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"Virtual Staining of Label-free Tissue Using Deep Learning"

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Submitted Abstracts

1. Wirelessly Actuated Ciliary Airway Stent for Excessive Mucus Transportation

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Small-scale cilia-like devices that can manipulate fluids in narrow spaces have great potential in microfluidics, biomechanics, biomedical engineering, and other applications. However, prior studies mostly focused on artificial cilia for pumping fluids for lab-on-a-chip microfluidic applications. The design and control of artificial cilia for transporting viscous mucus in confined and tubular structures remains challenging and medical devices such as airway stents with ciliary function are still missing. Here we report a method that enables integrating artificial cilia arrays on 3D curved surfaces and showcase an airway ciliary stent for excessive mucus transportation. The method allows encoding bioinspired non-reciprocal motion and metachronal waves for efficient fluid pumping in tubular structures. The method also introduces a lubricant hydrogel coating layer on artificial cilia inspired by the periciliary layer in airway cilia which further enhances viscous fluid transportation. We demonstrate that a novel ciliary airway stent can transport viscous porcine mucus in a lung phantom even faster than the respiratory cilia in a healthy human lung. Our methods of designing, integrating, and controlling artificial cilia on 3D curved surfaces thus enable the unprecedented function of removing excessive mucus beyond traditional airway stents for treating various lung diseases in a minimally invasive manner.

2. Regularized Kelvinlet Functions to Model Linear Elasticity for Image-to-Physical Registration of the Breast

Morgan Ringel [1], Jon Heiselman [1,2], Winona Richey [1], Ingrid Meszoeley [3], and Michael Miga [1]

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Image-guided surgery requires fast and accurate registration to align preoperative imaging and surgical spaces. The breast undergoes large nonrigid deformations during surgery, compromising the use of imaging data for intraoperative tumor localization. Rigid registration fails to account for nonrigid soft tissue deformations, and biomechanical modeling approaches like finite element simulations can be cumbersome in implementation and computation. We introduce regularized Kelvinlet functions, which are closed-form smoothed solutions to the partial differential equations for linear elasticity, to model breast deformations. We derive and present analytical equations to represent nonrigid point-based translation (“grab”) and rotation (“twist”) deformations embedded within an infinite elastic domain. Computing a displacement field using this method does not require mesh discretization or large matrix assembly and inversion conventionally associated with finite element or mesh-free methods. We solve for the optimal superposition of regularized Kelvinlet functions that achieves registration of the medical image to simulated intraoperative geometric point data of the breast. We present registration performance results using a dataset of supine MR breast imaging from healthy volunteers mimicking surgical deformations with 237 individual targets from 11 breasts. We include analysis on the method’s sensitivity to regularized Kelvinlet function hyperparameters. To demonstrate application, we perform registration on a breast cancer patient case with a segmented tumor and compare performance to other image-to-physical and image-to-image registration methods. We show comparable accuracy to a previously proposed image-to-physical registration method with improved computation time, making regularized Kelvinlet functions an attractive approach for image-to-physical registration problems.

3. Sensing Mucus Physiological Property In Situ by Wireless Millimeter-Scale Soft Robots

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The physiological property of mucus is an important biomarker for monitoring the human health conditions and helping understand disease development, as mucus property such as viscosity is highly correlated with inflammation and other diseases. However, it remains challenging to sense mucus viscosity using pure medical imaging. Collecting and analyzing mucus sample in vitro using flexible endoscopes and capsule endoscope robots is also challenging due to their difficulty of accessing very confined, tortuous, and small spaces, and the sample may not reflect the real mucus property. Here a novel method is proposed to enable sensing mucus viscosity in situ by wireless miniature sensors actuated by magnetic fields and tracked by medical imaging. These miniature viscosity sensors could be delivered with minimal invasion using a novel sensor delivery mechanism by controlling a magnetically actuated millimeter-scale soft climbing robot. As the soft robot can access confined and narrow spaces, and reliably deploy the sensor on soft tissue surfaces, multiple sensors could be delivered on soft biological tissues to sense biofluid viscosity spatiotemporally. The proposed minimally invasive robotic delivery and viscosity sensing method thus paves the way towards sensing biofluid properties deep inside the body for future disease monitoring and early diagnosis functions.

4. False Negative/Positive Control for SAM on Noisy Medical Images

Xing Yao, Han Liu, Daiwei Lu, Ruining Deng, and Ipek Oguz are with the Department of Computer Science, Vanderbilt University, Nashville, TN, USA. **Dewei Hu, Ange Lou, and Hao Li** are affiliated with the Department of Electrical and Computer Engineering, Vanderbilt University, Nashville, TN, USA. **Gabriel Arenas, Baris Oguz, and Nadav Schwartz** are part of the Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA. **Lastly, Brett C Byram** is associated with the Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA.

The Segment Anything Model (SAM) is a recently developed all-range foundation model for image segmentation. It can use sparse manual prompts such as bounding boxes to generate pixel-level segmentation in natural images but struggles in medical images such as low-contrast, noisy ultrasound images. We propose a refined test-phase prompt augmentation technique designed to improve SAM's performance in medical image segmentation. The method couples multi-box prompt augmentation and an aleatoric uncertainty-based false-negative (FN) and false-positive (FP) correction (FNPC) strategy. We evaluate the method on two ultrasound datasets and show improvement in SAM's performance and robustness to inaccurate prompts, without the necessity for further training or tuning. Moreover, we present the Single-Slice-to-Volume (SS2V) method, enabling 3D pixel-level segmentation using only the bounding box annotation from a single 2D slice. Our results allow efficient use of SAM in even noisy, low-contrast medical images.

5. Comparison Study between Different Calibration Methods for Augmented Reality Device

Bowen Xiang, Michael Miga

Vanderbilt University

Purpose: To study the difference between two manual calibration methods for AR device (HoloLens 2).

Approach: A new calibration method for HoloLens 2 was developed to improve the accuracy for the mapping between the virtual space and the real world. The new methods was compared for the previous calibration method that was also developed by our lab to demonstrate If the new method could outperform the previous one. The new methods used a stair block which has nine platforms as the phantom. Nine virtual sphere are build in the HoloLens space and manually moved to match the center of each platform. After calibration, 6 virtual spheres are distributed at the boundary of the field of view (FOV) as the targets. The results for target registration error (TRE) are compared to the results of previous calibration method. n=5 datasets are acquired.

Results: The mean TRE for the previous calibration method is 10.25 mm. The mean target registration error for the tested calibration method is 7.73 mm. The tested calibration method performed better than the previous calibration method.

Conclusion: The tested calibration method outperformed the previous calibration method. Even though both methods involved hand operation, the tested calibration eliminated the influence of hand instability by moving the virtual spheres to the center of the phantom. Thus, the researcher could try multiple times until they are assure that the correspondence points perfectly matched, and decrease the error for accuracy.

6. Measuring Anastomotic Tension in Robotic Surgery: A Feasibility Study Using Da Vinci Research Kit On Ex Vivo Colons

Hao Yang • Chi Phuong Huynh • Aimal Khan • James Weimer • Jie Ying Wu

Anastomosis, reconnecting parts of organs such as the colon or gut, is a critical part of gastrointestinal surgeries with dire consequences in the event of a leak. Despite being a key risk factor for anastomotic leaks, there is no objective method of measuring tension intraoperatively. In practice, instead of quantitative measurements, surgeons commonly rely on subjective perceptions to assess tension in an anastomosis. This research, therefore, is the first to provide quantitative measurements to analyze tissue tension as a risk factor for anastomotic leaks. We conducted a feasibility study to apply our deep-learning-based method of measuring the force exerted on tissue using a surgical robot. We aim to determine the tension required to disrupt an ex vivo porcine colonic anastomosis with the da Vinci Research Kit (dVRK)¹. Through experiments, we observed that the Spearman Correlation Coefficient of our algorithm predicted force over Cartesian z-direction and ground truth force sensor reading is larger than 0.7, across all the 9 trials we conducted. The result suggests our algorithm successfully captures the relative trends of force changes.

1. Kazanzides, Peter & Chen, Zihan & Deguet, Anton & Fischer, Gregory & Taylor, Russell & Dimaio, Simon. (2014). An open-source research kit for the da Vinci® Surgical System. Proceedings - IEEE International Conference on Robotics and Automation. 6434-6439. 10.1109/ICRA.2014.6907809.

7. Wireless Millimeter-Size Soft Climbing Robots With Omnidirectional Steerability on Tissue Surfaces

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Wirelessly actuated miniature soft robots actuated by magnetic fields that can overcome gravity by climbing soft and wet tissues are promising for accessing challenging enclosed and confined spaces with minimal invasion for targeted medical operation. However, existing designs lack the directional steerability to traverse complex terrains and perform agile medical operations. Here we propose a rod-shaped millimeter-size climbing robot that can be omnidirectionally steered with a steering angle up to 360 degrees during climbing beyond existing soft miniature robots. The design innovation includes the rod-shaped robot body, its special magnetization profile, and the spherical robot footpads, allowing directional bending of the body under external magnetic fields and out-of-plane motion of the body for delivery of medical patches. With further integrated bio-adhesives and microstructures on the footpads, we experimentally demonstrated inverted climbing of the robot on porcine gastrointestinal (GI) tract tissues and deployment of a medical patch for targeted drug delivery.

8. Towards Diabetes Risk Assessment from Large-Scale 3D Pancreas Imaging

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Pancreas volume and shape have been shown to change over time in MR imaging of individuals with type 1 diabetes when compared against controls. We aim to investigate how these findings can be validated in large-scale clinical CT imaging. Clarifying pancreas structural changes will lead to better understanding of disease progression. By leveraging ImageVU, we can investigate these characteristics in thousands of clinically acquired CT scans from Vanderbilt University Medical Center. Alongside imaging, we will incorporate other features from the electronic medical record. Additionally, we will computationally leverage the models from MR to increase the learning capabilities on the coarser CT imaging.

9. Segmentation of the Facial Nerve Using a Weakly Supervised GAN

Minh Vu, Yubo Fan, Jack H. Noble

Vanderbilt University

Cochlear implants (CI) are a highly successful neural-prosthetic device, recreating the sensation of hearing by directly stimulating the nerve fibers inside the cochlea for individuals experiencing severe to profound hearing loss. Installing the implants traditionally required invasive procedure such as mastoidectomy, however minimally invasive techniques such as percutaneous cochlear access are also being utilized. This method involves drilling a single hole through the skull surface, granting direct access to the cochlea where the CI can be threaded. The trajectory of this insertion typically involves traversing the facial recess, a region approximately 1.0-3.5 mm in width bounded posteriorly by the facial nerve and anteriorly by the chorda tympani. The determination of a safe drilling trajectory is highly important, as damage to these structures during surgery may result in a loss of taste (chorda) or facial paralysis (facial nerve). It is therefore very important that these clinical structures are segmented accurately for the drilling trajectory planning process. In this work, we propose the use of a conditional generative adversarial network (cGAN) to automatically segment the facial nerve. Our method can also make up for noisy and disconnected generated segmentations using a minimum cost path search function between the endpoints. Our network utilized weakly supervised approach, being trained on a small sample of 12 manually segmented image and supplemented with 120 automatically segmented image created through atlas-based image registration. Our method generated segmentations with an average mean surface error of only 0.22mm, improving upon the original method by ~50%.

