RCM alignment.

34. Enhancements to a Steerable Needle System to Enable Therapeutic Delivery

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Josephine Granna - Mechanical Engineering, VU **Jason Mitchell -** Mechanical Engineering, VU **Michael Lester -** Department of Medicine and Thoracic Surgery, VUMC
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We present two additions to a steerable needle system that increase the feasible workspace of the needle and improve the ability to deliver therapeutics. Current steerable needles offer the potential to access hard-to-reach areas of the body, but typically do not directly deliver biopsy and therapy delivery, since the embedded tracking sensor coils that enable accurate steering fill the inner lumen of the needle. To address this, we propose a new multi-material sheath design consisting of a catheter with good axial stiffness joined to a distal tip with low bending stiffness. Additionally, we present a new aiming device for steerable needles that locally adjusts needle launch orientation. The device consists of a tendon-actuated, notched tube design, which enables adjustment of the needle's initial orientation, increasing the effective workspace for targeting. Together, these additions to our steerable needle system ensure a more effective device with better clinical implications.

35. Correction of signal void artifact around metallic probes in MRI

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Artifacts caused by large magnetic susceptibility differences between metallic needles and tissue are a significant problem in many interventional MRI applications. The signal void caused by the probe can obscure procedure targets and prevent accurate image-based monitoring. Here, we introduce a solution to this problem by designing, simulating, fabricating and testing an active shim insert inspired from degaussing coils used in ships and submarines for defense against sea mines, to correct the field disturbance ($\Delta B0$) caused by the needle. The field disturbance induced by a 4/3 mm OD/ID mm bevelled Titanium needle at 3 Tesla is modeled and an active 2 coil shim insert is designed, and shimming is simulated. Simulations are followed by experiments on a 3 Tesla MRI scanner. A shim insert is fabricated from a 2.5 mm cylindrical former with 26-gauge wire. The shim set is inserted into the titanium rod and placed in a water phantom to match the simulation condition. 3D GRE imaging with field mapping is performed to assess shimming performance. Simulations predict significant reduction of the field disturbance outside the needle with active shimming. Experiments agreed with simulations and showed large reduction in the signal void and field inhomogeneity around the Titanium needle with active shimming. Significant degree of lost signal around the needle was recovered. We demonstrate that it is possible to recover signal losses around metallic probes with active shim coils, which can have significant benefits in a variety of qualitative and quantitative IMRI applications.

36. Real-time Therapeutic Drug Monitoring in Blood Using Electrochemical Method with the plasticized PVC coated sensor

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Electrochemical sensors are well known and established analytical tool for chemical analysis. The most successful field in which the electrochemical sensors established their application is medical application mainly in whole blood analysis. In this area electrochemical sensors were integrated into fully automated clinical laboratory analyzers, hand-held instruments for short turnaround time (STAT) and point of care testing (POCT) instruments. We have previously shown that by coating the surface of glassy carbon (GC) electrodes with a plasticized PVC membrane to measure propofol, the detection limit of the propofol measurement could be extended from micromolar to nanomolar levels. The focus of the presentation is to show plasticized PVC coated GC electrode for determination and monitoring lipophilic drugs in whole blood. The detection of analyte is based on electrochemical reaction within the PVC membrane. Lipophilic analyte partitions between sample and plasticized PVC membrane according to the partition coefficient. Due to high partition coefficient the concentration in the membrane is orders of magnitude higher than in the sample solution. That effect allows to achieve very low detection limit down to nano molar/L concentration. The proposed sensor was used to detect Amitriptyline, Rapamycin and Propofol in PBS buffer solution and whole blood. We tested the sensor in both voltammetric and chronoamperometric modes. The sensor was also used as a detector in a continuous flow analysis and flow injection analysis system to evaluate other analytical techniques for possible clinical applications. The detection limits for the tested drugs are below the therapeutic level concentration which allows to measure them in whole blood samples.

37. The impacts of temporal lobe epilepsy on Rey Complex Figure Test performance

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Temporal lobe epilepsy (TLE) is a neurological disorder that is often treated surgically. Prior to surgery, neuropsychological tests, such as the Rey Complex Figure Test (RCFT), are administered to assess the function of regions that may be resected and to help explain the risks of the procedure to the patient. The RCFT assesses visual memory abilities by measuring the patient's capability to reproduce a complex figure over three phases: 1) copy, 2) immediate (short delay after taking figure away), and 3) delayed (~30 minutes after figure has been removed). Using data acquired from the RCFT, we investigated the effects that laterality of TLE, duration of TLE, age, depression, and anxiety had on visual memory abilities. We found that as duration of epilepsy increased, performance on the delayed portion of the test decreased ($r = 0.404$, $p<0.05$). Left TLE (LTLE) patients performed worse than right TLE (RTLE) patients on the immediate and delayed phases of the test (immediate phase LTLE < RTLE: $p<0.001$, delayed phase LTLE < RTLE: $p<0.01$). This result is unexpected, as prior literature supports stronger visual memory ability in the right hemisphere, so we had hypothesized that RTLE would have a stronger negative impact on visual memory abilities. Overall, scores on the RCFT were not significantly affected by age, depression, or anxiety. Our results suggest that visual memory abilities may worsen more over time in LTLE patients compared to RTLE.

