6th Annual

Surgery, Intervention, and Engineering Symposium

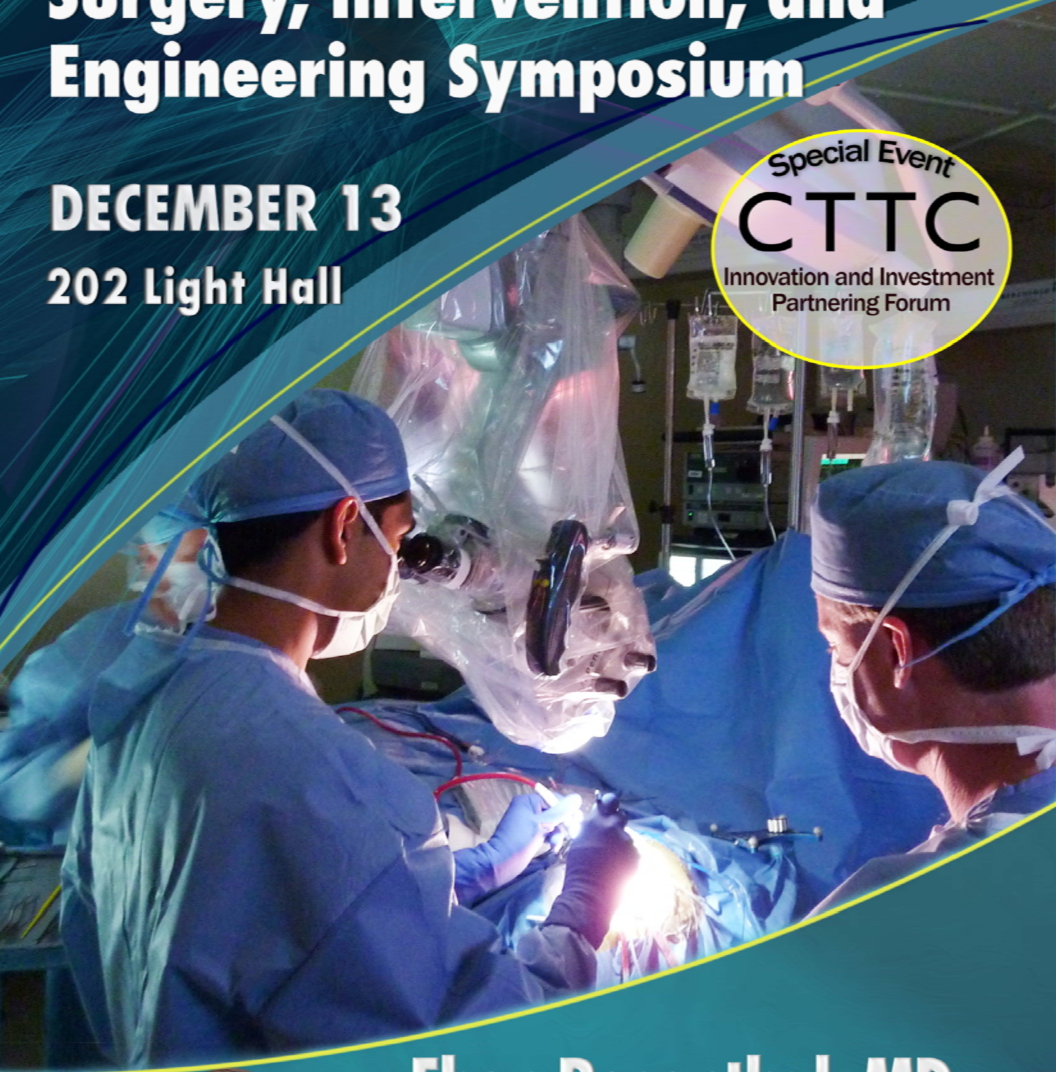
DECEMBER 13

202 Light Hall

Special Event

CTTC

Innovation and Investment Partnering Forum



Eben Rosenthal, MD

John and Ann Doerr Medical Director of the Stanford Cancer Center,
Professor of Otolaryngology-Head and Neck Surgery, and Radiology

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VISE VANDERBILT INSTITUTE FOR SURGERY AND ENGINEERING

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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 outcome. 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 symbiotically 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 seminar 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.

VANDERBILT

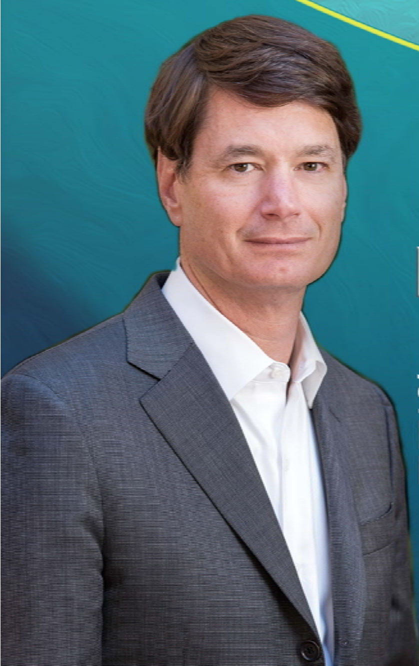
CTTC

Center for Technology Transfer & Commercialization

The Vanderbilt Center for Technology Transfer and Commercialization, in conjunction with VISE, is hosting a commercialization and investment event immediately prior to the annual VISE Symposium. The event features a panel discussion by nationally recognized experts in the field of advanced surgical devices and systems, and explores how these experts evaluate, conduct due diligence and invest in such technologies. Following the discussion, the panelists will lead an interactive small-group exercise centered on valuing several next-gen surgical technologies for their investment potential. Participants then engage with VISE researchers as they provide live demonstrations of their surgical device innovations.

"Leveraging Light in the OR: Finding an Optical Contrast Agent"

Presented by



Eben Rosenthal, MD

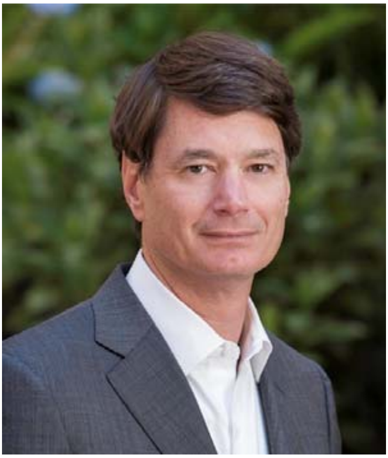
John and Ann Doerr Medical Director of the Stanford Cancer Center,
Professor of Otolaryngology-Head and Neck Surgery, and Radiology

Keynote Abstract

"Leveraging Light in the OR: Finding an Optical Contrast Agent"

Eben Rosenthal, M.D.
John and Ann Doerr Medical Director, Stanford Cancer Center
Professor of Otolaryngology-Head and Neck Surgery, and Radiology

Over the past two decades, synergistic innovations in imaging technology have resulted in a revolution in which a range of biomedical applications are now benefiting from fluorescence imaging. Specifically, advances in fluorophore chemistry and imaging hardware, and the identification of targetable biomarkers have now positioned intraoperative fluorescence as a highly specific real-time detection modality for surgeons in oncology. In particular, the deeper tissue penetration and limited autofluorescence of near-infrared (NIR) fluorescence imaging improves the translational potential of this modality over visible-light fluorescence imaging. Rapid developments in fluorophores with improved characteristics, detection instrumentation, and targeting strategies led to the clinical testing in the early 2010s of the first targeted NIR fluorophores for intraoperative cancer detection. The foundations for the advances that underline this technology continue to be nurtured by the multidisciplinary collaboration of chemists, biologists, engineers, and clinicians. In this Review, we highlight the latest developments in NIR fluorophores, cancer-targeting strategies, and detection instrumentation for intraoperative cancer detection, and consider the unique challenges associated with their effective application in clinical settings.



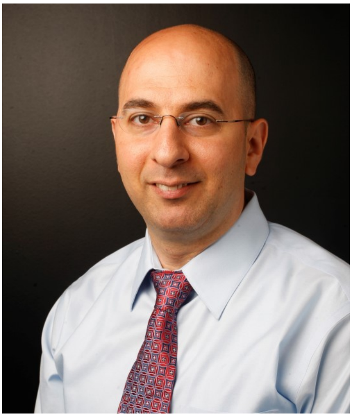
Eben Rosenthal, M.D.
Symposium Keynote Speaker

Eben Rosenthal is a surgeon-scientist who serves as the John and Ann Doerr Medical Director of the Stanford Cancer Center. He works collaboratively with the Stanford Cancer Institute and Stanford Health Care leaders to set the strategy for the clinical delivery of cancer care across Stanford Medicine and growing cancer networks. He is a professor of Otolaryngology and Radiology (courtesy) and a member of Molecular Imaging Program at Stanford (MIPS). He continues to be clinically active as an oncologic and microvascular reconstructive surgeon.

Dr. Rosenthal has conducted multiple early phase clinical trials for diagnostic and therapeutic agents for the treatment of solid tumors. He has been NIH funded for over a decade in targeted, translational research. He is part of a multidisciplinary team of clinical and basic scientists that have successfully performed preclinical studies, nonhuman primate IND-enabling studies, successfully performed the first in human clinical trials using fluorescently labeled antibodies as a cancer specific contrast agent for use in the operating room. Ongoing clinical trials include brain, pancreas, skin and head and neck tumors.

Participating Laboratories

Advanced Robotics and Mechanism Applications (ARMA)



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

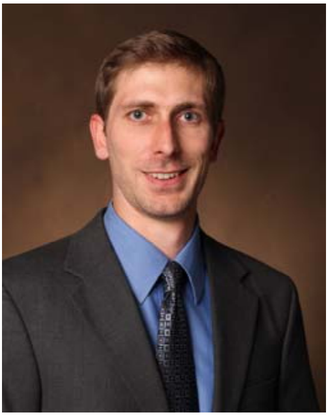
ARMA is focused on advanced robotics research including robotics, mechanism design, control, and telemanipulation for medical applications. We focus on enabling technologies that necessitate novel design solutions that require contributions in design modeling and control. ARMA has lead the way in advancing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

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

Lab Youtube Channel: http://www.youtube.com/user/ARMAVU/videos

Contact: nabil.simaan@vanderbilt.edu, 615-343-0470

Biomedical Elasticity and Acoustic Measurement (BEAM) Laboratory

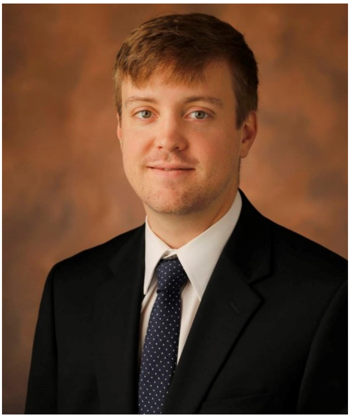


PI: Brett Byram, Ph.D.
Assistant Professor of Biomedical Engineering, Vanderbilt University

The biomedical elasticity and acoustic measurement (BEAM) lab is interested in pursuing ultrasonic solutions to clinical problems. Brett Byram and the BEAM lab's members have experience with most aspects of systems level ultrasound research, but our current efforts focus on advanced pulse sequencing and algorithm development for motion estimation and beamforming. 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 developing novel ultrasound transducers to enhance guidance for percutaneous procedures.

Contact: michael.i.miga@Vanderbilt.Edu

Biomedical Image Analysis for Image Guided Interventions (BAGL) Laboratory



PI: Prof. Jack H. Noble, Ph.D.
Assistant Professor of Electrical Engineering & 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 informatics to optimize hearing outcomes.

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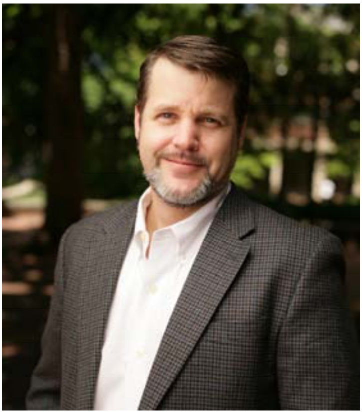
Biomedical Modeling Laboratory (BML)



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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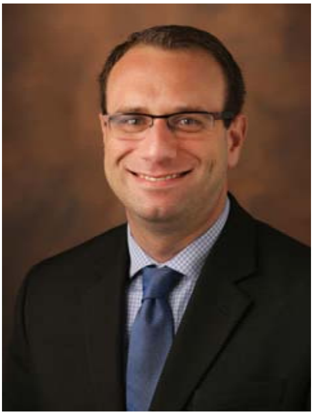
Brain Imaging and Electrophysiology Network (BIEN)



PI: Dario J. Englot, M.D., Ph.D.
Assistant Professor of Neurological Surgery,
Vanderbilt University

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

Contact: dario.englot@Vanderbilt.edu

Computational Flow Physics and Engineering (CFPE) Laboratory

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

High-fidelity modeling and simulations of fluid flows provide critical understanding of many complex systems and have become an increasingly important tool in engineering for design and innovations. In biomedical areas, computational fluid dynamics and computational fluid-tissue interaction will lead to novel tools for improved diagnosis, therapy, and surgery planning. In our lab, we develop and utilize computational methods to study biological and biomedical flows (either gas or liquid), especially those involving fluid-structure interactions. The current thrusts focus on aerodynamics of animal swimming, vocal fold modeling in human phonation, and hemodynamics of heart valves and blood vessels.