10. A Unified Deep-Learning-Based Framework for Cochlear Implant Electrode Array Localization

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Cochlear implants (CIs) are neuroprosthetics that can provide a sense of sound to people with severe-to-profound hearing loss. A CI contains an electrode array (EA) that is threaded into the cochlea during surgery. Recent studies have shown that hearing outcomes are correlated with EA placement. An image-guided cochlear implant programming technique is based on this correlation and utilizes the EA location with respect to the intracochlear anatomy to help audiologists adjust the CI settings to improve hearing. Automated methods to localize EA in postoperative CT images are of great interest for large-scale studies and for translation into the clinical workflow. In this work, we propose a unified deep-learning-based framework for automated EA localization. It consists of a multi-task network and a series of postprocessing algorithms to localize various types of EAs. The evaluation on a dataset with 27 cadaveric samples shows that its localization error is slightly smaller than the state-of-the-art method. Another evaluation on a large-scale clinical dataset containing 561 cases across two institutions demonstrates a significant improvement in robustness compared to the state-of-the-art method. This suggests that this technique could be integrated into the clinical workflow and provide audiologists with information that facilitates the programming of the implant leading to improved patient care.

11. Inter-vendor harmonization of CT reconstruction kernels using unpaired image translation

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The reconstruction kernel in computed tomography (CT) generation determines the texture of the image. Consistency in reconstruction kernels is important as the underlying CT texture can impact measurements during quantitative image analysis. Harmonization (i.e., kernel conversion) minimizes differences in measurements due to inconsistent reconstruction kernels. Existing methods investigate harmonization of CT scans in single or multiple manufacturers. However, these methods require paired scans of hard and soft reconstruction kernels that are spatially and anatomically aligned. Additionally, a large number of models need to be trained across different kernel pairs within manufacturers. In this study, we adopt an unpaired image translation approach to investigate harmonization between and across reconstruction kernels from different manufacturers by constructing a multipath cycle generative adversarial network (GAN). We use hard and soft reconstruction kernels from the Siemens and GE vendors from the National Lung Screening Trial dataset. We use 50 scans from each reconstruction kernel and train a multipath cycle GAN. To evaluate the effect of harmonization on the reconstruction kernels, we harmonize 50 scans each from Siemens hard kernel, GE soft kernel and GE hard kernel to a reference Siemens soft kernel (B30f) and evaluate percent emphysema. We fit a linear model by considering the age, smoking status, sex and vendor and perform an analysis of variance (ANOVA) on the emphysema scores. Our approach minimizes differences in emphysema measurement and highlights the impact of age, sex, smoking status and vendor on emphysema quantification.

12. Immersive 3D Specimen Maps: Transforming Communication at Multidisciplinary Head and Neck Cancer Tumor Board

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Tumor board discussions are the current standard for communication of complex patients among oncologists. There is little visual data available to aid in understanding of specimen orientation and sites of margin sampling during pathologic processing. This study builds upon our prior ex vivo 3D scanning and specimen mapping protocol to investigate the use of 3D specimen maps at multidisciplinary head and neck tumor board. Faculty of various specialties completed a pre-survey regarding their level of comfort with currently available tools for understanding anatomic orientation and sites of margin sampling in head and neck cancer cases (responses set on a scale of 1 to 100; 1 = “Strongly Disagree”, 100 = “Strongly Agree”). One virtual model will be presented at weekly tumor board for ten weeks using a QR code that allows providers to manipulate the model on their own device. Providers will be surveyed at the conclusion of the study. Pre-study results demonstrate a mean level of comfort of 42.2 (SD 25.1, 95% CI -7.0, 91.4) with orienting a head and neck cancer specimen and a mean level of confidence in locating the site of a positive margin of 45.6 (SD 18.7, 95% CI 8.9, 82.3) using currently available discussion tools. Current methods of communication during multidisciplinary head and neck cancer tumor board fail to adequately orient the resected specimen and locate sites of positive margins for cancer care team members. This ongoing study will evaluate whether an interactive 3D model of the resected cancer specimen allows for improved communication.

13. Democratizing Pathological Image Segmentation with Lay Annotators via Molecular-empowered Learning

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Multi-class cell segmentation in high-resolution Giga-pixel whole slide images (WSI) is critical for various clinical applications. Training such an AI model typically requires labor-intensive pixel-wise manual annotation from experienced domain experts (e.g., pathologists). Moreover, such annotation is error-prone when differentiating fine-grained cell types (e.g., podocyte and mesangial cells) via the naked human eye. In this study, we assess the feasibility of democratizing pathological AI deployment by only using lay annotators (annotators without medical domain knowledge). The contribution of this paper is threefold: (1) We proposed a molecular-empowered learning scheme for multi-class cell segmentation using partial labels from lay annotators; (2) The proposed method integrated Giga-pixel level molecular-morphology cross-modality registration, molecular-informed annotation, and molecular-oriented segmentation model, so as to achieve significantly superior performance via 3 lay annotators as compared with 2 experienced pathologists; (3) A deep corrective learning (learning with imperfect label) method is proposed to further improve the segmentation performance using partially annotated noisy data. From the experimental results, our learning method achieved $F1 = 0.8496$ using molecular-informed annotations from lay annotators, which is better than conventional morphology-based annotations ($F1 = 0.7015$) from experienced pathologists. Our method democratizes the development of a pathological segmentation deep model to the lay annotator level, which consequently scales up the learning process similar to a non-medical computer vision task. The official implementation and cell annotations are publicly available at <https://github.com/hrlblab/MolecularEL>.

14. Feasibility of Universal Anomaly Detection without Knowing the Abnormality in Medical Images

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Abstract. Many anomaly detection approaches, especially deep learning methods, have been recently developed to identify abnormal image morphology by only employing normal images during training. Unfortunately, many prior anomaly detection methods were optimized for a specific “known” abnormality (e.g., brain tumor, bone fraction, cell types). Moreover, even though only the normal images were used in the training process, the abnormal images were often employed during the validation process (e.g., epoch selection, hyper-parameter tuning), which might leak the supposed “unknown” abnormality unintentionally. In this study, we investigated these two essential aspects regarding universal anomaly detection in medical images by (1) comparing various anomaly detection methods across four medical datasets, (2) investigating the inevitable but often neglected issues on how to unbiasedly select the optimal anomaly detection model during the validation phase using only normal images, and (3) proposing a simple decision-level ensemble method to leverage the advantage of different kinds of anomaly detection without knowing the abnormality. The results of our experiments indicate that none of the evaluated methods consistently achieved the best performance across all datasets. Our proposed method enhanced the robustness of the performance in general (average AUC 0.956)

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

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

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

16. Single-timepoint dynamic functional connectivity patterns in temporal lobe epilepsy

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Epileptic tissue produces interictal spikes, brief electrical events between seizures that are used to localize epileptic tissue. In patients with temporal lobe epilepsy (TLE), these spikes induce increased activity in the hippocampus and decreased activity in the posterior cingulate cortex (PCC), producing instances of negative functional connectivity (FC) between these two regions. Here we applied single-timepoint dynamic FC to detect patterns at moments of negative FC between the hippocampus and PCC in resting-state functional magnetic resonance imaging (fMRI) data. We included 96 healthy controls and 37 patients with right TLE in this study. We first detected “FC events,” timepoints of negative FC between the hippocampus and PCC, in participants’ fMRI scans. We then detected three recurring whole-brain FC patterns at these “FC events” using clustering. Patterns 1 and 3 involved strong FC between many brain regions, while Pattern 2 primarily involved the hippocampus and PCC. Patients with TLE had more frequent Pattern 2 events than controls ($p\text{FDR} = 5.4e-6$), while the frequencies of Patterns 1 and 3 were not different between groups ($p\text{FDR} > 0.05$). The frequency of Pattern 2 events was also negatively correlated with epilepsy duration, positively correlated with consciousness-impairing seizure frequency, and was lower in patients who had a hippocampal lesion visible on MRI ($p < 0.05$). This study found a single-timepoint dynamic FC pattern that was increased in TLE, correlated with disease severity, and may be related to interictal spikes. Funded by NIH T32EB021937, R01NS075270, R01NS108445, R01NS110130 and R00NS097618.

17. Effects of mild TBI on the optic radiations and occipital lobe: a multimodal analysis with machine learning

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This research analyzed the effects of mild traumatic brain injury (mTBI) on the optic radiations and occipital lobe using multimodal analyses and applied machine learning models to identify potential imaging biomarkers. Currently, the pathophysiology of mTBI-related visual impairment is unclear and variability in mTBI-related visual impairment can delay diagnosis and treatment. This matched pair case-control study (n=36, age=33±7 years) included mTBI with Glasgow coma scale (GCS) score of 13-15 and control groups. Exclusion criteria were TBI with GCS <13, age <18 years old, non-mTBI vision pathology, pregnancy, and metallic implants. T1 and diffusion-weighted (DWI) MRI were acquired during a single session with the same acquisition protocols across participants and 3D whole brain segmentation into 135 regions with the spatially localized atlas network tiles (SLANT) deep learning pipeline was applied on each T1 MRI. DWI scans were preprocessed with PreQual and the optic radiations were extracted using the tractography pipeline (Tractoflow, RecoBundlesX, TractometryFlow). The machine learning model with full cross validation included optic radiations tractography macrostructure and microstructure metrics and 14 occipital lobe segments, normalized by total brain volume, primarily involved in vision. Overall, this multimodal analysis showed significant differences in optic radiations macrostructure and occipital lobe regions between mTBI and control groups, suggesting their potential as novel imaging biomarkers for mTBI-related visual impairment.

18. DABS-LS: Deep Atlas-Based Segmentation Using Regional Level Set Self Supervision

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Cochlear implants (CIs) are neural prosthetics used to treat patients with severe-to-profound hearing loss. The implant is an array of 12-22 electrodes implanted into the patient's cochlea. After implantation, the device has various parameters which can be optimized by an audiologist to improve hearing performance. This process can require dozens of programming sessions and often does not lead to optimal results. Previous research suggests that providing the audiologist with information about the location of the auditory nerve fibers (ANFs) and surrounding anatomy can greatly expedite and improve the optimization process. The ANFs travel from the cochlea to the brain via the internal auditory canal (IAC). In a past paper, we've used atlas-based segmentation to localize the IAC by deforming an atlas IAC localization to a target CT image. The method used a 3D U-Net with architecture and loss terms inspired by the VoxelMorph framework. In this paper, we expand upon that idea by improving our existing gradient loss term and creating a new loss term based on level sets. These modifications provide significant improvement when evaluated on our IAC dataset. In addition, we analyzed the impact of these terms on datasets for the trachea and kidneys, and found similar improvement.

