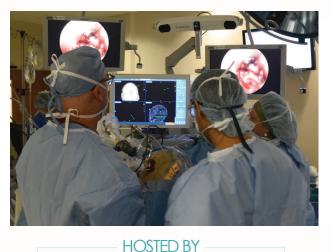
#### VANDERBILT INITIATIVE IN SURGERY AND ENGINEERING

Department of Surgery Research Collaborative

# **Surgery & Engineering** SYMPOSIUM & POSTER SESSION

December 12 • 3-5 p.m. 202 Light Hall • North Atrium





VANDERBILT INITIATIVE IN SURGERY AND ENGINEERING Rese

Department of Surgery Research Collaborative

### Dr. Reed Omary Symposium Keynote Speaker

Reed A. Omary, MD, MS, is the Carol D. & Henry P. Pendergrass Professor and Chairman of the Vanderbilt University Department of Radiology and Radiological Sciences. Dr. Omary is a translational physician-scientist who is active in education, patient care, research, and administration.



His clinical practice in interventional radiology is focused on imageguided therapies for hepatocellular carcinoma (HCC). Dr. Omary's major interests include the use of MRI to guide and functionally monitor catheter-based drug delivery. Dr. Omary has clinically translated these techniques using an innovative combined magnetic resonance imaging—x-ray digital subtraction angiography unit.

Dr. Omary is principal investigator (PI) on two separate NIH RO1 grants (one clinical, one pre-clinical) aiming to improve therapies for HCC. He has previously served as PI or co-PI on NIH, RSNA, and SIR training grants. His trainees at the medical student, graduate student, resident, and junior faculty levels have been awarded 32 national and 17 local research prizes. A Fellow in the Society of Interventional Radiology (SIR), Dr. Omary served as Chair of the SIR Foundation Grant Review Study Section from 2007-2011. He is a full member of the NIH Medical Imaging (MEDI) study section, and has participated in numerous other NIH grant review panels.

Dr. Omary has 10 patents pending in the areas of image-guided therapies and, with his research partner, runs one of the most active VX2 rabbit tumor laboratories in the world. In 2011, Dr. Omary co-founded Interventional Oncology Research and Development, LLC, a preclinical contract research organization that specializes in interventional oncology.

### Registrants

Elizabeth Adolph Hanbing An Andrea Bajo Ramya Balachandran Dan Beauchamp Marco Beccani Nicole Behnke Charreau Bell Barbara Blackford Steve Boronyak Trevor Bruns Jason Castellanos **Charles Coffey** David Comber Rebekah Conley Ryan Datteri Benoit Dawant Natasha Deane Michael DeLisi Neal Dillon Christian DiNatali Edwin Donnelly Katelyn Flint **Catherine Frame** Tanner Freeman Jean-Nicolas Gallant Robert Galloway Pooja Gaur Barbara Gibson Hunter Gilbert Todd Giorgio Jenna Gorlewicz William Grissom **Richard Hendrick** Duke Herrell

Jarod Hershberger Kate Hisev Karen Joos Imad Khan Mary Ellen Koran Krystian Kozek Louis Kratchman Ankur Kumar Robert Labadie Bennett Landman Ray Lathrop Yuan Liu M. Ahammed Machingal Michael Miga Victoria Morgan Nagaraj Nagathihalli Joseph Neimat Alan Nelson Erika Nelums T. Quyen Nguyen Jack Noble Srivatsan Pallavaram Manik Paul Virginia Pensabene **Thomas Pheiffer** Jason Pile Fitsum Reda William Riddle Lisa Robins **Diane Rohrer** Bernard Rousseau Kevin Sexton Jin Shen Jana Shirey-Rice **Robert Singer** 

Melissa Skala Byron Smith Suseela Somarajan Kay Sun Philip Swaney Robyn Tamboli Manish Tripathi Pietro Valdastri Robert Webster Thomas Withrow Yifei Wu Haoran Yu

#### 36. Wireless Tissue Palpation: Proof of Concept for a Single Degree of Freedom

Marco Beccani, Christian Di Natali, Mark E. Rentschler, Pietro Valdastri; Department of Mechanical Engineering, University of Colorado, Boulder, S. Duke Herrell Vanderbilt University Medical Center, Department of Urologic Surgery

Minimally invasive surgery (MIS) is today a widely accepted practice with a less postoperative pain, recovery time, and smaller incisions if compared to open surgery. However, unlike open surgery, during MIS the surgeon has few chances to leverage on tactile and kinesthetic feedback. So far, research toward restoring tactile and kinesthetic sensations in MIS has focused on the distal sensing element or on the proximal rendering of haptic cues. In this work, we present a pilot study to assess the feasibility of wireless tissue palpation, where a magnetic device is deployed through a standard surgical trocar and operated to perform tissue palpation without requiring a dedicated entry port. The setup consists of a wireless intra-body device and an external robotic manipulator holding a load cell and a permanent magnet. Embedded in the wireless cylindrical device (12.7 mm in diameter and 27.5 mm in height) is a sensing module, a wireless microcontroller, a battery, an accelerometer, and a permanent magnet. This platform achieved a precision in reconstructing the indentation depth, based on magnetic field measurements, of 0.1 mm. Experimental trials demonstrated the effectiveness of wireless vertical indentation in detecting the elastic modulus of three different silicone tissue simulators (elastic modulus ranging from 50 kPa to 93 kPa), showing a maximum relative error below 3%. This innovative approach to tissue palpation has the potential to open a new paradigm in the field of intraoperative palpation devices, where no mechanical link between the external platform and the target region is required anymore.



The Vanderbilt Initiative in Surgery and Engineering (ViSE) is a transinstitutional center that promotes the creation, development, implementation, clinical evaluation and commercialization of methods, devices, algorithms, and systems designed to facilitate interventional processes and their outcome. It 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.

Initiatives supported by ViSE include financial support for interdisciplinary seed projects, financial support and technical assistance with the rapid-prototyping of small devices, and the organization of a seminar series held bi-weekly. This first Symposium in Surgery 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.

### Department of Surgery Research Collaborative

The Department of Surgery Research Collaborative was developed to provide synergy between the basic sciences and clinical research as a means of enhancing research opportunities within the Section of Surgical Sciences. The Collaborative hosts research conferences with a reception on the second Tuesday of every month in the Hermitage Room at the University Club from 5:00 – 6:30 p.m., offering opportunities for informal discussion and presentations from basic sciences and translational research. Conferences and the reception are open to the Vanderbilt community and listings of upcoming events can be found under the Research tab of the Department of Surgery website (<u>http://www.mc.vanderbilt.edu/root/vumc.php?</u> <u>site=deptsurg&doc=32554</u>).

Upcoming talks for Spring 2013 include presentations by Claudia Andl, PhD on the role of E-cadherin and TGF-beta signaling in esophageal cancer (January 8), Dan Beauchamp, MD on Smad4 signaling in colon cancer (March 12) and Ki Taek Nam, PhD on gastric cancer (April 9).

#### **Biomedical Modeling Laboratory**

PI: Michael I. Miga, Biomedical Engineering, Radiology & Radiological Sciences, and Neurological Surgery

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. This involves not only the resolution of large scale systems of equations but also the integration of computations within measurement and software pipelines. With respect to the rapeutic applications, efforts in deformation correction for image-guided surgery applications in brain, liver, breast, and kidney are being investigated. Other applications in deep brain stimulation, neoadjuvant chemotherapy, and convective chemotherapy are also being investigated. With respect to diagnostic imaging, applications in biomechanics, elastography, and strain imaging are also of particular interest. All work involves both pre-clinical and clinical models. 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 direct therapy or characterizing tissue changes in an active way.

The laboratory has: numerous computational platforms to include parallel processing, telepresence capabilities, two 3D topographical laser range scanners with integrated tracking, Northern Digital OPTOTRAK Certus and 2 Hybrid Polaris Spectra Cameras for optical tracking, a Siemens Antares Ultrasound system with the Ultrasound Research Interface and Elasticity Imaging Module with the VFX9-4 sector array, and the PX4-1 linear array transducer, a state-of-the-art material tester for soft tissue mechanics (Enduratec ELF 3100), and numerical software libraries that contain sparse matrix solvers, mesh generation routines, many soft-tissue models, visualization libraries, 3D data rendering capabilities, and medical imaging software (AnalyzeAVW-Biomedical Imaging Resource).