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CAOS - Computer Assisted Otologic Surgery Laboratory

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

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

Contact: robert.labadie@vanderbilt.edu

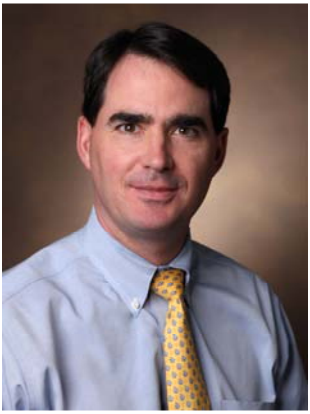
Diagnostic Imaging and Image-Guided Interventions (DIIGI) Laboratory

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

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

Contact: yuankai.tao@vanderbilt.edu

Fissell Laboratory

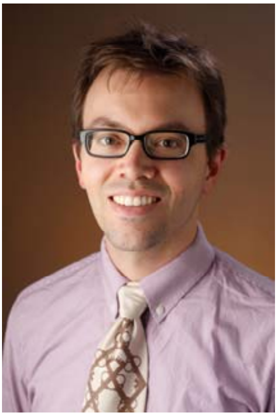


PI: William H. Fissell, M.D.
Associate Professor of Medicine,
Vanderbilt University

Our laboratory applies physical and mathematical tools to address unmet needs in care of patients with kidney disease and kidney failure. Our team developed the first new membrane technology for blood separations in 30 years. This high-efficiency membrane allows us to construct miniaturized, implantable devices for renal care.

Contact: william.fissell@vanderbilt.edu

Grissom Laboratory: MRI-Guided Focused Ultrasound



PI: William Grissom, Ph.D.
Assistant Professor of 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. Our current clinical applications are 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, blood-brain barrier disruption, and sonothrombolysis for treatment acute ischemic stroke.

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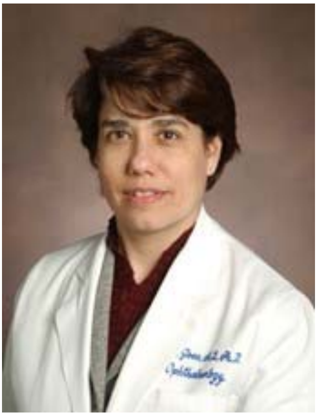
Joos Laboratory- Ophthalmology Research

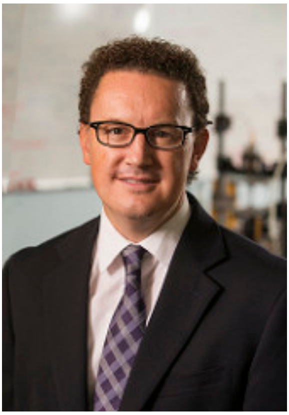


PI: Karen Joos, M.D., Ph.D.,
Joseph and Barbara Ellis Professor of Ophthalmology and Visual Sciences,
Vanderbilt University Medical Center
Biomedical Engineering,
Vanderbilt University

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 and Simaan laboratories have a continuing long-standing collaboration. A new collaboration has developed between the Joos and Tao laboratories.

Contact: karen.joos@vanderbilt.edu

Laboratory for the Design and Control of Energetic Systems

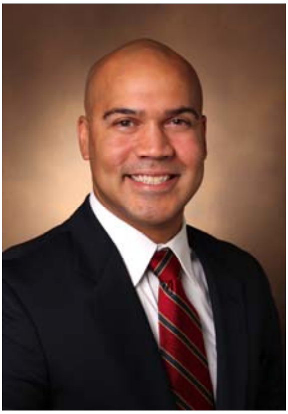


PI: Eric Barth, Ph.D.
Associate Professor of Mechanical Engineering,
Vanderbilt University

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.

Contact: eric.j.barth@vanderbilt.edu

Laryngeal Biology Laboratory

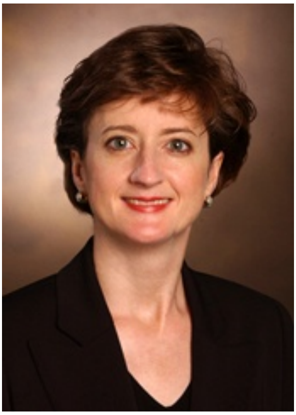


PI: Bernard Rousseau, Ph.D.
Associate Vice Chair for Research, Otolaryngology;
Chancellor Faculty Fellow and Associate Professor of
Otolaryngology, Hearing and Speech Sciences,
and Mechanical Engineering,
Vanderbilt University

There are several significant stresses (e.g. impact, stretching, and shear) that develop within the vocal fold tissues during vibration that differ in magnitude, direction, and distribution. It has been suggested that the high impact stress at the mid-portion of the vocal folds results in increased trauma to this region during phonation. This area has been described as a critical strike zone, or region of maximum impact, where the greatest collision between the two medial surfaces occurs during phonation. The Laryngeal Biology Laboratory under the direction of Bernard Rousseau, Ph.D., and the Computational Flow Physics Laboratory under the direction of Haoxiang Lou, Ph.D., are working towards the development of patient specific high-fidelity computational models to quantify the magnitude and spatial distribution of mechanical stresses during phonation. We are also working on the development of pre-operative surgical planning tools to improve outcomes in the treatment of vocal fold paralysis. This work is performed in collaboration with C. Gaelyn Garrett, M.D., Professor, Vice-Chair, and Medical Director of the Vanderbilt Voice Center and David Francis, M.D., Assistant Professor of Otolaryngology, Vanderbilt Voice Center.

Contact: Bernard.rousseau@vanderbilt.edu

Mawn Laboratory

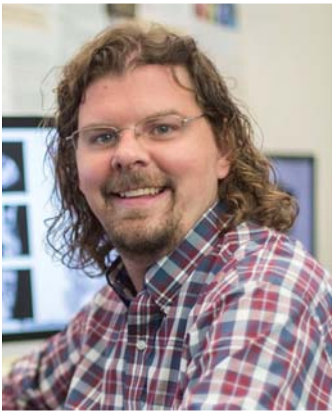


PI: Louise Mawn, MD,
Associate Professor of Ophthalmology,
Vanderbilt University

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

Contact: louise.mawn@vanderbilt.edu

Medical-image Analysis and Statistical Interpretation (MASI) Laboratory

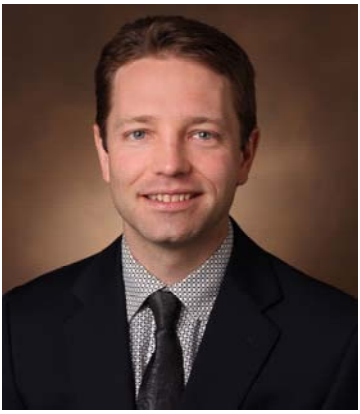


PI: Bennett Landman, Ph.D.
Electrical Engineering, Biomedical Engineering, Computer Science, Radiology and Image Science, Vanderbilt University

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.

Contact: bennett.landman@vanderbilt.edu

Medical Engineering and Discovery (MED) Laboratory



PI: Robert J. Webster III, Ph.D.
Mechanical Engineering, Electrical Engineering, Otolaryngology, Neurological Surgery, and Urologic Surgery,
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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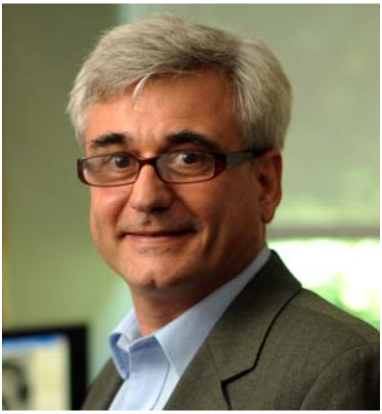
Medical Image Processing (MIP) Laboratory



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

The medical image processing (MIP) laboratory of the Electrical 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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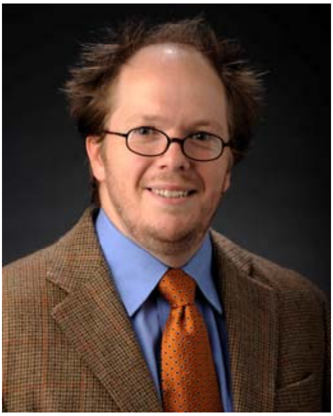
Merryman Mechanobiology Laboratory (MML)



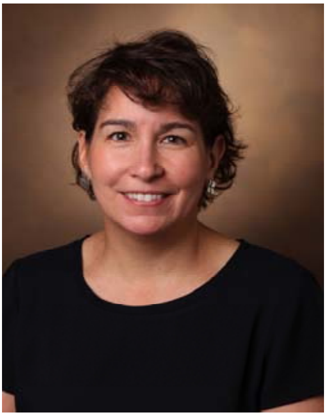
PI: W. David Merryman,
Associate Professor of Biomedical Engineering, Pharmacology, Medicine and Pediatrics,
Vanderbilt University

The Merryman Mechanobiology Laboratory (MML) is devoted to cardiovascular and pulmonary mechanobiology research with emphasis on cellular response and functional changes (phenotypic and biosynthetic) to altered mechanical stimuli and various biochemical agents. Areas of expertise include: cellular and soft tissue biomechanics, in-vitro bioreactor environments for tissue engineering, and mechanistic studies of cytokine activity and mechanical stimuli. Primary laboratory goals are to elucidate the mechanisms leading to multiple cardiovascular diseases and develop non-surgical strategies to prevent and treat them, with particular focus on heart valves.

The Merryman MechanoBiology Laboratory has four areas of research focus: Mechanobiology – the study of how mechanical forces or deformations alter cellular signaling, phenotype, and biosynthetic function; GPCR targeted drug strategies, mechanobiology and we have begun exploring potential therapeutic strategies to prevent heart valve disease via serotonergic receptors; General area of percutaneous interventions for heart valve disease where we are currently developing a novel catheter for percutaneous treatment of myxomatous mitral valve disease by altering the intrinsic biomechanical compliance of the mitral valve leaflets; and Mechanically tunable biomaterial for cardiovascular tissue engineering. WE are developing unable biomaterials that can be dynamically modified via multiple mechanisms to facilitate endothelial-to-mesenchymal transformation.

Contact: david.merryman@vanderbilt.edu

Morgan Laboratory



PI: Vicky Morgan, Ph.D.
Associate Professor of
Radiology & Biomedical Engineering,
Institute of Imaging 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 use functional MRI to localize eloquent cortex in the brain to aid in surgical planning to minimize functional and cognitive deficits post-surgery. In addition, our lab focuses on mapping functional and structural brain networks in epilepsy to elucidate the effects of seizures and predict post-surgical seizure and cognitive outcomes. 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 collaborations with the Englot Lab, the Medical Imaging Processing Laboratory (Dawant) and researchers throughout the Vanderbilt Institute of Imaging Science (VUIIS).

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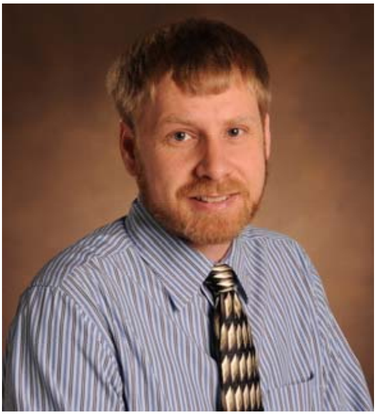
Orthopaedic Biomechanics Laboratory

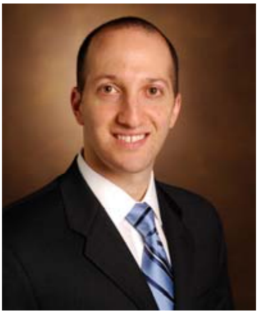


PI: Jeffry Nyman, PhD
Assistant Professor, Surgery – Orthopaedics, Vanderbilt University

The ultimate goal of the research in our lab is to lower the number of bone fractures associated with osteoporosis, diabetes, cancer, genetic diseases, and aging. Towards that end, we investigate ways to improve the clinical assessment of fracture risk and to identify regulators of bone toughness (lack of brittleness). Specifically, there are projects in the lab i) to determine whether matrix-bound water and pore water, as determined by 1H Nuclear Magnetic Resonance (or MRI), can explain age- and diabetes-related decreases in bone's resistance to fracture, ii) to identify the determinants of matrix-bound water, and iii) to elucidate the mechanisms by which tissue confers resistance to crack growth. In addition, we are developing Raman Spectroscopy techniques to assess tissue organization and composition as a potential biomarker of bone fragility. This technology could potentially be transferred to a hand-held probe for intra-operative use during orthopaedic surgeries, thereby providing real-time information on the quality of bone tissue.

Contact: jeffry.s.nyman@vanderbilt.edu

Science and Technology for Robotics in Medicine (STORM) Laboratory



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

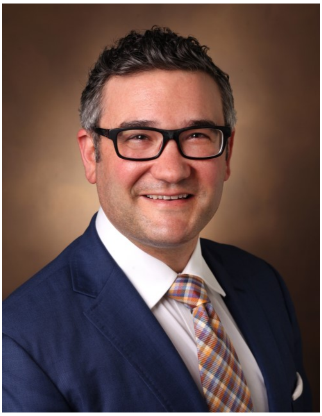
At the STORM Lab we strive to improve the quality of life for people undergoing endoscopy and abdominal surgery by creating miniature and non-invasive capsule robots.

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.

Contact: keith.obstein@vanderbilt.edu or p.valdastri@leeds.ac.uk

Surgical Analytics Laboratory



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

The Surgical Analytics Lab focuses on novel methods of real-time surgical data collection and analysis. We are presently developing a novel, wearable video platform for open surgical procedures as well as a dry lab model that replicates surgeon body motion for rapid testing of wearable devices.