19. Label Augmentation Method for Medical Landmark Detection in Hip Radiograph Images

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This work reports the empirical performance of an automated medical landmark detection method for predicting clinical markers in radiograph images. Notably, the detection method was trained using a label-only augmentation scheme; our results indicate that this form of augmentation outperforms traditional data augmentation and produces highly sample efficient estimators. We train a generic U-Net-based architecture under a curriculum consisting of two phases: initially relaxing the landmarking task by enlarging the label points to regions, then gradually eroding these label regions back to the base task. We measure the benefits of this approach on six datasets of radiographs with gold-standard expert annotations.

20. Predicting Age from White Matter Diffusivity with Residual Learning

Chenyu Gao, Michael E. Kim, Ho Hin Lee, Qi Yang, Nazirah Mohd Khairi, Praitayini Kanakaraj, Nancy R. Newlin, Derek B. Archer, Angela L. Jefferson, Warren D. Taylor, Brian D. Boyd, Lori L. Beason-Held, Susan M. Resnick, The BIOCARD Study Team, Yuankai Huo, Katherine D. Van Schaik, Kurt C. Schilling, Daniel Moyer, Ivana Išgum, Bennett A. Landman

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Imaging findings inconsistent with those expected at specific chronological age ranges may serve as early indicators of neurological disorders and increased mortality risk. Estimation of chronological age from structural MRI data has become an important task for developing biomarkers that are sensitive to such inconsistency. Complementary to structural analysis, diffusion tensor imaging (DTI) has proven effective in identifying age-related microstructural changes within the brain white matter, thereby presenting itself as a promising additional modality for brain age prediction. Although early studies have sought to harness DTI's advantages for age estimation, there is no evidence that the success of this prediction is owed to the unique microstructural and diffusivity features that DTI provides, rather than the macrostructural features that are also available in DTI data. We seek to develop white-matter-specific age estimation from DTI scalar images, deliberately disregarding the macrostructural information, using two distinct methods. The first method relies on extracting only microstructural features from regions of interest. The second applies 3D residual neural networks (ResNets) to learn features directly from the images, which are non-linearly registered and warped to a template to minimize macrostructural variations. When tested on unseen data, the first method yields mean absolute error (MAE) of 6.11 years for cognitively normal participants and MAE of 6.62 years for cognitively impaired participants, while the second method achieves MAE of 4.69 years for cognitively normal participants and MAE of 4.96 years for cognitively impaired participants. We find that the ResNet captures subtler, non-macrostructural features for brain age prediction.

21. Nonlinear Gradient Field Estimation in Diffusion MRI Tensor Simulation

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Gradient nonlinearities not only induce spatial distortion in magnetic resonance imaging (MRI), but also introduce discrepancies between intended and acquired diffusion sensitization in diffusion weighted (DW) MRI. Advances in scanner performance have increased the importance of correcting gradient nonlinearities. The most common approaches for gradient nonlinear field estimations rely on phantom calibration field maps which are not always feasible, especially on retrospective data. Here, we derive a quadratic minimization problem for the complete gradient nonlinear field ($L(r)$). This approach starts with corrupt diffusion signal and estimates the $L(r)$ in two scenarios: (1) the true diffusion tensor known and (2) the true diffusion tensor unknown (i.e., diffusion tensor is estimated). We show the validity of this mathematical approach, both theoretically and through tensor simulation. The estimated field is assessed through diffusion tensor metrics: mean diffusivity (MD), fractional anisotropy (FA), and principal eigenvector (V1). In simulation with 300 diffusion tensors, the study shows the formulation is not ill-posed and remains stable. We find when the true diffusion tensor is known (1) the change in determinant of the estimated $L(r)$ field and the true field is near zero and (2) the median difference in estimated $L(r)$ corrected diffusion metrics to true values is near zero. We find the results of $L(r)$ estimation are dependent on the level of $L(r)$ corruption. This work provides an approach to estimate gradient field without the need for additional calibration scans. To the best of our knowledge, the mathematical derivation presented here is novel..

22. Characterizing Low-cost Registration for Photographic Images to Computed Tomography

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Mapping information from photographic images to volumetric medical imaging scans is essential for linking spaces with physical environments, such as in image-guided surgery. Current methods of accurate photographic image to computed tomography (CT) image mapping can be computationally intensive and/or require specialized hardware. For general purpose 3-D mapping of bulk specimens in histological processing, a cost-effective solution is necessary. Here, we compare the integration of a commercial 3-D camera and cell phone imaging with a surface registration pipeline. Using surgical implants and chuck-eye steak as phantom tests, we obtain 3-D CT reconstruction and sets of photographic images from two sources: Canfield Imaging's H1 camera and an iPhone 14 Pro. We perform surface reconstruction from the photographic images using commercial tools and open-source code for Neural Radiance Fields (NeRF) respectively. We complete surface registration of the reconstructed surfaces with the iterative closest point (ICP) method. Manually placed landmarks were identified at three locations on each of the surfaces. Registration of the Canfield surfaces for three objects yields landmark distance errors of 1.747, 3.932, and 1.692 mm, while registration of the respective iPhone camera surfaces yields errors of 1.222, 2.061, and 5.155 mm. Photographic imaging of an organ sample prior to tissue sectioning provides a low-cost alternative to establish correspondence between histological samples and 3-D anatomical samples.

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

Elan Z. Ahronovich(1), Neel Shihora(1), Jin-Hui Shen(2), Karen Joos(2), Nabil Simaan(1)

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

24. Microstructure properties open new window toward understanding brain structure in the patients with behavioral variant frontotemporal

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Antisocial behaviors are common symptoms in patients with behavioral variant frontotemporal dementia (bvFTD). Our hypothesis is that microstructural changes in brain structures occurred before macrostructural changes in the early stages of bvFTD, and that microstructure information is related to the severity of antisocial behaviors in bvFTD patients beyond what can be explained by macrostructural brain atrophy. This study aimed to investigate the relationship between microstructural changes in brain regions and antisocial behavior in bvFTD patients. T1-weighted images were used to extract microstructural information through texture analysis. Antisocial behavior was measured using the social behavior questionnaire (SBQ). Linear regressions were used to measure the relationship between texture and SBQ scores within each region of interest. Patients were categorized into high and low antisocial behavior based on the median SBQ scores, and an ANOVA was used to compare autocorrelation between healthy control, and patients with low and high antisocial behavior. Our results showed that autocorrelation was negatively correlated to antisocial behavior in several brain regions. Patients with low antisocial behavior tended to have positive autocorrelation suggesting larger clusters of abnormal pixel intensities, whereas patients with higher antisocial behaviors had negative autocorrelations suggesting smaller, more diffuse clusters of abnormal pixel intensities. None of the identified regions showing macrostructural abnormalities associated with antisocial behaviors and volume. Our findings suggest that microstructural changes may help to explain the differing degrees of antisocial behavior seen across patients. The study also suggests that certain problematic behaviors may be better explained by irritative micro-lesions rather than destructive macro-lesions.

25. Learning Site-specific Styles for Multi-institutional Unsupervised Cross-modality Domain Adaptation

Han Liu (Vanderbilt CS), **Yubo Fan** (Vanderbilt CS), **Zhoubing Xu** (Siemens Healthineers), **Benoit M. Dawant** (Vanderbilt ECE), **Ipek Oguz** (Vanderbilt CS)

Unsupervised cross-modality domain adaptation is a challenging task in medical image analysis, and it becomes more challenging when source and target domain data are collected from multiple institutions. In this paper, we present our solution to tackle the multi-institutional unsupervised domain adaptation for the crossMoDA 2023 challenge. First, we perform unpaired image translation to translate the source domain images to the target domain, where we design a dynamic network to generate synthetic target domain images with controllable, site-specific styles. Afterwards, we train a segmentation model using the synthetic images and further reduce the domain gap by self-training. Our solution achieved the 1st place during both the validation and testing phases of the challenge.

26. An adaptable model for estimating patient-specific electrical properties of the implanted cochlea

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Disabling hearing loss can significantly decrease the quality of life for individuals who do not receive adequate treatment, but fortunately, a variety of treatments exist depending on the nature of the loss. For individuals with severe-to-profound sensorineural hearing loss who have not achieved sufficient restoration of hearing with other treatments, the cochlear implant (CI) may be an option. The CI is a surgically-inserted neural prosthetic that converts sounds to electrical stimuli to directly stimulate auditory nerve fibers, bypassing the causes of dysfunction in the inner ear. While many recipients experience significant success with their implants, others receive little or no benefit. Multiple factors can affect hearing outcomes, including the quality of the program that controls the device. Prior research has endeavored to provide clinicians with objective information about a patient to assist them in identifying the optimal parameters for this program. Multiple comprehensive computational models that simulate electrical activity in the cochlea have been created for this task. However, these models are often not fully customizable or are highly customized to single sets of clinical measurements, requiring the model to be recomputed as measurements change. Our overall goal is to create a new model of equal or better quality that is fully customizable and can adapt to changing clinical measurements without having to recompute the entire model. In this work, we present preliminary results of a methodology for one component of such a model, which uses simulations of voltage spread in the cochlea to estimate patient-specific electrical tissue resistivity values.

27. AAn Increase in Orbitofrontal Cortex High Frequency Activity Precedes Risk Taking

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Helen Qian - Undergraduate Student Researcher, Vanderbilt University **Zixiang Zhao, MS** - Research Analyst, Vanderbilt University Medical Center **Michael Zargari, BS** - Medical Student, Vanderbilt University School of Medicine **Balbir Singh, PhD** - Research Assistant Professor in Department of Biomedical Engineering, Vanderbilt University **Zhengyang Wang**, Graduate Student, Vanderbilt University **Jenna N. Fulton, BS** - Research Assistant, Vanderbilt University Medical Center **Christos Constantinidis, PhD** - Professor of Biomedical Engineering, Vanderbilt University **Shawniqua Williams Roberson, MD** - Assistant Professor of Neurology, Vanderbilt University Medical Center **Dario J Englot, MD, PhD** - Associate Professor of Neurological Surgery, Vanderbilt University Medical Center **Sarah K. Bick, MD** - Assistant Professor of Neurological Surgery, Vanderbilt University Medical Center

Understanding neural activity underlying risky decisions may identify therapeutic targets in risk-taking disorders such as substance use and bipolar disorders. Human neuroimaging studies have implicated the orbitofrontal cortex (OFC) in risk-taking. However, existing research into the OFC's role in risk-taking with electrophysiology in humans is limited. We recruited 10 patients with pharmacoresistant epilepsy who underwent stereotactic electroencephalography (SEEG) to perform a gambling task. In each trial, patients were shown a playing card and wagered on their card being higher than a hidden card, either betting low or high. Recordings were aligned to time of patient's card presentation. We compared trials where patients bet high to trials where they bet low during both high-risk (<50% winning) and low-risk (>50% winning) scenarios. After EEG filtering and re-referencing to a common average, Z-scored power was calculated aligned to the cue to respond. Cluster-based permutation testing was used to identify neural activity that predicted high versus low bets in high-risk scenarios. A 40-100Hz power increase before high bets was identified ($p=0.001$) at an average time of 0.4s after card presentation. The power within this cluster was found to be influenced by both the bet choice and risk level (Two-way ANOVA, $p=0.007$), with Z-scored power greatest in the high-risk high-bet scenario (mean=0.11, standard error=0.03). These findings identify that an increase in OFC high-frequency predicts risky decisions, and support future research into the OFC as a potential therapeutic target for disorders of risk taking.

