Webinar: FUS/US/Ablation
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Transcranial MR-guided histotripsy for non-invasive brain surgery

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Objective:
Transcranial MR-guided focused ultrasound (tcMRgFUS) has been investigated as a noninvasive ablation method in the brain. Ultrasound is delivered from outside the skull and heat up a focused target inside the brain. tcMRgFUS is used clinically to treat essential tremor. However, due to the overheating of the skull, tcMRgFUS is limited to treat a small volume in the center of the brain. Unlike tcMRgFUS that relies on heating produced by continuous sonication, histotripsy uses microsecond-length ultrasound pulses to generate focal cavitation with millimeter accuracy to mechanically liquefy the target tissue into acellular homogenate. With long cooling times between pulses (ultrasound on-time/off-time <0.1%), overheating to the skull and surrounding tissue can be avoided. Our prior ex vivo data show that histotripsy applied through excised human skulls was used to treat both shallow and deep brain volumes inside the skull, while keeping the temperature increase in the skull under 4°C. We aim to develop transcranial MR guided histotripsy (tcMRgHt) that can overcome the treatment location and volume limitations of tcMRgFUS for non-invasive brain surgery and test the feasibility in the brain of in vivo pigs and whole-body human cadavers.

Methods:
We have designed and built a 700-kHz, 360-element, hemispherical, tcMRgHt phased-array transducer with a 15 cm focal distance. To study the in vivo feasibility, TcMRgHt treatment was delivered to 8 pigs inside a 3T MRI scanner. After craniotomy to open an acoustic window to the brain, histotripsy was applied through an excised human calvarium to target inside the pig brain based on pretreatment MRI scans. MR images were acquired pre-treatment, immediately post-treatment, and 2-4 hours post-treatment to evaluate the treated zone and any off-target brain damage. In addition, we have performed transcranial histotripsy in the brain of whole-body human cadavers (<96 hours postmortem). Approximately 1cm3 of the brains of two whole-body cadavers were treated by electronically steering the focus with a 1.1 mm spacing using 1-cycle pulses, 200Hz PRF, p- of >28 MPa, and 50 pulses per focal location. Aberration correction was done with Kranion and pre-treatment CT head scans.

Results:
For the in vivo experiments, successful histotripsy ablation was observed in all eight pigs. The MR-evident lesions were well-confined within the targeted volume, without evidence of excessive brain edema or hemorrhage outside of the target zone. Histology revealed tissue homogenization within the ablation zones with a sharp demarcation between treated and untreated tissue, which correlated well with the radiographic treatment zones on MRI. The targeting accuracy was measured to be 2.32±1.23 mm. For the human cadaver study, three lesions were successfully generated in the septum, thalamus, and corpus callosum, and identified by the post-treatment MR images. Apparent Diffusion Coefficient (ADC) images best showed the histotripsy homogenized region in the human cadaveric brain.

Conclusion:
These results are the first to show the in vivo feasibility of tcMRgHt in the pig brain through an excised human skull and the first transcranial histotripsy human cadaver study. The results enable further investigation on the use of tcMRgHt for non-invasive brain surgery.

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Neuronavigation-guided sonobiopsy for brain tumor genetic diagnosis without surgery

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Objective
Currently, neuroimaging modalities (e.g., MR and CT) are often used to evaluate brain tumor lesions followed by surgical resection or stereotactic biopsy for histologic and genetic confirmation of imaging findings. Brain surgery, however, carries risk, is not feasible for repeated sampling, and may not be possible at all because of the location of the tumor. There is an unmet critical need for noninvasive methods to interrogate the genetic information of a brain tumor.

Methods
Our group introduced the focused ultrasound-enabled brain tumor liquid biopsy technique, which we term sonobiopsy, for noninvasive and spatially targeted molecular diagnosis of brain tumors. Sonobiopsy uses focused ultrasound in combination with microbubbles to induce blood-brain barrier (BBB) disruption and release brain tumor-specific biomarkers from the brain into the blood circulation to diagnose brain tumors by blood tests. Existing MR-guided focused ultrasound devices can be adapted for performing sonobiopsy, but they are limited by their design complexity, high cost, and high technical barrier, which prohibits their broad application as a diagnostic tool. To enable widespread use of sonobiopsy, we developed a neuronavigation-guided FUS device for sonobiopsy diagnosis of brain tumors. The sonobiopsy device integrated a commercially available neuronavigation system with a nimble, lightweight FUS transducer.

Results
We found that the targeting accuracy of the neuronavigation-guided sonobiopsy device was < 2 mm as measured in a water tank with a hydrophone and < 4 mm as measured in using a healthy pig model by calculating the offset between the targeted location and the centroid of the blood-brain barrier opening. Numerical simulation using the K-Wave toolbox was conducted to assess the targeting accuracy of the FUS transducer in 54 glioblastoma patients, measured as the offset between the targeted location in the tumor and the location of the peak acoustic pressure. Based on the numerical simulation, the transcranial targeting accuracy of the FUS transducer in glioblastoma patients was 5.49 mm ± 4.92mm. The neuronavigation-guided FUS device was then used to perform sonobiopsy in a pig model of glioblastoma. Droplet digital PCR (ddPCR) analysis of blood samples collected before and after FUS sonication found that sonobiopsy significantly increased the plasma levels of EGFRvIII circulating tumor DNA (ctDNA) by 270-fold and TERT C228T ctDNA by 9-fold. As a result, sonobiopsy increased the detection sensitivities for EGFRvIII and TERT C228T by 71.43% and 28.57%, respectively, compared with conventional blood-based liquid biopsy. No significant off-target tissue damage was observed from sonobiopsy-treated animals.

Conclusions
These findings demonstrated that the neuronavigation-guided sonobiopsy device provides a promising technique for the genetic diagnosis of brain tumors.

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Ultrasound as a tool for image-guided tumor therapy: from localized energy deposition to site-specific triggered drug delivery.

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[Objectives]
The general objective of this study is to use a combination of ultrasound and sonosensitive particles (such as microbubble complexes, perfluorocarbon nanodroplets and RBC drug carriers) for targeted tumor therapy. Medical ultrasound has a unique capability to focus mechanical energy into tightly controlled spots deep inside the body, even across the skull. Gas-filled micrometer-diameter bubbles compress and expand in the ultrasound field. Some of microbubble formulations are already in clinical use, in cardiology and radiology, applied as ultrasound contrast blood pool imaging agents. Superheated perfluorocarbon submicrometer nanodroplets, with boiling point below physiological temperature convert to gas bubbles only in response to ultrasound treatment. In response to the application of focused ultrasound, mechanical compression and expansion can lead to the triggered localized release of drugs, sequestered in the carrier cells, such as RBCs, micro- and nanoparticles, or enhance local energy deposition in the treated tissues.

[Methods]
Perfluorobutane gas microbubbles decorated with biotin were prepared by high shear mixing sonication of the aqueous medium that contained phospholipid, PEG-lipid surfactant stabilizer, and biotin-PEG-phospholipid. Biotinylated liposomes were prepared in ammonium citrate buffer medium, and then post-loaded with doxorubicin. Biotinylated liposomes were complexed with microbubbles via a streptavidin link, to create pendant structures. Perfluorocarbon nanodroplets were prepared by Nuclepore filtration from perfluoropentane or perfluorobutane and stabilized with a lipid monolayer shell that contained cationic lipid. Conversion of superheated nanodroplets to gas bubbles upon the action of ultrasound was assessed by microscopy and by contrast ultrasound imaging. RBCs were loaded with fluorescent dyes and heparin by osmotic loading process and resealed in an isotonic buffer. Doxorubicin was remote-loaded into heparin-carrying RBCs. Nanodroplet adhesion to the RBC membrane was achieved via electrostatic binding. Contents release from microbubble-liposomes and RBC-nanodroplet complexes upon insonation was monitored by fluorescence microscopy. In vivo testing was performed in a subcutaneous murine tumor model (MC38 cells). Upon intravenous administration of microbubble-liposome complexes or perfluorocarbon nanodroplets, tumor treatment with 1 MHz ultrasound was performed biweekly, and tumor size assessed.

[Results]
Doxorubicin was loaded into RBCs and liposome-microbubble pendant complexes, reaching 1 pg drug per particle, using remote loading, where the drug was absorbed and retained inside the carrier. This load level was necessary to achieve 6mg/kg in vivo drug dose. Ultrasound treatment resulted in contents release from microbubble-liposomes and nanodroplet-decorated RBCs. Repeated administrations of superheated perfluorocarbon nanodroplets, followed by biweekly focused ultrasound treatments reduced the rate of tumor growth in the MC38 murine model, as compared with untreated controls or treated controls that did not receive nanodroplets. Repeated biweekly administrations of doxorubicin-liposome complexes, followed by tumor insonation resulted in the suppression of tumor growth. It was important to moderate ultrasound intensity (acoustic pressure ~200 KPa) to maintain tumor perfusion during insonation, as visualized by contrast ultrasound imaging.

[Conclusion]
Ultrasound can be used for remote triggering of micro- and nanoparticles via localized energy deposition inside the body, specifically, within the tumor vasculature. A combination of intravascular administration of sonosensitive particles with tumor insonation suppresses tumor growth in a subcutaneous murine model.

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Model-Based Conformal Ablation Planning for MRI-Guided Robot-Assisted Needle-Based Therapeutic Ultrasound Treatment of Brain Tumors: Development and in vivo Validation in Survival Swine Studies of FEM-based Modeling and Reinforcement Learning-based Preoperative Planning

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Objective:
Thermal ablation using needle-based therapeutic ultrasound (NBTU) applicator is a minimally invasive cancer treatment option that can achieve appropriate margins and reduce collateral damage. We propose combining FEM-based acoustic & thermal modeling of ablation, RL-based planning, and robotic delivery using the determined trajectory under live MRI guidance.

Methods:
Stationary Simulation: 2D acoustic pressure deposition from 90 degree NBTU applicator was modeled using COMSOL, and simulations of thermal propagation in real brain tissue parameter-based media were produced. in vivo Trials: NBTU applicator was coupled to the seven degree-of-freedom NeuroRobot, which was attached to the MRI bed and connected to the shielded in-room control box with only fiberoptic connection through penetration panel for external connections. OpenIGTLink communication is implemented between robot control application, MRTI software (interfaces directly with MRI scanner), and ablation controller. Simulated heating was validated in four swine that underwent MR-guided robotically assisted NBTU using varying treatment duration and power. Serial MRTI was obtained and isodose lines overlaid on the MR images, which were compared to brain tissue acquired post-mortem which underwent histopathologic analysis.

Conformal Planning:
Based on the validated simulation data, a model-based closed-loop controller for MR-guided conformal ablation with robot-driven applicator was implemented. Conformal performance was experimentally validated using six virtual tumor boundaries. The robot controlled rotation of the NBTU applicator within a homogeneous gelatin phantom with similar thermal properties to brain tissue. Combining predicted simulation data and the closed-loop controller, a reinforcement learning (RL) model was developed to compute the optimal rotation trajectory for a desired tumor boundary given heat diffusion in the simulation environment.