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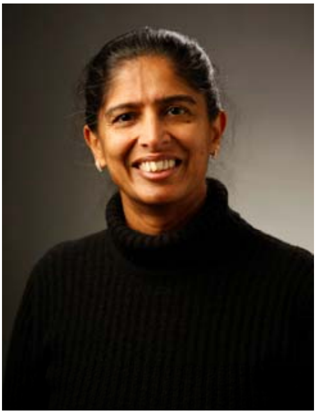
Vanderbilt Biophotonics Center



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: Cancer 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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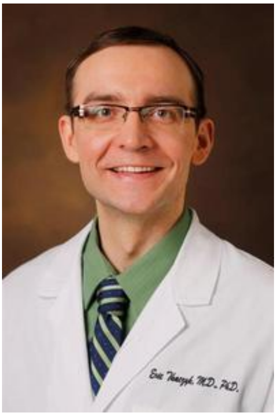
Vanderbilt Cutaneous Imaging Clinic



PI: Eric Tkaczyk, M.D., Ph.D.,
Assistant Professor of Medicine (Dermatology)
Assistant Professor of Biomedical Engineering

The Vanderbilt Cutaneous Imaging Clinic (VCIC) is a multidisciplinary team of clinicians and engineers whose mission is to seamlessly integrate patient care, clinical investigation, and fundamental technology research with application in dermatology, oncology, hematology, and other specialties.

Contact: eric.tkaczyk@vanderbilt.edu

Submitted Abstracts

1. Retinal vascular biometry in wild-type and a retinal vascular leakage model in Zebrafish using OCT angiography

Bozic, Ivan[1]; Spitz, Kathleen[1]; Pollock, Lana M.[2]; Anand-Apte, Bela[2]; Tao, Yuankai[1]

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[2] Cole Eye Institute, Cleveland Clinic, Cleveland, OH, United States.

In vivo assays enable longitudinal imaging of pathogenesis and response to novel therapeutics. Optical coherence tomography (OCT) and OCT angiography (OCT-A) allow for noninvasive visualization of structural and functional changes in the retina, respectively. In vivo zebrafish, retinal datasets were imaged using a custom-built spectral domain OCT system (855±45 nm and 125 kHz line-rate) under an IRB-approved protocol. OCT-A volumes were acquired with a 5 repeated B-scans at each position and vascular maps were calculated using wOMAG in post-processing. Animals were anesthetized using a 0.14% Tricaine solution and imaged air. A subset of study animals was treated with 10 μM diethylaminobenzaldehyde (DEAB) and 0.04% dimethyl sulfoxide in 1 L of water for 26 h to induce vascular leakage. Wild-type (WT, nWT=10) and vascular leakage model (nDEAB=10) zebrafish were imaged longitudinally in both eyes at multiple time-points: tWT=10 and tDEAB=6 (pre-treatment and 1, 3, 6, 8, 10 days posttreatment). Custom-developed segmentation algorithms were used to extract biometric features from OCT-A vessel maps including vessel segment length, curvature, and branch angle. OCT-A vascular maps showed distinct biometric features that may be used to uniquely identify each animal. WT animals showed no significant changes in vascular biometry during longitudinal time-points. We observed retinal vascular occlusion followed by reperfusion in DEAB treated animals. OCT-A enabled noninvasive visualization of retinal vascular occlusion and reperfusion. These preliminary results motivate potential applications of OCT-A as a tool for studying pathogenesis and therapeutic screening in zebrafish models of vascular disease.

2. Image-guided Cochlear Implant Procedures

Ahmet Cakir [1], Raul Gonzalez [1], Dongqing Zhang [1], Yiyuan Zhao[1], Srijata Chakravorti[1], Rene H. Gifford [2], Robert L. Labadie [3], Jack H. Noble [1], Benoit M. Dawant [1]

[1]Vanderbilt University, Department of Electrical Engineering and Computer Science, Nashville TN USA.
[2] Vanderbilt University Medical Center, Department of Otolaryngology-Head & Neck Surgery, Nashville TN USA
[3] Vanderbilt University Medical Center, Department of Hearing and Speech Sciences, Nashville TN USA

To date, over 200,000 hearing impaired individuals in the US have received cochlear implants (CIs) in which an electrode array designed to substitute natural nerve stimulation by electrical stimulation is threaded into the cochlea. While speech understanding outcomes are typically good among CI users, very few users report experiencing the fidelity of natural hearing. Additionally, a significant minority do poorly. We have developed a series of image processing algorithms that operate on clinical CT images and permit for the first time the precise localization of both the inner ear anatomy and individual CI electrodes. This will fundamentally change the preoperative planning, intraoperative placement, and the postoperative management of CI recipients. Preoperatively, quantitative information about temporal bone and cochlear anatomy can assist the surgical team in selecting the most adequate CI model for an individual recipient. Intraoperatively, knowledge of cochlear shape can guide the insertion process. Postoperatively, knowledge of the position of contacts with respect to the nerve endings they stimulate permits the development of custom electrode programing strategies that are informed by objective imaging data. We have developed such an Image-Guided Cochlear Implant Programming (IGCIP) strategy and we have demonstrated that it can substantially and sometimes dramatically improve hearing in long term CI users without requiring an additional surgical procedure. The success rate of our approach is also remarkable with the new setting being preferred over 70% of the time by the more than 200 long term CI users including children who have participated in our ongoing study.

3. A model-based approach to cochlear implant programming

Ahmet Cakir (1), Robert T. Dwyer (2), Rene H. Gifford (2), Robert F. Labadie (3), Benoit M. Dawant (1), Jack H. Noble (1)

(1) Department of Electrical Engineering and Computer Science, Vanderbilt University
(2) Department of Hearing and Speech Sciences, Vanderbilt University Medical Center
(3) Department of Otolaryngology-Head & Neck Surgery, Vanderbilt University Medical Center

Cochlear implants (CIs) are considered standard treatment for patients who experience sensorineural hearing loss. Although these devices have been remarkably successful at restoring hearing, it is rare to achieve natural fidelity, and many patients experience poor outcomes. Our group has developed the first image-guided CI programming (IGCIP) technique where the positions of the electrodes are found in CT images and used to estimate neural activation patterns, which is unique information that audiologists can use to define patient-specific processor settings. In our current system, neural activation is estimated using only the distance from each electrode to the neural sites. Even though the clinical studies have shown that our method leads to better hearing outcomes, it is possible that the method could be improved with a better estimate of the electrodes' neural activation patterns. In this work, we are evaluating a model-based method we propose to estimate neural activation patterns. This modeling approach involves 2 steps: (1) A patient-customized electro-anatomical model is used to estimate the distribution of voltage in neural tissue created by the electrode array. (2) Auditory nerve fiber models are semi-automatically created and activation is simulated using the NEURON package. This approach was used to simulate a physiological measurement that is available via patient's CI called electrically evoked compound action potentials (eCAPs) for 6 patients. The simulation results were compared to the acquired patient data to show how accurately the auditory neural responses could be simulated. In future work we will use these models to generate model-based IGCIP programs.

4. Ultra-low-cost Endoscopy for Gastroesophageal Cancer Screening in Low-Income Countries

Federico Campisano (1), Simone Calo' (2), Joseph Norton (2), Doug L. Morgan (3), Keith L. Obstein (1,3), Pietro Valdastri (1,2)

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(2) STORM Lab UK, School of Electronic and Electrical Engineering, of Leeds, Leeds, United Kingdom
(3) Medicine - Gastroenterology, Vanderbilt University Medical Center, Nashville, TN, United States

Globally, gastric and esophageal cancer accounts for 10% of incident cases, with nearly 70% of cases occurring in Low-Income Countries (LIC). Although screening programs have been shown to be effective in reducing the mortality rate through early detection, these programs are resource intensive and rarely seen in LIC. The HydroJet seeks to address these issues through a low-cost (2-5 USD per procedure) platform for primary screening of the upper gastrointestinal tract. The current platform design, along with implications for the medical efficacy and controllability of the device, are explored in this work. The jet actuators used to control the capsule are experimentally modeled and characterized in terms of both range and resolution of actuation force. The capsule workspace is also investigated using single and multiple jet actuation, and demonstrated maneuverability within a quasi-hemispherical workspace. A comparative trial between the HydroJet and a traditional gastroscope is conducted demonstrating adequate maneuverability of the HydroJet for screening procedures.

5. Compensation of lung deflation during Video Assisted Thoracoscopic Sugery

Pablo Alvarez [1,3], Simon Rouzé [1,2], Fanny Morin [3], Yohan Payan [3], Jean-Louis Dillenseger [1], Matthieu Chabanas [3]

[1] INSERM U1099; University of Rennes 1, LTSI; Rennes, France
[2] Univ. Hospital, Department of Thoracic, Cardiac and Vascular Surgery; Rennes, France
[3] Univ. Grenoble Alpes, CNRS, Grenoble-INP, TIMC-IMAG; Grenoble, France

An emerging treatment of early-stage lung cancer is Video Assisted Thoracoscopic Surgery (VATS). However this minimally invasive procedure requires the creation of a pneumothorax, an air pocket between the lung and the chest wall, to make room for the manipulation of the organ. This results in a collapse of the lung in a deflated state, which invalidates any measurement formerly calculated on preoperative CT. While intraoperative Cone-Beam CT (CBCT) could be used, poor image quality and constrast make the localization of small or subsolid nodules challenging. A first source of lung deformation is due to the change of positioning of the patient, from supine during CT acquisition to lateral decubitus in the operating room. This is corrected by non-rigid registration of the chest cavity using Mutual-Information between CT and CBCT. To compensate for the pneumothorax, a biomechanical model of the lung is then built, with a linear elastic constitutive law solved with a corotational approach. Lagrangian Multipliers constraints are used so that the model's lateral surface fits the deflated lung border segmented in the intraoperative images. A preliminary evaluation study was performed on a single retrospective case of Low-Dose CT acquired after an accidental post-biopsy pneumothorax. The TRE is reduced from 21.5 mm to 9 mm, which is a promising results toward intraoperative assistance in nodule localization.

6. A Structural Connectivity Approach to Validate a Model-based Technique for the Segmentation of the Pulvinar Complex

Srijata Chakravorti (Department of Electrical Engineering and Computer Science, Vanderbilt University), **Victoria L. Morgan** (Department of Radiology and Radiological Sciences, Vanderbilt University Institute of Imaging Science, Vanderbilt University Medical Center), **Paula Trujillo-Diaz** (Department of Neurology, Vanderbilt University Medical Center), **Raul Wirz-Gonzalez** (Department of Electrical Engineering and Computer Science, Vanderbilt University), **Benoit M. Dawant** (Department of Electrical Engineering and Computer Science, Vanderbilt University)

The pulvinar of the thalamus is a higher-order thalamic nucleus that is responsible for gating information flow to the cortical regions of the brain. It is involved in several cortico-thalamocortical relay circuits and is known to be affected in a number of neurological disorders. Segmenting the pulvinar in clinically acquired images is important to support studies exploring its role in brain function. In recent years, we have proposed an active shape model method to segment multiple thalamic nuclei, including the pulvinar. The model was created by manual delineation of high resolution 7T images and the process was guided by the Morel stereotactic atlas. However, this model is based on a small library of healthy subjects, and it is important to validate the reliability of the segmentation method on a larger population of clinically acquired images. The pulvinar is known to have particularly strong white matter connections to the hippocampus, which allows us to identify the pulvinar from thalamic regions of high hippocampal structural connectivity. In this study, we obtained T1-weighted and diffusion MR data from 43 healthy volunteers using a clinical 3T MRI scanner. We applied the segmentation method to the T1-weighted images to obtain the intrathalamic nuclei, and we calculated the connectivity maps between the hippocampus and thalamus using the diffusion images. Our results show that the shape model segmentation consistently localizes the pulvinar in the region with the highest hippocampal connectivity. The proposed method can be extended to other nuclei to further validate our segmentation method.

7. Computational Model of Microwave Ablation with Inverse Approach to Reconstructing Patient-Specific Tissue Properties

Jarrod A. Collins[1], Jon S. Heiselman[1], Logan W. Clements[1], Jared A. Weis[2], and Michael I. Miga[1].

[1] Department of Biomedical Engineering, Vanderbilt University
[2] Department of Biomedical Engineering, Wake Forest Baptist Health

Clinically accurate modelling of microwave ablation procedures can provide powerful planning and navigational information to physicians. However, patient-specific tissue properties are generally unavailable in a clinical setting. Therefore, a need exists for modeling frameworks that can account for patient-specific variations in organ tissue properties. We propose a novel inverse approach to patient-specific computational modelling of microwave ablation that reconstructs underlying tissue properties from a series of temperature recordings collected during treatment. The modeling framework is based on iteratively updating a set of tissue and environmental properties to minimize the difference between the model-predicted and observed temperature data. We validate the model predictions of ablation extent and transient thermal profiles with experimental measurements from a series of agar-albumin phantom procedures. Additionally, we compare the model-predicted ablation margins and measurements of true volumetric overlap to corrected vendor-specified predictions. Our model yielded thermal profiles in close agreement with experimental measurements (average root-mean-square error of 2.23 ± 0.97 K), which we accredit to the reconstruction of tissue properties within the model. The model-predicted ablation zones showed strong volumetric overlap with the observed ablation zones (average dice similarity coefficient of 84.2 ± 4.9 %). Furthermore, these results demonstrate an average improvement of 11.8% in volumetric overlap when comparing the presented model to the corrected vendor-specified predictions. In summary, these results have demonstrated close correspondence between observed and model-predicted temperatures and ablation volumes in a series of phantom experiments and show substantial potential for being able to account for varying tissue properties that can present clinically.