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### **Submitted Abstracts**

location on the video stream was displayed with a crosshair to aid in navigation. The surgeon was able to correctly identify the target by color, with an approximate intervention time of 20 minutes for the first three pigs and 3 minutes for the last three.

#### <u>35. Use of Probabilistic Efficacy and Adverse-Effect Maps of Stimulation Response</u> for Deep Brain Stimulation Programming Assistance in Essential Tremor

Srivatsan Pallavaram, Fenna T. Phibbs, Pierre-Francois D'Haese, Joseph S. Neimat, Peter E. Konrad, Benoit M. Dawant, Thomas L. Davis Electrical Engineering & Computer Science, Neurosurgery, Neurology Background: Post-operative neurological management of DBS patients is a complex and dynamic process aiming at alleviating symptoms while avoiding adverse effects. In clinical practice, identifying the optimal contact to achieve this goal can be a challenging and time-consuming process. Anatomy-driven approaches have their limitations due to lack of consensus on the location of optimal targets. Methods: Stimulation response observations recorded in a population of essential tremor patients were mapped onto individual Vim-DBS patients using non-linear image normalization to build probability maps of efficacy and paresthesia. For all cases, the neurologist first identified the clinically optimal contact based on symptom assessment while being blinded to the maps. They then selected the optimal contacts based on the probability maps overlaid on the MRIs, while being blinded to their clinical selections. The contacts selected based on the maps and those chosen clinically were compared.

Results: The map-based selections matched with clinical selections in all cases that had been programmed using a single contact. In 90% of cases, at least one of the clinically selected contacts matched with the map-based selection. In all cases when the efficacy map recommended multiple contacts, the paresthesia map helped break the tie.

Conclusions: Our results show the potential clinical utility of probability maps of stimulation responses tailored to individual subjects for post-operative programming. Using functional data our method provides an approach to circumvent the limitations of existing anatomical-driven methods.

#### 33. Towards Experimental Validation of MR-ARFI Aberration Tomography

William A Grissom, Elena Kaye, Alexander Volovick, Kim Butts Pauly, Yuval Zur, Desmond Yeo, Yoav Medan, Cynthia Davis, Ted L Anderson; Biomedical Engineering and Obstetrics and Gynecology

Background and Motivation: Phase aberrations and attenuations caused by bone can prevent the application of high-intensity focused ultrasound (HIFU) surgery in the brain. Using MR acoustic radiation force imaging (MR-ARFI), the HIFU field can be refocused by measuring the relative tissue displacement that each transducer element produces. We recently presented an autofocusing method called MR-ARFI Aberration Tomography, which uses the entire MR-ARFI image to determine the aberrations, dramatically reducing the number of image acquisitions required compared to other methods that use only the voxel at the center of the focus, and enabling autofocusing in a clinically-feasible time. Here we present progress towards experimentally validating our method, in the form of simulations using MR-ARFI-measured HIFU pressure fields of a brain transducer.

Methods and Results: To validate MR-ARFI Aberration Tomography, the pressure fields of a 4-element brain HIFU transducer were measured in a 1.5 T MRI scanner. Random phases were applied to the measured fields, and simulated aberrated MR-ARFI measurements were synthesized both for MR-ARFI Aberration Tomography (1 measurement) and a Conjugate Green's method (13 measurements). The two methods were then applied to refocus the array. Both methods refocused the array, but MR-ARFI Aberration Tomography enabled refocusing to within machine error, and required only one MR-ARFI acquisition, while 13 were required for the Conjugate Green's method.

#### 34. Transorbital Target

Michael P. DeLisi, Louise A. Mawn, Robert L. Galloway Biomedical Engineering, Ophthalmology, Neurological Surgery

Current pharmacological therapies for the treatment of chronic optic neuropathies such as glaucoma are often inadequate due to their inability to directly affect the optic nerve and prevent neuron death. While drugs that target the neurons have been developed, existing methods of administration are not capable of delivering an effective dose of medication along the entire length of the nerve. We have developed an image-guided system that utilizes a magnetically tracked flexible endoscope to navigate to the back of the eye and administer therapy directly to the optic nerve. We demonstrate the capabilities of this system with a series of targeted surgical interventions in the orbits of live pigs. Target objects consisted of NMR microspherical bulbs with a volume of 18 µL filled with either water or diluted gadoliniumbased contrast, and prepared with either the presence or absence of a visible coloring agent. A total of 6 pigs were placed under general anesthesia and two microspheres of differing color and contrast content were blindly implanted in the fat tissue of each orbit. The pigs were scanned with T1-weighted MRI, image volumes were registered, and the microsphere containing gadolinium contrast was designated as the target. The surgeon was required to navigate the flexible endoscope to the target and identify it by color. For the last three pigs, a 2D/3D registration was performed such that the target's coordinates in the image volume was noted and its

### **Participating Laboratories**

#### **Biomedical Photonics Laboratories**

PI: Anita Mahadevan-Jansen, Biomedical Engineering

The Biomedical Photonics laboratories are focused on the applications of light in medicine and biology. By bringing together researchers from throughout the University and the Medical Center, Vanderbilt has established an international presence in the field of biomedical photonics. Our researchers develop and implement various optical technologies for diagnosing and treating both physiological and pathological processes in the human body. Ongoing research projects are structured as follows:

Optical Diagnosis- Diagnosis of disease is the most challenging clinical problem as it is important to not only recognize the presence of non-normal conditions but to also differentially diagnose what benign or malignant condition it might be. We use different optical methods (fluorescence, diffuse reflectance, Raman scattering, optical coherence tomography) to diagnose diseases in patients in vivo, in real-time.

Optical Guidance- Optical techniques can be used to differentiate between the target tissue (that needs to be removed) and other tissues as well as used to guide therapy in general and in surgery in particular.

Optical Imaging- This research focuses on the development of optical imaging tools that monitor biological markers such as cellular metabolic rate, molecular expression, blood oxygenation and blood flow.

Optical Stimulation- Our labs have pioneered the application of pulsed infrared lasers for the activation of neural tissues in a damage free, artifact free, and contact free. Based on this discovery, we have numerous ongoing projects that focused on infrared neural stimulation (INS). These projects span from the fundamental discovery of what makes INS work to the clinical translation of this technique in human nerves in vivo.

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#### Computer-Assisted Otologic Surgery lab

PI: Robert F Labadie, Associate Professor of Otolaryngology -Head and Neck Surgery, Associate Professor of Bioengineering

The Computer-Assisted Otologic Surgery lab consists of members with clinical and engineering background from Otolaryngology, Electrical Engineering and Computer Science, and Mechanical Engineering. The aim of the lab is to develop methods and tools to enable and assist in minimally-invasive surgeries. Some of the projects that the group is current working on include minimally-invasive image-guided targeting of ear structures specifically the cochlea, the endolymphatic sac, and the petrous apex, endoscopic visualization of the cochlea, assessment of electrode placement and audiological outcomes in cochlear implant patients, utilization of robots to perform mastoidectomy, and development of bone-attached parallel robots for skullbased surgery.

Equipment available in the lab includes Polaris Spectra (Northern Digital, Waterloo, Ontario, Canada), MicronTracker (Claron Technology Inc, Toronto, Ontario, Canada), a XarTrax steerable laser system (Traxtal, Inc, Toronto, Canada), two robots—a Mitsubishi RV-3S (Mitsubishi Electric & Electronics USA, Inc., Cypress, CA) and a Motoman YR-SV035 (Motoman, Inc., West Carrollton, OH), two surgical stations with electric and pneumatic drills, a rigid endoscope with 1.7 mm diameter explorENT 23-5200 (Gyrus Acmi, Southborough, MA) and a 3 Megapixel USB camera EM310C (BigCatch, Torrance, CA) as well as a video processer unit for micro cameras IntroSpicio 120 (Medigus Ltd., Omer, Israel) and a DVI2USB converter (Epiphan Systems Inc., Ottawa, Ontario, Canada) for digital recordings of video data, surgical microscopes, two CNC milling machines, FARO Gage-Plus measuring system (FARO Technologies, INC., Atlanta, GA), and a xCAT portable fpVCT scanner (Xoran Technologies; Ann Arbor, MI).