Results:
Intraoperative MRTI thermal isodose contours were characterized and comprehensively mapped to postoperative MRI images and correlated with histological tissue sections postmortem. NBTU 360o ablations of MRTI volumes (1 cm3; 120 s, 3W; 1.2 cm3, 180s, 4W), 180o ablations (0.9 mm3, 120 s, 3W; 1.1cm3; 180 s; 4W) and 90o ablation (0.46cm3, 690s, 6W) validated the FEM results of 360o (1.0110 cm3; 120 s, 3W; 1.2677 cm3, 180s, 4W), 180o (0.9375 mm3, 120 s, 3W; 1.1631cm3; 180 s; 4W), and 90o (0.4746cm3, 690s, 6W). The results of fused MRTI and model-based controller to conformally ablate six desired brain tumor boundaries showed good agreement with average maximum Hausdorff distance 2.63mm and average Dice coefficient 0.88. Comparing a

controlled directional applicator to omnidirectional, the controller approach required 35.5% smaller ablation volume. Average area of ablation outside desired treatment area was 91.6mm2 by the baseline and 33.75mm2 by the controller.
Preliminary results of the RL agent using a directional beam to conformally ablate the six boundaries show good agreement between the selected shape and the RL ablated shape with average Hausdorff distance 2.75mm and average Dice coefficient 0.91. Average ablation area outside desired treatment was 172.5 mm2 by the baseline approach and 57.78 mm2 by the RL approach, demonstrating greater healthy tissue conservation.

Conclusion:
We present a series of technology for MR-guided robot-actuated ultrasound ablation including FEM simulation, in vivo survival experiment validation, and preliminary advanced controller model design. Future work will focus on integrating hybrid RL planning & closed-loop control in animal trials.

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Feasibility of Quantitative MR-Based Hypoxia Measurements in the Setting of Interstitial High Dose Rate Brachytherapy of the Cervix

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Objectives: High dose rate (HDR) interstitial brachytherapy is an essential component of radiation therapy for large gynecologic cancers. Magnetic resonance imaging is the modality of choice for pelvic brachytherapy. Tumor hypoxia is associated with radiation resistance, and cervical cancer patients with hypoxic tumors have increased local failure rates and reduced disease-free survival.(1) Silicone materials have been demonstrated to have oxygen-dependent T1 relaxation times. (2) This study assesses the feasibility of quantitative MR measurement of brachytherapy catheters incorporating a custom oxygen sensitive silicone.

Methods: An IRB-approved pilot study was opened to assess the feasibility of MR measurement of custom oxygen-sensitive silicone as part of a standard MR-guided interstitial brachytherapy implant procedure. Brachytherapy catheters were modified to incorporate custom silicone with oxygen sensitive MR properties. During 3T MR-guided interstitial brachytherapy procedures, one to two oxygen sensing catheters were placed at the beginning of the procedure. These catheters were measured with MR at the end of the implantation procedure and were then replaced with standard brachytherapy catheters. The study has a 2-stage design with a four-patient safety lead-in followed by three additional patients for a total accrual of seven patients. Feasibility was defined as acquisition of data from at least one oxygen sensor per patient.

Results: All seven participants had at least one oxygen-sensing catheter placed. Feasibility was successfully achieved in all seven patients.

Conclusions: Quantitative MR measurements of a custom oxygen-sensitive silicone is feasible in a clinical 3T scanner. Experience from this study will be used to inform chemical composition and mechanical design for the next generation of MR-measurable HDR brachytherapy catheters that could be implanted for the duration of the HDR treatments. Because HDR brachytherapy may be delivered in as many as five fractions, such catheters could enable hypoxia measurements at many points throughout the tumor and at multiple times during treatment. These measurements could be combined with adaptive HDR planning(3) to drive the high dose regions inherent to brachytherapy onto the hypoxic regions to counteract the radio-resistance of hypoxic cells and improve

treatment outcomes.

Funding Sources: GE serves as PI of an NIH SBIR (NIH R43CA261401) in his role as CEO of Stratagen Bio. JT is supported by the Image Guided Therapy Center (NIH P41EB015898). This work was supported by a Bridge Project Grant. GE was previously supported by the Koch Institute Quinquennial Cancer Research Fellowship and the Kavanaugh Translational Innovation Fellowship.

References: (1) Knocke, TH et al., Radiother Oncol, 1999. 53(2):99-104. (2) Liu, VH et al, Proc Natl Acad Sci USA 2014 111(18):6588-93. (3) Guthier, C.V. et al. Med Phys. 2017 4(12):6117-27.

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2:10 PM - 2:20 PM

Multi-Functional Photoacoustic Image-Guided Ablation Therapy

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[Objectives]
Ablation therapy is a minimally invasive procedure, using thermal doses to destroy abnormal tissue or tumors in the heart, prostate, liver, kidney, and brain. This talk introduces an image-guidance strategy for ablation therapy via functional photoacoustic (PA) imaging. PA imaging is real-time, non-invasive, non-ionizing, and highly selective and specific, depicting optical absorbance characteristics of endogenous and exogenous contrasts. We have explored the use of functional PA imaging to enhance the therapeutic outcome by addressing three needs. First, the targeted ablation lesion, such as tumor boundary and malignancy, must be identified and localized. Second, success in ablation therapy, such as in the prostate, often comes at the expense of damaging the neurovascular bundles (NVBs), i.e. the network of nerves and blood vessels running adjacent to the prostate and responsible for erectile function. These structures are embedded into soft tissue (i.e. the “fascia” layers surrounding the prostate) and are thus invisible from the surface, making their detection challenging. Thus, the procedure must avoid damaging these structures. Third, the current ablation therapies are performed under CT or MRI guidance with uncertainty in the degree of ablation-induced tissue necrosis and its boundary with non-necrotic tissue during the procedure, resulting in high recurrence and procedural complications due to incomplete and excessive ablation. Intraoperative monitoring of the ablated lesion evaluation has room to improve. In summary, there are unmet needs to offer an imaging solution to guide “where should be treated”, “where should not be ablated”, and “when to pause and stop treatment”.

[Methods]
We have explored multi-functional PA imaging to enhance the therapeutic outcome by tackling the above motivated three aspects. We develop a molecular-targeted PA imaging approach to detect cancer abnormality, highlighting “where should be treated”. Moreover, we develop a PA-based visualization of the NVB-specific contrasts for the avoidance of the damage, highlighting “where should not be treated”. Further, we explore the PA-based identification of ablation-induced tissue necrosis to allow intraoperative monitoring, highlighting “when to pause or stop treatment”.

[Results]
We validated the feasibility of the three PA imaging modes and their applicability to different imaging targets through ex-vivo and in vivo studies. 3D PA imaging could visualize the molecularly targeted contrast agents in ex-vivo tumors with a sub 300-micron spatial resolution. In addition, the PA imaging could detect the lipid-based endogenous nerve contrast and vascular contrast to highlight NVB region in an ex-vivo rat. Finally, in vivo validation of the ablation lesion identification was conducted in a swine model. The ablation-induced necrotic

lesion at the surface of a live tissue was depicted throughout a cardiac cycle through the cardiac-gated sPA imaging.

[Conclusion]
The proposed combined PA imaging strategy has the potential to reduce recurrence and postoperative complications by improving detection, avoidance, and monitoring for ablation therapy.

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Repurposing color Doppler ultrasound imaging to guide targeted cardiac injections in preclinical animal models using acoustically active needles.

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Objectives: A therapeutic or investigative agent is typically delivered into the cardiac cavity or muscle by a transthoracic needle or an intracardiac injection catheter. The common goal is to target the injection precisely to achieve the expected effect of the agent and simultaneously minimize injury to the heart. Ultrasonography is frequently used as a broadly available technique for image-guided interventions. However, the conventional brightness (B)-mode ultrasound is prone to reverberation and attenuation artifacts when tracking a needle. Color Doppler imaging fundamentally differs from B-mode by using longer transmission pulses (i.e., more acoustic energy) and Doppler frequency shift (i.e., not brightness) to detect blood flow. Our main objective was to develop a Doppler guidance technique for cardiac injections that would eliminate the shortcomings of B-mode navigation by leveraging the fundamental differences.

Methods: We can guide a cardiac injection by Doppler because the needle is made “acoustically active” by a small piezoelectric crystal embedded in its tip and producing an acoustic field. The acoustic field interacts with an incoming Doppler signal of known frequency. This interaction produces a new signal at a Doppler shift frequency. The ultrasound machine interprets the new signal as “motion” and generates a color band at the interaction location. In this way, the ultrasound machine identifies the needle within a color Doppler scan plane. The method works instantaneously and, therefore, tracks the insertion of the needle during injection in real-time. Our recently advanced version of the color Doppler guidance utilizes a deep learning algorithm, which combines B-mode and color Doppler imaging data, simulates human interpretation of the two modalities in combination, and identifies the Doppler-guided object exactly as a cross-shaped marker (i.e., not as a color band).

Results: We have built and will demonstrate several working prototypes of acoustically active needles and injection catheters with piezoelectric crystals of sub-mm size embedded in their tips. A hair-thin wire carries a signal with typically single-MHz frequency and single-V voltage from a waveform generator to the crystal. To document our results, we will present sequences of screenshots demonstrating how the color Doppler guides a) an injection catheter from its location in the aorta retrogradely through the aortic valve to the left ventricle and navigates its needle into the myocardial wall in an anesthetized pig and b) the insertion of a transthoracic needle into the myocardial wall of an anesthetized laboratory rat. We will also share preliminary results obtained after initial training of the learning algorithm that localizes the color Doppler-guided object.

Conclusion: Color Doppler imaging is typically used to analyze blood flow or myocardial motion. Our study introduces a new purpose for color Doppler – image-guided cardiac injections. Moreover, in conjunction with color Doppler guidance, we describe the concept of acoustically active needles that overcome the limitations of

conventional B-mode ultrasound navigation. A learning algorithm demonstrates our future direction towards user-independent needle localization and therapeutic or investigative cardiac injection guidance.

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Development of a forward-viewing 3D intravascular ultrasound imaging system for functional coronary imaging-guided intervention

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Objectives
> 8 million people in the U.S. suffer from stable coronary artery disease (CAD). Approximately 10% of these patients will experience a major adverse cardiac event (MACE) within a given two year period. Several independent indicators of adverse events have been identified:
1. Lesion morphology.
2. Plaque composition.
3. Hemodynamics - in particular, elevated wall shear stress (WSS) in the proximal part of the stenosis is predictive of MI.

However, no current technology can simultaneously measure these indicators in vivo to comprehensively characterize the mechanics that drive plaque rupture processes and guide treatment accordingly.

We have previously demonstrated 3D intravascular imaging of hemodynamics in the femoral artery of a pig using a 4 mm, 5 MHz forward-viewing device. Here we present the development of a 1.7 mm, 30 MHz 3D forward-viewing intravascular ultrasound system for risk stratification in coronary arteries in the cardiac catheterization lab.

Methods
A. Transducer array. A forward-viewing, 30 MHz 2D array transducer was developed. The array has a 1.7 mm diameter aperture with 120 elements. Each element is 100 μm ? 90 μm ? 60 μm (width ? height ? thickness). A via-less interconnect of 10 unique flexible printed circuit layers was developed. Electrical and acoustic properties of the array were characterized.