8. ADMIRE applied to fundamental and harmonic data acquired from a modern clinical platform

Kazuyuki Dei, Adam Luchies, and Brett Byram BEAM Lab, '

Department of Biomedical Engineering, Vanderbilt University

Motivation/Objective: Previous studies demonstrated that our aperture domain model image reconstruction (ADMIRE) beamforming algorithm mitigates some common ultrasound imaging artifacts. Many of our previous efforts have occurred on research oriented platforms that necessitated a limited field of view when acquiring imaging channel data. To address this limitation, we developed a channel data acquisition scheme using a modern clinical system (Siemens ACUSON SC2000) that enables a substantially larger field of view. We also implemented channel data acquisition in conjunction with a pulse inversion sequence to enable second harmonic imaging. The objective of this study is to demonstrate the feasibility of acquiring channel data from a modern clinical platform with and without pulse inversion in a way conductive to the application of the ADMIRE algorithm. **Contribution/Methods**: Using the developed channel data acquisition tool, we acquired single channel data from tissue-mimicking phantom for fundamental and harmonic imaging. We applied the ADMIRE algorithm to the data and compared the resulting images of fundamental B-mode and harmonic B-mode before and after ADMIRE. We also captured in vivo channel data from a human subject's abdomen and liver. We then quantified image quality using measured contrast and contrast-to-noise ratio (CNR). **Results:** When evaluating in vivo images, ADMIRE improves contrast by +10.3 dB relative to fundamental B-mode, and boosts contrast by +11.0 dB with harmonic B-mode image. Based on these findings, ADMIRE improves in vivo fundamental and harmonic B-mode image quality. Finally, we successfully acquired channel data using our modified ultrasound system with a large field of view.

9. Continuum Robot with multiscale motion manipulation and image -base biopsy.

Giuseppe Del Giudice, **Long Wang** and **Nabil Simaan** are at Advanced Robotics and Mechanism Applications (ARMA) Laboratory, Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37240, USA.

Karen Joos and **Jin-Hui Shen** are at Department of Ophthalmology, Vanderbilt Medical Center, Nashville, TN 37240, USA

Existing robots for multi-scale motion (MSM) are unsuitable for micro-surgery in deep surgical sites where miniaturization and traversal of often tortuous anatomical passageways is required. Also, new emerging surgical paradigms for natural orifice surgery and image-based diagnosis and guidance at the micro-scale level promise to provide accurate verification of tumor resection margins. To overcome the limitations of current robot architectures, and to enable image-based biopsy and micro-surgery in confined spaces, we present a new concept of continuum robots with equilibrium modulation (CREM). CREM robots are a modification of multi-backbone continuum robots that achieve micro-motion by using indirect actuation through modulation of their static equilibrium by change of the distribution of their cross-sectional flexural rigidity. As a first step towards modeling the micro-scale kinematics of these robots, solutions for micro-motion tracking are presented and verified to achieve tracking accuracies of better than 2 μ m. Preliminary evaluation of the micro-motion capabilities of a first prototype demonstrates motion resolutions at 1 μ m level and hysteresis of less than 10 μ m - despite the use of inexpensive actuators with significant backlash. A demonstration of a first effort at integrating such a robot with a custom-made optical coherence tomography (OCT) probe is presented.

10. Needle-Size Robots for Endoscopic Brain Surgery

Margaret F. Rox[1], Tayfun E. Ertop[1], Richard J. Hendrick[1], R.P. Naftel[2], and Robert J. Webster III[1]

[1]Department of Mechanical Engineering, Vanderbilt University, Nashville, TN, USA
[2]Department of Neurosurgery, Vanderbilt University Medical Center, Nashville, TN, USA

Due to various medical conditions, abnormalities such as tumors and lesions (which require surgical intervention) can occur deep inside brain tissue. Being so far inside the brain, operating and even reaching the surgical site are challenging tasks. The standard for neurosurgery is the open craniotomy, which is highly invasive, but some pioneering surgeons have started using neuroendoscopy for procedures deep inside the brain. This minimally invasive method involves drilling a hole in the skull and placing an endoscope through brain tissue up to the surgical site. However, in order to have mobility at the tip surgeons are required to manually tilt the conventional rigid endoscopes. Depending on severity of the tilt, this puts pressure on the delicate brain tissue, causing damage to surrounding cells. This study explains a new robotic system with two dexterous concentric tube manipulators deployed through a rigid endoscopic channel to provide mobility at the surgical site. Experiments were performed to compare the performance of the robotic system and manual endoscopic operation using a phantom model for colloid cysts removal scenario. Maximum tilt angles of the endoscope within the brain measured 1.16o with the robotic system and 17.09o with manual operation. Additionally, the robotic system enabled a single surgeon to operate bimanually whereas the conventional method only allows one tool and customarily requires two surgeons operating. The proposed dexterous robotic system has potential benefits over conventional manual endoscopic operation for neuroendoscopy in terms of safety and ease of use by reducing tilting motion and providing bimanual manipulation.

11. Image Guidance for the da Vinci Robot

James M. Ferguson [1], Leon Y. Cai [2], Alexander Reed [4], Michael Siebold [4], Smita De [3], S. Duke Herrell III [1,3], and Robert J. Webster III [1,3]

[1] Vanderbilt University, Department for Mechanical Engineering
[2] Vanderbilt University, School of Medicine
[3] Vanderbilt Medical Center, Department of Urologic Surgery
[4]Vanderbilt University, Department of Electrical Engineering and Computer Science

Our goal is to facilitate wider adoption of partial nephrectomy kidney surgery through image guidance, which can enable a surgeon to see subsurface anatomy and instrument locations in real time with the da Vinci robotic surgical system. There are compelling lifelong health benefits of partial nephrectomy, but radical nephrectomy remains the standard of care for most kidney cancer because of the difficulty in localizing targets or critical anatomical features intraoperatively. Image guidance may increase the surgeon's confidence and ability to maintain negative margins in the robotic partial nephrectomy procedure. During the procedure, periodic re-registration of physical space to image space is necessary because the kidney is not always completely stationary. Here we explore, test, and compare various re-registration approaches for the da Vinci robot that would enable updates to the display of segmented preoperative images within its console. We first consider using point clouds acquired from tracing a kidney with the robot's tool tip and next point clouds acquired from the robot's stereo endoscope. Finally we consider a hybrid, 'virtual fiducial' method combining these two techniques. We tested the accuracy and repeatability of each of these methods by localizing targets (with each of the robot's arms) after the execution of these re-registrations and comparing their locations to a ground truth. Intraoperative calibration processes will also be necessary for image guidance with the da Vinci system. Previously, these processes required the use of additional optical tracking hardware. Here, we present and assess methods using only the stereo endoscope on the robot.

12. A Disposable Continuum Endoscope Using Piston-driven Parallel Bellow Actuator

Nicolo Garbin [1], Long Wang [1], James H. Chandler [2], Keith L. Obstein [3], Nabil Simaan [1], Pietro Valdastri [2]

[1] Department of Mechanical Engineering, Vanderbilt University
[2] Department of Electronic and Electrical Engineering, University of Leeds
[3] Department of Gastroenterology, Hepatology, Nutrition, Vanderbilt University Medical Center

This work presents a novel low cost disposable continuum endoscope based on a piston-driven parallel bellow actuator design. The parallel bellow actuator achieves motion by being pressurized via displacement-controlled pistons. The displacements are generated by rack-and-pinion mechanisms using inexpensive stepper motors. The design concept provides a potential alternative solution to upper gastrointestinal (UGI) diagnosis. The modularity and the use of inexpensive components allow for low fabrication costs and disposability. The use of robotic assistance could facilitate the development of an easier interface for the gastroenterologists, avoiding the nonintuitive manipulation mapping of the traditional UGI endoscopes. We adapt existing kinematic solutions of multi-backbone continuum robots to model continuum parallel bellow actuators. An actuation compensation strategy is presented and validated to address the pneumatic compressibility through the transmission lines. The design concept was prototyped and tested with a custom control platform. The experimental validation shows that the actuation compensation was demonstrated to significantly improve orientation control of the endoscope end-effector. This paper shows the feasibility of the proposed design and lays the foundation toward clinical scenarios.

13. Disturbances of Brainstem Functional Connectivity in Temporal Lobe Epilepsy Patients May Recover after Successful Epilepsy Surgery

Hernan F.J. Gonzalez, M.S. (Biomedical Engineering, Vanderbilt University Institute of Imaging Science) Peter E. Konrad MD/PhD (Biomedical Engineering, Neurological Surgery) Hong Yu MD (Neurological Surgery) Michael I Miga PhD (Biomedical Engineering, Neurological Surgery, Radiology and Radiological Sciences) Victoria L Morgan PhD (Biomedical Engineering, Radiology and Radiological Sciences, Vanderbilt University Institute of Imaging Science) Dario J Englot MD/PhD (Neurological Surgery, Biomedical Engineering, Vanderbilt Institute of Imaging Science)

Introduction: Focal seizures in temporal lobe epilepsy (TLE) are associated with widespread brain network perturbations and neurocognitive problems. We hypothesize that over time, recurrent ictal events lead to interictal dysfunction of brainstem ascending reticular activating system (ARAS) centers, which may contribute to neurocognitive deterioration. This is supported by our recent studies of preoperative TLE patients, which showed decreased ARAS connectivity associated with neuropsychological deficits. Patients demonstrated decreased connectivity between 3 ARAS structures and frontoparietal regions. However, it is not known whether connectivity disturbances can improve in patients who achieve seizure freedom after epilepsy surgery. Methods: We evaluated 10 adult TLE patients who achieved postoperative seizure freedom and 10 matched control subjects, using resting-state functional MRI to measure functional connectivity (FC, partial correlation) between 3 ARAS structures (CSC, PPN, VTA) and 6 bilateral frontoparietal regions. FC patterns in patients before and after (> 1 year) surgery were compared to each other and to those in controls. Results: Compared to controls, preoperative TLE patients demonstrated significant decreases in FC between ARAS structures and the neocortex ($p < 0.05$, ANOVA, posthoc LSD). After successful epilepsy surgery, patients demonstrated significant increases in connectivity between ARAS structures and the neocortex compared to preoperative baseline ($p < 0.01$, ANOVA, posthoc LSD), with postoperative connectivity patterns resembling those in controls ($p > 0.6$, ANOVA, posthoc LSD). Postoperative CSC (but not PPN or VTA) connectivity increases were positively correlated with time since surgery ($r = 0.79$, $p < 0.01$), while PPN and VTA connectivity increases after surgery were positively correlated with preoperative frequency of complex-partial seizures ($r= 0.68\text{-}0.74$, $p < 0.05$ for each). Conclusions: Significant impairments in brainstem-neocortical connectivity are observed in preoperative TLE patients, but may recover after surgery, resembling connectivity patterns in controls. Some postoperative connectivity patterns may increase with time after surgery, suggesting progressive recovery after achieving seizure freedom, while others may be more dramatic in individuals with a higher frequency of consciousness-impairing seizures before surgery. These results are the first to demonstrate connectivity improvements after epilepsy surgery, and may lead to the identification of brainstem neuromodulation targets to address aberrant connectivity patterns and neurocognitive sequelae in this devastating disorder.

14. Comparing functional MRI low frequency fluctuations and connectivity in brainstem regions in temporal lobe epilepsy

Sarah E. Goodale, BE (1,2,4) Hernán F. J. González, M.S. (2,4) Victoria L. Morgan, Ph.D. (2,3,4) Dario J. Englot, M.D., Ph.D. (1,2,3,4)

Departments of
(1) Neurological Surgery,
(2) Biomedical Engineering,
(3) Radiology and Radiological Sciences
and
(4) The Vanderbilt University Institute of Imaging Science, Vanderbilt University Medical Center, Nashville, Tennessee, USA.

Introduction: Temporal lobe epilepsy (TLE) is a neurological disease that is associated with disturbances in brain networks. We have shown reduced functional MRI (fMRI) connectivity in TLE patients between brainstem ascending reticular activating system (ARAS) and frontoparietal neocortex, which is associated with neurocognitive problems. However, connectivity measurements between two regions do not allow insight in which of the two regions is 'driving' the abnormality - in this case, the brainstem vs. the neocortex. The amplitude of low frequency fluctuations (ALFF), which measures spontaneous fMRI signal fluctuations in individual brain regions, may lend insight to this question. Methods: We studied 10 adult patients with TLE who achieved postoperative seizure freedom before and after (>1 year) epilepsy surgery and 10 age, gender, and handedness matched control subjects. Using a resting-state fMRI in all subjects, we measured global ALFF (0.01-0.08 Hz) in 3 ARAS structures and 20 frontoparietal cortical regions, and also measured brainstem-neocortical functional connectivity between these regions. Results: ALFF values in the brainstem ARAS regions differed significantly between preoperative TLE patients and controls ($p < 0.01$, Wilcoxon rank-sum test), but neocortical ALFF was not significantly different between these groups ($p > 0.4$ for all comparisons, Wilcoxon rank-sum test). Interestingly, while patients showed increases in brainstem-neocortical functional connectivity after successful epilepsy surgery ($p < 0.01$, ANOVA, posthoc LSD), reaching levels comparable to control subjects, ALFF values in patients did not change significantly in either brainstem ($p < 0.01$) or neocortex after surgery ($p > 0.4$). Conclusions: Significant ALFF differences in the brainstem but not neocortex in patients vs. controls support our hypothesis that brainstem abnormalities are present in TLE, and may 'drive' connectivity impairments seen in these patients. ALFF measurements may aid the interpretation of functional connectivity differences in fMRI studies.