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### **Submitted Abstracts**

#### 31. Self-adhesive Patch for Fetal and Obstetrical Surgery

Virginia Pensabene. Britnev Nola Lizama-Manibusan.Todd D. Giorgio. BethAnn Mc Laughlin, Robert Singer, Noel Tulipan, Todd Giorgio; Biomedical Engineering Department, Department of Neurological Surgery, Department of Neurology During the last decade, ultrasonic imaging, fetoscopy and fetal surgery developed and lead to a wide adoption of preventive diagnostic screening techniques and to new therapeutic options for special fetal conditions (e.g. prenatal repair of myelomeningocele). These procedures however caused to an increased incidence of iatrogenic preterm rupture of fetal membranes. There is thus an urgent, unmet need for suturing techniques particularly appropriate for special membranes and for the reduction of invasiveness of surgical fetal procedures. Available solutions limit and delay the clinical introduction of innovative techniques and present a major obstacle to the further development of this field. Therefore, we propose this innovative polymeric and ultrathin patch that works as a suturing method in fetal surgery and in invasive endoscopic \fetoscopic procedures, which can be deployed and fixed by using minimally invasive tools, thus simplifying and reducing the duration of the intervention and favoring protection and regeneration of defects of the spinal tissue of the fetus. The adhesive properties of the patch (a single laver of biocompatible polymer with 100 nm thickness) were evaluated by ex vivo experiments. A dedicated setup allowed to measure the mechanical properties of the membranes in a multi-axial stress state by applying a fluid pressure which mimics the physiological conditions. Performance of the patch for suturing ruptures and holes generated by instruments in prenatal interventions (diameter 1-5 mm) were evaluated. Neurotoxicity studies, performed by preserving explanted rat embryos wrapped in the film, showed viability of neurons & permeability to nutrients and oxygen through the film.

#### 32. Surgeon Specific Automatic Path Planning Algorithm for Deep Brain Stimulation

Yuan Liu, Jack H. Noble, Srivatsan Pallavaram, Joseph S. Neimat, Peter E. Konrad, Pierre-François D'Haese, Ryan D. Datteri, Bennett A. Landman, and Benoit M. Dawant; VU Dept of Electrical Eng. and Comp. Science & VU Dept of Neurosurgery In deep brain stimulation surgeries, stimulating electrodes are placed at specific targets in the deep brain to treat neurological disorders. Reaching these targets safely requires avoiding critical structures in the brain. Meticulous planning is required to find a safe path from the cortical surface to the intended target. Choosing a trajectory automatically is difficult because there is little consensus among neurosurgeons on what is optimal. Our goals are to design a path planning system that is able to learn the preferences of individual surgeons and, eventually, to standardize the surgical approach using this learned information. In this work, we take the first step towards these goals, which is to develop a trajectory planning approach that is able to effectively mimic individual surgeons and is designed such that parameters are used to describe an individual surgeon's preferences. The approach is quantitatively evaluated in experiments that rely on expert assessment of trajectory quality. The overall rating of the computed trajectories was found to be comparable to interexpert performance ratings. Thus, no clear differences between computed and manually selected trajectories were found. These results demonstrate the potential clinical utility of computer-assisted path planning.

#### 29. Raman Spectroscopy to Evaluate Surgical Margin Status in Soft Tissue Sarcoma

*Xiaohong Bi, Zain Gowani, Quyen Nguyen, Isaac Pence, Anita Mahadevan-Jansen, Holt Ginger; Department of Biomedical Engineering; Department of Orthopaedics and Rehabilitation; Department of Medicine* 

Soft tissue sarcomas (STS) are a heterogeneous group of malignant tumors that arise from mesenchymal. Standard treatment for primary STS involves surgical excision of the tumor with a margin of surrounding tissue. The quality of resection margin status has been regarded as an important risk factor for the local recurrence of STS and is related to the curative success of surgical treatment of STS. Current clinical practice employs frozen section pathology as an intraoperative technique to provide a definitive diagnosis of margin status, which prolongs the surgical procedure and can increase the risk of surgical complication. This study explored the feasibility of Raman spectroscopy in evaluating surgical margin of STS. Raman spectra were collected using a portable fiber optic system. Tumor and control samples from 20 patients were tested yielding 44 spectra from tumor and 33 spectra from control muscles. Multivariate statistical analysis classified spectra into tumor and control groups with 100% sensitivity and 100% specificity. These results suggested the potential of Raman spectroscopy in differentiating soft tissue sarcomas and controls, and thus providing a new avenue for intraoperative surgical margin assessment.

#### 30. Segmentation of Abdominal Wall in Ventral Hernia CT

Zhoubing Xu, Wade M. Allen, Benjamin K. Poulose, Bennett A. Landman General Surgery, Electrical Engineering

The treatment of Ventral hernias (VH) has been a challenging problem for medical care. Repair of these hernias is fraught with failure; recurrence rates ranging from 24-43% are reported, even with the use of mesh. While Computed tomographic (CT) scanning is only used to make qualitative clinical judgments, we proposed that image segmentation methods to capture the three-dimensional structure of the abdominal wall would provide a foundation on which to measure geometric properties of hernias and surrounding tissues. In this pilot study with four clinically acquired CT scans, we extracted the bone skeleton with threshold methods for determination of landmarks, segmented the skin and outer abdominal wall with level set methods. A tentative coordinate system was built in terms of the shortest spatial distances to the selected landmarks (two anterior iliac crests and all visible ribs in CT scans). and skin was colored with RGB values converted with normalized distances. For segmentation of outer abdominal wall, we addressed massive segmentation difficulties (noise, artifacts, disruptions, intensity inhomogeneity) with appropriate mathematical morphological operators. All segmentation results were quantitatively validated with surface errors based on manually labeled ground truth on sample points. Surface errors for bones, skin, and outer abdominal wall were 2.24mm±3.28mm, 1.17mm±0.88mm, 1.58mm±1.56mm respectively.

### **Participating Laboratories**

#### Gastrointestinal SQUID Technology (GIST) Laboratory

PI: Alan Bradshaw, General Surgery/Physics & Astronomy

The Vanderbilt Gastrointestinal SQUID Technology (GIST) Laboratory is an interdisciplinary initiative by the Department of Surgery at the Vanderbilt University School of Medicine and by the Departments of Physics and of Biomedical Engineering at Vanderbilt University. The purpose of the GIST Lab is to investigate GI disease through the noninvasive use of a Superconducting Quantum Interference Device (SQUID) magnetometer. A SQUID magnetometer is a highly sensitive hardware device that has the ability to measure the weak magnetic fields of the human GI system without contact to the human body. The goal of the research in our lab is to develop novel noninvasive methods for the diagnosis of various diseases that are very difficult to detect otherwise, such as gastroparesis and intestinal ischemia.

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#### Laryngeal Wound Healing Laboratory

PI: Bernard Rousseau, Otolaryngology (Primary); Hearing and Speech Sciences (Secondary)

Optimal function of the vocal fold lamina propria is essential to human voice production. The lamina propria is an area of connective tissue that is uniquely different from tissues found elsewhere in the body. No other tissue in the body undergoes mechanical forces similar to the vibration that the vocal folds experience during phonation. Our federally funded research program investigates the cellular and molecular events underlying phonotrauma and the identification of unique mechanisms involved in protection of the vocal fold from injury. We are also deeply committed to the understanding of outcomes and the availability of health-related services in the treatment of phonotrauma. Our research efforts are funded by the National Institutes of Health, National Institute on Deafness and Other Communication Disorders and the American Academy of Otolaryngology-Head and Neck Surgery Foundation. Finally, as a necessary and logical next step towards improving treatment outcomes and advancing standard of care, we are moving systematically towards translation, with parallel investigations focusing on outcomes and the role of adherence in the wound-healing milieu.

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#### J.B. Marshall Laboratory

PI: Robert J. Singer, Assistant Professor of Neurological Surgery, Assistant Professor of Radiology

The J.B. Marshall Laboratory is interested in translating basic science research into the development of novel endovascular therapeutics for stroke, subarachnoid hemorrhage, CNS tumors, and functional CNS disease. Recent developments in endovascular surgery allow for an unprecedented level of access to the brain in the acute setting. In the operating room, members of the J.B Marshall Laboratory navigate catheters into the neurovasculature and deliver therapies directly to the site of disease. The lab's clinical research aims to optimize existing treatments and uncover biomarkers of disease. Preclinical research in the J.B. Marshall Lab focuses on vetting new pharmaceuticals to be used in human patients. To this end, the lab's research is geared towards developing and utilizing animal models for stroke and subarachnoid hemorrhage to uncover potential therapeutic targets.