B. Blood flow velocity and WSS estimation. Two approaches for 3D blood flow velocity and WSS estimation with an intravascular array were compared with computational fluid dynamics (CFD): 1) particle image velocimetry (PIV), and 2) Doppler with transverse oscillation. The coronary artery geometry of a healthy adult was 3D printed with 25 μm resolution to form an individual-specific phantom. A 23 MHz linear array transducer (Visualsonics MS400) was positioned at the outlet of the vessel. Steady flow at a rate of 15 mL/min was introduced towards the transducer and images were acquired at 10k frames/s.

Results
A. Electromechanical transducer simulations show a -6 dB bandwidth of 70%. Acoustic simulations indicate a beam with of 0.35 mm at a depth of 10 mm. The first prototype array has been fabricated and testing is in

progress. Fabrication of te next generation array with 240 elements is also in progress.

B. When two velocity estimation approaches were compared at the center plane of the vessel along the long axis of the artery across depths from 3 mm to 11 mm, the Doppler approach estimated the maximum velocity magnitude to be 2.9±1.1% (0.4±0.08 cm/s) higher than PIV. Doppler-estimated WSS averaged in depth at the same center plane was 10.3±3.93% (0.03±0.01 Pa) higher than PIV. To our knowledge, this is the first demonstration of ultrasound-based estimation of blood flow velocity and WSS in an individual-specific coronary artery.

Conclusion
Building on prior in vivo demonstration of 3D intravascular imaging of hemodynamics, we have developed the first forward-viewing array for coronary imaging with >100 elements and strategies for blood flow velocity and WSS estimation and using this device. When completed, the system will be used to simultaneously characterize the 3D coronary biomechanical environment.

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Feasibility of Quantitative MR-Based Hypoxia Measurements in the Setting of Interstitial High Dose Rate Brachytherapy of the Cervix

Gregory J. Ekchian[1], Junichi Tokuda[2], Robert A. Cormack[3], Michael Dyer[3], Evangelia Kaza[3], Michael J. Cima[4,5]

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Objectives: High dose rate (HDR) interstitial brachytherapy is an essential component of radiation therapy for large gynecologic cancers. Magnetic resonance imaging is the modality of choice for pelvic brachytherapy. Tumor hypoxia is associated with radiation resistance, and cervical cancer patients with hypoxic tumors have increased local failure rates and reduced disease-free survival.(1) Silicone materials have been demonstrated to have oxygen-dependent T1 relaxation times. (2) This study assesses the feasibility of quantitative MR measurement of brachytherapy catheters incorporating a custom oxygen sensitive silicone.

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Funding Sources: GE serves as PI of an NIH SBIR (NIH R43CA261401) in his role as CEO of Stratagen Bio. JT is supported by the Image Guided Therapy Center (NIH P41EB015898). This work was supported by a Bridge Project Grant. GE was previously supported by the Koch Institute Quinquennial Cancer Research Fellowship and the Kavanaugh Translational Innovation Fellowship.

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Webinar: Imaging and sensing
1:20 PM - 1:30 PM

Targeted Contrast Agents for Image-Guided Drug Delivery and Cancer Therapy

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Two fundamental and unsolved problems facing image-guided drug delivery and image-guided cancer surgery are nonspecific uptake of intravenously administered diagnostic and/or therapeutic agents by normal tissues and organs, and incomplete elimination of unbound targeted agents from the body. To solve these problems, we have synthesized a series of indocyanine near-infrared (NIR) fluorophores that varied systematically in net charge, conformational shape, hydrophilicity-lipophilicity, and charge distribution. Using 3D molecular modeling and machine learning, we have defined the relationship among the key independent variables that dictate biodistribution and tissue-specific targeting, such as lung and sentinel lymph nodes, human prostate cancers, and human melanomas (1-3).
Recently, we have developed a new pharmacophore design strategy, “structure-inherent targeting,” where tissue-specific targeting is engineered directly into the non-resonant structure of an NIR fluorophore, thus creating the most compact possible optical contrast agent for bioimaging and nanomedicine (4). The biodistribution and targeting of these compounds vary with dependence on their unique physicochemical descriptors and cellular receptors, which permit 1) selective binding to the target tissue/organ, 2) visualization of the target specifically and selectively, and 3) provide curing options such as image-guided surgery or targeted therapy (5). Our study solves two fundamental problems associated with image-guided drug delivery and image-guided cancer surgery and lays the foundation for additional targeted agents with optimal optical and in vivo performance.

References 1.Choi HS, Liu W, Misra P, Tanaka E, Zimmer JP, Itty Ipe B, Bawendi MG, Frangioni JV. Renal clearance of quantum dots. Nat Biotechnol. 2007; 25: 1165-70.
2.Choi HS, Liu W, Liu F, Nasr K, Misra P, Bawendi MG, Frangioni JV. Design considerations for tumour-targeted nanoparticles. Nat Nanotechnol. 2010; 5(1): 42-7.
3.Choi HS, Gibbs SL, Lee JH, Kim SH, Ashitate Y, Liu F, Hyun H, Park G, Xie Y, Bae S, Henary M, Frangioni JV, Targeted zwitterionic near-infrared fluorophores for improved optical imaging. Nat Biotechnol. 2013; 31: 148-53.
4.Hyun H, Park MH, Owens EA, Wada H, Henary M, Frangioni JV, Choi HS. Structure-inherent targeting of near-infrared fluorophores for parathyroid and thyroid gland imaging. Nat Med. 2015; 21: 192-7.
5.Kang H, Gravier J, Bao K, Wada H, Lee JH, Baek Y, El Fakhri G, Gioux S, Rubin BP, Coll JL, Choi HS. Renal clearable organic nanocarriers for bioimaging and drug delivery. Adv Mater. 2016; 28(37):8162-8.

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Webinar: Imaging and sensing
1:30 PM - 1:40 PM

Deformable motion compensation for 3D image-guided interventional radiology

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[Objective] Availability of robotic C-arms in the interventional radiology (IR) suite has enabled widespread use of CBCT for procedure guidance. However, CBCT image acquisition time remains moderately long, making CBCT susceptible to patient motion that challenges image quality, particularly in soft-tissue abdominal imaging, in which motion arises from a complex combination of quasi-independent sources, including respiratory, cardiac, and irregular peristaltic motion.
Our research aims at the development of image-based methods for compensation of soft-tissue motion in abdominal CBCT, via combination of autofocus techniques and data-informed models, following three research lines: i) Targeted autofocus acting on specific target anatomy; ii) Deep autofocus methods based on anatomy-aware learned metrics; and, iii) Deep simulation methods to synthesize random motion representative of patterns observed in clinical scenarios.

[Methods] Targeted autofocus for vascular CBCT used deep learning approach to identify regions containing contrast-enhanced vascularity in the projection domain. Identified regions were used to inform an autofocus framework that iteratively optimized a targeted metric designed to promote characteristics of motion-free images in vascular CBCT, i.e., presence of conspicuous tubular shapes.
An anatomy-aware deep autofocus metric (DL-VIF) was designed with a context-aware deep-CNN trained with realistic simulated data. DL-VIF aimed at reproducing a reference-based structural similarity metric (Visual Information Fidelity – VIF), that capture alignment between the structural content of the corrupted and reference (motion-free) images and the structural distortion induced by motion, but without any reference (motion-free) counterpart. DL-VIF overcomes issues associated with conventional autofocus metrics that can enforce solutions displaying properties associated to motion-free CBCT (e.g., sharpness or piecewise constancy), but that might depict unrealistic structural content. Methods for generation of realistic synthetic motion were developed leveraging the capability of deep CNNs to capture features associated to motion distortion, the availability of high-fidelity simulation methods for motion-free CBCT, and the availability of motion-corrupted CBCT data obtained as part of the routine clinical practice. Motion generative models were built following a domain translation approach, trained with a randomly perturbed cyclic adversarial strategy, requiring only motion corrupted data and simulated, motion-free, data.

[Results] The vascular targeted motion compensation yielded restoration of vascular structures. Threshold-based segmentation of the vascular anatomy in the motion-compensated CBCT demonstrated an intersection-over-union improvement of 25% compared to the motion-affected image, using the motion-free volume as reference. DL-VIF was tested in rigid motion in head/brain CBCT, and in deformable motion in abdominal CBCT, showing reduced motion artifacts that yielded an average increase in structural similarity index, computed against a motion-free reference, of 0.129 (0,113) in regions with severe (mild) motion, superior to that achieved with conventional autofocus.
Studies on deep motion simulation in controlled scenarios resulted in simulated motion trends following those in the training dataset: i) diffeomorphic motion fields; ii) static anatomical structures (e.g., spine) showed nearly static trajectories; and iii) motion was predominantly allocated in directions included in the training cohort.
[Conclusion] The proposed multi-faceted approach will yield a robust, practical set of methods for simulation and compensation of deformable soft-tissue motion in CBCT, removing a critical impediment to 3D guidance in IR.

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Webinar: Imaging and sensing
1:40 PM - 1:50 PM

Clinical impact of a volumetric image method for confirming tumour coverage with Ablation on patients with malignant Liver Lesions COVER-ALL Trial

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General study info: High rates of local tumour progression (LTP) remains a major limitation for widespread acceptance of liver thermal ablation (LTA). Insufficient minimal ablation margin (MAM) has been linked to treatment failure and LTP. Although MAM can be modified during LTA, no prospective studies have evaluated the role of ablation confirmation (AC) software as an intraprocedural decision-making tool.

Purpose: To evaluate if the intra-procedure use of a novel AC software increases the MAM on a three-dimensional computed tomography-generated quantitative (3D-MAM) analysis.

Methodology: This single-center, prospective phase II, intent-to-treat, randomised (1:1) trial is enrolling 100 patients with primary and secondary liver tumours (? 3 tumours, 1 - 5 cm diameter) undergoing LTA. A biomechanical deformable image registration method (Morfeus), incorporating ablation-specific AI-segmentation algorithms was built and retrospectively validated as part of our grant aims. This model is then utilized to prospectively evaluate tumour targeting and 3D-MAM analysis. For the experimental arm, AC is performed using Morfeus intraprocedurally. For the control arm, AC is performed by standard-of-care semiquantitative evaluation of pre- snf post-ablation contrast-enhanced CT images (visual inspection assisted with imaging co-registraion). Re-ablation is allowed on both arms. Herein, we will summarize the interim analysis of the first 50 patients enrolled.

Endpoints: Primary endpoint: 3D-MAM using Morfeus on pre- and final post-ablation contrast-enhanced CT (continuous variable, t-test or Wilcoxon rank-sum test based on underlying distribution of data, stopping rule for control arm enrolment at interim analysis based on superiority analysis using alpha spending function). Secondary endpoints: 2-year LTPFS, complication rates, quality of life, liver function, oncological outcomes, and Morfeus impact on procedure workflow. Expected data/impact on IR: Improving intraprocedural 3D-MAM might translate in improvement of LTA efficacy and LTP rates.