Funding: NIH NS075270, NS110130, NS108445

38. Computer-Aided Change Detection in Longitudinal Skin Photographs: Application to Cutaneous Chronic Graft-Versus-Host Disease

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Longitudinal tracking of skin change is of high importance in dermatology because it provides clinicians with information on disease progression, resolution, and treatment efficacy. We developed a computer-aided method that detects change in active skin inflammation (erythema) in longitudinal skin photos of cutaneous chronic graft-versus-host disease (cGVHD), the leading cause of long-term non-relapse mortality and morbidity following allogeneic hematopoietic stem cell transplantation. We acquired 3D photos with a Vectra H1 (Canfield Scientific) of 8 body sites of a cGVHD patient at 7 sessions over a 172-day period, including baseline skin appearance (t0) before the development of cGVHD erythema (t1-t6). Due to the lack of a "ground truth" of areas of active inflammation, two dermatologist-trained annotators marked only high-certainty regions within each image: 1) definitely affected skin ("do not miss", DNM), and 2) definitely unaffected skin ("do not include", DNI). This resulted in 48 DNM/DNI pairs of cross-polarized 3D images. We developed a pixel-wise, feature-based skin change segmentation algorithm based on DNM/DNI areas by utilizing a VGG16 feature extractor of a pre-trained convolutional neural network. With parameters fixed by only one single DNM/DNI pair, our developed algorithm achieved an average accuracy of 0.71 to detect skin change between baseline and any timepoint and skin site of active cGVHD. Color constancy and use of both cross-polarized and non-polarized images improved algorithm performance. Two board-certified dermatologists independently evaluated algorithm output as acceptable (average score of 0.9 on a scale 0-2).

39. Towards Semi-Autonomous Assistive Ischemic Stroke Treatment Using Intelligent Dexterous Continuum Robots

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In the United States, someone has a stroke every 40 seconds and someone dies from a stroke every 4 minutes. Worldwide, stroke is the leading cause of permanent disability. Since 2015, mechanical thrombectomy (MT), i.e. the endovascular retrieval of blood clots using stent retrievers and/or aspiration catheters, has become the standard of care for patients who present with acute large vessel occlusion strokes. This shift stemmed from multiple randomized controlled trials that showed the benefits of MT in increasing recanalization rates, and consequently reducing disability and death rates. The recent awareness to the importance of early revascularization via MT stands in contrast to the current availability of this intervention. This scarcity is partly due to the skill barrier associated with the complexity of navigating and steering through thin, tortuous, and branched vasculature using passive guidewires and catheters. The goal of our ongoing research is to lower this skill barrier and expand access to MT, through the use of a semi-autonomous self-steering catheters. As part of this effort, we have developed an ex-vivo experimental setup for testing and evaluation of catheter prototypes. We report our experience with creating various patient-specific vasculature phantoms (rigid, soft, and hybrid) and mock blood clots. We also present a method for intraoperative catheter tracking using image segmentation of bi-plane fluoroscopy image stream and Kalman filtering.

40. Patch-based abnormality maps for improved deep learning-based classification of Huntington's disease

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Deep learning techniques have demonstrated state-of-the-art performances in many medical imaging applications. These methods can efficiently learn specific patterns. An alternative approach to deep learning is patch-based grading methods, which aim to detect local similarities and differences between groups of subjects. This latter approach usually requires less training data compared to deep learning techniques. In this work, we propose two major contributions: first, we combine patch-based and deep learning methods. Second, we propose to extend the patch-based grading method to a new patch-based abnormality metric. Our method enables us to detect localized structural abnormalities in a test image by comparison to a template library consisting of images from a variety of healthy controls. We evaluate our method by comparing classification performance using different sets of features and models. Our experiments show that our novel patch-based abnormality metric increases deep learning performance from 91.3% to 95.8% of accuracy compared to standard deep learning approaches based on the MRI intensity.

41. Feasibility of Remote Landmark Identification for Cricothyrotomy using Robotic Palpation

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Cricothyrotomy is an emergency airway management procedure for treating airway obstruction. An incision is made in the skin and the cricothyroid membrane to establish a definitive airway. A successful cricothyrotomy largely depends on the accurate and rapid identification of the cricothyroid membrane. The location of this landmark is determined through the visual inspection and concurrent palpation of the Larynx. Enabling robot-assisted remote cricothyrotomy may extend this life-saving procedure to injured soldiers or patients who may not be readily accessible for on-site intervention during search-and-rescue scenarios. As a first step towards achieving this goal, we explore the feasibility of palpation-assisted remote landmark identification for cricothyrotomy. Using a cricothyrotomy simulator (from Simulaids®), we explored several alternatives for in-situ remote localization of the cricothyroid membrane. These alternatives included a) unaided telemanipulation, b) telemanipulation with direct force feedback c) telemanipulation with superimposed motion excitation for on-line stiffness estimation and display, and d) fully autonomous palpation scan initialized based on user's understanding of percutaneous anatomical landmarks. Using the autonomous mechanical raster scan of the anatomy as ground truth, we compared these four methods for accuracy and repeatability of identifying the cricothyroid membrane, time of completion, and ease of use based on user feedback. The results suggest that the remote cricothyrotomy landmark identification is most feasible when the user is aided with visual and force cues. These preliminary results show that, with proper user initialization, remote landmark identification is feasible - therefore satisfying a key pre-requisite for future robotic solutions for remote cricothyrotomy.

42. Image Guidance for the da Vinci Robot

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Partial nephrectomy kidney surgery involves removing a tumor while sparing as much surrounding healthy kidney tissue as possible. Compared to total kidney removal, partial nephrectomy improves outcomes for patients; however, it is currently underutilized because it is challenging to accomplish minimally invasively, requiring accurate spatial awareness of unseen subsurface anatomy. Over the past several years, we have developed an image guidance system for the da Vinci robot that could help surgeons perform robot-assisted partial nephrectomy, ultimately increasing the practice of this underutilized procedure. Our system improves robotic surgery by enhancing a surgeon's spatial awareness. As the surgeon operates, renderings of their robotic tools move seamlessly alongside translucent 3D models of patient anatomy derived from accurate medical imaging. This improved spatial awareness could help surgeons avoid critical subsurface anatomy such as blood vessels and target the tumor prior to resection. We present experimental results validating the accuracy of our system in phantom models. Additionally, we present our current study which is the first in human study of its kind.