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

PI: Bennett Landman, Electrical Engineering, Computer Science, Biomedical Engineering, Radiology, Institute of Image Science

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

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within the operating microscope environment, adds a beneficial diagnostic dimension to image guided surgery (IGS) systems in neurosurgery. An optically tracked laser range scanner (LRS) furnishes 3D coordinates of the cortical surface, as a 3D point cloud, in the surgical field of view and has been a vital component of intraoperative data acquisition for brain shift correction. However, integration of the LRS acquired data into a clinically acceptable IGS system has been limited because of acquisition time and disruption to the surgical workflow. The feature-rich stereo surgical video data provided by the operating microscope is the alternative to the LRS. The accuracy of 3D point clouds extracted from the stereo video system and the LRS for phantom objects are compared for a better understanding of the tradeoffs involved in using either as an input to an IGS system.

#### 28. Pose Estimation for Robotically Controlled Magnetic Endoscope Teleoperation

Charreau S. Bell, Keith Obstein, Pietro Valdastri

Mechanical Engineering, Gastroenterology

Commercial entities in the field of gastrointestinal endoscopy are moving toward magnetically manipulated endoscopes. Position and orientation (pose) estimation are limiting factors toward the development of a real-time, closed-loop system as current pose estimation systems have components incompatible with magnetically actuated systems. The novel pose estimation system we propose utilizes a multi-layer feed-forward artificial neural network (NN) to learn the relationship between the optical flow and change in pose of the endoscope in sequential endoscopic images. To enhance feature extraction, narrow band imaging (NBI) is applied and compared with standard white light illumination. Two spatial partitions, lumen-centered and grid-based, createthe NN input. The NN pose predictions were compared to a state-of-the-art magnetic tracker.

NBI combined with lumen-centered partitioning was superior to the NNs using white light illumination or grid-based partitioning. When comparing the NN performance to that of the magnetic tracker, the average accuracy was comparable for positional degrees of freedom (DOF) (0.5 mm $\pm$ 2.8 mm v. 0.1 mm $\pm$ 2.5 mm) and for rotational DOF (0.12° $\pm$ 1.28° v. 0.14° $\pm$ 0.86°).

Our novel system successfully identified the pose of the endoscope with no significant difference compared to the reference magnetic tracker. NBI, combined with feature partitioning based on mucosal patterns within the colon, provided a mechanism for endoscopic camera pose estimation through streaming images. This novel approach takes advantage of commercially available components and can be used for real-time closed-loop control. Our method represents a first step toward enabling technology to redefine endoscopy. In-vivo animal studies focused on validating the method are in progress.

#### 25. Optical Metabolic Imaging Identifies Early Treatment Response in Breast Cancer

Alex J Walsh, Rebecca S Cook, H. Charles Manning, Donna J Hicks, Alex Lafontant, Carlos Arteaga, and Melissa C. Skala; Biomedical Engineering, Cancer Biology Abnormal cellular metabolism is a hallmark of many diseases, yet there is an absence of quantitative methods to dynamically image this powerful cellular function. Optical metabolic imaging (OMI) is a non-invasive, high-resolution, quantitative tool for monitoring cellular metabolism. Here, we confirm that OMI is sensitive to cellular glycolytic levels. Additionally, OMI resolves differences in the basal metabolic activity of untransformed from malignant breast cells, and between breast cancer sub-types, including triple-negative, estrogen receptor positive, and human epidermal growth factor receptor 2 (HER2)-amplified. In vivo OMI is sensitive to metabolic changes induced by clinically-relevant HER2 inhibition with trastuzumab in responsive, but not resistant, xenografts within 48 hours of treatment, a time point preceding any other reported in vivo marker of trastuzumab response. Changes in FDG-PET uptake are not apparent until 12 days of treatment. This attractive suite of metabolic imaging tools has significant implications for rapid assessment of metabolic response to molecular expression and drug action at the cellular level, which would greatly accelerate drug development studies.

# 26. Optimizing the Delivery of Deep Brain Stimulation Using Electrophysiological Atlases and an Inverse Modeling Approach

Kay Sun, Srivatsan Pallavaram, William Rodriguez, Pierre-Francois D'Haese, Benoit M. Dawant, Michael I. Miga; Biomedical Engineering, Electrical Engineering and Computer Science

The use of deep brain stimulation (DBS) for the treatment of neurological movement degenerative disorders requires the precise placement of the stimulating electrode and the determination of optimal stimulation parameters that maximize symptom relief (e.g. tremor, rigidity, movement difficulties, etc.) while minimizing undesired physiological side-effects. This study demonstrates the feasibility of determining the ideal electrode placement and stimulation current amplitude by performing a patient-specific multivariate optimization using electrophysiological atlases and a bioelectric finite element model of the brain. Using one clinical case as a preliminary test, the optimization routine is able to find the most efficacious electrode location while avoiding the high side-effect regions. Future work involves optimization validation clinically and improvement to the accuracy of the model.

#### 27. Phantom-based Accuracy Comparison of 3D Point Clouds Extracted from Stereo Cameras and Laser Range Scanner

#### Ankur N. Kumar, Reid C. Thompson, Michael I. Miga, and Benoit M. Dawant; Electrical Engineering, Biomedical Engineering, Neurosurgery

The intraoperative surgical microscope used in neurosurgery can deliver pertinent and temporally dense intraoperative information in the form of stereo video. This acquired video is cost-effective, undemanding of the surgical team, does not cause disruptions in the surgical workflow, and motivates its use in craniotomy applications. The ability to intraoperatively digitize the cortical surface in real-time and track surgical instruments' tip registered to preoperative images of the patient,

### **Participating Laboratories**

#### Medical & Electromechanical Design (MED) Laboratory

PI: Robert J. Webster III, Mechanical Engineering, Otolaryngology

The Vanderbilt School of Engineering's Medical & Electromechanical Design (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 GI tract.

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#### Medical Image Processing (MIP) Laboratory

PI: Benoit Dawant, Electrical Engineering and Computer Science, Biomedical Engineering, Radiology and Radiological Sciences

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 to treat Parkinson's disease, (3) localize critical structures 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 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 other collaborative institutions.

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#### **Omary Laboratory**

PI: Reed Omary, Department of Radiology and Radiological Sciences

Dr. Omary's lab group currently resides at Northwestern University. The lab has a very active pre-clinical program to test local drug delivery therapies in the following animal models of liver cancer: VX2 rabbits; N1-S1 rats; and McA-RH7777 rats. The group also runs a tumor biology lab for cell culture and HPLC analysis, and a materials science lab that develops nanoparticles as drug delivery vehicles for cancer. Imaging capabilities includes x-ray digital subtraction angiography and MRI. Drug delivery strategies occur via catheter based routes, systemic administration, and/or needle injections. Through collaboration and future recruitment, the goal is to transition these capabilities to Vanderbilt.

Contact: Robbie Luckett, (615) 343-1187

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

PI: Pietro Valdastri, Mechanical Engineering

The Science and Technology for Robotics in Medicine (STORM) Lab research is focused on the design and creation of mechatronic and self-contained devices to be used inside specific districts of the human body to detect and cure diseases in a non-invasive way. STORM Lab strongest expertise lies in the remote and real-time teleoperation of magnetic capsule robots for gastrointestinal endoscopy and abdominal surgery. The STORM Lab, in collaboration with the MED Lab and ISIS, has been recently awarded with a NSF-CPS Medium Grant to create a focused cyber-physical design environment to accelerate the development of miniature medical devices in general and capsule-like systems in particular. The project will develop new models and tools including a web-based integrated simulation environment, capturing the interacting dynamics of the computational and physical components of devices designed to work inside the human body, to enable wider design space exploration, and, ultimately, to lower the barriers which have thus far impeded system engineering of miniature medical devices.

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### **Submitted Abstracts**

#### 23. Novel Endovascular Therapeutics for Blood-Brain Barrier Modulation in Acute Ischemic Stroke – An Animal Model

*Imad Saeed Khan, M.D., Mitchell Odom, Moneeb Ehtesham, M.D., Brandon Davis, M.D. Ph.D., Daniel Colvin, Ph.D., Robert J. Singer, M.D.; Department of Neurosurgery and VU Institute of Imaging Sciences* 

The blood-brain-barrier (BBB) is a system of tight-junctions between endothelial cells protecting the brain environment from harmful exogenous agents. Acute ischemic stroke can lead to disruption of the BBB and increased damage to the brain parenchyma. We aimed to develop a rat stroke model to study the effects of various intra-arterial neurotherapeutic agents on the modulation of the BBB after an episode of ischemic stroke and subsequent reperfusion.