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Webinar: Imaging and sensing
1:50 PM - 2:00 PM

Estimation of High Framerate Digital Subtraction Angiography at Low Radiation Dose

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[Context] Digital Subtraction Angiography provides high resolution image sequences of blood flow through arteries and veins and is the gold standard for visualizing cerebrovascular anatomy for neurovascular interventions. However, acquisition frame rates are typically limited to 1-3 fps to reduce radiation exposure, and thus DSA sequences often suffer from stroboscopic effects.

[Objectives] We present the first approach that permits generating high frame rate DSA sequences from low frame rate acquisitions eliminating these artifacts without increasing the patient's exposure to radiation.

[Methods] Our approach synthesizes new intermediate frames using a phase-aware Convolutional Neural Network. This network accounts for the non-linear blood flow progression due to vessel geometry and initial velocity of the contrast agent.

[Results and Conclusion] Our approach outperforms existing methods and was tested on several low frame rate DSA sequences of the human brain resulting in sequences of up to 17 fps with smooth and continuous contrast flow, free of flickering artifacts.

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Webinar: Imaging and sensing
2:00 PM - 2:10 PM

High Temporal Resolution Using 1000 fps Angiography for Endovascular Interventional Procedures

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Objectives: At the 7th NIGT Workshop in 2014, our group presented initial work on an NIH supported project for developing a new high spatial resolution angiographic system designated the Micro-Angiographic Fluoroscope (MAF) that has subsequently become a widely distributed Canon (Toshiba) product called HiDef. We now present initial work on another NIH-supported project for developing a new high temporal as well as high spatial resolution angiographic system based on 1000 frame per second (fps) detectors used for High-Speed Angiography (HSA). This grant application received a 1% score from the NIH Study Section.

Methods: The new system is capable of recording imaging sequences showing details of blood flow in the vasculature including velocity distributions that can be used to obtain measures of important hemodynamic parameters such as wall shear stress involving aneurysms, blood shear involving platelet activation potentially leading to stroke, and other phenomena in the neuro and cardio vasculature where blood velocity is too high to be observed in detail by current angiography, which is typically done at a few fps. The HSA system includes a standard x-ray source with constant exposure times of large fractions of a second as well as a contrast media injector used to develop streams that purposely do not fill the vessels unlike what is normally done for standard angiography where determination of vessel morphology rather than dynamic function is the aim. The special high-speed x-ray detectors now used are direct CdTe photon counting detectors capable of noise-free, zero dead-time operation with 1 millisecond per frame and with 100 um pixels. A test flow-loop was built where the ECG-like signal from the pulsatile fluid pump was used to synchronize the detector and contrast-media injector. Various 3D-printed patient-specific neuro-vascular aneurysm and stenosis models were connected to the flow loop and detailed velocity distributions within the models as well as wall shear stresses were investigated.

Results: The output flow from a 3D-printed model of a Left Ventricular Assist Device (LVAD) bypass graft anastomosed to the aorta was studied and resulted in a demonstration of the flow advantages of a reduced graft angle in decreasing shear and vorticity in the fluid entering the aorta model. To calculate velocity distributions,

the pros and cons of three methods were tested including Optical Flow (OF) used for distributed contrast media, X-ray Particle Image Velocimetry (XPIV) using Ethiodol droplets and microspheres labeled with iodine contrast, and Computational Fluid Dynamic (CFD) calculations used for mathematical modeling. Of these, OF is clinically possible currently. The long times and restrictive assumptions required for CFD calculations make its use impractical during a clinical intervention. XPIV is superior for testing interventions in models with immediate results, but is not clinically compatible currently. In addition, the use of two simultaneous projections at different angles are being investigated for 3D hemodynamic analysis. Finally, patient dose requirements for these various applications are being evaluated.

Conclusion: Initial studies of High-Speed Angiography (HSA) appear to be leading to a rich potential for future benefit in image-guided vascular interventions.

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Webinar: Imaging and sensing
2:10 PM - 2:20 PM

Renal mass angiography using QUTE-CE-MRA with Ferumoxytol contrast agents in chronic kidney disease patients

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[Objectives] Ferumoxytol clears out through the liver instead of the kidney, thus it is considered as a safe contrast agent for chronic kidney disease (CKD) patients with low estimated glomerular filtration rates (eGFR) who are contra-indicated for gadolinium enhanced MRA. Currently, there is limited publication on renal mass imaging using ferumoxytol-enhanced MRI and the qualitative assessment on the contrast enhancement may bring uncertainty to renal mass characterization. The purpose of this study is to demonstrate our approach to quantitatively assessing the signal enhancement in renal masses with Ultrashort-Time-to-Echo (UTE) sequences and share our experience in first-pass imaging with ferumoxytol in the abdominal region.

[Methods] Subjects previously diagnosed with CKD were recruited from Massachusetts General Hospital and scanned at the Martinos Center for Biomedical Imaging. Five subjects with eGFR < 30 mL/min/1.73m2 who are not eligible for gadolinium based MR or iodinated CT contrast agent were referred to this study and received first-pass ferumoxytol infusion at the dose of 4 mg/kg body weight. Scans were performed using the 3T scanner with a variety of pulse sequences, including a prototype 3D stack-of-spirals UTE VIBE sequence, T1-weighted sequence, T2-weighted sequence and diffusion-weighted sequence. When the ferumoxytol is slowly infused, the 13-seconds breath-hold UTE scans were acquired simultaneously. 6-minutes free-breathing UTE scans were acquired pre- and post- contrast injection for blood volume quantification. The blood volume (BV) map was calculated by scaling the free-breathing UTE post- and pre- subtraction image from 0 to 1.

[Results] Positive contrast images captured the vascular networks of the kidneys. Good first-pass images were obtained, with venous phase, arterial phase, delayed phase images showing selectively enhancement of the veins and arteries in the abdomen. One complex mass was identified in one subject (74 year-old male, CKD stage 4, eGFR = 29 mL/min/1.73m2). No visible vessels were found feeding into the renal mass. However, the renal mass appears highly heterogeneous in both pre-contrast and post-contrast QUTE-CE scans. BV in entire renal mass is (17±8)%, with two sub-regions of the renal mass (32±10)% and (30±7)%, exceeding the contra-lateral BV (14±7)% and ipsi-lateral cortex BV (21±4)%. It suggests that there exists micro-vessel structure in the sub-regions of the complex renal mass.

[Conclusion] This technique combining the UTE pulse sequence and the safe contrast agent ferumoxytol

provides strong positive contrast vascular images superior to Gd CEMRA and is a useful tool in renal mass assessment. The use of UTE sequences provides homogenous intraluminal signal intensity which is a function of contrast concentration. The BV map derived here provides a quantitative measurement of the distribution of micro-vessel density across the renal mass and other region-of-interest, even below the limits of vessels which can be resolved at the resolution. This will potentially benefit surgical planning, renal mass characterization, and disease progression in patients with impaired renal function.

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Webinar: Imaging and sensing
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Extract the cardiac cycle signal and respiratory signal directly for 2D cine MR images and CBCT projection images

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Objectives: Cardiac and respiratory signals are essential in the analysis of cardiac imaging and creating the joint cardiac and respiratory motion models. Such motion analysis and motion modeling efforts are critical for image-guided radiation therapy treatment for cardiac diseases. In this study, we developed a novel approach, purely based on the image intensity, to directly extract both respiratory and cardiac cycling signals from different image modalities. The extracted motion cycling signals could be lately used for supporting motion phase based image reconstruction, motion analysis and modeling. 2D cine MRIs and x-ray cone-beam CT projection images are covered by this study. The proposed method can be used as an alternative when cardiac and respiratory signals, such as ECG, are not available on the image-guided treatment machines.

Methods: For images with a consistent field-of-view (FOV) such as the 2D Cine MRIs, the main contributors of the image intensity changes are the cardiac and respiratory motions. The proposed procedure to extract and separate both respiratory and cardiac cycling signals was 1) calculating the average intensity of the whole 2D Cine MR image, and 2) filtering the intensity signal based on the common frequency of the respiratory and cardiac motions (0.1 – 0.3 Hz for respiratory signal, and 0.8 – 1.2 Hz for the cardiac signal). For CBCT projection images acquired with rotating gantry on radiation therapy treatment machines, the signals were extracted by 1) manually selecting cardiac boxes (to cover the largest and visible portion of the heart) in several frames with obviously different heart position such as the 90 180 360 in a 360 rotation; 2) generating the cardiac boxes for the middle frames by interpolating the sizes of the manually placed cardiac boxes on the key frames, then applying a smooth-fitting; 3) calculating the average image intensity in the moving cardiac boxes to obtain the raw signal which contains 3 information – the gantry rotation, respiratory motion and cardiac motion; 4) using smoothing-spline-fitting to remove the baseline signal caused by the gantry rotation; and 5) generating the respiratory and cardiac signals by applying band-pass filters (0.1 – 0.3 Hz for respiratory signal, and 0.8 – 1.2 Hz for the cardiac signal).

Results: The proposed respiratory and cardiac signal extraction approach was tested on 2D cine MRIs and CBCT projections from 15 different subjects. The extracted cardiac and respiratory signals were consistent and synchronized with motions appearing in the images. A comparison with the landmark-based cardiac signals from ICD lead locations in three subjects showed that the two cardiac signals were consistent.

Conclusion: A novel approach was developed to extract the respiratory and cardiac signals from 2D Cine MRIs and Cone-Beam CT projection images. The proposed approach will be useful for supporting cardiac and respiratory motion studies for image-guided radiation therapy treatments.

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4D motion modeling and real-time online 3D motion tracking for MR image guided radiotherapy

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Objectives:
Real-time monitoring, estimation, and prediction of the respiratory movement of tumors and nearby organs-at-risk (OARs) are very challenging for treating thoracic and upper abdominal cancers with MR image guided radiation therapy (MRIGRT). The latest MRI-guided radiotherapy system (Viewray MRI-Linac) can acquire 2D Cine MRIs at 8Hz during radiation beam delivery and perform real-time 2D image-based tumor motion tracking and beam gating. However, 2D Cine imaging is often inadequate to accurately track 3D motion of tumors and OARs.

Methods:
A novel motion modeling and estimation approach named Low-Resolution-Motion-Modeling (LRMM) was developed to enable 3D motion tracking with two stages: 1) pre-delivery motion measurement and modeling; 2) 3D motion estimation during treatment delivery. Forty low-resolution (10 slices, 4.5x4.5x7 mm3) free-breathing 3D-Cine MRIs (2 volumes per second, in coronal view, in total 20 seconds) were added after the clinical standard breath-hold 3D MRI patient setup scan (1.5×1.5×3 mm3, 17 seconds). A groupwise deformable registration AI model was developed and applied to compute the 4D motion on the 3D Cine volumes before radiation beam delivery. To compute 3D motion during radiation beam delivery, each frame of the continuously acquired 2D-Cine MRIs (4.5x4.5x7 mm3, a single 2D slice, 8 frames per second) was approximated from the central slices of the 3D Cines. The corresponding 3D motion field for each 2D-Cine frame was estimated from the weighted sum of the determined weights with corresponding deformation fields calculated in the modeling stage.