43. Intraoperative spectrally encoded coherence tomography and reflectometry (iSECTR) for ophthalmic surgical guidance

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Ophthalmic surgery is conventionally performed under white-light microscopy which has limited benefit for identifying tissue layers and providing depth-resolved feedback. Intraoperative optical coherence tomography (iOCT) has enabled depth-resolved intraoperative imaging of retinal microstructures, including epiretinal membranes, macular holes, and retinal detachment. Recent advancements have enabled faster imaging speeds and video-rate, volumetric iOCT imaging of surgical dynamics. However, iOCT of surgical maneuvers remains challenging because the imaging field-of-view (FOV) requires manual adjustment and tracking. To overcome this limitation, we previously demonstrated multimodal spectrally encoded coherence tomography and reflectometry (SECTR), which simultaneously acquires an en face spectrally encoded reflectometry (SER) frame with cross-sectional OCT B-scans. SER provides a complementary en face retinal view that enables robust visualization of surgical instruments for tool-tracking. Here, we demonstrate multimodal ophthalmic imaging with an intraoperative SECTR (iSECTR) system. iSECTR optical design and scan-head were integrated with a Zeiss VISU 200 surgical microscope with optimized optical performance and optomechanical stability. The system was evaluated by performing widefield in vivo retinal imaging on a healthy volunteer. Simulated retinal surgery in ex vivo porcine eyes demonstrated co-registered surgical microscope views and iSECTR volumes. We believe that overcoming the static FOV limitation of current-generation iOCT systems will allow for more robust real-time feedback on the location and depth of surgical instruments relative to anatomic microstructures of interest to better guide ophthalmic surgery.

44. Evaluating the Effect of Anti-Epileptogenic Drugs on Functional Connectivity Measures in Stereo-Electroencephalography

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Introduction: Patients with medically-refractory focal epilepsy often undergo stereo-electroencephalography (SEEG) to assist in localization of epileptogenic zones (EZ) for surgical treatment. Previous research demonstrates there are differences in functional connectivity measures between EZs and non-EZs using SEEG, however, it is unknown whether anti-epileptic drugs (AEDs) affect connectivity measures.

Objective: Determine if SEEG measures of connectivity are stable over time or if they vary with AED dosage.

Methods: In 9 patients with medically-refractory focal epilepsy who underwent SEEG, 2 minutes of clean pseudo-rest (eyes open, sitting quietly with minimal talking and no food or beverage consumption) data was collected post-implantation of depth electrodes, on post-operative days 1-7 while patients were weaned from AEDs, when available. One non-directed connectivity measure, between imaginary coherence, and one directed connectivity measure, partial directed coherence (PDC) inward strength, were calculated.

Results: There was a trend towards higher between imaginary coherence values in EZs compared to non-EZs over time with significant findings on days 2, 3, and 7 ($p<0.05$, t-test). PDC inward strength trended to be higher in EZ regions compared to non-EZ regions over time with significant findings on days 2-7 ($p<0.05$, t-tests). Qualitative observations suggest a relatively stable difference in PDC inward strength over time between EZ and non-EZ regions, whereas this difference appears less stable for between imaginary coherence.

Conclusions: Connectivity differences between EZs and non-EZs in SEEG are more stable over time in PDC inward strength compared to between imaginary coherence. Future directions include further quantifying the effect of AEDs on connectivity measures.

45. Asymmetry, Instability, and Functional Deficits in Transtibial Prosthesis Users During Squatting, Lifting, and Sit-to-Stand

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Lower limb prosthesis users (LLPUs) experience mobility challenges that can impair their ability to carry out activities of daily living, affecting quality-of-life and independence. Most LLPUs use a passive ankle-foot prosthesis where the ankle joint and foot keel are locked at a fixed angle. The lack of ankle and toe joint mobility may contribute to task performance deficits LLPUs experience. Prosthetic design modifications could potentially improve their comfort, safety, and ability to complete these tasks. To investigate this, we are conducting a comprehensive human movement study evaluating transtibial LLPUs during sit-to-stand, squatting, lifting, and lunging movements. These activities were all identified as tasks that LLPUs completely avoid or find challenging, and have the potential to be improved by modifying prosthetic ankle-foot design. We are collecting data with each participant wearing their prescribed passive prosthesis and the Vanderbilt Powered Ankle, used to emulate specific device design modifications that are expected to improve the ability of LLPUs to complete these tasks, i.e., adding ankle and/or toe articulation. For each task, we are collecting participant feedback on perceived effort, stability, and comfort in addition to full motion capture and ground reaction force data. Preliminary data from one participant has been collected. During each task, the participant's intact lower limb experienced more than twice the magnitude of force as their prosthetic limb. In pilot testing of the powered prosthesis, there were noteworthy improvements in subjective feedback related to effort, stability and comfort when utilizing increased ankle dorsiflexion during sit-to-stand.

46. Multimodal Directed Connectivity in Mesial Temporal Lobe Epilepsy Patients

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Introduction: Approximately 50 million people globally suffer from epilepsy. Functional magnetic resonance imaging (fMRI) noninvasively samples the brain but has limited success in identifying epileptogenic zone(s). Stereotactic electroencephalography (SEEG) is minimally invasive technique and the gold standard for localizing epileptogenic zone(s) but is limited by sampling bias. This investigation explores directed connectivity using both modalities in mesial temporal lobe epilepsy (mTLE) patients.
Methods: Fifty-two mTLE patients (15 left mTLE) and matched controls, we acquired 10-minutes of resting-state fMRI. Four left mTLE (LmTLE) and 6 right mTLE (RmTLE) patients had 2-minutes of resting-state SEEG collected. Brain regions were designated with Desikan-Killany atlas. We studied bilateral hippocampi, amygdale, and caudal anterior cingulate. For resting-state fMRI, we utilized dynamic causal modeling (DCM) (SPM12 DCM12.5) to compare endogenous coupling of an optimal network containing all regions, and we used Granger causality to compare directed connectivity. For resting-state SEEG, we used inward Partial Directed Coherence (PDC) strength (http://www.fieldtriptoolbox.org/) to compare these regions to others sampled.
Results: DCM analysis revealed endogenous coupling from right hippocampus to left hippocampus was lower in RmTLE versus matched controls ($p<0.01$,t-test). While not significant in Granger causality, the connection from left hippocampus to right hippocampus was lower in RmTLE versus matched controls ($p<0.05$,t-test). PDC inward strength was higher in right/left hippocampi versus other sampled regions in RmTLE/LmTLE patients ($p<0.05$,t-test).
Conclusions: Resting-state fMRI and SEEG studies of directed connectivity in mTLE elucidated differences in hippocampal connectivity. Further investigation could aid in ultimately employing fMRI as a noninvasive modality to localize epileptogenic zones.