15. Nonrigid registration for laparoscopic liver surgery using sparse intraoperative data

Jon S. Heiselman [1,2] Jarrod A. Collins [1,2] Logan W. Clements [1,2] Jared A. Weis [1,2] Amber L. Simpson [3] Sunil K. Geevarghese [4] T. Peter Kingham [3] William R. Jarnagin [3] Michael I. Miga [1,2,5,6]

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[5] Department of Radiology and Radiological Sciences, Vanderbilt University Medical Center, Nashville, TN
[6] Department of Neurological Surgery, Vanderbilt University Medical Center, Nashville, TN

Organ deformations associated with laparoscopic liver surgery can be substantially different from those concomitant with open approaches due to intraoperative practices such as abdominal insufflation and variable dissection of supporting ligaments. Insufflation distends the abdominal wall and diaphragm and places tension on the anterosuperior ligaments. Previous mechanics-based deformation correction methods that were developed for the open environment therefore need to be adapted for laparoscopic organ configurations where ligament attachments may play an important role. In this work, we propose a new deformation correction strategy that accounts for additional mechanical support by ligaments through enforcing boundary conditions reflective of the laparoscopic anatomy. Perturbations of anatomically distributed control points on a finite element model are used to iteratively reconstruct an organ shape that best matches sparse measurements of the intraoperative surface. A liver phantom that replicates intraoperative laparoscopic deformations was used to examine three possible scenarios of ligament support based on intraoperative organ mobilization. From a set of 147 targets dispersed throughout the volume of the phantom, the nonrigid registration method yielded an average target registration error (TRE) of 6.37±0.47 mm whereas rigid registration produced average TRE of 14.68±1.22 mm, representing a 56.6% improvement. The proposed method also performed 19.4% better than a direct application of an open nonrigid correction method that does not account for ligament attachments.

16. Efficient and Distributable Deep Learning Platform for Large-scale Image Processing

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Deep convolution neural networks (CNN) have been widely used in the medical imaging research. We proposed three CNN based abdomen segmentation methods: (1) Deep Fully Convolutional Network (FCN) were trained to perform whole body segmentation on MRI and CT. (2) Spleen Segmentation Network (SSNet) was proposed to perform spleen segmentation for both normal spleen and splenomegaly on MRI. (3) An end-to-end MRI and CT synthesis and segmentation network (EssNet) was proposed to achieve the unpaired MRI to CT image synthesis and CT splenomegaly segmentation simultaneously without using manual labels on CT. However, to distribute such deep CNN based methods to users (e.g., researchers, collaborators and clinical practitioners) under a user friendly and efficient manner is still challenging. To address this issue, we developed the Docker based deep learning platform, which enables the users to deploy the deep CNN algorithms on their ends efficiently. In the demo, we demonstrate that anyone with internet access can use our methods to process their images just with several clicks on a website.

17. Optical tracking-guided MR-ARFI for targeting focused ultrasound neuromodulation

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Magnetic resonance-acoustic radiation force imaging (MR-ARFI) pulse sequences permit localization and targeting during focused ultrasound (FUS) therapy. MR-ARFI uses motion-encoding gradients (MEGs) to visualize the tissue displacement caused by the acoustic beam's radiation force. However, a priori knowledge of the acoustic beam's position and orientation in space is critical for MR-ARFI so that the MEGs can be placed in the proper orientation. We used an optical tracking system to inform the geometry of MR-ARFI acquisitions. The proposed methods will be used to guide ongoing experiments that use MR-ARFI to produce acoustic beam maps for targeting ultrasound neuromodulation in real-time.

18. 'Cleopatra' Wearable Surgical Video Camera

Alex Roed, Eric Noonan, Doug Manogue, Chris Savoca, Kevin Barrow, Lindsey Nestor, Thomas Withrow, Bill Rodriguez, Alexander Langerman

All authors affiliated with Engineering Department except Alexander Langerman, who is affiliated with the Otolaryngology Department

Surgery requires expert performance of critical, intricate tasks, yet surgery has lagged behind other industries in adopting video technology for performance assessment. Ubiquitous acquisition of high-quality video would allow surgeons to review their procedures, disseminate best practices for educational purposes, and provide clarity for medical records. In addition, a platform which records and analyzes video data would be the basis for the formation of normative surgical standards and lead to understanding of how to perform optimal surgery. One of the primary challenges to widespread adoption is difficulty in capturing consistent, high-quality video in 'open' (as opposed to endoscopic) surgical procedures. Current state-of-the-art boom mounted cameras suffer from obstructed views of the surgical field, and head-mounted cameras are subject to instability and add uncomfortable weight to the surgeon's head. We have developed a novel, lightweight camera system, 'Cleopatra', designed specifically for use in open surgical procedures. The camera is worn at the top of the surgical gown - close enough to the surgical field to allow high-quality images and avoid viewing obstructions. This location has proved inherently stable. We are continuing to refine this prototype and test it across multiple procedures.

19. Dry Lab Testing of Wearable Devices for the Operating Room

Lindsey Nestor, Kevin Barrow, Chris Savoca, Doug Manogue, Eric Noonan, Alex Roed, Thomas Withrow, Bill Rodriguez, Alexander Langerman

All authors affiliated with Engineering Department except Alexander Langerman, who is affiliated with the Otolaryngology Department

Dry Lab Testing of Wearable Devices for the Operating Room Our lab focuses on enabling high-quality data acquisition in the OR, with a current special emphasis on a wearable video camera for surgeons. The OR environment presents special challenges to testing wearables: data collection must be HIPAA compliant, the sterile environment limits on-body placement, surgical maneuvers can be highly physical and complex, and the high-stakes nature of surgical care forbids unnecessary distractions during operations. Furthermore, surgeons and appropriate surgical procedures may not be available on a time schedule conducive to rapid prototyping and experimentation. For these reasons, we have begun modelling surgeon body movement in a dry lab setup. We have begun with on-body testing of surgeon movement using accelerometers and estimation of working distances using infrared sensors. We have also utilized in-field light meters to map the normative lighting landscape during actual surgical procedures. We are currently testing the utility of the Microsoft Kinect to estimate larger-scale surgeon movement in a de-identified fashion. To translate these findings into a model of surgeon movement, we are developing a Stewart platform replica of surgeon-in-the-OR activity. We will use this dry lab to accelerate testing and iterative development of our on-body surgical video camera prototype; this dry lab setup also has numerous additional applications for testing surgeon wearables and devices for operating room use.

20. Deep Neural Networks for Ultrasound Beamforming

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We investigated using deep neural networks (DNNs) to suppress off-axis scattering in ultrasound images. This approach operates on sub-band data in the frequency domain. Networks were trained using the simulated responses from individual point targets. The network inputs consisted of the separated in-phase and quadrature components observed across the aperture of the array. The output had the same structure as the input and an inverse short-time Fourier transform was used to convert the processed data back to the time domain. Simulations, physical phantom, and in-vivo scans were used to assess performance of this method in terms of ultrasound image quality.

21. A Novel Molecular Imaging Probe for Optical Surgical Navigation of Pancreatic Cancer

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Objectives: Pancreatic cancer is among the most aggressive types of cancer. Early detection and treatment can play an active role in the disease therapy. This work established the correlation between translator protein (TSPO) expression and premalignant pancreatic lesions. Based upon these findings, a near-infrared-based TSPO ligand was developed and showed very promising in the disease imaging. It was further observed that the probe can be utilized to aid in surgical navigation. We anticipate that the novel probe can help the early detection, clear visualization, and precision removal of pancreatic tumor, especially the early stage lesions. Methods: Pancreatic TMAs were generated from samples collected from 220 patients at Vanderbilt University Medical Center. TSPO IHC expression was assessed using an intensity score-derived methodology. The Ptf1a-Cre;LSL-KrasG12D/+;Smad4fl/fl GEM was generated by housing the mice with LSL-KrasG12D/+;Smad4fl/fl and Ptf1a-Cre;Smad4fl/fl .Excised tissues were imaged using Odyssey Imaging Systems and surgical navigation was carried out on Pearl Small Animal Imaging System.

Results: TSPO expression was evaluated in premalignant pancreatic lesions in comparison with normal pancreas and chronic pancreatitis (CP). In the first group of 155 patients, pancreatic intraepithelial neoplasia (PanIN) exhibited significantly increased IHC score. The mean IHC score of normal pancreas was 1.025 ± 0.104, with CP being moderately higher as 1.385 ± 0.136. PanIN showed elevated TSPO levels with scores of 2.500 ± 0.167, 2.000 ± 0.333, and 2.000 ± 0.548 for PanIN 1-3 lesions, respectively. In the second group of patients, intraductal papillary mucinous neoplasm (IPMN) positive patients had significantly higher TSPO expression than IPMN negative patients (chi-square test $p<0.0001$). 78% (36/46) IPMN positive patients had moderate to strong TSPO expression compared to 21% (4/19) IPMN negative patients. Based upon this relationship, a novel TSPO near-infrared-based (NIR) probe has been developed by conjugating the TSPO ligand unit with LI-COR 800CW. The probe exhibited exceptional binding affinity to TSPO (Ki = 4.47 nM) and was applied to image the Ptf1a-Cre;LSL-KrasG12D/+;Smad4fl/fl pancreatic mouse model. Excised tissue imaging showed that pancreas tissues collected from the 4-9 week genetically engineered tumor mice exhibited about ten times higher in signal intensity compared with the normal pancreas. H&E and trichrome staining demonstrated the existence of cystic lesion and early stage invasive lesion in the young age genetically engineered mice. TSPO IHC staining confirmed that TSPO was overexpressed in the lesion by comparing the level of immunoreactivity with the normal cells. We further utilized the probe for optical surgical navigation. The probe was found to be accumulated in pancreatic tumor instead of normal pancreas, and can play an active role to help the surgeons precisely locate and remove the tumor. **Conclusion:** Overall, we established the relationship between TSPO and pancreatic cancer, and developed a novel TSPO NIR probe which showed very promising in pancreatic cancer imaging. We envision this probe can help with pancreatic cancer diagnosis and surgery, and possibly be used in other TSPO related disease, such as colon and breast cancer.

22. Comparing model-based deformation correction to intraoperative magnetic resonance imaging for image-guided neurosurgery: a retrospective study of nine cases

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Soft tissue deformation, or brain shift, during tumor resection compromises the spatial validity of registered preoperative imaging data, which is critical to image-guided neurosurgery. Current clinical solution to mitigate the impact of brain shift is to re-image the patient using intraoperative magnetic resonance (iMR) imaging. While iMR demonstrates benefits in accounting for preoperative-to-intraoperative tissue changes, its cost and encumbrance are major considerations for medical centers. Although iMR will be employed for challenging cases, a cost-effective model-based brain shift compensation strategy is needed as a complementary technology for standard resections. We have performed a retrospective study of nine tumor resection cases, comparing iMR measurements to intraoperative brain shift predictions with our model-based strategy, driven by sparse intraoperative cortical surface data. For quantitative assessment, homologous subsurface targets near the tumor were selected on preoperative and registered intraoperative MR images, which provide measured intraoperative subsurface deformation measurement. The measured subsurface deformation is compared to its model-predicted counterpart as estimated by the model-based brain shift correction framework. When considering moderate and high shift (> 3 mm, $n = 13 \pm 6$), alignment error due to brain shift decreased from 5.7 ± 2.6 to 2.3 ± 1.1 mm, representing an approximately 59% correction.

23. Establishing a Forward Model and Reconstruction for Background Oriented Schlieren Imaging of High Intensity Focused Ultrasound Pressure Fields

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High-intensity focused ultrasound(HIFU) is a non-invasive technique for thermal or mechanical treatment of tissues that can lie deep within the body. The ability to quantitatively map HIFU beams and beam aberrations is essential for treatment safety, quality assurance and technical research. However, currently no method directly provides quantitative spatially-resolved beam maps at therapeutic pressure levels, and at the same time is inexpensive, simple, and portable. Background-oriented schlieren (BOS) imaging is a technique just requiring a background pattern and a camera. Photographs of the background pattern taken with and without a nonuniform refractive index field in front of it can be related to the pressure distribution in a water tank. We are developing BOS imaging and tomography for rapid, cheap, and noninvasive mapping of continuous-wave HIFU pressure fields.

In this initial work, we developed a forward imaging model for BOS imaging. Given a spatially- and temporally-resolved steady-state pressure field calculated using the KZK equations, a background image and its position relative to the HIFU beam, simulated images are reconstructed from finite differencing in in-plane image dimensions and numerical integration through the projected dimension. We then built dictionaries of 2D blurring patterns and their corresponding projected steady-state pressure waveforms. BOS images were constructed using this dictionary by matching the projected pressure waveform at each spatial location to a dictionary entry, and tiling that entry's blurring pattern into the image. Next we will incorporate time delays in the projection data which will also be estimated.