Results:
Real-time 3D motion computation (0.012 second per frame) during beam delivery was accomplished without computationally expensive iterative optimization. Synthetic experiments and healthy subject studies were conducted to demonstrate and evaluate the proposed approach. An average 0.5±0.4 mm 3D motion tracking accuracy was obtained after registration and motion modeling on XCAT digital motion phantom simulations. Data from three healthy human subjects were processed and visually evaluated.

Conclusion:
A novel 4D motion management procedure was successfully developed. It allows tracking tumor and OAR motions in 3D and real-time, which is an important advancement over the current 2D tracking and gating.

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In Vivo 3-D Gamma-Ray Spectrometry for Molecular Theranostics

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(Objective) We will discuss our recent progress in developing the world-first clinical hyperspectral SPECT system (Dynamic Extremity (DE)-SPECT system) that allows the user to derive voxel-by-voxel, high-fidelity gamma-ray spectra with an unprecedented energy resolution (<1.5% at 140 keV to <1% at 500 keV) over a wide energy range (50-600 keV). The DE-SPECT system would allow X-Y-Z-E 4-D mapping of gamma-ray emission across a clinically relevant FOV of 28 cm diameter, which makes it particularly attractive for simultaneous imaging of multiple-molecular pathways using virtually any combination of commonly used SPECT isotopes (Tl-201, Tc-99m, I-125/123, In-111, etc.). We are also exploring the DE-SPECT system for the mapping distribution of the primary and secondary radioisotopes following the delivery of therapeutic radionuclides (Ac-225, Ra-223, Lu-177, At-211, etc.).

(Methods) The DE-SPECT system is constructed with 192 3-D imaging spectrometers, each having a CZT crystal of 2 cm x 2 cm x 1 cm (thickness) to ensure a reasonable sensitivity for gamma rays of 50-600 keV. The CZT detectors utilize sophisticated electrode design and signal processing hardware to provide precise 3-D position resolution (0.7 mm), an unmatched spectroscopic performance, and the ability to detect multiple simultaneous gamma-ray interactions inside the detector. These characteristics represent a significant step-up from existing hardware employed in modern clinical SPECT systems. The DE-SPECT system is also equipped with a variable aperture system to allow the user to select, on-the-fly, between a wide FOV (28 cm diameter) overview mode and a focused (16 cm) high-resolution/sensitivity mode for local tomographic studies. Furthermore, the DE-SPECT system will be installed inline with the GE Discovery NM570c SPECT/CT or 530 SPECT systems to allow multi-organ and multi-modality (SPECT/CT) imaging of patients.

(Results) In this presentation, we will discuss the design and construction of the DE-SPECT detector hardware, variable apertures, and system gantry. We will also present the preliminary assessment of the CZT sensor performance and imaging resolution, and sensitivity of the DE-SPECT system.

(Conclusion) The development of the DE-SPECT system is a critical step to extend the horizon of modern emission tomography (SPECT and PET) from single-functional/monoenergetic imaging to multi-functional/colorful spectral imaging of gamma-ray emission for integrated focused organ and whole-body clinical imaging. It would uniquely allow users to perform voxel-by-voxel gamma-ray spectrometry and from which derive the concentrations of multiple radiotracers and therapeutic radionuclides in user-selected local targeted regions. This capability would make it particularly attractive for various forms of molecularly-guided interventions.

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Webinar: Robot
1:20 PM - 1:30 PM

Telerobotic neurovascular interventions with magnetic manipulation

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Advances in robotic technology have been adopted in various subspecialties of both open and minimally invasive surgery, offering benefits such as enhanced surgical precision and accuracy with reduced efforts and fatigue. Despite the advantages, robotic applications to endovascular neurosurgery have remained largely unexplored due to technical challenges such as the miniaturization of robotic devices that can reach the complex and tortuous vasculature of the brain. Although some commercial robotic systems enable precise manipulation of convention-al guidewires for coronary and peripheral vascular interventions, they remain unsuited for neurovascular applications due to the considerably smaller and more tortuous anatomy of cerebral arteries. Here we present a teleoperated robotic neurointerventional platform based on magnetic manipulation. Our system consists of a magnetically controlled guidewire, a robot arm with an actuating magnet to steer the guidewire, a set of motorized linear drives to advance/retract the guidewire and a microcatheter, and a remote-control console to operate the system under feedback from real-time fluoroscopy. We demonstrate our system's capability to navigate narrow and winding pathways both in vitro with realistic neurovascular phan-toms representing the human anatomy and in vivo in the porcine brachial artery with accentuated tortuosity for preclinical evaluation. We further demonstrate telerobotically assisted therapeutic procedures including coil embolization and clot retrieval thrombectomy for treating cerebral aneurysms and ischemic stroke, respectively. Our telerobotic neurointerventional system could enable safer and quicker access to hard-to-reach lesions while minimizing the radiation exposure to interventionalists and open the possibility of remote procedural services to address challenges in current stroke systems of care.

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Webinar: Robot
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MERLIN: An MRI-Guided Steerable Needle to Replace Open Brain Surgery for Epilepsy Patients

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For the 3.4 million individuals in the United States who experience epilepsy, drug-based treatments can cause significant side effects, while approximately 30% are medically refractory. For individuals where the epileptic seizures can be localized to the hippocampus, amygdalohippocampectomy can be a curative treatment for epilepsy. MRI-guided Laser Interstitial Thermal Therapy (LITT) has emerged as a promising alternative to surgical resection for neurosurgical procedures since it can be performed without a craniotomy. Recent advances in laser neural tissue ablation and MR thermal imaging underscore the promise of minimally invasive therapies for the treatment of temporal lobe epilepsy. However, existing LITT tools are rigid straight manipulators; targeting features in the deep brain (such as the hippocampus) requires traversing through regions of the brain that control speech and language comprehension, with some patients experiencing strokes or Broca's aphasia due to the trauma caused by surgical treatment. Smaller, more dextrous surgical manipulators, combined with real-time MRI-guidance have the potential to deliver LITT therapy to deep brain targets without the risk of damaging regions of the brain that would be traversed using a cranial approach with existing tools. In contrast with existing LITT technologies which deliver tools through a cranial burr hole, the use of concentric tube steerable needle technology enables a percutaneous approach through a natural opening in the facial-skeletal structure called the foramen ovale. Our previous work has demonstrated the potential for helical needles to traverse the foramen ovale to reach the hippocampus using a follow-the-leader approach. We hypothesize that the use of a curved needle delivery system will enable a more customizable ablation volume than ablation using conventional straight LITT tools, which have been shown to be capable of ablating at most 70% of the volume of the

hippocampus, which can potentially result in recurrence of epileptic seizures after treatment. To deliver the concentric-tube laser ablation probe to the hippocampus, we have designed a modular, MRI-compatible, pneumatically actuated robotic system that is capable of independently actuating the curvilinear guide needle and the optical fiber for thermal ablation. The pneumatic actuation is achieved using additively manufactured stepper motors that are capable of being powered off a hospital air supply line, and do not noticeably affect the SNR of the MRI image since they do not produce electrical interference. Conventional MR thermometry, based on Proton resonance frequency shift (PRFS) loses signal in areas with steep off resonance gradients that appear near metallic objects. To enable imaging near the delivery needle, we have developed a novel temperature imaging scan that enables MRTI near metallic features, by refocusing phase dispersion in tissue near a wire using through-slice z-shim gradient pulses placed before the gradient-recalled echo MR signal readouts. With the real-time thermal feedback from the MRI, closed loop control will be implemented to actuate the needle through the hippocampus while adjusting the laser intensity to ablate the target volume. MR-guided concentric tube manipulators for percutaneous access of neurosurgical targets represent a promising advancement towards reducing the invasiveness and increasing the efficacy of laser thermal therapy.

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Webinar: Robot
1:40 PM - 1:50 PM

Image-Guided Robotic Steerable Needles for Enhanced Access to Lung Nodules

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[Objective] Lung cancer kills over 130,000 Americans each year and survival depends on early diagnosis, which requires biopsy to be definitive. Even with the latest devices, current approaches for accessing suspicious nodules for biopsy are unable to accurately reach many nodules in the peripheral lung (i.e., those not adjacent to a bronchial tube) or risk pneumothorax (lung collapse), which can be life-threatening to older patients and those with comorbidities. A new approach is needed to enable accurate and safe access to nodules throughout the lung.

[Methods] We present a novel semi-automatic robotic system that harnesses the capabilities of a new class of steerable needles to extend the range of bronchoscopes to accurately biopsy nodules throughout the lung. Our team brings together computer scientists, engineers, and physicians at the University of North Carolina at Chapel Hill and Vanderbilt University. Compared to percutaneous biopsy, our approach decreases the risk of pneumothorax since the needles are deployed from within the lung, without puncturing the pleura. Compared to the latest transoral approaches, our device extends their reach by steering through the lung parenchyma to nodules throughout the lung.

[Results] We present a three-stage, image-guided, semi-automatic robotic device for bronchoscopically deploying steerable needles to targets in the lung. In a procedure, the physician first guides a bronchoscope through the airways to a desired exit point and pierces into the lung parenchyma. Then a needle-diameter aiming device, deployed through the bronchoscope, enters the lung parenchyma and is tele-operated to aim at the nodule. The steerable needle then launches through the aiming device and semi-automatically maneuvers through the lung parenchyma around anatomical obstacles and accurately hones in on the target. Using early-stage prototypes, we have achieved targeting errors averaging under 3mm in ex vivo porcine animal models.

[Conclusion] We created a new robotic system with the potential to significantly broaden the class of patients for which early-stage definitive diagnosis of suspicious nodules can be safely and accurately obtained. Increasing rates of chest imaging and new lung cancer screening guidelines are expected to increase the number of incidentally discovered lung nodules, further increasing the potential applicability of the presented system. We also will discuss ongoing and future work to enable accurate, precise, safe, and automatic access to nodules throughout the lung.

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Webinar: Robot
1:50 PM - 2:00 PM

Shape-Sensing and Prediction using FBG-Sensorized Needles

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Objectives: In prostate cancer diagnosis and treatment, inaccurate needle placement may cause false-negative biopsies and suboptimal cryoablation. This project aims to mitigate these issues through the development of adaptive needle guides to compensate needle deviation on-the-fly allowing for fast and accurate needle placement during needle insertion interventions, as well as provide a needle shape prediction framework for proper needle insertion planning. To enable on-the-fly needle deviation compensation we developed a unique, sensorized, shape-sensing needle embedded with biocompatible fiber Bragg grating (FBG) strain sensors. The sensorized needle utilizes the FBG sensors' capabilities for real-time sensing and high accuracy in conjunction with a novel sensor-based shape-sensing model to enable real-time shape feedback and shape prediction. The goal of this study is to prototype a sensorized needle, and to validate our real-time shape-sensing and shape-prediction system. In this study, we tested our shape-sensing and shape-prediction framework for C-shaped needle insertions in single-layer soft and hard phantom tissue under stereo camera visualization for ground truth measurement. Furthermore, we evaluate our shape-sensing framework for C-shaped needle insertions in real tissue under C-arm visualization for ground truth measurement.