47. FMRI Functional Connectivity Perturbations Between Arousal Structures and Resting-State Networks in Persons with Temporal Lobe Epilepsy

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Introduction: Temporal lobe epilepsy (TLE) is a focal epilepsy but results in broad neural deficits. Arousal structures, understudied in TLE, may be paramount to explaining these deficits. In many neurological diseases resting-state networks (RSN) display altered connectivity, however, arousal network-RSN connectivity is unexplored in TLE. Here, we examine directed and non-directed connectivity between arousal structures and RSN (Salience Network (SN), Default Mode Network (DMN), Frontoparietal Control Network (FPCN), Visual Network (VN)) in TLE patients and effects of epilepsy surgery.
Methods: We acquired resting-state fMRI in 50 TLE patients and 50 matched controls. In 29 patients, we repeated fMRI >1yr after epilepsy surgery. We calculated non-directed (correlation) and directed connectivity (Granger Causality Laterality Index: GC) between arousal structures (brainstem ascending reticular activating system (ARAS), intralaminar thalamus, and nucleus basalis of Meynert (NBM)) and RSN.
Results: Before surgery patients displayed altered non-directed connectivity between multiple arousal structures and all four RSN examined ($p<0.05$, t-test). ARAS and NBM exhibited markedly altered GC with SN, DMN, and FPCN ($p<0.05$, t-test). Interestingly, ARAS non-directed connectivity with SN, DMN, and FPCN was lower in patients with good and moderate surgical outcomes (Engel 1-2) than bad outcomes (Engel 3-4, $p<0.05$ ANOVA). Additionally, some connectivity abnormalities recovered after surgery.
Conclusion: TLE patients exhibit abnormal connectivity between arousal structures and resting-state networks. These perturbed connectivities may be related to broad brain network disturbances seen in TLE and potentially associated with surgical outcomes. Further work studying arousal network connectivity may inform novel surgical approaches to treat this devastating disorder.

48. Inter-rater and intra-rater reliability of leukocyte adhesion and rolling in upper dermal blood vessels via in vivo reflectance confocal video microscopy

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Background: In a previous study, we found increased number of adherent and rolling leukocytes in the upper dermal blood vessels of cutaneous acute graft-versus-host disease (aGVHD) patients via in vivo reflectance confocal microscopy (RCM).
Objective: Test the inter-rater and intra-rater reliability of the assessment of the number of adherent and rolling leukocytes in in vivo RCM videos.
Methods: We collected 1522 RCM videos of various groups including aGVHD patients and healthy subjects from sites of interest (i.e. forearm, chest, or cutaneous aGVHD-affected lesion). Two blinded and trained raters counted adherent and rolling leukocytes in 88 videos. Based on a discussion of the discrepancies, they developed a guideline and utilized it for analyzing the remaining 1434 videos. One blinded rater re-analyzed 20 videos after more than a month since the initial post-guideline assessments. We calculated the intraclass correlation coefficients (ICCs) based on a single-rating, absolute-agreement, 2-way random effects model.
Results: The inter-rater ICCs of adherent (pre-guideline ICC: 0.056; post-guideline ICC: 0.791) and rolling (0.385; 0.626) leukocyte counts increased post-guideline. The intra-rater ICCs of adherent and rolling leukocytes post-guideline were 0.953 and 0.956, respectively.
Conclusion: We developed a guideline that improved the inter-rater reliability of assessing adherent and rolling leukocytes. The guideline clarified the types of scenarios that mimic adherent (e.g. keratinocytes) and rolling (e.g. sliding) leukocytes in RCM videos. The guideline aids in the reproducibility of future human cutaneous microvasculature studies utilizing in vivo RCM.

49. Continuum Robots with Equilibrium Modulation: Micro/Macro Motion Control and OCT-guided Visual Servoing for Future Targeted Drug Delivery and Image-Based Biopsy

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Multi-backbone continuum robots (MBCR) are parallel robots with constrained flexible legs that can provide a large workspace and high precision by controlling their leg lengths. We recently introduced a new design extending the motion capabilities of MBCRs to the micro-scale by introducing joints dedicated to modulating the static equilibrium of these devices. We call this new approach for micro-motion continuum robot equilibrium modulation (CREM). By using CREM, MBCRs can provide macro and micro-scale motion capabilities suitable for several potential applications such as image-based biopsy, micro-surgery, cellular-level surgery or ophthalmic surgery where a micro-motion workspace with micrometer-level precision is needed. Deriving a closed-form solution for the micro-motion induced by equilibrium modulation as a function of equilibrium modulation joint values is a complicated task involving the solution of nonlinear differential equations. To overcome this challenge, we first present a modeling approach that explains the source of the equilibrium modulation behavior. Another approach that allows experimental-based micro-kinematics modeling of these devices is also presented. Using this approach for micro-motion control, we present our system integration and approach for achieving closed-loop OCT-guided visual servoing and 3D OCT. We demonstrate the utility of our approach for OCT-guided needle targeting into a microchannel in agar. These experiments suggest that continuum robots may be used in the future as interventional surgical tools with integrated sensory capabilities such as OCT biopsy or confocal laser endo-microscopy.

50. Repairing transient artifacts in PPG signals acquired during fMRI

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Photoplethysmography (PPG) is a fast and noninvasive way of measuring pulse rate and other valuable physiological variables during functional magnetic resonance imaging (fMRI) scans. However, large chunks of noise in the waveform can result from slight subject movement and interfere with the data, undermining its utility in data processing such as its use in fMRI denoising. Oftentimes, to correct for the noisy region, pulse intervals will have to be manually calculated and filled in. Since the PPG waveform can have large variations in amplitude over time, generating reasonable waveforms to replace such regions can be challenging.