24. Cortical Surface-based Shape Analysis Pipeline in Neuroimaging Study

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A population analysis of human cortical morphometry is critical for insights into brain development or degeneration, which allows for investigating sulcal and gyral folding patterns. The main focus here is to develop a fully automatic pipeline and its application to a population analysis of local cortical folding changes. The proposed pipeline consists of three novel components to overcome the challenges in the population analysis: 1) automatic sulcal curve extraction for stable/reliable anatomical landmark selection, 2) group-wise registration for establishing cortical shape correspondence across a population with no template selection bias, and 3) quantitative methods of local cortical folding.

25. Resolution and throughput optimized intraoperative spectrally encoded coherence tomography and reflectometry (iSECTR) for multimodal imaging during ophthalmic microsurgery

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Limited visualization of semi-transparent structures in the eye remains a critical barrier to improving clinical outcomes and developing novel surgical techniques. While increases in imaging speed has enabled intraoperative optical coherence tomography (iOCT) imaging of surgical dynamics, several critical barriers to clinical adoption remain. Specifically, these include (1) static field-of-views (FOVs) requiring manual instrument-tracking; (2) high frame-rates require sparse sampling, which limits FOV; and (3) small iOCT FOV also limits the ability to co-register data with surgical microscopy. We previously addressed these limitations in image-guided ophthalmic microsurgery by developing microscope-integrated multimodal intraoperative swept-source spectrally encoded scanning laser ophthalmoscopy and optical coherence tomography. Complementary en face images enabled orientation and co-registration with the widefield surgical microscope view while OCT imaging enabled depth-resolved visualization of surgical instrument positions relative to anatomic structures-of-interest. In addition, we demonstrated novel integrated segmentation overlays for augmented-reality surgical guidance. Unfortunately, our previous system lacked the resolution and optical throughput for in vivo retinal imaging and necessitated removal of cornea and lens. These limitations were predominately a result of optical aberrations from imaging through a shared surgical microscope objective lens, which was modeled as a paraxial surface. Here, we present an optimized intraoperative spectrally encoded coherence tomography and reflectometry (iSECTR) system. We use a novel lens characterization method to develop an accurate model of surgical microscope objective performance and balance out inherent aberrations using iSECTR relay optics. Using this system, we demonstrate in vivo multimodal ophthalmic imaging through a surgical microscope.

26. Intraoperative Assessment of Parathyroid Viability using Laser Speckle Contrast Imaging

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Post-surgical hypoparathyroidism and hypocalcemia are known to occur after nearly 50% of all thyroid surgeries as a result of accidental disruption of blood supply to healthy parathyroid glands, which are responsible for regulating calcium. However, there are currently no clinical methods for accurately identifying compromised glands and the surgeon relies on visual assessment alone to determine if any gland(s) should be excised and auto-transplanted. Here, we present Laser Speckle Contrast Imaging (LSCI) for real-time assessment of parathyroid viability. Taking an experienced surgeon's visual assessment as the gold standard, LSCI can be used to distinguish between well vascularized (n = 32) and compromised (n = 27) parathyroid glands during thyroid surgery with an accuracy of 91.5%. Ability to detect vascular compromise with LSCI was validated in parathyroidectomies. Results showed that this technique is able to detect parathyroid gland devascularization before it is visually apparent to the surgeon. Measurements can be performed in real-time and without the need to turn off operating room lights. LSCI shows promise as a real-time, contrast-free, objective method for helping reduce hypoparathyroidism after thyroid surgery.

27. Multimodality optical coherence tomography and fluorescence confocal scanning laser ophthalmoscopy for image-guided feedback of intraocular injections in mouse models

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Sankarathi B. Mehanathan,
Edward M. Levine, and
Yuankai K. Tao

Rodent models are robust tools for understanding human retinal disease and function because of their similarities with human physiology and anatomy and availability of genetic mutants. Optical coherence tomography (OCT) has been well-established for ophthalmic imaging in rodents and enables depth-resolved visualization of structures and image-based surrogate biomarkers of disease. Similarly, fluorescence confocal scanning laser ophthalmoscopy (cSLO) has demonstrated utility for imaging endogenous and exogenous fluorescence and scattering contrast in the mouse retina. Complementary volumetric scattering and en face fluorescence contrast from OCT and cSLO, respectively, enables cellular-resolution longitudinal imaging of changes in ophthalmic structure and function. We present a non-contact multimodal OCT+cSLO small animal imaging system with extended working distance to the pupil, which enables imaging during and after intraocular injection. While injections are routinely performed in mice to develop novel models of ophthalmic diseases and screen novel therapeutics, the location and volume delivered is not precisely controlled and difficult to reproduce. Animals were imaged using a custom-built OCT engine and scan-head combined with a modified commercial cSLO scan-head. Post-injection imaging showed structural changes associated with retinal puncture, including the injection track, a retinal elevation, and detachment of the posterior hyaloid. When combined with image-segmentation, we believe OCT can be used to precisely identify injection locations and quantify injection volumes. Fluorescence cSLO can provide complementary contrast for either fluorescently labeled compounds or transgenic cells for improved specificity. Our non-contact OCT+cSLO system is uniquely-suited for concurrent imaging with intraocular injections, which may be used for real-time image-guided injections.

28. Combined fingerprint and high wavenumber Raman spectroscopy for in vivo assessment of the pregnant cervix

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Ton van Leeuwen (University of Amsterdam Medical Center),
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Previous studies have indicated that the hydration state of the cervix changes during pregnancy and may serve as a biomarker for preterm labor. However, there is currently no nondestructive method for assessing changes in cervical hydration in vivo. We have shown that Raman spectroscopy can be used to evaluate water content in biological tissues of interest based on the broad OH stretching band in the high wavenumber region. The accuracy of this approach has been validated in gelatin and chicken breast tissue phantoms. Here we demonstrate the use of a portable combined fingerprint and high wavenumber Raman spectroscopy system to track hydration and other biochemical changes in the cervix during pregnancy. In this pilot study, fingerprint and high wavenumber Raman spectra were measured in vivo in both nongravid mice and pregnant mice at term. Decomposition of the broad OH stretching band into its component Gaussian peaks provides insight into the interactions of water molecules with cervical tissue. This hydration information from the high wavenumber region is complimentary to the biochemical specificity of the fingerprint region. Raman spectroscopy is a highly sensitive and minimally invasive technique for the in vivo analysis of cervical remodeling, and as such may be a valuable clinical tool for understanding and predicting preterm labor.

29. In Vivo Modeling of Biphasic Mechanics in the Brain: A Poroelastic Constitutive Model with Enhanced Structural Description Approach

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Objective: The purpose of this investigation is to test whether a poroelastic model with enhanced structure could capture in vivo interstitial pressure dynamics in a brain undergoing mock surgical loads. Methods: Using interstitial pressure data from a porcine study, we use an inverse model in order to reconstruct these pressures and estimate material properties of the brain tissue. This is done in four distinct reconstruction parameterizations to isolate the influence of the three features studied. These features are the dural septa, the treatment of the ventricles, and treatment of the brain as a saturated media. Results: The approach demonstrates accurate capturing of the interstitial pressure dynamic, tissue deformation, and the presence of intracranial pressure compartmentalization. The best result reflects a model that employs tissue heterogeneity, the dural septa, a ventricular boundary condition, and the treatment of the tissue as not fully saturated. Conclusion: This study shows the appropriateness of using a poroeleastic model in conjunction with appropriate boundary conditions that reflect the anatomical features of the brain in the context of accurately capturing the behavior of the brain. Significance: To our knowledge there has not been a systematic study of the influence of anatomical features within brain models. Also, the quality of interstitial pressure fits shown here have not been seen before within previous literature. Lastly, the common assumption of saturated tissue is challenged and the noted compliance related to our fits likely reflects remaining anatomical structure not yet captured.

30. Visualization of Slow Velocity Blood Flow using Power Preserving Coherent Flow Power Doppler Ultrasound

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Power Doppler imaging is a widely adopted technique for ultrasonic blood flow detection, offering greater sensitivity to slow flow than conventional color Doppler imaging. However, a considerable deficiency of power Doppler is that it is susceptible to common sources of image degradation, including tissue clutter, reverberation, and thermal noise. To address this deficiency, we have developed a technique termed Power Preserving Coherent Flow Power Doppler (CFPDpp). This beamforming technique uses an aperture domain spatial coherence metric to suppress incoherent reverberation and thermal noise, and a novel singular value decomposition clutter filter to suppress tissue clutter. This CFPDpp technique has been evaluated using Field II simulations to demonstrate that CFPDpp offers greater sensitivity to slow flow in the presence of various clutter sources, while preserving blood signal energy. Overall, CFPDpp can provide a 5-10 dB increase in SNR, which enables perception of slow flow at velocities as low as 0.1 cm/sec.

31. MR imaging simulator and optimized multi-echo z-shimmed sequence for temperature mapping near metallic ablation probes

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The magnetic susceptibility of metallic ablation probes causes large signal voids that prevent precise magnetic resonance thermometry near the probes. This is especially a problem when the target lesion is small, such as for RF ablation of the hippocampus to treat epilepsy. Previously, we proposed an orientation-independent multi-echo Z-shimmed sequence that recovers signal near the probe for more precise temperature mapping. However, this method was hindered by the need to acquire high resolution off-resonance maps around the ablator and perform computationally-intensive optimization of the z-shim gradient moments prior to heating. Here we present an MR imaging simulator that calculates images near metallic ablation probes and use it for offline optimization of a multi-echo Z-shimmed pulse sequence. The simulated images and optimized sequence were validated in experiments using a nitinol RF ablation probe.

32. A system for automatic monitoring of surgical instruments and dynamic, non-rigid surface deformations in breast cancer surgery

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Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer related death. If the tumor is completely resected, breast conserving therapy (lumpectomy to resect the tumor with radiation therapy) offers patients improved cosmetic outcomes and quality of life with equivalent survival outcomes to mastectomy. However, high reoperation rates ranging from 10-59% indicate the need for improved intraoperative tumor localization. We propose a coupled optical tracker and stereo camera system for automated monitoring of surgical instruments and non-rigid breast surface deformations. Utilizing both devices allows for precise instrument tracking of multiple objects with reliable, workflow friendly tracking of dynamic breast movements. A bracket was designed to rigidly pair an optical instrument tracker with a stereo camera, maximizing their volume of overlap. Computer vision techniques were employed to automatic track fiducials, requiring one-time initialization with bounding boxes in stereo camera images. Point based rigid registration was performed between fiducial locations triangulated from the stereo camera images and fiducial locations recorded with an optically tracked stylus. Undeformed and deformed states were tested for three deformations of a phantom breast with five fiducials. An average FRE of 2.2 ± 0.7 mm demonstrates considerable promise for this approach in monitoring the surgical field. The method proposed could allow for continuous measurement of surgical instruments in relation to the dynamic deformations of a breast during lumpectomy.

33. Putting a Wrist and an Elbow on a Laparoscopic Tool

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Patrick Anderson,
Robert J. Webster III

Minimally invasive surgery offers significant advantages over open surgical alternatives. In certain surgeries involving challenging structures, minimally invasive procedures are impossible to perform with a non-robotic approach due to limitations of purely mechanical surgical tools. This poster describes a highly dexterous manual tool that features both a pinned joint 'wrist' (2 DOF) and a multi-backbone joint 'elbow' (2 DOF). This device overcomes the need of the tool to pivot about the entry point, reducing the overall tool range of motion while maintaining surgeon dexterity and high force transmission capability. This poster details the development and implementation of a static balance system that relieves the requirement that surgeons must hold the stiff continuum joint in place. It also describes the first example of a completely manual tool that features both a wrist and a statically balanced elbow to enhance surgeon capabilities. This highly dexterous tool could give surgeons the ability to perform surgeries manually that involve challenging structures that were previously impossible to do without a robotic platform.

34. Application of Computational Fluid Dynamics to Surgical Planning In Laryngeal Stenosis

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BACKGROUND: Laryngeal stenosis is a rare and life-threatening condition in which both vocal folds are fixed in a midline position. This results in severe airway obstruction associated with life-threatening respiratory compromise. Laryngeal stenosis primarily occurs secondary to scarring after endotracheal intubation (also termed posterior glottis stenosis: PGS). It can also arise following bilateral vocal cord paralysis (BVFP). Treatment of laryngeal stenosis is largely surgical and remains an unsatisfactory compromise between voice, breathing and swallowing. Current techniques aim to restore airway patency at the cost of worse glottic closure and vocal quality. The three main approaches to enlarge the airway include 1. endoscopic cordotomy, 2. endoscopic suture lateralization, and 3. expansion of the posterior cricoid plate. No comparisons between techniques currently exists. OBJECTIVES: We sought to employ computational modeling to delineate the optimal surgical approach. METHODS: Utilizing clinical computerized tomography (CT) in laryngeal stenosis patients, coupled with image analytics employing computational fluid dynamic (CFD) models, we compared the airflow gains between the three distinct surgical approaches. RESULTS: One geometric index (cross-sectional area of airway) and two CFD measures (airflow velocity, and airflow resistance) were significantly lower in posterior cricoid plate expansion surgery when compared to alternate surgical approaches. CONCLUSIONS: Computational fluid dynamic (CFD) modeling can provide discrete, quantitative assessment of the airflow through the laryngeal inlet, and offers preliminary data suggesting expansion of the posterior cricoid plate provides the greatest improvement in respiratory physiology.