28. Simulation of Image-Guided Microwave Ablation Therapy Using a Digital Twin Model

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Emerging computational tools such as healthcare digital twin models are enabling the creation of patient-specific surgical planning for interventional procedures, including microwave ablation to treat primary and secondary liver cancers. Healthcare Digital twins (DTs) are anatomically one-to-one biophysical models constructed from anatomical and biomarker-based imaging data to simulate patient-specific therapies accurately. In microwave ablation (MWA), tissue-specific factors, including tissue perfusion, hepatic steatosis, and fibrosis, affect therapeutic extent, but current thermal dosing guidelines do not account for these parameters. This study establishes an MR imaging framework to construct digital twins to predict ablation delivery in livers with varying fat content in the presence of a tumor. Patient anatomic scans, specifically fat-quantification images, were segmented to develop customized three-dimensional computational biophysical digital twins. Simulated microwave ablations were performed using 915 MHz and 2450 MHz antennae in Tumor Naïve DTs (control) and Tumor Informed DTs at five grades of steatosis. Across the range of fatty liver steatosis grades, fat content was found to significantly increase ablation volumes by approximately 29-42% in the Tumor Naïve and 55-60% in the Tumor Informed DTs in 915 MHz and 2450 MHz antenna simulations. The presence of tumor did not significantly affect ablation volumes within the same steatosis grade in 915 MHz simulations but did significantly increase ablation volumes within mild-, moderate-, and high-fat steatosis grades in 2450 MHz simulations. An analysis of signed distance to agreement suggests that accounting for patient-specific tumor tissue properties significantly impacts ablation forecasting for the preoperative evaluation of ablation zone coverage.

29. Design of a Concentric Push-Pull Robot for Colon Surgery

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Khoa Dang, University of Tennessee - Knoxville **Carter Hatch**, University of Tennessee
- Knoxville **Caleb Rucker**, University of Tennessee - Knoxville **Tony Qin**, University of
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Minimally invasive surgery offers a wide range of benefits to patients. For patients with local stage colorectal cancer, only small polyps can be removed using minimally invasive techniques. While procedures exist to remove larger lesions endoscopically, the difficulty, training required, and lack of proper tools often prevents their use. We aim to build a robotic system using concentric push-pull robots to give surgeons the tools they need to perform en bloc endoscopic removal of larger lesions. These flexible, dexterous tools can be deployed through the tool channel of commercial endoscopes and help reduce the training required to perform these difficult procedures. Creation of this device involves design of an actuation unit, design of a controller, and design and modeling of the concentric tube pairs. With the implementation of a controller, the robotic system can be teleoperated by surgeons to accomplish more challenging tasks. The design of the steerable concentric push-pull robots first requires an understanding of how the design parameters affect the achievable workspace. I present the preliminary designs of the actuation unit as well as a sweeping search within the tube design space to show the effects of design parameters on tool workspace.

30. Handheld spectrally encoded coherence tomography and reflectometry with clinical task automation technologies for point-of-care ophthalmic diagnostics.

Jacob J. Watson, BME Rachel Hecht, BME Dr. Yuankai K. Tao, BME

Compensation of ocular refractive error is essential for obtaining high-quality optical coherence tomography and angiography (OCT/OCTA) images for retinal diagnostics across patients with different refractive power. During point-of-care ophthalmic imaging with handheld OCT systems, the clinical ergonomics of operator-driven focal adjustments to accommodate refractive error can disrupt clinical workflow. Here, we present a closed-loop automated hands-free focus tracking method to overcome limitations of conventional manual focus adjustment, and demonstrate its performance when integrated with our handheld spectrally encoded coherence tomography and reflectometry (HH-SECTR) probe. We predict automated focus tracking will improve clinical ergonomics for more efficient point-of-care ophthalmic imaging.

31. 3D Shape Correspondence For Medical Applications Using Neural Descriptor Fields

Dingjie Su (Vanderbilt University Department of Computer Science), **Yubo Fan** (Vanderbilt University Department of Computer Science), **Yike Zhang** (Vanderbilt University Department of Computer Science), **Benoit Dawant** (Vanderbilt University Department of Electrical and Computer Engineering)

The problem this paper is concerned with is that of unsupervised learning for point cloud representation which can be used to build anatomy correspondence without need for registration. Inspired by a recently proposed technique, called neural descriptor fields (NDFs), we derive a latent embedding for each point on a point cloud using the activation values from layers in an occupancy network. This embedding is conditioned on the point cloud and is exactly invariant to rigid-body transformations and approximately invariant to deformable transformations. We improve this technique to make it suitable for building dense correspondence, including increasing the discriminative ability of the embeddings and regularizing the latent space to enhance the anatomical plausibility after correspondence mapping. We evaluate the performance of our method using the structure of the labyrinth, the ossicles and the left lateral ventricle and we compare it to a surface registration method designed for dense anatomy correspondence. Additionally, we perform experiments to demonstrate the network's ability to represent objects in different categories simultaneously and to process incomplete point clouds.

32. A maximum a posteriori method for quantitative T1 mapping with uncertainty using MP2RAGE

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Quantitative MRI methods like T1 mapping allow for measurements of tissue properties independent of scanner differences across sites. T1 mapping is important for a biological understanding of disease progression and tissue characterization. The MP2RAGE sequence allows for efficient quantitative imaging of T1 in the brain, but current point estimate methods do not provide a way to measure uncertainty in this mapping and do not allow for multi-echo MP2RAGE signals. Here, we use a Monte Carlo simulation to generate the posterior probability of T1 from MP2RAGE signals. From this distribution, we generate statistical measures like maximum a posteriori (MAP) estimate for T1, the expected value of T1, and the standard deviation of T1, which provides a measure of uncertainty. When compared with gold standard selective inversion recovery quantitative magnetization transfer image (SIR-qMT) T1 maps, our MAP estimate of T1 results in a slightly higher error than previous point estimate methods. Our standard deviation maps report high values in areas corresponding to higher error. The posterior distribution allows for T1 mapping with multi-echo MP2RAGE signals using only a minor modification to the acquisition sequence with no additional scan time, and it allows for mapping statistical measures of T1 like the standard deviation or expected value.

33. A Standardized Smartphone-based Total Body Photography to Automate Mpox Lesion Counting by Artificial Intelligence

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Mpox (associated with clade I monkeypox virus infection) is endemic in the Democratic Republic of the Congo (DRC) and has an estimated case fatality ratio of 11% (17% in children). In October 2022, the PALM007 randomized placebo-controlled clinical trial was launched at remote sites in the DRC to test the efficacy of tecovirimat against mpox. Lesion count is a key measure to assess disease progression, but accurately counting the hundreds to thousands of lesions typical of clade I mpox poses considerable human effort. Optical methods coupled with artificial intelligence (AI) algorithms could automate lesion counting. Based on the performance of our initial AI algorithm trained on non-standardized photos of mpox lesions, we established smartphone-based protocols for standardized total body photography. We will discuss key considerations to acquire high quality photos to train a reliable AI algorithm, including (i) homogenous background, (ii) consistent illumination, (iii) standardized body poses, (iv) focus on skin areas of interest, and (v) consistent angle and distance between the camera and the skin area of interest. In an optimal future, optical technologies will advance in response to this clinical need. Smartphone-based photography coupled with AI image analysis is becoming the benchmark for evaluating the performance of these novel optical technologies. The presented work is supported by the Institut National de la Recherche Biomédicale, NIAID, and funded by NCI Contract No. 75N910D00024, Task Order No. 75N91020F00025.

34. Endovascular Detection of Catheter-Thrombus Contact by Vacuum Excitation

Jared Lawson - Mechanical Engineering **Madison Veliky** - Mechanical Engineering **Collette Abah** - formerly Mechanical Engineering (graduated) **Mary Dietrich** - Biostatistics **Rohan Chitale** - Neurological Surgery **Nabil Simaan** - Mechanical Engineering

Objective: The objective of this work is to introduce and demonstrate the effectiveness of a novel sensing modality for contact detection between an off-the-shelf aspiration catheter and a thrombus.

Methods: A custom robotic actuator with a pressure sensor was used to generate an oscillatory vacuum excitation and sense the pressure inside the extracorporeal portion of the catheter. Vacuum pressure profiles and robotic motion data were used to train a support vector machine (SVM) classification model to detect contact between the aspiration catheter tip and a mock thrombus. Validation consisted of benchtop accuracy verification, as well as user study comparison to the current standard of angiographic presentation.

Results: Benchtop accuracy of the sensing modality was shown to be 99.67%. The user study demonstrated statistically significant improvement in identifying catheter-thrombus contact compared to the current standard. The odds ratio of successful detection of clot contact was 2.86 ($p=0.03$) when using the proposed sensory method compared to without it.

Conclusion: The results of this work indicate that the proposed sensing modality can offer intraoperative feedback to interventionalists that can improve their ability to detect contact between the distal tip of a catheter and a thrombus.

Significance: By offering a relatively low-cost technology that affords off-the-shelf aspiration catheters as clot-detecting sensors, interventionalists can improve the first-pass effect of the mechanical thrombectomy procedure while reducing procedural times and mental burden.

35. Finite Element Modeling for Realistic Tissue-Tool Interaction in Cholecystectomy Simulation

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Traditional haptic simulators often fail to provide a realistic tactile experience, potentially resulting in gaps in skill transfer to the operating room. This research addresses this limitation by accurately modeling tissue and tool interactions that occur during cholecystectomy procedures, to improve force feedback in haptic devices. While traditional finite element (FE) modeling offers accuracy, its real-time application is limited by its computational burden. To overcome this challenge, our methodology involves generating FE solutions as training data for a neural network, enabling real-time, biomechanically accurate force predictions without compromising computational efficiency. Our work focuses on developing detailed small-scale FE models that accurately represent soft tissue deformation and force predictions during tissue/tool interaction, with the goal of increasing the realism of haptic feedback in simulators. In our methodology, tissue damage is computed through a damage mechanics approach. When the strain in the material reaches a threshold, a cutting/crack is introduced, mimicking the process of tissue damage due to peeling the tissue with a grasper. Additionally, for electrocautery simulations, we coupled electric, thermal, and strain equations nonlinearly to address the phenomena. Tissue degradation occurs when either temperature or strain reaches predefined thresholds. Force predictions from our finite element simulations were found to be within the literature's range for tissue damage. While these results are preliminary and further validation is needed, they indicate that our approach accurately reproduces forces due to tissue-tool interaction.