To tackle this issue, a convenient and simple algorithm is developed to correct transient artifacts in the PPG waveform. The algorithm partitions the data waveform into a number of sections, calculates the standard peak interval and peak height across the region, then detects noisy regions with this information at hand. Interpolation and replacement of a noisy region is based on the standard information collected in its respective part, putting heavy weights especially on the periods before and after the noisy segment in order to estimate the correct amplitude, period, and phase. As a result, this algorithm is able to automatically detect outliers in the data and interpolate with precision close to a manual fix. This saves a significant amount of repetitive work in the preprocessing stage and allows for better and more extensive use of the data in preprocessing of fMRI data.

51. Altered Dynamic Response of Brain Networks in Temporal Lobe Epilepsy

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Temporal lobe epilepsy (TLE) is a neurological disorder characterized by recurrent and unpredictable seizures emanating from abnormal neuronal activity, typically arising from small, focal regions. However, many brain networks are impaired based upon their connection to this region, and as a result surgical resection of the focal region is not always successful at providing complete seizure remission. This uncertainty stems from not knowing the underlying network abnormalities involved in epilepsy and how surgical removal of entire regions affects wide-scale brain dynamics. Our goal was to investigate the difference in brain dynamics between TLE patients and healthy controls to identify markers of abnormal brain regions and understand how removal of these regions will affect brain function after surgery. We acquired diffusion weighted imaging in 40 TLE patients and 70 healthy controls to construct structural connectomes which define how brain regions are interconnected. We then computed a measure of network controllability (i.e. the impulse response) for each brain region. In the TLE cohort, we found significant reductions in the controllability of several regions associated with seizure activity compared to healthy controls: the temporal gyrus, temporal pole, and hippocampus. Understanding how these regions affect wide-scale brain dynamics may aid in tracking disease progression both before and after surgical interventions. This information could be used to identify patients who might respond to surgery or explain why some surgeries were not successful at reducing seizures based upon how the resected tissue altered network dynamics. This study is funded by NIH NS075270, NS110130, and NS108445.

52. Handheld spectrally encoded coherence tomography and reflectometry for point-of-care ophthalmic OCT and OCTA

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Current-generation optical coherence tomographic angiography (OCTA) systems are slit-lamp based, which limits ophthalmic imaging to patients who are able to sit upright and fixate. Prototype handheld OCTA has demonstrated imaging of supine patients, but these systems are susceptible to bulk-motion artifacts that degrade OCTA resolution and contrast. Here, we demonstrate bulk-motion correction and multi-volumetric mosaicking of OCTA volumes acquired using our handheld spectrally encoded coherence tomography and reflectometry (SECTR) system. In addition, we leverage variable-velocity scanning to reduce OCTA acquisition times. We believe SECTR overcomes the limitations of current-generation handheld OCT/OCTA and will enable functional ophthalmic imaging in bedridden patients and infants.

53. Image-to-physical deformable registration using intraoperative ultrasound and linearized iterative boundary reconstruction

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During image guided liver surgery, soft tissue deformation can cause considerable error when attempting to achieve accurate localization of the surgical anatomy through image-to-physical registration. In this work, a linearized iterative boundary reconstruction technique is proposed to account for these deformations. The approach leverages a superposed formulation of boundary conditions to rapidly and accurately estimate the deformation applied to a preoperative model of the organ given sparse intraoperative data of surface and subsurface features. With this method, tracked intraoperative ultrasound (iUS) is investigated as a potential data source for augmenting registration accuracy beyond the capacity of conventional organ surface registration. In an expansive simulated dataset, features including vessel contours, vessel centerlines, and the posterior liver surface are extracted from iUS planes. Registration accuracy is compared across increasing data density to establish how iUS can be best employed to improve target registration error (TRE). From a baseline average TRE of 11.4 ± 2.2 mm using sparse surface data only, incorporating additional sparse features from three iUS planes improved average TRE to 6.4 ± 1.0 mm. Furthermore, increasing the sparse coverage to 16 tracked iUS planes improved average TRE to 3.9 ± 0.7 mm, exceeding the accuracy of registration based on complete surface data available with more cumbersome intraoperative CT without contrast. Additionally, the approach was applied to three clinical cases where on average error improved 67% over rigid registration and 56% over deformable surface registration when incorporating additional features from one independent tracked iUS plane.

54. Breast Deformation from Supine Imaging to Surgery within an Image Guided Approach

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Image guidance frameworks for breast conserving surgery show great promise but currently rely on rigid registration to describe breast shift from supine magnetic resonance (MR) imaging to surgical position. We characterize and measure these deformations and evaluate the accuracy of rigidly aligning supine MR images to the surgical field. Depending on the location of the tumor, maximum error with a rigid registration framework can be expected to be between 10 and 30 millimeters. Data here suggest that nonrigid deformation will be an essential consideration in developing a novel image guidance system to compete with and outperform seed-based lesion localization methods.

55. Robustness of vigilance estimation due to fMRI preprocessing variations: multi-echo ICA vs. conventional preprocessing

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Fluctuating levels of alertness are accompanied by substantial neural, behavioral, and cognitive variability. Yet, most fMRI studies do not explicitly investigate changes in alertness, since it is oftentimes not feasible to gather external measures of alertness (such as scalp EEG and pupillometry) in routine fMRI scans. Our recent work has demonstrated that estimating alertness from fMRI data alone can predict behavioral responses to incoming sensory stimuli as well as improving specificity of task fMRI activation maps. We are currently testing the robustness and reproducibility of our vigilance estimation procedure by altering how the fMRI images were pre-processed. Our previous findings had a multi-echo ICA denoising step (DuPre et al., 2020; Kundu et al., 2012, 2013) separating fMRI signal components generated from BOLD mechanisms from those arising from non-BOLD signal sources. This technique has demonstrated efficacy in reducing artifacts including head motion, cardiac pulsatility, and breath-to-breath respiratory volume, but requires that data were gathered using particular pulse sequences. In this new study we pre-process the fMRI with a less complex and more conventional method that includes RETROICOR (Glover et al., 2000), which is meant to decrease noise and improve the statistical significance of activation signals correcting for respiration effects and cardiac pulsatility. Based on preliminary investigation we are finding our vigilance estimation method to be similar between these two pipelines. This suggests that our vigilance measure is not specifically dependent on the multi-echo denoising procedure, and therefore can be applied to data processed with different pipelines.