35. An 8-channel coil array for MR-guided focused ultrasound at 7

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A 7 Tesla 8-channel coil array was developed in increase SNR and improve resolution for Magnetic Resonance Imaging (MRI)-guided focused ultrasound (FUS), compared to an existing transducer-attached single surface loop coil. The array comprised 8 circular elements arranged in a hexagonal tiling pattern [2] on a 3-D printed substrate with non-zero Gaussian curvature designed to closely fit the head of a non-human primate (macaque), for an ongoing ultrasound neuromodulation study. The ultrasound transducer is acoustically coupled to the subject's head through a hole in the middle element of the array. Electromagnetic coupling between neighboring elements is minimized using overlap. The coil former features a Buna-N rubber sheet for water-proofing and robust strain relief for cables. We will present the design of the array and its substrate, as well as electromagnetic simulations of its fields and initial bench tests.

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36. TURBot: a Telerobotic System for Transurethral Bladder Cancer Resection & Surveillance

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S. Duke Herrell, Department of Urologic Surgery
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A new telerobotic surgical platform called TURBot is presented for bladder cancer resection and surveillance. The experimental evaluation of TURBot on a human bladder phantom is also presented where mock-up tumors are resected in two locations: left superior and bladder neck. Outcomes of in-vivo attempts where the system was tested in swine are explained. We successfully used laser for ablating tumors in the porcine bladder. We were also able to show feasibility of en-block resection. In the end, a redundancy resolution based on artificial potential field is developed to minimize the visual field occlusion caused by the presence of the robot in the field of view (FOV). The method drives the robot outside the FOV in attempting to reach static equilibrium while achieving the main task of tracking. Simulations confirmed the efficacy of the proposed method for a rotating camera. Although the proposed method was developed within the context of multi-backbone continuum robots, it can be generally applied to any redundant robot that requires to stay as clear of the visual field as possible.

37. Non-linear Beamforming Approaches for Sizing and Detecting

Siegfried Schlunk, Jaime Tierney, Mark George, Pranav Karve, Ravindra Duddu, Ryan S. Hsi, and Brett Byram.

Department of Biomedical Engineering, Vanderbilt University

Standard B-mode imaging has poor sensitivity and specificity for detecting kidney stones and consistently overestimates stone size. Because of this, the acoustic shadow and twinkling artifacts seen with color Doppler have been used as substitutes for conventional imaging for stone sizing and detection. However, often neither a shadow nor color Doppler artifact are present. In this study, the use of several non-linear beamforming strategies was investigated in conjunction with plane wave synthetic focusing (PWSF). These include aperture domain model image reconstruction (ADMIRE), short-lag spatial coherence (SLSC), and a new mid-lag spatial coherence (MLSC) method designed specifically for kidney stone detection. Evaluations of all four methods were performed in vitro and ex vivo. For the in vitro evaluation, various sized kidney stones (n=8 with width 9.88±5.96mm) were placed on top of a gelatin phantom doped with graphite, which served as a platform and provided a diffuse scattering background for comparisons. The stones were imaged at a depth of 4 cm and 8 cm. An ex vivo evaluation was also performed where several stones were implanted into pig kidneys immersed in water. The in vitro sizing errors for all stones at both depths for PWSF, ADMIRE, SLSC, and MLSC were 0.89±0.74mm, 0.57±0.69mm, 0.96±1.31mm, and -0.92±3.12mm, respectively. For sizing, ADMIRE performs best in vitro, but in the ex vivo study delineation of the border was unclear. For detection, the custom MLSC method was able to achieve excellent discrimination between the stones and the diffuse scattering media with a constant threshold across all sets.

38. Nanodroplets enhanced ablation using Multi-Focal High Intensity

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High intensity focused ultrasound (HIFU) is a non-invasive treatment that kills cells cells via heating with high frequency sound waves. Although HIFU is non-invasive compared to other ablative modalities, long treatment times and off-target heating remain significant hurdles when treating large volumes. One method to improve off-target heating is to selectively amplify heating in the focal region, which we achieve using phase shift nanodroplets (PSNDs) that can be activated from a liquid to gas phase using HIFU. Once in the gas phase, the particles absorb more sound and improve heating efficiency specifically within the intended region. We hypothesize that these droplets can also improve treatment times since multiple sites can be activated and then simultaneously treated, yielding a much larger heated volume than the HIFU focus. In this study, we present early tests of the activation of PSNDs in phantoms and confirm activation of the droplets with B-mode ultrasound. Droplet phase change of a single or multiple points was visualized with B-mode ultrasound. In the future, we seek to use this method to improve treatment time and energy efficiency by creating an ablation zone of different diameters and steering the focal spot along the activated regions. Overall, this work will result in overcoming the problems associated with off-target heating and low time efficiency, ensuring HIFU ablation occurs only in the intended region with lower treatment times.Off target heating occurs when HIFU ends up heating not only the intended region but also the nearby tissue. This can lead to mechanical stress and deformities in tissues. To combat this hurdle, we propose usage of nanodroplets to localize heating in intended region of tumor, thereby ablating only areas that have tumor cells and preserving healthy tissues. The issue of low time efficiency arises when we deal with a tumor volume that is much larger than the HIFU focus. In conventional HIFU, one would use point by point sonication to ablate the entire tumor volume, thereby increasing procedure time and lowering the time efficiency. To improve treatment time and energy efficiency, we propose a volumetric ablation wherein we would create an ablation zone of different diameters and steer the focal spot along those concentric circles to ablate tumor volume. Overall, this work will result in overcoming the problems associated with off-target heating and low time efficiency. This will ensure tumor ablation only in the intended region with lower treatment times.

39. Developing a clinical prototype for label-free rapid intraoperative parathyroid identification during thyroid and parathyroid surgeries

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Background: Difficulty in identifying parathyroids during thyroid and parathyroid surgeries, often leads to accidental parathyroid excisions and eventual post-surgical hypocalcemia. This necessitates time-consuming frozen section examinations for parathyroid identification. This study aims to translate a near-infrared fluorescence detection lab-built system into a clinical prototype for label-free intraoperative parathyroid identification. Method: A lab-built system was first tested for parathyroid identification across 20 patients undergoing thyroidectomy and/or parathyroidectomy with 134 parathyroid, 106 thyroid, 53 muscle, 57 fat and 53 tracheal measurements to validate previous findings obtained with this system. A clinical prototype called PTEye was subsequently designed with a user-friendly interface to function with operation room (OR) lights turned on. PTEye was then tested across 20 patients with 120 parathyroid, 109 thyroid, 40 muscle, 40 fat and 40 tracheal measurements. Accuracy was determined by correlating the acquired data with visual confirmation by surgeon for unexcised parathyroids or histology report for excised parathyroids, and then compared between the two systems. Results: The lab-built system had a sensitivity of 96.3% and specificity of 94.2% for in vivo parathyroid identification. In comparison, PTEye achieved a sensitivity of 100% and specificity of 96.1% for the same, despite ambient OR lights. Furthermore, PTEye did not require fluorescent dye injection and provided results in real-time.

Conclusion: PTEye demonstrated high accuracy for label-free intraoperative parathyroid detection. The intuitive interface of PTEye and its ability to rapidly detect parathyroid with ambient OR lights can ensure easy usability by surgeons. Eventual clinical translation will require multi-centric testing of PTEye.

40. Ultrasonic Non-Contrast Perfusion Imaging with Adaptive Demodulation

Jaime Tierney(1), Crystal L. Coolbaugh(2), Theodore Towse(3), and Brett Byram(1)

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Ultrasonic non-contrast perfusion imaging remains challenging due to spectral broadening of the tissue clutter signal caused by patient and sonographer hand motion. Simply, the velocity of the slowest moving blood has similar spectral support to the moving tissue. To address this problem, we developed an adaptive demodulation (AD) scheme to suppress the bandwidth of tissue prior to high-pass filtering. The method works by directly estimating the modulation imposed by tissue motion, and then removing that motion from the signal. Our initial implementation used a single plane wave power Doppler imaging sequence combined with a conventional high-pass IIR tissue filter. However, other recent advancements in beamforming and tissue filtering have been proposed for improved slow-flow imaging, including coherent flow power Doppler (CFPD) and singular value decomposition (SVD). Here, we aim to evaluate AD separately as well as in comparison and in conjunction with improvements in beamforming and filtering using simulations and an in vivo muscle contraction experiment. We show that simulated blood-to-background SNR is highest when using AD+CFPD and a 100ms ensemble, which resulted in a 9.88dB increase in SNR compared to CFPD by itself. Additionally, AD+SVD resulted in a 54.6% increase in mean power within the in vivo muscle after contraction compared to a 6.84% increase with AD and a conventional IIR filter.

41. Biomechanical Properties of Skin as Potential Biomarker for Sclerotic Chronic Graft-Versus-Host Disease Severity

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Skin sclerosis is a common manifestation of chronic graft-versus-host disease (cGVHD) resulting in significant morbidity. All existing scales to monitor sclerosis are subjective, suffer low reproducibility, and provide only coarse grading ability. These disadvantages limit the ability to accurately reflect changes in disease progression or treatment response. We propose a noninvasive approach to directly measure biomechanical properties of skin. In this preliminary study, we investigated the reproducibility and feasibility of using the commercial Myoton device to quantitatively measure sclerotic features of skin cGVHD. cGVHD patients (n=7) with NIH 2014 sclerosis score of 3 (most severe) and healthy subjects (n=5) were recruited. The Myoton was used to assess skin stiffness bilaterally on ten anatomical sites, resulting in 20 measurements per subject. Interobserver reproducibility, day-to-day repeatability, left-to-right differences, and variation across anatomic sites were evaluated. The ability to quantitatively differentiate sclerotic from normal skin was assessed in a cross-sectional study comparing skin stiffness of cGVHD patients to healthy subjects. Continuous variables were compared using a t-test. Measurements performed on a healthy subject demonstrated high day-to-day repeatability, minimal left-to-right discrepancy, and expected variations across anatomic regions. In a sclerotic cGVHD patient, differences between two independent observers were minimal. In cross-sectional study, sclerotic cGVHD patients showed significant increases ($p<0.05$) in skin stiffness measurements in five of the ten regions compared to healthy subjects. Our preliminary results indicate that direct biomechanical measurement of skin stiffness holds great potential for accurate and repeatable sclerotic cGVHD assessment, and merits further clinical investigation.

42. The Vanderbilt Cutaneous Imaging Clinic (VCIC) - 'Pioneering noninvasive skin measurements for clinical impact'

Arved Vain, PhD; Inga Saknite, PhD; Fuyao Chen; Jocelyn Gandelman; Laura Dellalana; Eric Tkaczyk, MD, PhD

VUMC Department of Medicine Vanderbilt Biomedical Engineering

This poster will give interested parties an overview of the patient care and translational dermatology imaging work going on in the VCIC. The Vanderbilt Cutaneous Imaging Clinic (VCIC) is a multidisciplinary team of clinicians and engineers whose mission is to seamlessly integrate patient care, clinical investigation, and fundamental technology research with application in dermatology, oncology, hematology, and other specialties.

43. Segmentation of Skin Lesions in Chronic Graft Versus Host Dis-

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Chronic graft-versus-host disease (cGVHD) is a frequent and potentially life-threatening complication of allogeneic hematopoietic stem cell transplantation and commonly affects the skin, resulting in distressing patient morbidity. The percentage of involved body surface area (BSA) is a commonly used feature for diagnosing and scoring the severity of cGVHD. However, the segmentation of the involved BSA from patient whole body serial photography is challenging because the appearance of cGVHD lesions can be drastically different from patient to patient. It is thus difficult to design hand-crafted algorithms capable of capturing textural information that could be used for localizing the lesions. In this study we explore the possibility of using a fully convolutional network (FCN) to segment the involved BSA in photography of cGVHD patients. We use the Vectra H1 (Canfield Scientific) 3D camera to acquire 227 3D photographs of 12 cGVHD patients aged between 22 and 72. A rotational data augmentation process is then applied, which rotates the 3D photos through 10 evenly distributed angles, producing one 2D projection image at each position. This results in 2270 2D images that constitute our data set. A FCN model is initialized using the weights of a classification network that is pre-trained on natural images and subsequently fine-tuned using images in our data set. We show that our method achieves encouraging results for segmenting cGVHD skin lesion in photographic images.

44. Raman Spectroscopy Predicts Fracture Toughness of Human Cortical Bone

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Although the crucial contribution of bone matrix to fracture resistance is largely understood, there is currently no clinical tool that assesses the matrix. Raman spectroscopy (RS) is uniquely well suited to address this unmet need. However, there is currently no consensus on which RS parameters are most important for assessing the fracture resistance of human bone. To establish the potential for RS in assessing the contribution of the matrix to the fracture resistance, we hypothesized that i) the new RS parameter developed by our group correlates with fracture toughness of human cortical bone and ii) more importantly, RS adds value helping volumetric BMD (vBMD) and age predict fracture toughness properties. Fifty-eight cadaveric cortical bone specimens (28M/30F, age = 21-101 yrs) machined into a single-edge notched beam specimen (SENB). Volumetric bone mineral density (vBMD) ahead of the crack tip was assessed by μCT (μCT50, Scanco Medical, and corresponding vBMD was calculated. A non-linear fracture mechanics approach (R-curve testing) was used to determine crack initiation (Kinit), crack growth toughness (Kgrow) and overall J integral (J-int). Thirty-two Raman spectra per sample were each acquired by 12 accumulations (5 s), and distributed throughout the entire surface of bone specimens neighboring each SENB (785 nm Horiba confocal RS, 20x obj). The new parameter, 1670/1640, was negatively associated with all fracture toughness properties and it explained 20% of variance in age, 48% of the variance in J-int and 35% of the variance for Kinit (reported as R2). Correlations between 1670/1640 and fracture toughness properties were modest, but greater than those between fracture toughness and avBMD (max. R2=0.23), suggesting that information about bone matrix could be more valuable than measure of BMD to assess bone fracture resistance. We included age and vBMD in multilinear regressions as covariates and 1670/1640 significantly improved the prediction of J-int (from adj-R2= 12.35 to 46.55) and the prediction of Kinit (from adj-R2= 40.73 to 50.49). In summary, the present research suggests that RS assessment has a great potential to assist existing clinical tools in assessing an individual's fracture risk with the unique advantage of probing disease and age-related changes in bone tissue at the nano-structural level of organization.