Methods: We built an 18 Ga (OD = 1.3mm) sensorized needle embedded with four active area FBG strain sensors. The sensorized needle was calibrated into a constant curvature jig to correlate needle sensor measurements with curvature information within an active area of the needle. Post-calibration, the needle was inserted into transparent phantom tissue using a robotic 4-axis insertion stage for varying insertion depths using stereo vision as the ground truth 3D needle shape. Shape-sensing and shape-prediction was evaluated for insertion depths up to 120mm in transparent tissue. Finally, the needle was manually inserted in real tissue for varying insertion depths using 3D volumetric CT scans as a ground truth 3D needle shape. Shape-sensing was evaluated for insertion depths up to 120 mm in the real tissue.

Results: We successfully built and tested a shape-sensing needle embedded with three optical fibers (? = 80 ?m) arranged in a trigonal pattern with each other. Each fiber has four active areas located at 10, 30, 65, and 100mm from the needle tip. Calibration results indicate an average root-mean-square shape-sensing error of 0.20mm for clinically relevant curvatures (? 1m-1). Experimental needle insertion results in soft and hard phantom tissue indicate accurate shape-sensing and shape-prediction with root-mean-square shape errors of 0.48mm and 0.89mm, respectively. Furthermore, accurate shape-sensing was demonstrated in real tissue with a root-mean-square shape-sensing error at the maximal insertion depth of 120mm of 1.12mm.

Conclusion: We demonstrated real-time accurate shape-sensing for FBG-based sensorized needles with preliminary shape-prediction for C-shaped needle insertions.

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Webinar: Robot
2:00 PM - 2:10 PM

Image-guided robotics for surgical reduction of complex joint dislocations

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Objectives. Surgical treatment of joint fractures requires accurate reduction and fixation of the joint space to restore anatomical integrity. In ankle fractures with syndesmotic injuries, realignment inaccuracies are associated with chronic functional impairment, mechanical instability, and increased risk of osteoarthritis. Despite the prevalent role of intraoperative fluoroscopic imaging, uncertainties in 3D spatial reckoning and challenges in hand-eye coordination can result in malreduction rates of up to 39–52%. This work develops a novel system that combines intraoperative imaging, using low-dose CBCT and 3D-2D image registration, with robotic manipulation of the anatomy to precisely restore joint integrity. The solution offers quantitative morphological analysis from 3D and 2D images and precisely guides a robotic instrument without the need for and the limitations associated with conventional surgical tracking.

Methods. The approach is developed on 3 major fronts: (1) image-based planning from intraoperative 3D CBCT to identify the target fibula pose; (2) a low-profile, radiolucent robot for manipulating the distal fibula; and (3) 3D-2D registration of the robot and multiple bones from fluoroscopic imaging to guide/confirm reduction. Image-based planning uses statistical shape and pose modeling to obtain 3D bone models and establish their pose relation to predict the necessary reduction. The robot has a table-mounted design that grasps the fibular fixation plate, has an embedded force/torque sensor, and allows 3-DOF motion of the fibula with respect to the secured tibia. Registration to fluoroscopic imaging uses standard views acquired as part of routine workflow to obtain a multi-body 3D-2D registration for tracking bones and guiding/confirming reduction. Initial studies were performed on phantom and cadaver specimens, with future studies underway to test system integration and evaluate end-to-end performance. Feasibility of the approach will be tested in clinical studies planned in the final year of the project.

Results. Initial work on robot design focused on addressing workflow requirements and characterizing operating forces on cadaveric specimen with intact and ligament-cut joint, demonstrating maximum forces/torques of 100 N and 2.5 Nm for 100 mm and 25° displacements/rotations, respectively. Statistical image-based planning used a 40-member atlas of ankle CT images and was able to predict the correct fibula pose to within 1.6 mm and 1.8° in leave-one-out analyses. The 3D bone models obtained from shape modeling were used in 3D-2D registration to yield 1.9 mm target registration error (comparable to conventional tracking). Robustness to modeling errors was demonstrated <5 mm registration error when using models with mean surface distance error of <0.9 mm.

Conclusions. Preliminary results demonstrate the basic feasibility of our approach, which combines modern robotics approaches with intraoperative imaging to satisfy the high technical demands of joint realignment, limit radiation dose to patient and staff, and provide accurate treatment to ultimately improve long-term patient outcomes. Success in this research will help to eliminate revision surgeries due to malreduction (a major cost burden) and improve long-term quality of life for >100,000 patients/year. The technology developed has impact trauma surgery beyond ankle repair and would be applicable to surgical treatment of other challenging joint dislocations and long-bone fractures.

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Webinar: Robot
2:10 PM - 2:20 PM

Medical Robotics for MRI-Guided Interventions

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Objectives. MRI-guided interventions are growing in popularity due to the superior imaging characteristics of MRI and the lack of ionizing radiation. We are developing several systems for MRI-guided interventions including: 1) a shoulder-mounted robot for arthrography; 2) a back-mounted robot for pain relief; 3) a head-mounted robot for intracerebral hemorrhage; and 4) a table-mounted robot for long bone biopsy.

Methods. The shoulder-mounted and back-mounted robots were developed in collaboration with Johns Hopkins Engineering and Cincinnati Children's. The shoulder-mounted robot includes a custom vacuum mounting bag to hold the robot stably on the shoulder. The back-mounted robot includes a custom single loop coil to provide additional signal for robot fiducial registration. The head-mounted robot is being developed through a team including Georgia Institute of Technology, Vanderbilt University, DePaul University, and George Washington University. This robot is a concentric tube design which includes a vacuum pump to evacuate the clot. The table-mounted robot was developed by Johns Hopkins Urology who also developed an MRI-compatible bone biopsy drill based on pneumatic actuation.

Results. Both phantom and cadaver studies have been completed on the various projects. We are also pursuing IRB and FDA approval for clinical trials. The workflow is similar across the robotic devices: 1) position robot on body/table; 2) obtain MRI images; 3) register robot to MRI coordinate system; 4) path planning on MRI images; 5) align robot along desired trajectory; and 6) perform the intervention.

Conclusions. MRI-guided interventions offer advantages in terms of image quality and radiation free imaging. Body and table mounted robots may allow precise interventions to be carried out in a minimally invasive manner. While the projects are in various stages ranging from pre-clinical development to early phases of clinical testing, our ultimate goal is to move them all to wide clinical adoption to benefit pediatric patients.

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Webinar: Robot
2:20 PM - 2:30 PM

Open Source Software Platform for Image-Guided Robot-Assisted Interventions

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Objectives. Percutaneous needle placement plays a fundamental role in diagnosing and treating prostate cancer. Nearly one million prostate biopsies are performed annually in the United States using a core biopsy needle for pathological examination. The confirmed lesions may then be focally treated with brachytherapy or thermal ablation using applicator needles. For those procedures, accurate needle placement is essential to avoid false negatives or achieve an optimal dose distribution. The demand for precise needle placement has been growing in recent years, thanks to the recent progress in imaging technologies, particularly multiparametric magnetic resonance imaging (MRI). Several groups, including us, attempted to improve needle placement accuracy in the prostate using image-guided robot-assisted intervention (IGRI) systems. However, the in vivo accuracies of those IGRI systems have never matched the level achieved in the benchtop setting. Those lower-than-expected accuracies are often attributed to needle deviation resulting from the physical interaction between the needle and

the heterogeneous tissue, underscoring the importance of modeling the needle and tissue deformations. While several needle and tissue models have been proposed, their advantages are yet to be demonstrated in patients because of a lack of practical methods to build a patient-specific model from data available in clinical practice and incorporate the model into the control process in the IGRI system. Particularly, software components for building a model based on image information and those for managing and controlling the robotic hardware are often incompatible and cannot be integrated into a single IGR system.

Methods. To address this engineering challenge, we are developing ROS-IGTL-Bridge as a mechanism to integrate two popular open-source software packages, namely Robot Operating System version 2 (ROS2) and 3D Slicer. ROS and 3D Slicer are separate modular software environments where users can combine existing plug-in modules or add new ones to customize the software for their applications. Both software packages are used by many researchers and engineers as de-facto standard software environments in the robotics and medical image computing communities, respectively. ROS-IGTL-Bridge interconnects ROS and 3D Slicer using a TCP/IP socket to facilitate seamless data exchange between the modules across the environments so that state-of-the-art robotics and image processing modules can work together in a single system.

Results. ROS-IGTL-Bridge enabled us to design a unified workflow consisting of image analysis, kinematics, control, and visualization by calling features available in these packages with relatively small engineering efforts. Since its initial launch in 2016, the platform has been used in several research projects that integrate needle-guiding robots and 3D-Slicer-based image-guidance software.

Conclusion. As 3D Slicer and ROS have been long supported by large user/developer communities, ROS-IGTL-Bridge enables us to incorporate a broad range of gold-standard image processing and robotics tools into our research IGRI system. It has the potential to help research projects where a patient-specific model derived from medical images is used to control the robotic hardware for better outcomes.

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Webinar: Robot
2:30 PM - 2:40 PM

Physician Assistance Technology in Image-guided Robotic Intervention of Prostate

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Recent advances in the multi-parametric MRI of the prostate have led to a surge in new research methods for the detection and diagnosis of prostate cancer - with the goal of accurate risk- stratification of prostate cancer. Specifically, a traditional Transrectal Ultrasound (TRUS)-guided biopsy tends to fail, as samples are randomly collected from the prostate without aiming at suspicious lesions often visible in MRI. Currently, several new MRI biopsy approaches have come to the forefront. They are being evaluated and adopted in clinical practice, including in-bore MRI- guided biopsy and TRUS-guided MRI-fusion biopsy, collectively called ‘MRI-targeted biopsy.’ While recent literature shows that MRI-targeted biopsies can detect more clinically significant cancer than a conventional TRUS-guided biopsy, there is still a substantial issue with the precision placement of the needle in these procedures particularly in transperineal approach, resulting in clinicians being overly conservative with the amount of tissue removal (Zhang et al., 2019). Need to address needle placement accuracy in transperineal biopsy is further heightened lately as the fluoroquinolone- resistant Escherichia coli is becoming a significant concern in public health, and clinicians are shifting to use transperineal biopsies to avoid post-biopsy infections and overuse of antibiotics. Literature, as well as our preliminary studies, found that needle deflection is a substantial obstacle for precision aiming in transperineal biopsies. Abundant literature on needle deflection analysis, needle steering, and image-guided robots are available in pre-clinical engineering studies. Yet, clinically viable or proven solutions to address the needle deflection is yet to be seen. Therefore, the

objective of this application is to develop and test a cooperative robotic intervention with closed-loop error compensation in MRI targeted biopsies and focal therapies, resulting in more precisely targeted instrument placement. Accurately, we will aim to address needle deflection by the synergic use of advanced imaging and robotics. Guided by robust preliminary data, this objective is achieved by pursuing three specific aims: 1) We will develop novel tracking techniques and clinically deploy a cooperatively controlled, hands-on robotic needle placement manipulator to enable fine instrument control at the periphery of the MRI bore. 2) We will test the usefulness of a cooperatively controlled robot to increase the accuracy of needle placement in animal studies mimicking MRI-guided biopsies of the prostate. Our approach is innovative in its application of novel cooperative robotic control, in which the clinician maintains ultimate control with the direction of motion being autonomous to ensure the desired path is followed to the intended target. The proposed study is also clinically significant since the completion of this current engineering study will enable machine- assisted semi-autonomous percutaneous therapy, much discussed in the recent editorial article in Science Robotics (Yang et al., 2018). The impact of the study reaches beyond MRI-targeted prostate intervention; the technology developed can be translated into other forms of MRI-guided or ultrasound-guided intervention.