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

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Kidney stones require surgical removal when they grow too large to be broken up externally or to pass on their own. Upper tract urothelial carcinoma are also sometimes treated endoscopically in a similar procedure. These surgeries are difficult, particularly for trainees who often miss tumors, stones or stone fragments, requiring re-operation. One cause of difficulty is the high cognitive strain surgeons experience in creating accurate mental models during the endoscopic operation. Furthermore, there are no patient-specific simulators to facilitate training or standardized visualization tools for ureteroscopy despite its high prevalence. We propose ASSIST-U, a system to automatically create realistic ureteroscopy images and videos solely using preoperative CT images to address these unmet needs. We train a 3D UNet model to automatically segment CT images and construct 3D surfaces. These surfaces are then skeletonized for rendering and camera position tracking. Finally, we train a style transfer model using Contrastive Unpaired Translation (CUT) to synthesize realistic ureteroscopy images. Cross validation on the UNet model achieved a Dice score of 0.853 ± 0.084 for the CT segmentation step. CUT style transfer produced visually plausible images; the Kernel Inception Distance to real ureteroscopy images was reduced from 0.198 (rendered) to 0.089 (synthesized). We also qualitatively demonstrate the entire pipeline from CT to synthesized ureteroscopy. The proposed ASSIST-U system shows promise for aiding surgeons in visualization of kidney ureteroscopy.

37. Improving the Temporal Accuracy of Eye Gaze Tracking for the da Vinci-Surgical System Through Automatic Detection of Decalibration Events

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Robust and accurate eye gaze tracking can play a role in advancing medical telerobotics by providing complementary data for surgical training, interactive instrument control, and augmented human-robot interactions. However, current gaze tracking solutions for systems such as the da Vinci Surgical System (dVSS) are limited to complex hardware installations. Additionally, existing methods do not account for operator head movement inside the surgeon console, invalidating the original calibration. This work provides an initial solution to these challenges that can seamlessly integrate into console devices beyond the dVSS. Our approach relies on simple and unobtrusive wearable eye trackers and provides calibration routines that are capable of contending with operator-head movements. An external camera tracks the wearable trackers to detect invalidation of the prior calibration from head movement and \red{slip-page}, and the system prompts another calibration sequence. In a study where users moved freely in the surgeon console after an initial calibration procedure, we show that our system that tracks the \red{eye tracking glasses} to initiate recalibration procedures can reduce the mean tracking error up to 89\% compared to the currently prevailing approach which relies on the initial calibration only. This work is an important first step towards incorporating user movement into gaze-based applications for the dVSS.

38. MERLIN: MRI-Enabled Robotic Nonlinear Incisionless Neurosurgery

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With 50 million people suffering worldwide, epilepsy is a highly prevalent and debilitating disease that plagues people with seizures. While some patients' seizures can be effectively managed with drug therapies, 30% of the population is drug resistant leaving surgical intervention as the primary option. 70% of patient seizures originate in the hippocampus, a hard-to-reach region in the deep brain. The main surgical options are open hippocampectomy, a successful, but rather invasive approach, and MR-guided, laser interstitial thermal therapy (LITT). The latter is much less invasive as it involves deploying a straight laser probe through small burr-holes drilled in the back of the skull. However, LITT procedures are currently limited to straight-line trajectories and the hippocampus is naturally curved. This results in limited ablation coverage and lower seizure freedom rates than traditional hippocampectomy. This research aims to address these issues using curved trajectories to achieve more complete lesioning as well as navigating a natural opening for a much less invasive, percutaneous procedure. A new robotic system has been developed around the harsh environment of the MRI scanner enabling the use of perioperative, real-time MR thermometry. The robot mechanically enforces a remote center at the natural opening, the foramen ovale, and can adjust the initial insertion vector to account for anatomical variations. MR-safe, pneumatic stepper actuators and an advanced controller were also developed for precise motion control. Preliminary curvilinear ablations were performed demonstrating our current lesion shaping capabilities.

39. Augmented-Reality Surgery to Guide Head and Neck Cancer Resections

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Background: Following head and neck cancer resections, head and neck surgeons often have difficulty relocating close or positive tumor margin sites for re-resection due to the complex three-dimensional (3D) anatomy of the head and neck. To address this challenge, we developed an augmented reality (AR) guidance system that allows surgeons to visualize holographic 3D specimens to guide re-resection.

Methods: This was a cadaveric feasibility study. A structured-light 3D scanner captured the photorealistic surface topography of ex vivo cadaveric specimens. The scans were exported to the HoloLens augmented reality environment. The surgeon manually aligned the 3D specimen hologram into the resection bed. Accuracy of manual alignment and time intervals throughout the protocol were recorded.

Results: The 5 resections were performed by 5 head and neck surgeons at various levels of training and included 2 oral cavity and 3 cutaneous head and neck cancer specimens. On average, an uploading time of 2.98 ± 2.30 min, visualization time of 1.05 ± 0.67 min, re-alignment time of 4.39 ± 2.59 min, and a total AR resection protocol time of 20.51 ± 3.15 min were achieved. The mean re-alignment error was 3.1 mm (range, 2-6 mm) with a standard deviation of 1.67 mm. There was no association between the size of the specimen and the realignment error.

Conclusions: This cadaveric study demonstrated the feasibility and accuracy of an augmented reality protocol for visualization and realignment of 3D holographic specimens in head and neck cancer surgery.

40. Novel OCT mosaicking pipeline with Feature- and Pixel-based registration

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High-resolution Optical Coherence Tomography (OCT) images are crucial for ophthalmology studies but are limited by their relatively narrow field of view (FoV). Image mosaicking is a technique for aligning multiple overlapping images to obtain a larger FoV. Current mosaicking pipelines often struggle with substantial noise and considerable displacement between the input sub-fields. In this paper, we propose a versatile pipeline for stitching multi-view OCT/OCTA en face projection images. Our method combines the strengths of learning-based feature matching and robust pixel-based registration to align multiple images effectively. Furthermore, we advance the application of a trained foundational model, Segment Anything Model (SAM), to validate mosaicking results in an unsupervised manner. The efficacy of our pipeline is validated using an in-house dataset and a large public dataset, where our method shows superior performance in terms of both accuracy and computational efficiency. We also made our evaluation tool for image mosaicking and the corresponding pipeline publicly available.

41. Assessing Test-time Variability for Interactive 3D Medical Image Segmentation with Diverse Point Prompts

Hao Li, Han Liu, Dewei Hu, Jiacheng Wang, Ipek Oguz

Vanderbilt University

Interactive segmentation model leverages prompts from users to produce robust segmentation. This advancement is facilitated by prompt engineering, where interactive prompts serve as strong priors during test-time. However, this is an inherently subjective and hard-to-reproduce process. The variability in user expertise and inherently ambiguous boundaries in medical images can lead to inconsistent prompt selections, potentially affecting segmentation accuracy. This issue has not yet been extensively explored for medical imaging. In this paper, we assess the test-time variability for interactive medical image segmentation with diverse point prompts. For a given target region, the point is classified into three sub-regions: boundary, margin, and center. Our goal is to identify a straightforward and efficient approach for optimal prompt selection during test-time based on three considerations: (1) benefits of additional prompts, (2) effects of prompt placement, and (3) strategies for optimal prompt selection. We conduct extensive experiments on the public Medical Segmentation Decathlon dataset for challenging colon tumor segmentation task. We suggest an optimal strategy for prompt selection during test-time, supported by comprehensive results.

42.A Point Cloud Approach for Soft Tissue Deformation Modeling

Ashkan Shahbazi, Soheil Kolouri

Department of Computer Science

In the complex field of surgical training, the precision and predictability of procedures are critical. Since interacting with tissues is a crucial part of the training procedure, understanding the nuanced responses of soft tissues to manipulation becomes important. Soft tissue deformation modeling offers a predictive framework for tissue behavior upon interaction. In this project, I will be using the LiverMesh dataset provided by the Department of Biomedical Engineering at Vanderbilt University. This dataset consists of 250 simulations from a nonlinear FEM model which is not publicly available. These simulations are based on the real-world behavior of the liver tissue under different manipulations such as lifting a lobe or cutting a part of the tissue. My data is represented by the mesh points and the manipulation information are added as feature of vertices. I aimed to tackle the soft tissue deformation task by using a graph convolutional neural network. By using the implicit geometrical symmetries of GCNs I could effectively train a model to predict the deformations. My model attained a 90% accuracy in capturing deformations when lifting lobes of the Liver Mesh. Also, my model's forward pass time is recorded at 1.17 ± 0.10 ms, notably 4-5 order of magnitude quicker than a classical deformation solver.

43. Prognosis of Crohn's Disease

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This research endeavors to significantly improve prognosis and treatment strategies for Crohn's Disease (CD), focusing on accurately predicting transitions between its various stages-ranging from Normal and Quiescent to Mild, Moderate, and Severe. In the United States, the impact of inflammatory bowel diseases (IBD), including CD, is profound, with over 3 million affected individuals. CD remains a condition without a known cure, making advances in treatment and prognosis particularly crucial. Our methodology centers on analyzing Hematoxylin and Eosin (H&E) stained colon biopsy whole slide images (WSIs) from CD patients. This analysis is instrumental in uncovering intricate cell relationships and characteristics, essential for formulating an accurate prognosis. The significance of this lies in its potential to influence key decisions regarding treatment and management, thereby enabling the development of personalized and effective care strategies that could dramatically improve patient outcomes. Our study is further enriched by incorporating multi-instance learning frameworks, cross-scale attention features, and acknowledging the critical role of neutrophils in predicting disease states. We utilize advanced cell neighborhood analysis techniques, allowing us to discern subtle yet critical distinctions between cells in CD and non-CD conditions. This detailed computational analysis, focusing on the cellular microenvironment, is pivotal in understanding the complexities of CD. Our initial steps involve setting baseline predictions through a basic Deep Learning network, analyzing cellular relationships and local microenvironment interactions within tissue samples. We aspire to achieve an Area Under the Curve (AUC) of at least 0.6, thereby establishing a robust benchmark for prognosis accuracy in the field of CD. This study's findings have the potential to revolutionize the understanding and management of CD, paving the way for more targeted and effective treatments.

44. Quantification of subretinal injection volumes with intraoperative OCT using intraocular reference features

Rachel Hecht, Jacob J. Watson, and Yuankai K. Tao

Biomedical Engineering

Intraoperative optical coherence tomography (iOCT) provides depth-resolved visualization of retinal microstructures and surgical dynamics during ophthalmic surgery. There has been a recent push to augment real-time feedback using 2D and 3D iOCT imaging with image-based quantitative metrics to potentially improve surgical outcomes and develop novel surgical maneuvers. Surgeons currently rely on visual estimations, infusion duration, or microinjector readings to approximate injection volumes. However, this can result in high variability of actual delivered volumes. Previous studies have implemented iOCT imaging and segmentation to quantify subretinal injection volumes, but these previous studies required complex modeling of iOCT scanning parameters and required introduction of external reference standards into the eye to perform validation studies. Here, we demonstrate a simple and robust method to quantify subretinal volumes using volumetric iOCT data imaged immediately before and after injection. We use iOCT images of subretinal cannula with known dimensions as an intraocular reference feature to estimate intraocular dimensions, which are then used to quantify segmented injection of microliter-scale subretinal injections. The additional examination of several axial eye length models demonstrated the versatility of the technique for quantifying volume injections. This quantitative method for determining the volume of subretinal volumetric injections by using a subretinal cannula as an intraocular reference may be extended to ex vivo eye studies. Future improvements of the quantitative method and expanded injection studies will allow for more detailed evaluation of the potential translatability of the proposed method.