56. Learning white matter fingerprints from structural information

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Here, we present a tool and reconstruction method to label white matter pathways directly on structural images without the need for diffusion MRI or tractography. A 3D U-net was trained utilizing 1109 scan sessions where fiber pathways were segmented using two different segmentation schemes (defining 53 and 72 white matter bundles, respectively). Results on testing datasets show anatomically viable segmentations and moderate-to-high volume overlaps with ground truth pathways, on par with scan-rescan reproducibility of tractography on the same datasets. We envision the use of this tool for visualizing the expected course of white matter pathways when diffusion data are not available.

57. Pandora: 4-D white matter bundle population-based atlases derived from diffusion MRI fiber tractography

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Brain atlases have proven to be valuable neuroscience tools for localizing regions of interest and performing statistical inferences on populations. Although many human brain atlases exist, most do not contain information about white matter structures, often neglecting them completely or labelling all white matter as a single homogenous substrate. While few white matter atlases do exist based on diffusion MRI fiber tractography, they are often limited to descriptions of white matter as spatially separate “regions” rather than as white matter “bundles” or fascicles, which are well-known to overlap throughout the brain. Additional limitations include small sample sizes, few white matter pathways, and the use of outdated diffusion models and techniques. Here, we present a new population-based collection of white matter atlases represented in both volumetric and surface coordinates in a standard space. These atlases are based on 2443 subjects, and include 216 white matter bundles derived from 6 different automated state-of-the-art tractography techniques. This atlas is freely available and will be a useful resource for parcellation and segmentation.

58. Learning white matter subject-specific segmentation from structural MRI

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Mapping brain white matter (WM) is essential for building understanding of brain function and dysfunction. Tractography-based methods derived from diffusion weighted MRI (dMRI) are the principle tool for investigating extended connections within WM. These procedures rely on time-consuming acquisitions that may not always be available, especially for legacy or time-constrained studies. Structural MRI acquisitions, on the other hand, are ubiquitous. Herein, we hypothesize that extended WM relationships may be inferred from structural MRI through WM segmentation with deep learning. We explore this hypothesis in the context of deep learning on structural MRI. Following recently proposed innovations in structural anatomical segmentation, we evaluate the feasibility of training multiple spatially localized convolution neural networks to predict WM pathways. We focus on 6 widely used dMRI bundle segmentation routines, and create deep neural networks to learn these techniques based on about 3870 T1-weighted images from Baltimore Longitudinal Study of Aging (BLSA), Human Connectome Project (HCP) S1200 release and Vanderbilt University. The proposed framework identifies fiber bundles with high agreement against dMRI pathways with median Dice from 0.62 to 0.87. We demonstrate generalizability of the proposed framework on three external available datasets.

59. A Deep Pattern Recognition Approach for Inferring Respiratory Volume Fluctuations from fMRI Data

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Functional magnetic resonance imaging (fMRI) is one of the most widely used non-invasive techniques for investigating human brain activity. Yet, in addition to local neural activity, fMRI signals can be substantially influenced by non-local physiological effects stemming from processes such as slow changes in respiratory volume (RV) over time. While external monitoring of respiration is currently relied upon for quantifying RV and reducing its effects during fMRI scans, these measurements are not always available or of sufficient quality. Here, we propose an end-to-end procedure for modeling fMRI effects linked with RV, in the common scenario of missing respiration data. We compare the performance of multiple deep learning models in reconstructing missing RV data based on fMRI spatiotemporal patterns. Finally, we demonstrate how the inference of missing RV data may improve the quality of resting-state fMRI analysis by directly accounting for signal variations associated with slow changes in the depth of breathing over time.

60. Construction of a Multi-Phase Contrast Computed Tomography Healthy Kidney Atlas

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The construction of three-dimensional multi-modal tissue maps provides opportunity to spur interdisciplinary innovations across temporal and spatial scales through information integration. While the preponderance of effort is allocated to the cellular and molecular level mapping to explore the changes in cell interactions and organizations, contextualizing findings within organs and systems is essential to visualize and interpret higher resolution linkage across scales. There is substantial normal variation of kidney morphometry and appearance across body size, sex and imaging protocols in abdominal computed tomography (CT). A volumetric atlas framework is needed to integrate and visualize the variability across scales. However, there is no abdominal organs atlas framework for multi-contrast CT. Hence, we proposed a high-resolution CT abdominal atlas specifically optimized for the kidney across-non-contrast CT and early arterial, late arterial, venous and delayed contrast enhanced CT. Briefly, we introduce a deep learning-based volume interest extraction method and automated two-stage hierarchal registration pipeline to register abdominal volumes to a high-resolution CT atlas template. To generate and evaluate the atlas, multi-contrast modality CT scans of 500 subjects (without reported history of renal disease, age: 15-50 years, 250 males & 250 females) are processed. We demonstrate a stable generalizability of the atlas template for integrating the normal kidney variation from 64 cm3 (small) to 302 cm3 (large), across contrast modalities and populations with great variability of demographics. The linkage of atlas and the demographics provided a better understanding of the variation kidney phenotype across population and improved understanding of the anatomical characteristics of kidney organs.