Animal Model: Twelve week old spontaneously hypertensive rats (SHR) are subjected to middle cerebral occlusion via the intraluminal suture method. Briefly, a neck cut-down is carried out to expose the common carotid artery. The dissection is continued rostral to expose the length of the external carotid artery (ECA) till the hyoid bone. After cauterizing the superior thyroid and occipital branches of the ECA, a small arteriotomy is made to allow the insertion of a silicon-tipped intraluminal suture. The suture is routed into the internal carotid artery and advanced till it blocks the middle cerebral artery. The rats can then be subjected to ischemia for a variable amount of time before the suture is removed. Once reperfusion is established, the external carotid artery can be used to directly infuse pharmacologic agents into the recovering brain.

Conclusion: BBB disruption caused by stroke can lead to severe neurological injury in patients. We describe a rat stroke model that can used to study the effects of various intra-arterially administered drugs on the modulation of the BBB. Intraarterial therapy mimics the effects of endovascular treatment and allows translational stroke research.

#### 24. A Novel Iterative Approach for Accounting for Non-Rigid Deformations in Image-Guided Liver Surgery Using Sparse Surface Data

#### D. Caleb Rucker, Yifei Wu, Thomas S. Pheiffer, Amber L. Simpson, Michael I. Miga Biomedical Engineering

In open abdominal liver surgery, image-guidance systems aim to accurately depict tool locations with respect to the anatomy while maintaining the workflow of the surgical team. Partial surface measurements can be obtained intraoperatively with relatively little impact on the surgical workflow, as opposed to other intraoperative imaging modalities. This data can be used to (1) rigidly register the preoperative CT image volume to physical OR space, and (2) compensate for intraoperative deformation by non-rigid registration based on a tissue-mechanics model of the organ. We present a novel approach for non-rigid registration by iteratively reconstructing the displacement field on the posterior side of the organ in order to optimize the surface fit. Experimental results with a phantom liver show a mean target registration error (TRE) of 4.1 mm in the prediction of 58 locations inside the phantom. This represents a 49% reduction in mean error over rigid registration alone.

# 21. NFAT Regulates a Gene Expression Program Associated with Invasiveness and Poor Prognosis in Colorectal Cancer

Manish K. Tripathi, Shinji Mima, Zhiao Shi, Naresh Prodduturi, Jing Zhu, Connie Weaver, Kristen K. Ciombor, Xi Chen, Natasha G. Deane, R. Daniel Beauchamp, Bing Zhang; Department of Surgery, Department of Cancer Biology, Department of Biomedical Informatics, Vanderbilt Ingram Cancer Center, Hematology/Oncology, Advanced Computing Center for Research & Education

Colorectal cancer is the second leading cause of cancer-related death in the United States. In order to understand the regulatory mechanisms underlying poor prognosis in colorectal cancer, we analyzed fourteen human colorectal cancer microarray data sets and identified co-expressed modules using network analysis. We next filtered these modules using gene expression data from a mouse model of metastatic colon cancer, narrowing down to a candidate metastasis-related module, and identified NFAT as its potential transcriptional regulator. The NFAT family and their identified targets were found to be upregulated in human colorectal cancer patients. Analysis of NFAT family members expression in mouse and human microarray datasets, revealed NFATc1 to be differentially expressed between metastatic and non-metastatic, and between disease progression and no disease progression, respectively. We found that high NFATc1 expression correlated with significantly increased invasion (p<0.0001) and migration (p<0.005) in mouse colon cancer cells. We show that RNAi- based knockdown of NFATc1 and functional inhibition by the calcineurin inhibitor FK506 resulted in downregulation of predicted NFAT target genes from the metastatic module and decreased cancer cell invasiveness. Finally, we showed that the expression of NFAT target genes was significantly correlated with both disease-specific and disease-free survival in Stage II and III colorectal cancer patients. Our studies suggest a role for NFATs in colon cancer cell invasion and a potential application for the NFAT driven program as a biologically anchored prognostic gene expression signature.

#### 22. Noninvasive Biomagnetic Detection of Isolated Ischemic Bowel Segments

Somarajan S, Cassilly S, Obioha C , Bradshaw LA, and Richards WO General Surgery/Physics & Astronomy

We measured slow wave activity in the magnetoenterogram (MENG) of normal porcine subjects (N=5) with segmental intestinal ischemia. We determined the correlation of changes in enteric slow wave activity measured in MENG and serosal electromyograms (EMG). MENG recordings show significant changes in the frequency and power distribution of enteric slow wave signals during segmental ischemia, and these changes agree with changes observed in the serosal EMG. There was a high degree of correlation between the frequency of the electrical activity recorded in MENG and in serosal EMG (r = 0.97). The percentage of power distributed in bradyand normoenteric frequency ranges exhibited significant segmental ischemic changes. Our results suggest that noninvasive MENG detects ischemic changes in isolated small bowel segments.

### **Participating Laboratories**

#### Surgical Navigation Apparatus Research Lab (SNARL)

PI: Robert Galloway, Biomedical Engineering, Neurosurgery, Surgery

The Surgical Navigation Apparatus Research Lab (SNARL) develops guidance systems for the delivery of therapy: surgery, ablation or direct injection chemotherapy. We work in areas of surgical devices, system integration, software delivery, therapeutic visualization and image-space/physical-space registration. While the systems are developed in the SNARL space and tested on anthropomorphic phantoms, we progress to animal experimentation in the section of surgical sciences and ultimately deliver to the operating room or procedure rooms requiring particular attention to, and design for we pay attention to, and design for, workflow in those rooms.

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#### Urologic surgery & Cancer Research Laboratory

PI: Robert Matusik, Prostate Cancer Center

Urologic surgery & Cancer Research Laboratory is in unit of Prostate Cancer Center where Dr. Matusik serves as director with a team of several Research Assistant professors, Post. doctoral fellow and technical staff. My personal description of work is mainly Histology including processing, embadding, sectioning and staining mainly H&E. In addition acquiring patient samples from Surgical Pathology mainly blood & urine. I am also responsible for scheduling seminars & journal clubs for our unit and collaborating departments including Meharry Medical College.

Contact: manik.paul@vanderbilt.edu

#### Vanderbilt University Institute of Imaging Science (VUIIS)

PI: William A Grissom, Biomedical Engineering and Radiology

VUIIS is interested in developing novel magnetic resonance imaging techniques for guiding interventions. Our current development focus is MR guidance of high-intensity focused ultrasound (HIFU) surgery, including temperature imaging, closed-loop control methods, autofocusing methods, and assessment of treatment. Clinical HIFU applications of interest include ablation of uterine fibroids and adenomyosis, bone metasteses, and brain tumors, as well as drug delivery by mild targeted hyperthermia.

#### 1. Automatic Segmentation of the Labyrinth in CT

*Fitsum A. Reda, Benoit M. Dawant, Theodore R. McRackan, Robert F. Labadie, and Jack H. Noble; Electrical Engineering & Computer Science; Otolaryngology–Head and Neck Surgery* 

Many otologic procedures would benefit from automatic segmentation of the labyrinth for planning and guidance. In this poster we will present an active shape model (ASM)-based automatic method we have developed for segmenting the labyrinth in CT. To build the ASM, first, the labyrinth surface was manually segmented by an expert in a reference volume and 17 training volumes. Next, the training surfaces are registered to the reference surface. Finally, eigenanalysis is used to build the ASM of the labyrinth according to the procedure described by Cootes et al. in 1995. To locate the labyrinth in a new target image, first, an initial segmentation is generated by projecting the labyrinth model from the reference volume onto the target image through the non-rigid registration transformation that registers the two images. Next, the segmentation is refined using an iterative search. In each iteration, a new candidate location is found for each point in the model and the ASM is fitted to those candidate points. This process is iterated until convergence is reached, which finalizes the segmentation. Using a leave-one-out approach, we validated our system by comparing automatic segmentations of the 17 training CT scans to manually delineated segmentations, which are used as a ground truth. We found that our approach results in overall mean and maximum errors of 0.24 and 1.82 mm, respectively. These results suggest that our automatic labyrinth segmentation approach is accurate enough for use in many important otologic applications.