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Webinar: Surgery
1:20 PM - 1:30 PM

Margin Detection for Oral Squamous Cell Carcinoma Using Dynamic Optical Contrast Imaging

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Introduction and Objective
Surgical resection of oral squamous cell carcinoma (OSCC) requires establishing appropriate margins that carefully balance oncologic outcomes and preservation of function. While positive margins negatively affect prognosis and increase rate of recurrence, excessive excision of healthy tissue can result in significant patient morbidity including speech and swallowing deficits. Intraoperative margins are currently determined through palpation, surgeon experience, and frozen section. In this study, we utilize dynamic optical contrast imaging (DOCI), a novel and non-invasive imaging system, to accurately identify margins in OSCC.

Study Type
Prospective study

Methods
In vivo and ex-vivo oral tongue, mandible skin, buccal mucosa, and floor of mouth specimens from OSCC patients were first imaged using the DOCI system followed by permanent histologic sectioning. A pathologist annotated the histopathology slides for epithelial, mucosal, muscle, fat, and malignant tissue types. Annotations were then transferred to DOCI images, and signature emission was compared between malignant and adjacent healthy tissue across 8 different spectral channels.

Results
In all specimens, DOCI images of gross specimens clearly demarcate margins as well as perineural invasion (PNI) between healthy tissue and OSCC. DOCI real time images are acquired in less than 18 seconds with a clinically relevant wide field of view (6.5 cm2) and 70 micron resolution. Across all 8 spectral channels, there was a statistically significant difference in DOCI values between different healthy tissue types and OSCC ($p>0.01$).

Conclusion
DOCI allows for visualization and accurate delineation of OSCC and adjacent healthy tissue in real-time. This study demonstrates that DOCI has the potential to revolutionize cancer care by allowing the surgeon to precisely

determine margins intraoperatively and improving patient oncologic and functional outcomes

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Webinar: Surgery
1:30 PM - 1:40 PM

A Lensless Wireless Fluorescence Image Sensor for Real-time in vivo Imaging in Cancer Immunotherapy

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[Objectives]
Cellular-level in vivo imaging is critical in obtaining high-resolution, multicellular information in cancer therapy. One key application is monitoring the immune response in immunotherapy, a game-changing therapeutic that unleashes the immune system to attack cancer. While immunotherapy results in durable responses for responders, detailed cellular-level information from multiple immune cell types is essential to assess efficacy of the treatment and adapt it based on the mechanism of resistance in nonresponders. Current microscopy systems (MRI/CT, etc.) capture entire body images to guide diagnostics; however, due to their low sensitivity (centimeter-scale), any change is detected only after a significant accumulation of cells resulting in long (months) delays and potential loss of the curative window. Ideally, a repeated biopsy would provide the requisite information; however, this is impractical. In lieu of bringing the tissue to the microscope, we consider the possibility of bringing the microscope into the tissue. Fluorescence microscopy enables detection of multiple cell types, including activating and immune-suppressing components, but is yet to be deployed inside the body on a platform compatible with long-term implantation. While state-of-the-art fluorescence imagers provide high-resolution microscopy, they are impractical for chronic real-time in vivo monitoring due to external wiring.

We propose a proof-of-concept “wireless microscope-on-chip”, leveraging innovations in optics and CMOS technology to detect small cell foci (via systemic injection of a fluorophore-labeled antibody) in real-time and transmit the data through an ultrasonic link. Miniaturization is achieved by: (1) a custom 36×40 pixel CMOS imager with integrated angle-selective gratings to remove bulky optics, (2) a single mm-sized piezoceramic for wireless power and data transfer eliminating external wiring and batteries, and (3) a sub-mm-sized laser diode replacing optical fibers to provide illumination inside the body.

[Methods]
To obtain a detectable fluorescence signal from 200 cells (~200fW) labeled with typical fluorophores, a laser diode with a 50mW/cm2 excitation power is controlled by the wireless sensor. An ultrasound link is chosen for minimum tissue attenuation and higher FDA-approved power transfer density.
To supply the high-power excitation source from limited instantaneous power of ultrasound waves, the wireless sensor is operated with a heavily duty-cycled (0.04%) illumination within a 150.5s frame. An 11.52kbit image is captured by the 2.5x4.9mm2 integrated circuit, quantized and transmitted wirelessly via ultrasound backscattering.

[Results]
Performance of the system is verified using a fluorescent Cyanine5.5-NHS dye distributed over a USAF test target and the image is wirelessly transmitted to an ultrasound transducer placed 2cm away inside canola oil to replicate tissue attenuation properties. The imager captures 150?m structures on the test target after a 64ms integration time making it possible to visualize comparable sizes of cell foci in real-time.

[Conclusion]

This work presents a prototype for a wireless lensless image sensor enabling real-time monitoring of the immune response at early stages of cancer progression in immunotherapy. We demonstrate an unprecedented proof-of-concept wireless fluorescence microscope-on-chip with a frame time of 150.5s to capture minute-scale cell movements without focusing lenses, fiber optics, batteries or external wiring.

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Webinar: Surgery
1:40 PM - 1:50 PM

Near Infrared Nerve-Specific Fluorophores to Improve Nerve Sparing Radical Prostatectomy

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Objective: Iatrogenic nerve injury represents one of the most feared surgical complications and remains a major morbidity across all surgical specialties. Nerve-sparing radical prostatectomy is a compelling clinical example of significant patient morbidity, where nerve damage is reported in up to 60% of patients resulting in incontinence and impotence. Surprisingly, no clinically approved technology can enhance intraoperative nerve visualization, typically performed through neuroanatomical knowledge and conventional white light visualization alone. Development of a near infrared (NIR) fluorophore that specifically highlights nerve tissue in the operating room would have direct clinical translation to nerve sparing prostatectomy through the FDA approved fluorescence channel in the da Vinci surgical robotic system (Firefly, Intuitive Surgical, Inc.), which is used in >80% of prostatectomies performed in the United States today. The proposed work will directly address this unmet clinical need. Fluorescence Guided Surgery (FGS) has successfully integrated into clinical medicine with only two FDA-approved NIR fluorophores (i.e., indocyanine green [ICG] and methylene blue). FGS systems operate almost exclusively in the NIR (700-900 nm), where tissue chromophore absorbance, autofluorescence and scatter fall to local minima, allowing high contrast and high resolution imaging at up to centimeter depths. All clinical FGS systems have an “800 nm” channel designed to image ICG.

Methods: To facilitate rapid clinical translation, the overall goal of this work is to generate a nerve-specific small molecule fluorophore with spectral properties matched to ICG, enabling both nerve imaging at depth and future clinical translation using existing clinical FGS infrastructure. Design and development of a small molecule nerve-specific fluorophore that can be imaged using FGS systems optimized for ICG has been a significant challenge because these probes need to have a low enough molecular weight to cross the tight blood nerve barrier junction with a sufficient degree of conjugation for NIR excitation and emission.

Results: In exciting recent studies, our team has synthesized first-in-class NIR nerve-specific small molecule fluorophores that can be imaged with standard FGS systems optimized for ICG. Herein, we will report on our novel probe development, translation to swine and canine models using the da Vinci as well as preclinical pharmacology and toxicology (pharm/tox) studies, enabling a future IND application to the FDA for clinical translation to robotic assisted radical prostatectomies (RARP).

Conclusion: Successful completion of this project will result in an optimal NIR nerve-specific fluorophore suitable for use with all clinical FGS systems and validation of nerve-specific contrast for RARP using the da Vinci Firefly.

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Webinar: Surgery
1:50 PM - 2:00 PM

Robot-Enabled Natural Orifice Prostatectomy

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The objective of this proposal is to create a hand-held surgical robot for endoscopic transurethral radical prostatectomy. The new robot will deploy needle-sized arms through the endoscope, for independent tissue manipulation, laser aiming, and visualization, enabling resection of the prostate and reconstructive suturing. Clinical significance comes from (1) the large number of patients who could benefit (1 in 7 men will have prostate cancer in their lives) and the high rates of complications including impotence and incontinence of current surgical approaches. We hypothesize that the key to reducing complication rates is minimal disruption to the delicate tissues surrounding the prostate, especially the neurovascular bundles that run on the outside of the prostate. Current surgical techniques approach the prostate from the abdomen, and thus require large dissection of the structures that surround the prostate including endopelvic fascia and prostatic ligaments, and manipulation and retraction of the neurovascular bundles. In contrast, we propose the novel approach of reaching the prostate from within, through the urethra, which is enabled by needle-size, tentacle-like robot manipulators delivered through an endoscope, to enable laser-based resection and dexterous reconstructive suturing. We hypothesize that such a system will improve functional outcomes and reduce complication rates, providing a much less invasive approach to performing prostate surgery. The innovation of our new robot is the ability to deliver needle-sized robotic arms through an endoscope. They are made up of telescoping, curved, elastic tubes. By axially rotating these tubes and telescopically extending them, our robot will provide the surgeon with two small tentacle-like arms at the tip of the endoscope. One arm will carry a holmium laser fiber for cutting, the other will enable tissue retraction, and both will work together to perform reconstructive suturing. This is the first hand-held robotic system to provide two-handed dexterity. It will enable suturing within a lumen as small as the urethra, a major technical innovation that we expect to be useful. in many other surgical contexts in the future. We have designed a robotic system and demonstrated suturing in both synthetic and biological tissues in anthropomorphic phantoms.

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Webinar: Surgery
2:00 PM - 2:10PM

Image Guided Robotic Nephron-Sparing Surgery

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The importance of preserving renal function during surgical interventions through nephron-sparing (“partial nephrectomy”) surgical techniques has garnered considerable and growing recent recognition. Total kidney removal (“radical nephrectomy”) permanently compromises renal function and leads to increased morbidity and mortality, with substantial negative impact on long-term patient quality of life. In contrast, partial nephrectomy improves long-term outcomes by sparing a maximal amount of healthy kidney tissue. However, minimally invasive partial nephrectomy is rarely attempted because it is extremely challenging to accomplish. The surgeon must make critical intraoperative decisions (which can mean life or death for the patient), based on imprecisely mentally inferred and registered three-dimensional anatomical relationships. The surgeon must view a series of 2D preoperative images and build a mental 3D model of patient anatomy. He/she must then intraoperatively

guess how this remembered anatomical map should be registered to the patient. The inherent inaccuracies in this process prevent many surgeons from attempting minimally invasive partial nephrectomy, since positive margins (or inadvertent damage to internal kidney structures) are disastrous outcomes, while taking a large negative margin defeats the purpose of the partial nephrectomy procedure. Our overall goal is to create an image-guided surgical system that makes localization, dissection, and isolation of critical vascular and organ structures, as well as correct margin selection, easier and more accurate for the surgeon (and thus the procedure safer and more effective for the patient), thereby increasing the number of surgeons and hospitals able to adopt nephron sparing techniques. Toward this goal, our specific objective in this proposal is to test the hypothesis that image guidance can increase the accuracy and/or time efficiency of the surgery. To test this hypothesis, we have built and are currently clinically evaluating an image guidance system that brings preoperative CT images into the da Vinci surgeon console and accurately registers them to patient anatomy by using he da vinci tool tips to trace the organ surface. We are currently conducting a clinical pilot study where two surgeons participate, one who performs the surgery according to the standard of care (never seeing the image guidance display), and a second who intermittently steps in momentarily to use the image guidance display and collect accuracy data for post processing. Success of this work could, in principle, be widely clinically translated almost immediately because it requires no new pieces of hardware or other infrastructure; it could be deployed to the thousands of installed da Vinci systems as a simple software upgrade.