61. An Exploratory Project: Predictive modeling of hypertrophic response to portal vein embolization

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Aside from transplantation, surgical resection is considered to be the gold-standard of treatment for primary and secondary liver cancers. Post-resection liver failure, occurring in ~30% of cases, is the major cause of death following resection and most often results from insufficient future liver remnant (FLR). For patients with limited FLR, portal vein embolization (PVE) is the most common method to stimulate growth of the FLR, allowing for potentially curative resection in patients that otherwise would not be considered candidates. PVE is a preoperative procedure where an occlusive agent is injected to block venous blood flow, inducing atrophy in the planned resection area and hypertrophy of the FLR. PVE is a low risk procedure, but limitations include metastatic progression in the two- to eight-week period between PVE and resection, and insufficient hypertrophy for prevention of postoperative liver failure. Numerous studies focus on prediction of postoperative liver failure from metrics obtained after PVE, including studies by our group that identify post-PVE growth rate as a significant predictor of outcome and propose a surgical planning model to accurately predict FLR volume. However, few studies predict PVE response or model parenchymal changes to more precisely align treatment with patient candidacy. We investigate the importance of PVE and the potential impact of a pre-PVE computational model of the FLR growth and vascular changes. Clinically, a liver hypertrophy model may assist with predicting procedural outcome of PVE to better select candidacy for and optimize the timing of subsequent resection to improve patient survival and curative outcome.

62. Local Drug-Delivery Strategies for Prolonged MMP13 RNA interference (RNAi) to Block Progression of Post-Traumatic Osteoarthritis (PTOA)

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Osteoarthritis (OA) is a debilitating and prevalent chronic disease, but there are no approved disease modifying OA drugs (DMOADs), only pharmaceuticals for pain management. OA progression, particularly for post-traumatic osteoarthritis (PTOA), is associated with inflammation and enzymatic degradation of the extracellular matrix. In particular, matrix metalloproteinase 13 (MMP13) breaks down collagen type 2 (CII), a key structural component of cartilage extracellular matrix, and consequently, matrix degradation fragments perpetuate inflammation and a degenerative cycle that leads to progressive joint pathology. As drug delivery strategy 1, we created matrix-anchored nanoparticles (mAbCII-siNPs) that target exposed collagen 2 in OA-afflicted joints meanwhile delivering an anti-MMP13 small interfering RNA (siRNA) therapeutic. mAbCII-siNPs were synthesized comprising an endosome-escaping, RNA-condensing core and a passivating, colloidally-stabilizing poly (ethylene glycol) (PEG) surface amenable to antibody conjugation. The collagen II targeting monoclonal antibody (mAbCII) was conjugated to COOH-PEG-ECT by sNHS/EDC chemistry. Successful conjugation of PEG-bl-DB to mAbCII was validated by size exclusion chromatography. For drug delivery strategy 2, we designed a nano-in-micro system (siMMP13-NPs/μPLs). A top-down approach was employed for synthetizing shape defined poly (D,L-lactide-co-glycolide) (PLGA) microPlates (μPLs) for local and sustained release of MMP13-siRNA nanoparticles (siMMP13-NPs). Both formulations (mAbCII-siNPs and siMMP13-NPs/μPLs) were physico-chemically characterized and their therapeutic efficacy was assessed in a mechanically-induced OA mouse model (PTOA). Overall, mAbCII-siNP/siMMP13 and siMMP13-NPs/μPLs were able to provide prolonged, localized, knockdown of MMP13 leading to a significant improvement in PTOA/OA phenotype; these results demonstrate the unique ability of targeted nano and nano-in-micro formulations for sustained delivery of intracellular-acting biologics, such as siRNA.

63. A Real-Time, GPU-Based Implementation of Aperture Domain Model Image REconstruction

Christopher Khan, Kazuyuki Dei, Siegfried Schlunk, Kathryn Ozgun, and Brett Byram

Delay-and-sum (DAS) is the primary ultrasound beamforming method that is used in the field of ultrasound imaging. This is mainly due to the ability of this algorithm to be implemented in real time. The first step of DAS is to time-delay the ultrasound channel data in order to adjust for path length differences between the transducer elements and the returning acoustic wavefronts, and the second step is to coherently sum the received signals across the aperture. Now, although DAS is able to be implemented in real time, one of its main disadvantages is that it is less effective than more advanced beamforming methods when it comes to addressing mechanisms such as off-axis and multipath scattering, which produce acoustic clutter that degrades ultrasound image quality. To address these mechanisms, we have recently proposed Aperture Domain Model Image REconstruction (ADMIRE), which is an advanced beamforming method that uses a model-based approach in order to suppress sources of acoustic clutter. This method has shown promise in improving the quality of ultrasound images, but its large computational requirements has made it infeasible to implement it in real time on a CPU. However, by using graphics processing units (GPUs), the speed of ADMIRE can be dramatically improved due to each GPU containing hundreds to thousands of computational cores. Therefore, in this work, we have developed a GPU-based implementation of ADMIRE, and we demonstrate the feasibility of this implementation to be used for real-time imaging.

64. Intrinsic functional connectivity of spinal cord of monkeys using Independent Component Analysis of resting state fMRI and its clinical significance

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Recent reports of resting state blood oxygenation level dependent fluctuations in the spinal cord (SC) using functional Magnetic Resonance Imaging (fMRI) suggest that similar to brain, there exists a functional architecture in SC. However very less is known about the function circuits in SC beyond the conventional '4 horn model' at bilateral dorsal and ventral regions of gray-matter. Even less is known about possible changes in functional circuits after a SC injury. In this study, we implemented a data driven technique called Independent Component Analysis (ICA) on fMRI data from the cervical region (C3-C7) of SC of squirrel monkeys to obtain robust networks at bilateral intermediate region and gray-matter commissure region apart from the conventional '4 horn model'. A unilateral dorsal column lesion was made to study changes following a SC injury. ICA based connectivity measures showed that there was a reduction in connectivity both below and above lesion post-injury which slowly recovered back to normalcy with time. Inter-slice connectivity was more affected compared to intra-slice connectivity. This observation was further substantiated by Graph-Theory analysis which found that there was a rise of intra-slice community structures and drop in inter-slice community structures following a SC injury. A machine learning framework based on Support-Vector-Machine classifier was able to predict different stages of injury using functional connectivity measures at a low classification error of 14.28 %. Overall, this study reveals new insights into the SC architecture, and demonstrates the clinical potential of ICA derived functional connectivity measures in case of SC injury.