#### 2. Bench-Top Reaction of Sodium Bicarbonate and Citric Acid for Insufflation of Gastrointestinal Tract

Brian Fang, Byron Smith, Charreau S. Bell, Jason Gerding, Pietro Valdastri, Keith Obstein STORM Lab, Mechanical Engineering, VUSE, & Div Gastroenterology, VUMC Medical use of capsule endoscopy has become much more prevalent in the past years, but there are still obstacles that hold this technology from reaching its full potential. One such obstacle is the need for dependable and safe method of insufflation. The CO2 producing reaction between sodium bicarbonate and citric acid was found to be the most effective method for insufflation because this reaction produces the most CO2 without any heat released or toxic byproducts and within a relatively short time period. A bench-top test of the gas production for the reaction was conducted to determine the temperature change caused by the reaction, the time taken for the reaction to reach completion, and the volume of CO2 produced. One milliliter of powdered sodium bicarbonate and one milliliter of powdered citric acid was reacted with two milliliters of deionized water in a flask. Eleven trials were conducted. Six of the eleven trials showed the temperature of the air inside the flask decreasing initially, suggesting that the reaction is endothermic. Four of the trials showed the temperature remaining constant. Only one trial showed the temperature increasing steadily throughout the whole reaction. The results show that the reaction will be endothermic and, therefore, will be safe for medical use. The average time for the reaction to reach completion was nine minutes. The average volume of CO2 produced was 510 mL.

### **Submitted Abstracts**

#### 19. Minimally-Invasive Image-Guided Cochlear Implantation

Ramya Balachandran, Jack H Noble, Grégoire Blachon, Jason E Mitchell, Fitsum Reda, Benoit M Dawant, J Michael Fitzpatrick, Robert F Labadie; Otolaryngology, Electrical Engineering and Computer Science, Mechanical Engineering Cochlear implantation is a surgical procedure for treatment of patients with sensorineural hearing loss. The traditional surgical procedure involves invasively drilling out a major portion of the bone behind the ear to expose anatomic structures and achieve access to the cochlea followed by insertion of an electrode array into the cochlea to simulate the auditory nerve. A minimally-invasive surgical (MIS) technique has been proposed to reduce the invasiveness and time of the surgery and post-surgery recovery. This MIS technique involves drilling a linear path from the lateral skull to the cochlea avoiding damage to vital anatomy such as the facial nerve. To implement this technique, we have developed custom software that processes preoperative CT images of patients to automatically identify the pertinent anatomy and compute a safe linear path and custom microstereotactic frame that can be fabricated in five minutes, mounts on bone-implanted markers, and constraints the drill to the desired path. Following preoperative path planning, the current intraoperative workflow involves implanting three markers in the mastoid bone surrounding the ear, acquiring intraoperative CT scan, intraoperative path planning, designing and fabricating a custom microstereotactic frame, sterilizing the frame, mounting the frame on the bone-implanted markers and drilling the tunnel to the cochlea, performing the cochleostomy, and inserting the electrode array through the drilled tunnel into the cochlea. We present the results of the in vivo validation and preliminary implementation studies of this MIS technique.

#### 20. Monitoring Surgical Resection of Tumors with Ultrasound Strain Imaging

#### Thomas S. Pheiffer, Brett C. Byram, Michael I. Miga. Biomedical Engineering Biomedical Engineering

Resection of tumors is often performed by the surgeon using tactile sensory information to distinguish between normal and abnormal tissue. Ultrasound strain imaging has potential to supplement conventional guidance methods with quantitative information about tissue stiffness at depth. It has been suggested that strain imaging may be capable of distinguishing tumor from normal tissue during surgery. With respect to diagnostic lesion inspection, localization with strain imaging of a potential surgical target is well understood. In this work, we assess the efficacy of this modality to monitor resection via two phantom experiments. In the first, a surgical procedure was simulated by resecting a phantom tumor in several stages. At each stage, the tumor remnant was imaged with ultrasound strain imaging. This experiment showed that strain imaging could successfully localize a tumor remnant during surgical conditions. In the second experiment, the resection simulation was repeated with the addition of CT imaging of the phantom at each stage of resection. and all ultrasound data was tracked with an optical tracking system and registered to the CT volumes. The tracked ultrasound data validated the spatial correspondence between the strain image lesion and CT lesions. There was consistent misalignment on the order of several millimeters between the strain and CT tumor borders due to compression of the tissue by the probe, to be addressed in future work.

#### 17. The Insertable Robotic Effector Platform for Single Port Access Surgery

Nabil Simaan, Andrea Bajo, Long Wang; Mechanical Engineering

Single Port Access Surgery is driven by the potential for additional patient benefits due to reduction of the number of access incisions to only one (or to no incisions when using a natural orifice). These potential benefits include improved cosmesis. reduced risk of incisional hernia and wound site infection, and reduced pain compared to open surgery or laparoscopic minimally invasive surgery. To validate these patient benefits, new technologies are needed to address the technical demands of SPAS. As an effort towards achieving this goal, our team developed the Insertable Robotic Effector Platform (IREP). The IREP, is the smallest system for SPAS requiring an access port of only *Æ*15 mm while offering dual arm dexterous operation with sub-millimeter accuracy, 3D visualization, and automated instrument tracking. The total number of actuated Degrees-of-Freedom (DoF) of the IREP is 21. We carried out preliminary ex-vivo tests to evaluate the tele-manipulation framework of the IREP. For evaluation, we used two tasks of the Fundamentals of Laparoscopic Surgery (FLS) Manual Skills testing component (Peg Transfer and Simple Suture with Intracorporeal Knot). In addition, vision tracking algorithms, repeatability, and micromanipulation capabilities were also tested. Our results demonstrate telemanipulation accuracy of better than 0.3 mm when high zoom visualization is used and better than 0.5 mm when using its stereo-vision module. Results also pointed out the need to increase the workspace of the roll wrist used for passing circular sutures. These results inform our ongoing redesign of system components in preparation for future in-vivo animal testing.

#### 18. Intraoperative Digitization with a Handheld Optically Tracked Laser Device

A. L. Simpson, Y. Wu, J. Burgner, T. S. Pheiffer, D. C. Rucker, K. Sun, W. R. Jarnagin, R. C. Thompson, R. J. Webster III, and M. I. Miga; Biomedical Engineering, Mechanical Engineering, Surgery

Intraoperative organ deformation compromises the accuracy of image-guided interventions if not corrected by either intraoperative imaging or computational modeling. The latter requires intraoperative sparse measurements for constraining and driving model-based compensation strategies. Conoscopic holography, an interferometric technique that measures the distance of a laser light illuminated surface point from a fixed laser source, was recently proposed for non-contact surface data acquisition in image-guided surgery and is used here for organ surface digitization and validation of our modeling strategies. In this contribution, we describe our recent research endeavors with the device which represents a collaborative project with researchers at Vanderbilt University in biomedical and mechanical engineering and with clinical collaborators in liver surgery at Memorial Sloan Kettering Cancer Center and in neurosurgery at VUMC. The results of our work indicate that conoscopic holography is a promising method for surface acquisition since it requires no contact with delicate tissues and can characterize the extents of structures within confined spaces. We demonstrate that for two clinical cases, the acquired conoprobe points align with our model-updated images better than the uncorrected ones lending further evidence that computation modeling approaches improve the accuracy of image-guided surgical interventions in presence of soft tissue deformations.

### **Submitted Abstracts**

# 3. Biomechanical Effects of Radiofrequency Ablation with Simultaneous Cryogenic Anchoring

Steven M. Boronvak and W. David Merryman: Biomedical Engineering The increased surface area of mitral valve (MV) leaflets with myxomatous disease leads to mitral regurgitation (MR), hence there is a need for treatment options that avoid open-chest surgery. Radiofrequency (RF) ablation uses resistive heating to reduce leaflet size via collagen contracture. One challenge of using RF ablation to percutaneously treat myxomatous MV leaflets is maintaining contact between the RF electrode on the catheter tip and a functioning MV leaflet. To meet this challenge, we have developed an RF ablation catheter with a cryogenic anchor for stable attachment to MV leaflets to accurately and reliably apply RF energy. The results from biaxial mechanical testing indicate that while cryo-anchoring reduces the effect of RF ablation, this can be mitigated by increasing RF energy output in order to induce the same geometric and biomechanical changes in MV leaflets. IR imaging indicates that RF ablation and cryo-anchoring can function in close proximity, on the same MV leaflet. A percutaneous catheter using RF ablation combined with cryoanchoring could represent a possible alternative treatment strategy for MV prolapse by reducing the size of redundant MV leaflets.