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Webinar: Surgery
2:10 PM - 2:20 PM

Optical phantoms and computational tools for advancing development of fluorescence guided surgery

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Introduction: Fluorescence-guided surgery is increasingly being adopted by surgeons for the potential to obtain real-time feedback that augments their ability to identify normal and diseased tissues through enhanced contrast of markers for perfusion, molecular phenotype or even genotype of tissue. Much of this field's first generation clinical successes have been based upon functional assessment of vascular perfusion imaging with indocyanine green (ICG). There are currently nearly 500 active clinical trials incorporating fluorescence imaging, and 39 unique fluorescent compounds under investigation, including four phase III trials. Yet, even with this growing adoption, there is a stark lack of standardized system characterization or routine performance monitoring, largely because the optical technologies vary considerably in their geometry, configuration, components and ultimately their uses.

Methods: A novel 3D-printing technique has been developed which provides the ability to tune optical parameters and embed fluorophores at fixed concentrations. This manufacturing process is being utilized to produce a set of reference targets to test system sensitivity for ICG-equivalent concentration, depth sensitivity and fluorescence resolution. This manufacturing process is also being used to demonstrate biomimetic features and the ability to incorporate other fluorophores. A web-portal has been developed to analyze fluorescence images of the reference targets collected with a range of systems to help identify parameters appropriate for system characterization and inter-system comparisons. These web-enabled tools are currently being expanded to reduce the operator burden of running Monte Carlo simulations for fluorescent optical interactions in tissue-equivalent material.

Results: Characterization of our 3D-printing process shows minimal autofluorescence of the base photo-curable resin. Doping resin with absorbing (i.e. carbon, hemin, nigrosin, etc.) and scattering (i.e. TiO2, BaSO4, Al2O3, etc.) agents provide the ability to mimic tissue optical properties, specifically at 800nm. An ICG-equivalent

fluorophore (IR125) as well as methylene blue, rhodamines and quantum dots have been demonstrated to provide fluorescence contrast. Using a multi-step quality assurance protocol, we demonstrate our percent standard deviation of intensity for assembled targets to be approximately 3% within our initial five manufacturing runs.
Conclusions: Optically appropriate reference targets and phantoms, produced in a cost effective manner, are a key component for performance characterization in fluorescence imaging applications. Computational tools for standardizing image analysis and simulating light-tissue interactions are additional tools in an ecosystem for efficiently developing and characterizing the next generation of fluorescence imaging systems. Feedback from a panel of academic, medical and industry experts is being utilized to direct the next phase of development.

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Technology and Framework for Image-guided Transoral Robotic Surgery igTORS

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Significance: Cancers of the head and neck (oral cavity, pharynx, and larynx) are the 5th most common cancers worldwide. Trans-oral surgical approaches such as trans-oral robotic surgery (TORS) and trans-oral laser microsurgery (TLM) are effective, reducing complications and long-term treatment morbidity. Challenges and Opportunities: One of the drawbacks of the trans-oral approach is the difficulty in intraoperatively assessing tumor extent and locating critical vascular structures, resulting in positive margins and risks of vascular complications. Image guidance and surgical navigation play a significant role in sinus, skull base, and neurosurgery, demonstrating improvement in the safety and efficacy of these procedures. It is expected that similar advantages could be realized by applying this approach to trans-oral surgery in the context of improving assessment of tumor depth and avoiding neurovascular structures. Image guidance however is currently not feasible for trans-oral robotic surgery due to the significant intraoperative tissue deformation that occurs with the introduction of retractors needed to provide surgical access. This intraoperative deformation limits the ability to accurately register preoperative imaging to the intra-operative state. Further, current metallic instrumentation required for exposure and airway management during trans-oral robotic surgery creates significant artifact on CT imaging. Our Approach: With the availability of intra-operative CT and MRI imaging at Dartmouth's Center for Surgical Innovation (CSI), intra-operative imaging is feasible. We have developed a suite of novel 3D printed polymer laryngoscopes and retractors that enable us to safely acquire artifact free images of patients during trans-oral surgery procedures including TORS (Fig 1). These devices provide equivalent tissue retraction and surgical working volume as compared to standard-of-care metal retractors. In addition, we are developing a surgical navigation framework that leverages in-room optical tracking to register surgical tools and robot arms to an intraoperatively acquired CT. 3D slicer coupled with OpenIGT are being used to co-ordinate tracker sampling, coordinate frame registration, and live-view updates (Fig 1). Live updates from the 3D slicer GUI are being projected through the TilePro feature on the daVinci surgical platform to provide screen-in-screen visualization of both the stereoendoscopic view and a 3D rendering of the registered patient CT. The CT is registered to the optical view of the stereoendoscope so that the CT view is aligned with the standard visual view the surgeon uses to operate. As the stereoendoscope pans through the surgical working volume the 3D CT volume tracks synchronously. Phantom and cadaver head studies are being evaluated to assess improved accuracy in terms of target localization errors when navigation is used during image guided transoral robotic surgery (igTORS) as compared to conventional TORS. We will present our current experience in developing igTORS and discuss future plans for evaluating this approach in preparation for in vivo deployment.

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Trackerless Navigation System for Lateral Skull-base Surgery

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Objectives: Lateral skull base surgery for repairing temporal bone defects or resecting tumors is extremely challenging. This is primarily due to two main reasons: 1) there is a lack of reliable anatomical landmarks to identify the underlying structures during surgery, 2) there are numerous sensitive structures around the resection cavity. Inadvertent damage to these sensitive structures could lead to potentially catastrophic consequences including permanent hearing loss, significant blood loss, loss of facial muscle activity, vertigo and disequilibrium. There is, therefore, an urgent unmet need to provide real-time and accurate visual guidance to the surgeon while performing lateral skull base surgery to visualize the surrounding anatomical structures in real-time while drilling through the skull or operating on the delicate structures in the inner ear.

Methods: We have developed a trackerless navigation system to provide real-time visualization of the inner ear structures intraoperatively. The navigation system consists of three steps. (1) We build three-dimensional (3D) model of the tissue surface from stereo microscopy images using the simultaneous localization and mapping (SLAM) method. (2) To register the CT data to the 3D surface model, and (3) we re-project the anatomical models generated from the preoperative CT images to the microscopy images during the surgery. No additional tracking or hardware devices will be required to provide enhanced guidance to the surgeon.

Results: A pilot evaluation of the stereoscopic surface reconstruction technology was completed using one side of a single cadaveric head. Five torus shaped fiducials (~1 cm diameter) were sutured in place around the cadaveric pinna. Using 3D endoscopy and high-resolution CT imaging, surface reconstruction and segmented CT models were generated as described above. The surface and segmented CT models were registered by aligning their respective fiducial centers, which were manually defined. We performed a preliminary assessment of registration accuracy and calculated target registration errors for the five fiducials of 2.51, 1.23, 1.09, 1.57, and 0.76 mm. The 3D Slicer-based user interface was designed to provide (1) the 3D visualization of the pinna surface and internal structures, and (2) the augmented microscopy images by reprojecting the 3D CT models to the microscopy images.

Conclusion: The expected benefits of our method include (1) the ability to allow the surgeon to "see through" the opaque bone while drilling within millimeters of critical structures, and (2) the ability to provide feedback of the relative positions between the critical structures and the instrument to avoid overexposure. In addition, since no external tracking devices are needed, the developed technologies may reduce the cost of existing navigation systems and easy integration with the clinical workflow without any OR footprint. In future, the developed technologies may also be transferred to other types of surgeries with small modifications.

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Establishing extensible open source infrastructure for managing IGT data

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Objectives
With the advancing role of AI in the clinic, current applications that utilize imaging and image computing for supporting image-guided medical procedures are becoming increasingly "data thirsty". At the same time, rapid growth and increasing complexity of the datasets with different imaging modalities, annotations, and clinical attributes necessitates implementation of robust and scalable data management approaches. Moreover, the approaches must meet the needs of various groups of users - including software developers, clinical experts, and project managers.

Methods
We are establishing an open source data management platform that leverages and extends existing open source tools and data management best practices. The desired solution will include the following components: * Interactive interface for search and exploration of the available data * Interactive data visualization * Flexible and configurable capabilities to support annotation of image data * Ability to extend the platform with AI-based analysis tools

Our approach extends the existing Joint Imaging Platform (JIP) Kaapana (1) within the Google Cloud Platform (GCP). We extend the existing capabilities of the platform with the ability to perform annotation of imaging data using a custom extension in 3D Slicer (https://slicer.org). We evaluate the platform utilizing a representative dataset collected during in-bore MRI guided prostate biopsy (2) and implement standard DICOM representation (3) of the image-derived data.

Results
We successfully deployed an instance of the Kaapana platform within a GCP-provisioned virtual machine, and confirmed operation of the data import, metadata indexing, cohort building, and image visualization. Once installed and the VM is activated, the user can access the functionality through the web browser, without the need to install any special tools.

To support annotation of image data, we are developing the 3D Slicer mpReview extension, which supports streamlined segmentation of multiparametric datasets, in particular prostate MRI. The module automatically loads patient data from a local database or remote DICOM server using DICOMweb interface, and provides a simplified interface that can be used to annotate various anatomical regions which are serialized as standard DICOM Segmentation objects; this in turn enables interoperability with the other components of Kaapana. The module can also be adapted for use in any multiparametric dataset apart from prostate MR.

To facilitate evaluation we have identified the test dataset that includes planning and intra-procedural MRI DICOM studies, localized image findings, segmentations of selected structures and pathology outcomes based on the collected biopsy samples.

Conclusions
Our current experience establishes the initial evidence for the utility of Kaapana and included components for the purposes of managing IGT data. We believe the proposed approach outperforms the current research practices of data management.

References
1. Scherer et al. Joint Imaging Platform for Federated Clinical Data Analytics. JCO Clin Cancer Inform. 2020.
2. Penzkofer et al. Transperineal in-bore 3-T MR imaging-guided prostate biopsy: a prospective clinical observational study. Radiology. 2015.
3. Fedorov et al. DICOM for quantitative imaging biomarker development. PeerJ. 2016.

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