45. Evaluation of U-Nets for Object Segmentation in Ultrasound Images

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Ultrasound is a commonly used modality for medical imaging. While this modality has great advantages in terms of safety and cost relative to other imaging modalities, it also has several limitations. Signal-to-noise ratio varies greatly depending on the acoustic properties of the tissue being imaged and the depth of the target structures. In this work, we evaluate the use of deep learning based methods to reconstruct 3D surfaces of general objects imaged with ultrasound. We evaluate three variants of the 3D U-Net with different training scenarios. We were able to train networks to reconstruct three distinct categories of objects relatively well when trained on limited data from each category. However, when testing on categories of objects not included in the training, the networks struggled to generalize. These results provide a baseline for exploring modifications to the U-Net framework to improve generalizability. A generalizable method could improve visualization for a number of medical imaging tasks.

46. DMD-based heads-up display integrated with ophthalmic surgical microscope oculars for high-contrast intraoperative OCT visualization

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Microscope-integrated intraoperative optical coherence tomography (iOCT) allows for depth-resolved volumetric imaging during ophthalmic surgery. Real-time visualization of iOCT data is conventionally displayed on an external monitor or heads-up display (HUD) optically coupled to surgical oculars. Stereoscopic surgical views are either completely lost or require the use of polarization glasses with limited viewing angles when displayed on external monitors. Intraocular HUD couples LED/OLED displays across a beamsplitter cube, but display contrast is limited by low panel brightness, display and surgical field brightness trades-off, and overlays are generally constrained to dark/unused regions of the surgical field-of-view (FOV). Here, we demonstrate a digital micromirror device (DMD) based HUD that overcomes contrast limitations of existing intraocular HUDs and enables high resolution display of iOCT data and surgical field overlays. Our DMD-HUD will be integrated with our iSECTR system for real-time surgical visualization to provide real-time intraoperative feedback and contextual overlays during ophthalmic surgery.

47. Learning site-invariant features of connectomes to harmonize complex network measures

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Multi-site diffusion MRI data is often acquired on different scanners and with distinct protocols. Differences in hardware and acquisition result in data that contains site dependent information, which confounds connectome analyses aiming to combine such multi-site data. We propose a data-driven solution that isolates site-invariant information whilst maintaining relevant features of the connectome. We construct a latent space that is uncorrelated with the imaging site and highly correlated with patient age and a connectome summary measure. Here, we focus on network modularity. The proposed model is a conditional, variational autoencoder with three additional prediction tasks: one for patient age, and two for modularity trained exclusively on data from each site. This model enables us to 1) isolate site-invariant biological features, 2) learn site context, and 3) re-inject site context and project biological features to desired site domains. We tested these hypotheses by projecting 77 connectomes from two studies and protocols (Vanderbilt Memory and Aging Project (VMAP) and Biomarkers of Cognitive Decline Among Normal Individuals (BIOCARD)) to a common site. We find that the resulting dataset of modularity has statistically similar means (p-value <0.05) across sites. In addition, we fit a linear model to the joint dataset and find that positive correlations between age and modularity were preserved.

48. Interactions between fMRI-derived arousal patterns and healthy aging

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Introduction In aging populations, daytime fatigue and sleepiness can be prominent and can impact everyday behavior and cognitive function (Carskadon et al. 1980; Beradi et al., 2001). Moreover, aging can be accompanied by disruptions of subcortical brain regions that are implicated in the regulation of arousal. Here, we leverage subject-specific arousal patterns to investigate how arousal-related hemodynamic fluctuations across the brain correlate with healthy aging.

Methods This study used 3T fMRI data from the Human Connectome Project - Aging dataset. We use an established arousal “template” map (Goodale et al., 2021), created from simultaneous EEG-fMRI data, to extract subject-specific arousal maps for each subject using a method akin to dual regression. We then evaluated how arousal patterns correlate to healthy adult aging using voxel-wise regression, co-varying for sex, race, education, and total intracranial volume. Significant clusters were identified using a threshold-free cluster enhancement (TCFE; FSL Randomise).

Results Voxel-wise regression analysis demonstrated that arousal-related fMRI activity was significantly ($p < 0.01$, TCFE multiple comparisons) associated with age in regions such as the lingual gyrus, superior temporal gyrus, insula, cuneus, post-central gyrus, amygdala, thalamus, and lateral ventricles.

Conclusions Overall, this analysis reveals significant relationships between age and fMRI arousal fluctuations, suggesting that further investigation of the functional circuits linked with arousal could contribute to our understanding of age-related changes in the brain. Future work will leverage other forms of tracking arousal such as simultaneous pupil data, and compare these findings with age-related changes in the fMRI global signal (Nomi et al., 2022).

49. Depression Attenuates Corticostriatal Beta Power Response to Reward Feedback and Positive Emotional Stimuli During Working Memory

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Depression is a prevalent mental disorder and a common comorbidity across neurological disorders. Common symptoms include anhedonia, negative emotional biases, and cognitive dysfunction. Beta (15-30 Hz) neural oscillations have been shown to increase during reward-based learning within fronto-striatal reward networks. Corticostriatal beta oscillations have also been implicated in cognitive functions including working memory. However, the relationship between beta oscillations and depression remains unknown. Using intracranial recordings, we investigated how depression modulates the spectral power of beta oscillations in corticostriatal structures during reward in a working memory task. Thirty movement disorder patients undergoing awake deep brain stimulation surgery with electrode trajectories traversing the caudate or dorsolateral prefrontal cortex (DLPFC) participated in this study. Subjects completed a 2-back task where they identified whether a word matched the word presented two trials prior, receiving reward in the form of visual feedback for correct answers. Word stimuli had either a positive, negative, or neutral emotional valence. Subjects completed the Beck Depression Inventory-II preoperatively, with a cut-off of 14 identifying patients with depression. Caudate and DLPFC beta power increased during reward. This increase was significantly greater for subjects without depression compared to depressed subjects. In non-depressed patients, positive word stimuli evoked significantly higher beta power in the caudate during reward compared to neutral and negative stimuli. In depressed patients, emotional valence did not affect reward-related spectral power. Our findings suggest depression suppresses beta power responsiveness to reward and emotional stimuli during working memory, indicating beta power attenuation may contribute to emotional and cognitive depression symptoms.

50. Identification of functional white matter networks in BOLD fMRI

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White matter signals in resting state blood oxygen level dependent functional magnetic resonance (BOLD-fMRI) have been largely discounted, yet there is growing evidence that these signals are indicative of brain activity. Understanding how these white matter signals capture function can provide insight into brain physiology. Moreover, functional signals could potentially be used as early markers for neurological changes, such as in Alzheimer’s Disease. To investigate white matter brain networks, we leveraged the OASIS-3 dataset to extract white matter signals from resting state BOLD-FMRI data on 711 subjects. The imaging was longitudinal with a total of 2,026 images. Hierarchical clustering was performed to investigate clusters of voxel-level correlations on the timeseries data. The stability of clusters was measured with the average Dice coefficients on two different cross fold validations. The first validated the stability between scans, and the second validated the stability between populations. Functional clusters at hierarchical levels 4, 9, 13, 18, and 24 had local maximum stability, suggesting better clustered white matter. In comparison with JHU-DTI-SS Type-I Atlas defined regions, clusters at lower hierarchical levels identified well-defined anatomical lobes. At higher hierarchical levels, functional clusters mapped motor and memory functional regions, identifying 50.00%, 20.00%, 27.27%, and 35.14% of the frontal, occipital, parietal, and temporal lobe regions respectively.

51. Seizure Onset Zones Demonstrate Unique Low Frequency Canonical Response Dynamics in Patients with Focal Epilepsy

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Epilepsy is a neurological condition that affects 1% of the global population. Nearly 40% of patients continue to have seizures despite maximal medical management. For these patients, surgical treatment can result in seizure freedom, but traditionally requires the localization of the area thought to be generating seizures (seizure onset zone, SOZ). Intracranial monitoring with stereotactic encephalography (SEEG) is often used to localize SOZs, but nearly 30% of patients will continue to have seizures. Direct intracranial stimulation can be performed while patients are implanted with SEEG and has shown promise in improved localization of SOZs. However, these single pulse electrical stimulation (SPES) trials cannot investigate critical low-frequency ranges due to responses occurring over less than 500ms. Canonical Response (CR) Parameterization is a low-assumption machine learning framework which extracts low frequency responses from the top eigenvector computed by Linear Kernel PCA on voltage tracings. Thus, we obtained SPES data from 15 patients who underwent SEEG at Vanderbilt and extracted canonical responses across all contacts. We then extracted average reparameterized response strength, explained variance, and response time for non-involved-zones (NIZ) to other NIZs (NIZ-NIZ), NIZ to SOZ (NIZ-SOZ), and SOZ to SOZ (SOZ-SOZ). Responses for each trial were normalized to the NIZ-NIZ responses on a per-patient basis. We found that NIZ-SOZ responses resembled baseline whereas SOZ-SOZ responses were significantly higher than the NIZ-SOZ responses (0.51 vs .01, $p=0.001$, two-sample t-test). This may suggest that SOZ-SOZ connections exhibit an enhanced low frequency hypercoupling. These results may improve localization of SOZs for surgical treatment of epilepsy.

52. A First Step Towards Accelerated Surgical Training for Developing Countries: A Data-Driven Design Approach

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Minimally invasive (laparoscopic) surgical interventions require surgeons to be adept at achieving constrained motions with a reverse kinematic mapping, the ability to judiciously control a forceful interaction with the anatomy, and the ability to delineate and perform safe resections around sensitive anatomy. The traditional apprenticeship training model followed in many countries requires a minimal cadre of dedicated expert clinicians for training new surgeons. This model is difficult to sustain in low-middle income countries with severe shortage of trained expert surgeons. This work presents our efforts to design a haptic device as part of a surgical training system for training surgeons the key steps of critical laparoscopic interventions including, cholecystectomy, appendectomy, and peptic ulcer repair. The process for extracting task specifications using motion tracking during phantom and explanted organ experiments for cholecystectomy is presented. This data was used to design a unique parallel-architecture haptic device that retains the use of traditional laparoscopic devices as a means for interacting with either virtual or physical anatomical models. The design process, electronics layout, and communication interfaces are presented along with initial assessment of tool tip stiffness and maximal force capabilities is also presented. Initial results suggest that our device has a uniquely large translational and orientation workspace suitable for minimally invasive surgery.

53. Periodic 3D white matter geometries for diffusion magnetic resonance imaging simulations

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Axonal damage is known to occur in a number of white-matter diseases. Diffusion weighted MRI is sensitive to axonal microstructure changes in white matter, and simulations and experimental works have shown that the apparent diffusion coefficient (ADC) in white matter is diffusion-time dependent and related to axon diameter. Monte Carlo simulation of diffusion of water molecules is a fast and inexpensive approach for further studies, but to-date has been largely limited to simulations in 2D or 3D with simplified geometry. Here, we introduce a framework for generating 3D axonal geometries with periodic boundary conditions for numerical substrates that capture orientation dispersion of in-vivo white matter axons. We were able to create an axon geometry that includes 128 fibers in a $40 \times 40 \times 40$ (μm)³ simulation box, with axon orientation sampled from Watson distribution with $\kappa = 200$. The geometry reaches an intra-axonal volume fraction of 0.83, which is close to the volume fraction of axon environment in-vivo. We anticipate our framework will be a utility for building complex 1) 3D axon environments 2) with periodic boundary condition for diffusion MRI simulation studies. With better in-vivo mimicking axon environment, we can better map the connection between the ADC obtained from diffusion weighted imaging signals and axon characteristics in white matter diseases.aging signals to axon characteristics in white matter diseases.