65. Deep Multi-path Network Integrating Incomplete Biomarker and Chest CT Data for Evaluating Lung Cancer Risk

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Clinical data elements (CDEs) (e.g., age, smoking history), blood markers and chest computed tomography (CT) structural features have been regarded as effective means for assessing lung cancer risk. These independent variables can provide complementary information and we hypothesize that combining them will improve the prediction accuracy. In practice, not all patients have all these variables available. In this paper, we propose a new network design, termed as multi-path multi-modal missing network (M3Net), to integrate the multi-modal data (i.e., CDEs, biomarker and CT image) considering missing modality with multiple paths neural network. Each path learns discriminative features of one modality, and different modalities are fused in a second stage for an integrated prediction. The network can be trained end-to-end with both medical image features and CDEs/biomarkers, or make a prediction with single modality. We evaluate M3Net with datasets including three sites from the Consortium for Molecular and Cellular Characterization of Screen-Detected Lesions (MCL) project. Our method is cross validated within a cohort of 1291 subjects (383 subjects with complete CDEs/biomarkers and CT images), and externally validated with a cohort of 99 subjects (99 with complete CDEs/biomarkers and CT images). Both cross-validation and external-validation results show that combining multiple modality significantly improves the predicting performance of single modality. The results suggest that integrating subjects with missing either CDEs/biomarker or CT imaging features can contribute to the discriminatory power of our model ($p < 0.05$, bootstrap two-tailed test).

66. Human Brian Extraction with Supervised and Transfer Learning

Hao Li, Ipek Oguz

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Brain extraction, also known as skull stripping, from magnetic resonance images (MRIs) is an essential preprocessing step for many medical image analysis tasks and is also useful as a stand-alone task for estimating the total brain volume. Currently, many proposed methods have excellent performance on T1-weighted images, especially for healthy adults. However, such methods do not always generalize well to more challenging datasets such as pediatric, severely pathological, or heterogeneous. In this paper, we propose an automatic deep learning framework for brain extraction on T1-weighted MRIs of adult healthy controls, Huntington's disease patients and pediatric Aicardi Goutières Syndrome (AGS) patients. We examine our method with supervised learning on the PREDICT-HD dataset and transfer learning on an AGS dataset. Compared to current state-of-the-art methods, our method produced the best segmentations on both datasets. These results indicate that our method has better accuracy on intra-dataset and generalizability for inter-dataset.

67. Training Program for Innovative Engineering Research in Surgery and Intervention.

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Over the past several decades, dramatic breakthroughs in biomedical science have been witnessed within laboratory research. The ability to translate those discoveries as well as to make new discoveries within human investigations has been a challenge and has been often characterized asthe bottleneck of clinical research. Added to this context has been the dramatic changes to healthcare organizational environments, constraints on delivery, efficiency, and reimbursements to include major structural changes to the investment in healthcare research, both federally, and industrially. Lastly, as a result of dramatic systemic changes in healthcare funding structure, the impact on higher educational graduates' careers, specifically doctoral graduates, has been quite profound. Within that changing dynamic landscape, we hypothesize that the fundamental bottlenecks associated with clinical translational research can be dramatically loosened with the training of engineers intimately familiar with human treatment and trained in the inception of novel technology-based platforms. We further hypothesize that continued scientific discoveries within the human environment as well as novel treatment approaches are highly dependent on these technology-based platforms. The purpose of this training programis to create a new cadre of researchers capable of creating, developing, implementing, clinically evaluating, and translatingmethods, devices, algorithms, and systems designed with a clear focus at one particular application of medicine, namely, to facilitate surgical/interventional processes and their outcomes.Thematically, our trainees and training program will have a central focus –innovative platform technologies for treatment and discovery. While this training program addresses pressingproblemsin biomedical research, namely the translation and facilitation of human investigative systems, the program also speakstoimprovinghigher education career trajectories by providing a novel professional development atmosphere. Briefly described, the training program is a year 2, 3 program that centers on a novel dual-course clinical immersion sequence(a first course that isa context heavy experience with physicians introducing their specialty and clinical realities, and a second course that isan intensively immersive environment withstudentsembedded within the clinical team).In both courses, students are required to engage in expository writing associated with disease and therapeutic analysis, provocative question solutions, clinical outcome analysis and reviews, and mock grant applications. This framework supports a unique educational paradigm brought to engineering education. Apart from this sequence, training continues with addition-course work among areas associated with surgical/interventional guidance and delivery, interventional imaging, medical image processing and analysis, robotics and medical device design, modeling & simulation,interventional therapeutics, and new to this cycle, interventional and surgical data science.This all takes place in one of the most strategically collocated environments for engineering, surgery, and intervention in the world.This is a Training Program for Innovative Engineering Research in Surgery and Intervention.

Registrants

Abbie Weeks
Adrian Florea
Alan Bentley
Alexander Langerman
Alice Ding
Allison Whitten
Andrew Janson
Andrew Orekhov
Andrew McNeil
Anirban Sengupta
Baxter Rogers
Benoit Dawant
Bill Rodriguez
Bohan Jiang
Bowen Xiang
Brett Byram
Cailey Kerley
Carlisle DeJulius
Cathy Cui
Catie Chang
Christian Navarro
Christopher Khan
Claire Landewee
Colette Abah
Colin Hansen
Dann Martin
David Pickens
Dario Englot
Dewei Hu
Diana Carver
Dominick Ropella
Elan Ahronovich
Emelina Vienneau
Emily Matijevich
Eric Tkaczyk
Eric Tang
Erin Bratu
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Giju Thomas
Giuseppe Del Giudice
Graham Johnson
Han Liu
Hannah Mason
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Hernán González
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Jack Noble
Jaime Tierney
James Ferguson
Jared Weis
Jianing Wang
Jim Stefansic
Joe Malone
Jon Heiselman
Jose Rico Jimenez
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Kenny Tao
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Kristy Walsh
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Lucas Sainburg
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Margaret Rox
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Michael MIga
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Mikail Rubinov
Morgan Ringel
Nhung Hoang
Nial Redha
Philip Swaney
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Robert Webster
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Xiaoqi Liu
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Yuankai Huo
Yubo Fan
Yuzhe Lu
Zheyu Zhu
Zijun Zhao
Ziteng Liu

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