# <u>4. Design, Calibration and Preliminary Testing of a Robotic Telemanipulator for OCT guided Retinal Surgery</u>

#### Haoran Yu; Vanderbilt Eye Institute

This research aims to develop a framework for OCT-Guided micro-vascular retinal surgery. We present an experimental system for testing dexterous ocular and intraocular manipulation with real-time OCT guidance. One of our goals is to develop algorithms and technology enabling the use of stents to maintain the structural integrity of artery/vein crossings in the retina. The design of an 11 degree of freedom (DoF) robot that includes a 6 DoF Stewart-Gough platform, a two DoF differential wrist, and a three DoF actuator for deployment of stent and bridge vessel separators is presented as a validated robotic system for ophthalmic microsurgery. The robot also allows for quick exchange of surgical graspers and the integration of a custom made B-mode OCT probe. We present the kinematic modeling and calibration of the robot for demonstration of ocular and intraocular manipulation. The system's telemanipulation framework was constructed and experimental evaluations of stent deployment and membrane peeling are shown with a verification of results using OCT probe images. We believe these preliminary results demonstrate new technology that may enable micro-vascular stenting for treatment of branch retinal vein occlusion while offering a general platform for dexterous retinal surgery.

#### 5. Design Feasibility Study of a Rapidly Deployable CI Robotic Tool

Jason Pile, Ishan Ann Tsay, Claudiu Treaba, James Dalton, Nabil Simaan Mechanical Engineering and Cochlear Ltd.

Our research aims to design and test the feasibility of using a robotic insertion tool for cochlear implant surgery. The robotic tool is designed to insert Contour Advance perimodiolar electrodes into the cochlea at smooth, controlled speeds and to incorporate real-time force data into the control algorithm. To facilitate portability and use scenarios where the device is handheld, the device dimensions were restricted to less than 300 mm in length and 400 grams in weight. Positional accuracy of the device was required to be less than 0.2 mm and force sensing capability with a resolution of better than 0.1 grams was required. Based on characterization of equilibrium shapes of Contour Advance electrodes, insertion plans were optimized to minimize intra-cochlear contact and to mitigate insertion force and trauma. The expected workspace was determined from these insertion trajectories and various mechanism designs were evaluated that could satisfy the requirements for size, weight, and precision. The final design prototyped was a three degree of freedom parallel robot with integrated six axis force sensing. The device easily loads an electrode prior to use and automatically releases the implant after the insertion procedure is complete. It is designed to work with the existing operating workflow and be fully sterilizable. This study has shown the feasibility of a small scale robotic insertion tool for cochlear implant procedures and developed the control and diagnostic algorithms. These algorithms have been tested on a rapidly produced prototype for implementation in our next generation prototype.

#### 6. Design of an Endonasal Graft Placement Tool for Repair of Skull Base Defects

Richard J. Hendrick, Ray A. Lathrop, John S. Schneider, and Robert J. Webster III Mechanical Engineering & Otolaryngology

A novel surgical tool design is presented for placement of grafts during minimally invasive, endonasal surgery to repair skull base defects. Endonasal placement of grafts at the skull base has proven difficult with current tools due to the tight nasal passages, varying graft size and rigidity, and the inability to simultaneously orient the graft and apply force to the graft site. This tool has been designed specifically for skull base graft placement, reliably accepts all graft types, and fills a gap for surgeons who currently struggle placing grafts using tools that are not well-suited for the task. The design utilizes a shelved tube with a Nitinol wire gripping mechanism actuated by the surgeon's hand that allows for simultaneous gripping, orienting, and force application. Preliminary benchtop testing with the prototype indicates this tool will increase surgeon confidence in skull base defect reconstruction quality while decreasing operating time.

### **Submitted Abstracts**

#### 15. Image-Guided Robotic Kidney Surgery

#### *Courtenay Glisson, Peter Clark, S. Duke Herrell, Robert L. Galloway Biomedical Engineering and Urology*

Over the past decade there has been considerable recognition of the importance of preserving renal function through surgical techniques for nephron-sparing (kidney preserving) surgery. Total or radical nephrectomy can result in significant and permanent compromise in renal function and has been associated with significant negative quality of life and increased mortality. In contrast, nephron-sparing surgeries (partial nephrectomy) as well as ablative therapies for both benign and malignant renal processes are associated with improved long-term patient outcomes. However, nephron-sparing surgeries dramatically increase the demands on the surgeon and intraoperative risk: requiring consideration of vascular control, minimization of ischemic damage, precise resection of the diseased kidney volume, and reconstruction of the kidney and collecting system. This proposal encompasses a methodology by which, in either open or minimally invasive surgeries, a surgeon is provided information about his or her proximity to lesion boundaries, blood vessels or sensitive structures such as the kidney collection system. This information is presented in real time, in three dimensions and updates continuously during surgery.

#### 16. Immersive Virtual Reality for Visualization of Abdominal CT

#### *Qiufeng Lin, Zhoubing Xu, Rebeccah Baucom, Benjamin Poulose, Bennett A. Landman, Robert E. Bodenheimer*

#### Computer Science, General Surgery, Electrical Engineering

Immersive virtual environments use a stereoscopic head-mounted display and data glove to create high fidelity virtual experiences in which users can interact with three-dimensional models and perceive relationships at their true scale. This stands in stark contrast to traditional PACS-based infrastructure in which images are viewed as stacks of two-dimensional slices, or, at best, disembodied renderings. Although there has substantial innovation in immersive virtual environments for entertainment and consumer media, these technologies have not been widely applied in clinical applications. Here, we consider potential applications of immersive virtual environments for ventral hernia patients with abdominal computed tomography imaging data. Nearly a half million ventral hernias occur in the United States each year, and hernia repair is the most commonly performed general surgery operation worldwide. A significant problem in these conditions is communicating the urgency, degree of severity, and impact of a hernia (and potential repair) on patient quality of life. Hernias are defined by ruptures in the abdominal wall (i.e., the absence of healthy tissues) rather than a growth (e.g., cancer); therefore, understanding a hernia necessitates understanding the entire abdomen. Our environment allows surgeons and patients to view body scans at scale and interact with these virtual models using a data glove. This visualization and interaction allows users to perceive the relationship between physical structures and medical imaging data. The system provides close integration of PACS-based CT data with immersive virtual environments and creates opportunities to study and optimize interfaces for patient communication, operative planning, and medical education.

# 13. Identification of Small Molecules that Reverse E-cadherin Loss in Carcinoma Cells

Hanbing An, Sydney Stoops, A Scott Pearson, Alex Waterson, Suzanne Brady, Craig Lindsley, and R. Daniel Beauchamp; Surgery, Department of Cancer Biology, Department of Pharmacology, and Vanderbilt Institute of Chemical Biology E-cadherin is the prototype of the large cadherin superfamily, required for the maintenance of epithelial cell adherence junctions. Epithelial tumors often lose Ecadherin partially or completely as they progress toward malignancy. Different mechanisms for inactivating E-cadherin have been identified in human cancers, including mutations, epigenetic and transcriptional silencing, and increased endocytosis and proteolysis. Thus, E-cadherin and their regulators become valuable potential therapeutic targets. To date, no compounds directly targeting E-cadherin restoration have been developed. Here, we report the development and use of a novel high-throughput immunofluorescent screen to discover lead compounds that restore E-cadherin expression in the SW620 colon cancer cells and H520 non-small cell lung cancer cells. Using this screen, we have identified compounds that restore E-cadherin protein at the plasma membrane and reduce cell invasion, but have minimal effect on cell proliferation. These compounds cause an increase in E-cadherin mRNA transcripts and we have narrowed the cis-acting effector site to a 200bp fragment of the proximal E-cadherin promoter. Our ultimate goals are to identify the molecular protein targets of the active compound, to uncover their mechanism of action and to test them as therapeutic agents in colon cancer.