54. Network State During Focal Impaired Awareness Seizures Resembles Deep Sleep

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Epilepsy affects nearly 1% of the global population with focal impaired awareness seizures (FIAS) being the most common seizure type. Seizures can drastically impact patients' lives, but the loss of consciousness in FIAS and focal-to-bilateral tonic-clonic (FBTCS) seizures can be particularly devastating. Surgical neuromodulation may aid in the preservation of consciousness in epilepsy, but it is not well understood what networks should be targeted. It has been hypothesized that the impaired consciousness in FIAS is like deep sleep, thus we analyzed network state in focal aware seizures (FAS), FIAS, and FBTCS. Stereotactic electroencephalography (SEEG) recordings of 74 patients were obtained and seizure types were designated. Bandpower and connectivity were computed in the delta(1-4Hz) and gamma(31-80Hz) frequency bands. Sleep staging was performed for each patient to identify REM and deep sleep. In the ipsilateral frontoparietal association cortex (FPAC), delta bandpower increased in consciousness-impairing seizures and in deep sleep ($p < 0.001$, one-way ANOVA). Gamma bandpower increased in FBTCS but did not change across sleep states, perhaps representing the seizure generalization ($p < 0.0001$). Delta-band segregation of the FPAC was increased for both FIAS ($p = 0.008$) and for deep sleep ($p = 0.002$), suggesting that the ipsilateral FPAC both FIAS and deep sleep is isolated from the rest of the brain. Furthermore, gamma-band segregation was decreased for FIAS ($p = 0.002$) and deep sleep ($p < 0.001$). Network-based approaches may improve surgical treatment of FIAS. Further study of the common networks between sleep and consciousness-impairing seizures may improve surgical neuromodulation through novel neuromodulation strategies and targets to preserve consciousness in epilepsy.

55. Thalamo-Cortical Functional Connectivity Differs in Low and High Vigilance States in Patients with Temporal Lobe Epilepsy

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Epilepsy is a common neurological disorder affecting 1% of the global population, with temporal lobe epilepsy (TLE) being the most common. In addition to recurrent seizures, patients can experience neurocognitive deficits associated with regions beyond the temporal lobe, such as executive function, attention, and concentration. These deficits may be due to abnormalities in subcortical-neocortical arousal pathways as neurocognitive functions are modulated by subcortical arousal structures. However, it is challenging to study subcortical-neocortical functional connectivity (FC) given that subcortical-neocortical FC is modulated by vigilance and vigilance fluctuates over time. Thus, vigilance may be a critical confounder in studying subcortical-neocortical FC. Therefore, we examined FC between thalamic arousal nuclei and cortical regions during both high and low vigilance states. We collected resting state functional magnetic resonance imaging (fMRI) data from 16 TLE patients and 24 controls. FMRI data was parcellated into subject-specific thalamic subnuclei and subject-specific cortical regions. Afterwards, FC was computed between all regions with a sliding window 2-minute epoch and the vigilance level was determined for each epoch. Thalamo-cortical FC was compared between patients and controls in the highest and lowest vigilance windows. We found that the medial nucleus had decreased FC in patients vs controls in the high vigilance state ($p=0.029$, 2-sample t-test), but there was no difference in the low vigilance state, suggesting that FC abnormalities in patients with epilepsy may be modulated by vigilance level. Future study of subcortical-neocortical FC while controlling for vigilance may elucidate novel neuromodulation targets to improve neurocognitive deficits in TLE patients.

56. SAMSNerF: Segment Anything Model (SAM) Guides Dynamic Surgical Scene Reconstruction by Neural Radiance Field (NeRF)

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The accurate reconstruction of surgical scenes from surgical videos is critical for various applications, including intraoperative navigation and image-guided robotic surgery automation. However, previous approaches, mainly relying on depth estimation, have limited effectiveness in reconstructing surgical scenes with moving surgical tools. To address this limitation and provide accurate 3D position prediction for surgical tools in all frames, we propose a novel approach called SAMSNerF that combines Segment Anything Model (SAM) and Neural Radiance Field (NeRF) techniques. Our approach generates accurate segmentation masks of surgical tools using SAM, which guides the refinement of the dynamic surgical scene reconstruction by NeRF. Our experimental results on public endoscopy surgical videos demonstrate that our approach successfully reconstructs high-fidelity dynamic surgical scenes and accurately reflects the spatial information of surgical tools. Our proposed approach can significantly enhance surgical navigation and automation by providing surgeons with accurate 3D position information of surgical tools during surgery.

57. Functional Connectivity in ICU Survivors

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INTRODUCTION Electroencephalography (EEG) is a clinical tool for measuring brain voltage fluctuations. EEG may be useful to characterize functional connectivity patterns associated with cognitive dysfunction during and after critical illness. Development of EEG-based biomarkers must account for the duration of recordings required to compute valid metrics. Since shorter duration of data signals artificially increases functional connectivity metrics, we sought to evaluate the relationship between EEG data quantity and computed functional connectivity in hospitalized inpatients.

METHODS We hypothesized that the quantity of EEG data impacts the functional connectivity characteristics. We selected a convenience sample of 5-minute, 19-channel EEG clips recorded in 4 hospitalized patients. After filtering and artifact reduction, signals were subdivided into 3-second epochs. For each EEG, we randomly selected subsets of 20, 30, 40 and 80 epochs. We thus generated 4 EEGs with 20 epochs each, 4 EEGs with 30 epochs each, etc. Using FieldTrip, we computed imaginary coherence (icoh) and weighted Phase Lag Index (wpli) in four frequency ranges: 1-4Hz, 4-8Hz, 8-13Hz, 13-25Hz. We used paired t-tests to compare metrics computed on 20, 30, or 40 epochs versus those computed on 80 epochs for the same patient. P values less than 0.05 were considered statistically significant.

RESULTS The mean difference in connectivity metrics between epoch lengths is presented in Table 1. Only datasets with 40 epochs showed stable connectivity computations.

Connectivity Measure		# of Epochs	Mean difference		95 % CI	p-value
icoh	20	0.0029	0.00176 to 0.0070		0.00465	0.00069
	to 0.0086	0.0242	-0.00073 to 0.0036			
wpli	20	0.04974	0.0002		0.02426 to 0.0843	0.0757
	to 0.0712	0.01520	-0.00178 to 0.0322			

CONCLUSION
Having a higher quantity of data does impact the quality of the signal analysis. These findings have relevance for development of EEG based biomarkers for clinical applications.

58. Relating fMRI Vigilance Patterns with Neurocognitive Measures in Temporal Lobe Epilepsy

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Introduction: Temporal Lobe Epilepsy (TLE) is a nuanced, focal neuropathology with widespread cognitive abnormalities spanning from sub-cortex to cortex. In this study, we seek to evaluate how cognition relates to full brain fMRI-derived vigilance spatial patterns in TLE patients.

Methods: Simultaneous fMRI-EEG scans were collected for 15 TLE patients (42.3 ± 13.6 years; 11 female). Scans consisted of a 20-minute eyes-closed, resting state sequence using a 3T MRI and 32 channel, MR compatible EEG devices. A gold standard-vigilance measure was derived using alpha/theta frequency band ratio extracted by our EEG. Cognitive ability was measured using 10 clinical neuropsychological tests administered by professional clinicians at Vanderbilt University Medical Center. Furthermore, we conducted a principal component analysis (PCA) of the neuropsychological testing data. In all, 14 voxel-wise regression maps were obtained (1 for each clinical test, and 1 for each principal component).

Results: In all, arousal-related brain fluctuation patterns in TLE patients were found to be significantly related ($p < 0.05$) to a well-documented semantic fluency test (Animal Naming test) and our second principal component of cognition, although the significance did not survive multiple comparisons correction.

Conclusion: Our results suggest that arousal-related brain fluctuations could explain another source of variance in cognitive measures among TLE patients.

59. Cochlear Implant Fold Detection in Intra-operative CT using Weakly Supervised Multi-Task Deep Learning

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Cochlear Implants (CI) are considered to be an effective treatment for severe-to-profound hearing loss [1]. In CI procedures, an electrode array is surgically inserted into the cochlea. The electrodes are used to stimulate the auditory nerve and restore hearing sensation for the recipient. If the array folds inside the cochlea during the insertion procedure, it can lead to trauma, damage to the residual hearing, and poor hearing restoration. Intraoperative detection of such a case can allow a surgeon to perform reimplantation. However, this intraoperative detection requires experience and electrophysiological tests sometimes fail to detect an array folding. Due to the low incidence of array folding (as demonstrated in the following table), we generated a dataset of CT images with folded synthetic electrode arrays with realistic metal artifacts. The dataset was used to train a multitask custom 3D-UNet model for array fold detection. We tested the trained model on real post-operative CTs (7 with folded arrays and 200 without). Our model could correctly classify all the fold-over cases while misclassifying only 3 non fold-over cases. Therefore, the model is a promising option for array fold detection.

60. MAP: Domain Generalization via Meta-Learning on Anatomy-Consistent Pseudo-Modalities

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Deep models suffer from limited generalization capability to unseen domains, which has severely hindered their clinical applicability. Specifically for the retinal vessel segmentation task, although the model is supposed to learn the anatomy of the target, it can be distracted by confounding factors like intensity and contrast. We propose Meta learning on Anatomy-consistent Pseudo-modalities (MAP), a method that improves model generalizability by learning structural features. We first leverage a feature extraction network to generate three distinct pseudo-modalities that share the vessel structure of the original image. Next, we use the episodic learning paradigm by selecting one of the pseudo-modalities as the meta-train dataset and perform meta-testing on a continuous augmented image space generated through Dirichlet mix-up of the remaining pseudo-modalities. Further, we introduce two loss functions that facilitate the model’s focus on shape information by clustering the latent vectors obtained from images featuring identical vasculature. We evaluate our model on seven public datasets of various retinal imaging modalities, and we conclude that MAP has substantially better generalizability.