45. Trackerless Image-guided Surgical Planning System Design Using a Collaborative Extension of 3D Slicer

Xiaochen Yang[1], Rohan Vijayan[2], Ma Luo[2], Logan W. Clements[2,5], Reid C. Thompson[3,5], Benoit M. Dawant[1,2,4,5], and Michael I. Miga[2,3,4,5]

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Conventional optical tracking systems combine cameras sensitive to near-infra-red (NIR) light and passively/actively NIR-illuminated markers to measure physical space in the operating room (OR). This technology is widely-used within the neurosurgical theatre and is a staple in the standard of care in craniotomy planning. To accomplish, planning is largely conducted at the time of the procedure and OR. In the work presented herein, we propose a framework to achieve this in the OR that is free of conventional tracking technology, i.e. a 'trackerless' approach. Briefly, we are investigating a collaborative extension of 3D slicer that combines surgical planning and craniotomy designation in a novel manner. While taking advantage of the well-developed 3D slicer platform, we implement advanced features to aid the neurosurgeon in planning the location of the anticipated craniotomy relative to the preoperatively imaged tumor, and then subsequently aid the physical procedure by correlating that plan with a novel MR-to-physical registered field-of-view display. These steps are done such that the craniotomy can be designated without use of a conventional optical tracking technology. To test this novel approach, an experienced neurosurgeon performed experiments on four different mock surgical cases using our module as well as the conventional procedure for comparison. The results suggest that our planning system provides a simple, cost-efficient, and reliable solution for surgical planning and delivery without the use of conventional tracking technologies. We hypothesize that the combination of this early-stage craniotomy planning and delivery approach, and our past developments in cortical surface registration and deformation tracking using stereo-pair data from the surgical microscope may provide a fundamental new realization of an integrated 'trackerless' surgical guidance platform.

46. Continuum Robots for Force-Controlled Semi Autonomous Organ Exploration and Registration

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To perform semi-automated surgical tasks or to assign virtual fixtures for telemanipulated surgical procedures, accurate correspondence between preoperative and intraoperative organ geometry is required. To overcome organ deformation and shift relative to pre-operative images, this paper proposes using force-controlled exploration to update the organ geometry using a deformable registration of a pre-operative model to the surgical scene. Since continuum robots can offer deep access into the anatomy, we explore the unique challenges associated with their use to achieve force-controlled shape exploration. To overcome these challenges, a mixed feedback control law is proposed whereby joint-level and end-effector position measurements are used to satisfy a reference motion trajectory. A hybrid force/position controller is presented using sensory input from magnetic tracking and force sensing. Validation of the control algorithms proposed in this paper is achieved on the IREP (a single port access surgical system). Experimental results show that, despite deformation of an organ, the surgical plan can be deformably registered using force-controlled exploration data via an implementation of coherent point drift registration. Future applications of this work include updating virtual fixture laws in the presence of organ deformations or swelling and semiautomation of surgical tasks.

47. Selecting electrode configurations for image-guided cochlear implant programming using template matching

Dongqing Zhang, Yiyuan Zhao, Jack H. Noble, Benoit M. Dawant

Department of Electrical Engineering and Computer Science

Cochlear implants (CIs) are neural prostheses that restore hearing using an electrode array implanted in the cochlea. After implantation, the CI processor is programmed by an audiologist. One factor that negatively impacts outcomes and can be addressed by programming is cross-electrode neural stimulation overlap (NSO). In the recent past, we have proposed a system to assist the audiologist in programming the CI that we call Image-Guided CI Programming (IGCIP). IGCIP permits using CT images to detect NSO and recommend deactivation of a subset of electrodes to avoid NSO. In an ongoing clinical study, we have shown that IGCIP significantly improves hearing outcomes. Most of the IGCIP steps are robustly automated but electrode configuration selection still sometimes requires manual intervention. With expertise, Distance-Vs-Frequency (DVF) curves, which are a way to visualize the spatial relationship learned from CT between the electrodes and the nerves they stimulate, can be used to select the electrode configuration. In this work, we propose an automated technique for electrode configuration selection. A comparison between this approach and one we have previously proposed shows that our new method produces results that are as good as those obtained with our previous method while being generic and requiring fewer parameters.

48. Leukocytes as Mobile Carriers of Anti-Cancer Therapeutics via Bispecific Liposomes

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More than 90% of cancer-related deaths are caused by cancer metastasis, in which cancer cells break away from the primary tumor, travel through the blood or lymph system as circulating tumor cells (CTCs), and form new tumors (metastases) in other parts of the body. Studies have shown that the neutralization of CTCs in circulation for the prevention of metastasis could represent an effective anti-cancer strategy. Here, we demonstrate a unique strategy to kill CTCs in the circulation that modifies the surface of circulating leukocytes with bispecific liposomes. The cancer-specific tumor necrosis factor (TNF) related apoptosis inducing ligand (TRAIL) is conjugated on the surface of liposomes along with E-selectin (ES) that recognizes and binds to circulating leukocytes. These bispecific liposomes, after intravenous administration, are expected to adhere to their target leukocytes and enable them to present TRAIL on their surface for the purpose of killing CTCs. A liposomal formulation method of TRAIL and ES has been established. The TRAIL/ES liposomes can kill cancer cells efficiently, and maintain their physical stability when stored as powder at -80°C. The liposome formulations can efficiently functionalize leukocytes in whole blood under shear force. The formulation also greatly extended the circulation life of TRAIL to ~72 h. These results strongly support TRAIL/ES liposome's potential to functionalize leukocytes in vivo and therefore convert them into 'circulating hunters' of CTCs. We expect that anticancer protein hitchhike on circulating leukocytes via liposomes could represent an effective strategy to directly target and kill CTCs for the prevention of cancer metastasis.

49. Validation of cochlear implant electrode localization techniques

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Cochlear implants (CIs) are neural prosthetics for treating hearing loss. Although these devices have been remarkably successful at restoring hearing, it is rare to achieve natural fidelity, and many patients experience poor outcomes. Our group has developed image-guided CI programming (IGCIP) techniques, in which image analysis techniques are used to locate the intra-cochlear position of CI electrodes to determine patient-customized settings for the CI processor. Clinical studies have shown that IGCIP leads to significantly improved outcomes. A crucial step is the localization of the electrodes, and rigorously quantifying the accuracy of our algorithms requires dedicated datasets. In this work, we discuss the creation of a ground truth dataset for electrode position and its use to evaluate the accuracy of our electrode localization techniques. Our final ground truth dataset includes 31 temporal bone specimens that were each implanted with one of four different electrode array types by an experienced Otologist. The arrays were localized in conventional clinical CT images using our automatic methods and manually in high resolution μCT images to create the ground truth. The conventional and μCT images were registered to facilitate comparison between automatic and ground truth electrode localization results. Our technique resulted in mean errors of 0.14 mm in localizing the electrodes across 31 cases. Our approach successfully permitted characterizing the accuracy of our methods, which is critical to understand their limitations for use in IGCIP

50. Quantitative Image Analysis to Guide Biopsy for Molecular Biomarkers

Derek J. Doss[1], Jon S. Heiselman[1,4], Ma Luo[1,4], Logan W. Clements [1,4], Michael I. Miga[1,2,3,4], and Filip Banovac[4,5]

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Resection or transplantation are the primary curative methods of treatment for hepatocellular carcinoma, however, many patients are not candidates. If the cancer has infiltrated both lobes or has metastasized, other treatment options must be used. It is well established that treatment can be customized based on tumor type and response. Analysis of biomarkers captured through biopsy could enable this tumor-specific treatment, but the tissue must be biopsied from biologically active portions of the tumor. While other methods exist to find biologically active portions of the tumor, such as positron emission tomography (PET) scans, these methods are not real time nor are they reliable in PET positive small tumors. The aim of this study was to create a method of displaying an overlay of the pre-treatment and post-treatment tumors to more effectively guide a biopsy into relevant areas of a tumor for continued longitudinal treatment. In this work, retrospective image data from 10 cases was used to perform an image-based nonrigid registration between the pre-treatment and post-treatment scans. The result of the registration was validated using feature target error and surface fit. The mean feature target error and surface fit was found to be 8.3±4.1mm and 1.8±0.4mm, respectively. To assess the tumor response, a bidirectional local distance (BLD) measure was used. The mean minimum BLD across all cases was 0.14±0.06mm and the mean maximum BLD across all cases was 17.5±6.3mm. These preliminary results suggest that the proposed method is an effective way of identifying the region of the tumor to biopsy.

51. Towards a Clinically-Ready Steerable Needle Robot in the Lung

Stephanie R. Amack,
Robert J. Webster III

Lung cancer is the most deadly form of cancer in part because of the challenges associated with accessing nodules for diagnosis and therapy. Transoral access is preferred to percutaneous access since it has a lower risk of lung collapse, yet many sites are currently unreachable transorally due to limitations with current bronchoscopic instruments. Vanderbilt's MED lab has developed a new robotic system for image-guided trans-bronchoscopic lung access. The system uses a bronchoscope to navigate in the airway and bronchial tubes to a site near the desired target, a concentric tube robot to move through the bronchial wall and aim at the target, and a bevel-tip steerable needle with magnetic tracking to maneuver through lung tissue to the target under closed-loop control. We seek to improve the robotic hardware and design an intuitive workflow for implementation of the complete system. The aim of this project is to design an actuation unit for the robotic system that is suitable for the operating room. By designing for ease of use with current bronchoscopic techniques while making the device compact, our work seeks to prepare the novel robotic lung system for clinical use.

52. PHOTON: Pathologies of the Human Eye, Orbit, and The Optic Nerve

Shikha Chaganti, EECS,
Xiuya Yao, EECS
Louise Mawn, VEI
Bennett Landman, EECS
Thomas Lasko, Biomedical Informatics

Millions of Americans are affected by diseases of the optic nerve, inducing billions of dollars in annual economic burden. The onset of eye diseases and impairment of vision are often accompanied by changes in physical characteristics of orbital structures. An objective evaluation of the role of imaging and related EMR data in diagnosis of these conditions would improve understanding of these diseases and help in early intervention. In our study, we conducted retrospective analyses on imaging and EMR data of 821 patients who visited the Vanderbilt University Medical Center and were diagnosed with four major optic nerve diseases: glaucoma, optic neuropathy, thyroid eye disease, and optic nerve edema. We developed an automated image-processing pipeline that identifies the orbital structures within the human eyes from computed tomography (CT) and magnetic resonance imaging (MRI) scans, calculates structural size, and performs volume measurements. We investigated the relationship between structural metrics of the eye orbit and visual function. In addition, we evaluated the predictive power of these structural metrics by developing diagnostic classifiers for the four eye disease groups. We also tested the role of EMR data to improve image-based studies. We found that structural metrics obtained from imaging as significantly ($p<0.001$) correlated with visual function, with a reasonable explained variance (R2 ~0.1-0.3). Addition of EMR data to the imaging metrics improved the R2 to up to 0.61. We found that structural metrics also have high predictive power with area under the curve (AUC) between 0.71 to 0.95 for the diagnostic classifiers. Addition of EMR data improved the AUC by an average of 15%. This work presents novel methods to analyze multi-modal data in ophthalmology to identify imaging and EMR features that are predictive of changes in visual function. The ultimate goal of this project is to improve prognosis prediction, aid timely intervention and improve disease management.

53. On-Axis Acoustic Radiation Force-based Quantitative Elasticity in Phantoms

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Shear wave elasticity imaging (SWEI) derives shear modulus from shear wave displacements arriving at locations lateral to the acoustic radiation force (ARF). Instead, we measure displacement of tissue directly along the ARF axis which can simplify hardware required for quantifying tissue stiffness. We measure the time-to-peak displacement and use a look-up table to quantify stiffness based on finite element method (FEM) and Field-II simulations of the ARF and transducer pushing and tracking configurations. Previously this method had too high of a displacement estimate variance for practical feasibility. To reduce displacement estimate error and achieve more accurate stiffness estimation, we apply our Bayesian displacement estimator and compare it to normalized cross-correlation (NCC). This method is tested in 20 experimental simulations and 15 tissue-mimicking phantoms. Near the focal depth, the 2 kPa simulations had a root mean square (RMS) error of 0.21 kPa using the Bayesian displacement estimator and 0.32 kPa using NCC. Using a lateral time-of-flight-based shear wave speed and converting to shear modulus, the 15 phantoms had a mean shear modulus of 2.07 kPa and a standard deviation of 0.12 kPa. The error in the phantoms was computed between the shear wave speed-derived estimates and the on-axis estimates. The phantoms had the lowest error at a depth of 5.45 cm with RMS errors of 0.32 kPa for the Bayesian displacement estimator and 0.88 kPa for NCC. The results show we can apply a simulated look-up table to real experimental data and produce stiffness estimates comparable to laterally offset shear wave methods.

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

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