#### 14. Image-guidance Enables New Methods for Customizing Cochlear Implant Stimulation Strategies

#### Jack H. Noble, Robert F. Labadie, René H. Gifford, and Benoit M. Dawant Electrical Engineering & Computer Science, Otolaryngology – Head & Neck Surgery, and Hearing & Speech Sciences

Cochlear implants (CIs) are considered standard of care treatment for severe hearing loss. Cls restore hearing by applying electric potential to neural stimulation sites in the cochlea with an implanted electrode array. Each recipient's CI processor is programmed by an audiologist to determine how it maps the spectrum of detected sound frequencies to the set of electrodes. Over the last 20 years, Cls have become what is arguably the most successful neural prosthesis to date. Despite this success, a significant number of CI recipients experience marginal hearing restoration, and, even among the best performers, restoration to normal fidelity is rare. In this poster, we will present new image processing techniques that can be used to detect, for the first time, the positions of implanted CI electrodes and the nerves they stimulate for individual Cl users. These techniques permit development of new, customized CI processor programming strategies. We present one such strategy that uses this patient-specific spatial information to decrease cross-electrode channel interactions and show that it leads to significant hearing improvement in an experiment conducted with 11 CI recipients. These results indicate that image-guidance can be used to improve hearing outcomes for many existing CI recipients without requiring additional surgical procedures.

### **Submitted Abstracts**

#### 7. Direct Reconstruction of Proton Resonance Frequency-shift Temperature Maps from K-space Data for Highly Accelerated thermometry

# *Pooja Gaur, Ted L Anderson, William A Grissom, Biomedical Engineering, Chemical and Physical Biology, and Obstetrics and Gynecology*

Real-time volumetric MR thermometry is desirable for several applications of MRguided focused ultrasound. While high frame rates can be achieved over limited volumes using standard imaging techniques, real-time 3D temperature imaging reguires some form of acceleration. Existing accelerated thermometry techniques use temporal regularization and/or parallel imaging and compressed sensing to suppress aliasing artefacts. However these approaches do not ensure artefact-free solutions while preserving temporal resolution. We propose and validate a constrained temperature reconstruction method that achieves accurate temperature map reconstruction without aliasing artefacts even at high acceleration. We fit a hybrid multibaseline and referenceless temperature model directly to accelerated k-space data. By constraining the magnitude of the accelerated image to match that of a previously-acquired image, the possibility of aliased temperature map solutions is eliminated. Additionally, high acceleration factors can be achieved without temporal regularization that sacrifices temporal resolution. The method will readily extend to 3D, where it will enable accurate real-time volumetric thermometry at a high frame rate.

#### 8. 6 DOF Real-time Pose Detection for Medical Magnetic Devices

#### Di Natali C., Beccani M., Obstein K., Valdastri P., Mechanical Engineering, Gastroenterology

Magnetic coupling is one of the few physical phenomena capable of transmitting motion across a physical barrier. In gastrointestinal endoscopy, remote magnetic manipulation has the potential to make screening less invasive and more acceptable, thus to save lives by early diagnoses and treatment. Through remote magnetic manipulation operations are less invasive, by allowing untethered miniature devices to enter the body through natural orifices, and then being maneuvered with minimum disruption to healthy tissue. Closed-loop control of the magnetic device position is crucial step for a safe and reliable operation. In order to implement closedloop control, the pose -position and orientation- of the device must be available in real-time. This becomes challenging if magnetic coupling is achieved by permanent magnets, since the strong magnetic field required for manipulation interferes with current localization techniques. In this work, we present a novel wireless real-time pose detection strategy that is compatible with magnetic manipulation based on permanent magnets. The system consists of a localization module placed on the capsule, which measures the magnetic field -generated by an external magnet- and the absolute orientation of the capsule. The localization algorithm combines multiple sensors readings with a pre-calculated magnetic field map. The proposed approach is able to provide an average detection error below 4 mm for the position, 10 degree for roll and 1 degree for yaw and pitch within a spherical workspace of 30 cm in diameter. The computational time is 10ms and, using a wireless microcontroller, the localization module can be operated wirelessly.

#### 9. Do you Have the Next Great Idea?

Vanderbilt Center for Technology Transfer and Commercialization (CTTC) CTTC's mission is to provide professional commercialization services to the Vanderbilt community, thus optimizing the flow of innovation to the marketplace and generating revenue that supports future research activities, while having a positive impact on society. We accomplish this by (i) serving as an efficient and effective conduit for the transfer of promising intellectual property to industry; (ii) contributing to regional economic development by licensing locally and supporting new venture creation; and (iii) encouraging greater collaboration between academia and industry. In the past year, CTTC has more than doubled the number of years of licensing experience and added expertise in key core research areas through strategic hiring. We have also streamlined our commercialization process to be transparent and business focused. We have introduced several outreach Initiatives aimed at greater engagement with the Vanderbilt community, including a series of departmental presentations, one-on-one inventor meetings, bi-weekly newsletters, inventor surveys and a technology transfer internship program. All these have resulted in increased commercialization activities at Vanderbilt evidenced by the record number of invention disclosures and licensing transactions that generated the largest biotech and engineering upfront licensing fees in Vanderbilt history.

#### 10. Engineering Better Surgical Outcomes for Lumpectomy

Rebekah Conley, PhD Candidate in Biomedical Engineering; Thomas S. Pheiffer, PhD Candidate in Biomedical Engineering; Yifei Wu, PhD Candidate in Biomedical Engineering; Thomas E. Yankeelov, PhD, Associate Professor of Radiology & Radiological Sciences & VUIIS; Mike Miga PhD, Associate Professor of Biomedical Engineering, Radiology and Radiological Sciences, and Neurological Surgery; Ingrid Meszoely MD, Associate Professor of Surgery, Clinical Director of the Vanderbilt Breast Center

An investigation towards engineering better outcomes for breast lumpectomy patients is underway. Over the past several decades, it has been shown that breast lumpectomy is as effective as mastectomy (total or radical) when clear margins are achieved, i.e. no cancer being evident in the margins as encapsulated cancerous breast tissue is resected. Unfortunately, the use of advanced surgical guidance technology towards breast lumpectomy is limited at this time. Generating surgical technologies that could improve the fidelity of resection would have dramatic impact to this considerable population of patients (nearly 230,000 women per year in the United States alone with 80% being detected at stages 0, 1, or 2). Given that preoperative imaging of the breast usually differs significantly from the intraoperative surgical presentation and that large deformations occur during surgery, the ability to perform image-guided lumpectomies is challenging. The work presented here represents preliminary work towards a realization of image-guided lumpectomy using preoperative imaging, intraoperative ultrasound, novel digitization methodologies, and computer models.

### **Submitted Abstracts**

#### 11. Estimation and Reduction of Target Registration Error through Registration Networks

## *Ryan D. Datteri and Benoit M. Dawant EECS*

Fiducial-based registration is often utilized in image guided surgery because of its simplicity and speed. The assessment of target registration error when using this technique, however, is difficult. Although the distribution of the target registration error can be estimated given the fiducial configuration and an estimation of the fiducial localization error, the target registration error for a specific registration is uncorrelated with the fiducial registration error. Fiducial registration error is thus an unreliable predictor of the target registration error in a particular case. In this work, we present a new method to estimate the quality of a fiducial-based registration. We show that the measure we introduce is correlated to the target registration error and that it can be used to reduce target registration error. This has direct implications on the attainable accuracy of fiducial-based registration methods.

#### <u>12. A Feasibility Study on Transurethral Radical Prostatectomy via Laser-Equipped</u> <u>Concentric Tube Robots</u>

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Department of Mechanical Engineering and Department of Urology Radical prostatectomy has driven much of the recent dramatic growth in sales and clinical use of surgical robots. However, despite improvements in dexterity and visualization, the transabdominal approach employed means that surgical instruments continue to approach the prostate from the intrapelvic space around it, and must work across the external prostate boundary during resection. Since the nerves and vessels that control continence and sexual function lie on the boundary of the prostate, an approach from within the prostate may reduce trauma to them and thereby lead to fewer complications. Thus, we propose a natural orifice approach in which surgical tools approach the prostate from within the gland itself. This approach is enabled by laser-equipped concentric tube robots deployed transurethrally through a cystoscope. To explore the feasibility of this approach, we evaluate the ability of the endoscope-robot system to aim the laser at the internal boundary of the prostate, as would be required for holmium laser based radical prostatectomy. These studies illustrate the feasibility of laser-equipped concentric tube robots to provide a less invasive approach for robotic radical prostatectomy.