61. Mpox Lesion Counting With Semantic And Instance Segmentation Methods

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Mpox is a viral illness with symptoms similar to smallpox. A key clinical metric to monitor disease progression is the number of skin lesions. Manually counting mpox skin lesions is labor-intensive and susceptible to human error. We previously leveraged a set of 66 photographs from 18 patients with manual lesion counts and segmentation masks to develop a counting method based on a UNet segmentation model. To build on this work, we have compared three additional methods for lesion counting: the instance segmentation methods Mask R-CNN and YOLOv8, in addition to a UNet++ model. To evaluate their performance, we designed a patient-level leave-one-out experiment, assessing each model on the unseen patient using two different metrics: lesion count, and precision + recall. Bland-Altman analysis of lesion count performance showed a limit of agreement width of 65.8 for Mask R-CNN, 68.2 for YOLOv8, and 62.1 for UNet++, with the baseline UNet model achieving 67.1. When assessing precision + recall, a more informative metric for the accurate detection of mpox lesions, UNet achieved a score of 1.60 compared to 1.54 for Mask R-CNN, 1.54 for YOLOv8, and 1.59 for UNet++. In our data, instance segmentation methods did not outperform UNet-based semantic segmentation methods for lesion counting. Furthermore, an ensemble of the trained models showed no performance increase over the best-performing individual model, likely because errors are frequently shared across models.

62. Thermoelectrics and Liquid Metal: A Pathway to Pumpless Variable Stiffness Robots

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Soft and continuum robots have garnered great interest in recent years due to their ability to reconfigure, navigate complex environments, and enhance safety during unplanned collisions. The surgical environment demands such capabilities in order to prioritize the safety of the patient and enable surgeons to perform dexterous tasks and apply clinically relevant forces. To combine the advantages (e.g. higher payloads, simpler kinematics) of rigid robots with these desirable attributes, we present here a manipulator which is able to switch back and forth between being a rigid-link manipulator and a soft continuum robot. Manipulator stiffness is altered using phase changes of a low melting point alloy. The robot can switch between stiff and flexible states using thermoelectric heat pumps which enable local heating and cooling of both robot sections and robot joints. When completely liquid the manipulator acts as a soft, continuum robot, able to navigate surgical scenes for tasks like endoscopy. Using the proposed localized heating and cooling, it is also possible to navigate to a specified location and then perform tasks by only mobilizing certain sections or by stiffening the entire backbone and deploying tools through the inner lumen. We evaluate the expanded reach afforded by the soft state, the overall workspace, and the increase in payload capacity enabled by the stiff state. Potential applications are demonstrated including flexible scope deployment and end effector gripping.

63. Intraoperative Gaze Guidance with Mixed Reality

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Efficient communication and collaboration are essential in the operating room for successful and safe surgery. While many technologies are improving various aspects of surgery, communication between attending surgeons, residents, and surgical teams is still limited to verbal interactions that are prone to misunderstandings. Novel modes of communication can increase speed and accuracy, and transform operating rooms. We present a mixed reality (MR) based gaze sharing application on Microsoft HoloLens 2 headset that can help expert surgeons indicate specific regions, communicate with decreased verbal effort, and guide novices throughout an operation. We test the utility of the application with a user study of endoscopic kidney stone localization completed by urology expert and novice surgeons. We observe improvement in the NASA Task Load Index surveys (up to 25.23\%), in the success rate of the task (6.98\% increase in localized stone percentage), and in gaze analyses (up to 31.99\%). The proposed application shows promise in both operating room applications and surgical training tasks.

64. Comparison of Structural and Functional Connectivity: Exploring Correlations and Disparities in Brain Pathways and Functionality

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Structural connectivity, derived from Diffusion Weighted Images(DWI), offers insights into the white matter pathways connecting different brain regions, highlighting anatomical links. Functional connectivity, assessed through Functional Magnetic Resonance Imaging(fMRI), reveals which brain regions are concurrently active, independent of direct anatomical connections. Emerging evidence points to detectable and meaningful fMRI signals in white matter, traditionally discounted as noise. Diffusion Magnetic Resonance Imaging(dMRI) has also been claimed to detect functional activations as changes in apparent diffusion coefficients. Both fMRI and dMRI have been studied extensively independently. fMRI studies have mostly focused on gray matter functional connectivity, while dMRI studies generally focus on white matter pathways. Recent studies have shown that both these modalities are more related than previously thought. This study aims to compare FC and SC and to find out how they relate to each other and how they differ from each other. The hope is that this will help us understand what common information SC and FC share and if one can be learned from the other. Furthermore, understanding BOLD signals in white matter could be crucial for advancing our knowledge of certain brain disorders, as alterations in these signals have been noted in various disease states.

65. Learning-based Free-Water Correction using Single-shell Diffusion MRI

Tianyuan Yao, Derek B. Archer, Praitayini Kanakaraj, Nancy Newlin, Shunxing Bao, Daniel Moyer, Kurt Schilling, Bennett A. Landman, Yuankai Huo

Diffusion magnetic resonance imaging (dMRI) offers the ability to assess subvoxel brain microstructure through the extraction of biomarkers like fractional anisotropy, as well as to unveil brain connectivity by reconstructing white matter fiber trajectories. However, accurate analysis becomes challenging at the interface between cerebrospinal fluid and white matter, where the MRI signal originates from both the cerebrospinal fluid and the white matter partial volume. The presence of free water partial volume effects introduces a substantial bias in estimating diffusion properties, thereby limiting the clinical utility of DWI. Moreover, current mathematical models often lack applicability to single-shell acquisitions commonly encountered in clinical settings. Without appropriate regularization, direct model fitting becomes impractical. We propose a novel voxel-based deep learning method for mapping and correcting free-water partial volume contamination in DWI to address these limitations. This approach leverages data-driven techniques to reliably infer plausible free-water volumes across different diffusion MRI acquisition schemes, including single-shell acquisitions. Our evaluation demonstrates that the introduced methodology consistently produces more consistent and plausible results than previous approaches. By effectively mitigating the impact of free water partial volume effects, our approach enhances the accuracy and reliability of DWI analysis for single-shell dMRI, thereby expanding its applications in assessing brain microstructure and connectivity.

66. Impact of preprocessing on the cross-modality reproducibility of the functional connectivity of arousal centers in the brainstem and basal forebrain

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Previous fMRI studies have shown that various neurological disorders are associated with impaired functional connectivity (FC) of arousal centers in the brainstem and basal forebrain (BF). However, reliably characterizing the FC of these structures is challenging because of localization and SNR limitations. Advanced acquisition and preprocessing techniques may alleviate some of these limitations. Therefore, we sought to compare the FC of the arousal structures across fMRI datasets with different acquisition parameters and across four preprocessing pipelines. This study included 3T and 7T single-echo fMRI from the Human Connectome Project (HCP; $n = 375, 176$) and 3T multi-echo fMRI collected at Vanderbilt ($n = 30$). The Vanderbilt and HCP 3T datasets contained simultaneous respiratory and cardiac recordings. The whole-brain correlation patterns of 9 brainstem and 4 BF nuclei were computed for four preprocessing pipelines in each dataset, and the spatial reproducibility of the FC across the datasets was evaluated for each pipeline. After regression of mean white matter (WM) and deep cerebrospinal fluid (CSF) signals, the reproducibility was moderate to strong (Dice coefficient > 0.4) for most nuclei, except the PAG and left MS/DBB in HCP 7T. Additionally regressing the mean fourth ventricle signal improved the reproducibility of the PAG and left MS/DBB. Regression of respiratory and cardiac confounds achieved a reproducibility similar to the CSF/WM regression while the aCompCor pipeline resulted in lower reproducibility for most nuclei. Our results indicate that reproducible FC patterns for the nuclei can be achieved with multi-echo fMRI, even in a relatively small sample size.

67. Monocular Microscope to CT Registration using Pose Estimation of the Incus for Augmented Reality Cochlear Implant Surgery

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For those experiencing severe-to-profound sensorineural hearing loss, the cochlear implant (CI) is the preferred treatment. Augmented reality (AR) aided surgery can potentially improve CI procedures and hearing outcomes. Typically, AR solutions for image-guided surgery rely on optical tracking systems to register pre-operative planning information to the display so that hidden anatomy or other important information can be overlaid co-registered with the view of the surgical scene. In this paper, our goal is to develop a method that permits direct 2D-to-3D registration of the microscope video to the pre-operative Computed Tomography (CT) scan without the need for external tracking equipment. Our proposed solution involves using surface mapping of a portion of the incus in surgical recordings and determining the pose of this structure relative to the surgical microscope by performing pose estimation via the perspective-n-point (PnP) algorithm. This registration can then be applied to pre-operative segmentation of other invisible anatomy during operation, as well as the planned electrode insertion trajectory to co-register this information for the AR display. Our results demonstrate promising accuracy with an average rotation error of less than 25 degrees and a translation error of less than 2 mm, 3 mm, and 300 mm for the x, y, and z axes, respectively. Our proposed method has the potential to be applicable and generalized to other surgical procedures while only needing a monocular microscope during intra-operation.

68. Improving Cardiac Ultrasound with a Semi-supervised Deep Learning Beamformer

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Deep learning beamformers have demonstrated potential to improve ultrasound images by removing artifacts including phase aberration, reverberation, and off-axis clutter. However, such beamformers may perform poorly on out-of-distribution data that differs too much from training data. In this work, we use GANs to separately model distributions of noisy and clean channel data in both synthetic and in vivo domains. We leverage these generators to train a beamformer that performs well on new in vivo images. Our training set comprises 12 cysts with clutter simulated with Field II, corresponding clutter-free synthetic data, and in-vivo cardiac cine loops from three subjects. The fourth domain - clean, in vivo data - is unavailable but can be inferred by establishing path- consistent training losses. We train two sets of generators to map between synthetic and in vivo data in the noisy and clean domains using separate cycleGANs. These generators let us construct losses for the beamforming regressor that involve all domains including the unavailable one. To evaluate the quality of the domain transforms, we passed 12 simulated diffuse targets through the generators on the noisy and clean side and computed van Cittert-Zernike (VCZ) curves. We captured beamforming regressor performance with contrast-to-noise ratio (CNR) and generalized CNR (gCNR) computed on a 32-frame test cine-loop distinct from the training set. On average, DAS and our method achieved a CNR of 1.05 ± 0.97 dB and 3.77 ± 0.99 dB, respectively and gCNR of 0.698 ± 0.09 and 0.982 ± 0.03 , respectively.

69. Combining gCNR with size and resolution for a clinically relevant image quality metric

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In medical ultrasound imaging research, image quality metrics are frequently used to judge the performance of different post-processing image formation techniques. However, in industry and clinical settings these metrics are at best correlated with subjective image quality, and at worst may not correlate at all. A growing concern in the community is that traditional image quality metrics may not be effective at analyzing many modern adaptive techniques, and therefore may not be indicative of real-world clinical performance. To address this, methods such as generalized contrast-to-noise ratio (gCNR) have been introduced that seek to compensate for certain types of image transformations that are known to not impact clinical assessment. In this work, we seek to take gCNR another step forward, and consider it in the context of the work done by Smith et al., who proposed SNRopt, which incorporates target size and system resolution. SNRopt was demonstrated to correlate well with subjective clinical evaluation, and further was more robust as it considered the size of the target. As it stands, SNRopt still falls prey to many of the same concerns that gCNR aims to correct, so by merging the strengths of both image quality metrics we may be able to create an objective metric that is robust and still correlates well with clinician assessment. Preliminary results suggest that a relation between gCNR and SNRopt exists, which would additionally allow us to compare this metric to the Rose Criterion, which is a popular threshold for signal-to-noise ratio considerations.