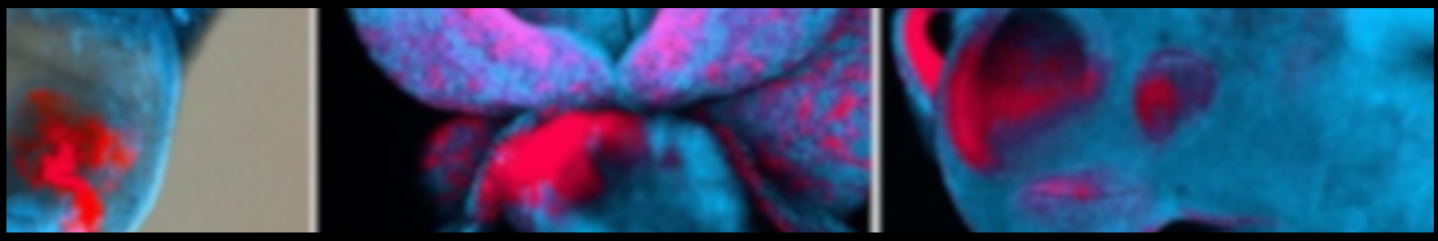
2nd Annual Translational Imaging Conference

AI and Machine Learning in Imaging



November 10, 2020

Gulf Coast Consortia

QUANTITATIVE BIOMEDICAL SCIENCES

The Gulf Coast Consortia (GCC), located in Houston, Texas, is a dynamic, multi-institution collaboration of basic and translational scientists, researchers, clinicians and students in the quantitative biomedical sciences, who benefit from joint training programs, topic-focused research consortia, shared facilities and equipment, and exchange of scientific knowledge. Working together, GCC member institutions provide a cutting-edge collaborative training environment and research infrastructure beyond the capability of any single institution. GCC training programs currently focus on Biomedical Informatics, Computational Cancer Biology, Molecular Biophysics, Pharmacological Sciences, Precision Environmental Health Sciences and Antimicrobial Resistance. GCC research consortia gather interested faculty around research foci within the quantitative biomedical sciences, and currently include AI in Healthcare, Antimicrobial Resistance, Cellular and Molecular Biophysics, Innovative Drug Discovery and Development, Immunology, Mental Health, Regenerative Medicine, Single Cell Omics, Theoretical and Computational Neuroscience, Translational Imaging and Translational Pain Research. Current members include Baylor College of Medicine, Rice University, University of Houston, The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, The University of Texas M. D. Anderson Cancer Center, and the Institute of Biosciences and Technology of Texas A&M Health Science Center.

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Agenda

9:00 Welcome - Robia Pautler, Baylor College of Medicine and
Jim Bankson, UT MD Anderson Cancer Center

Convener: Robia Pautler, Baylor College of Medicine

9:10 *Artificial Intelligence 101 in Medical Imaging: Open the Door to Discover Clinically Meaningful Imaging Markers in Precision Oncology*
Jia Wu, UT MD Anderson Cancer Center

9:40 *Keynote: Learning Brain States from Resting State fMRI*
Shella Keilholz, Georgia Tech/Emory University

10:15 Networking Break

Convener: Jim Bankson, UT MD Anderson Cancer Center

Session 1: Featured Speakers

10:40 *Translating AI's in Pediatric Radiology*
Ananth Annapragada, Baylor College of Medicine/Texas Children's Hospital

11:00 *Harnessing the Power of AI for Image Guided Cancer Therapy*
Kristy Brock, UT MD Anderson Cancer Center

11:20 *Effect of Training Size on Deep-Learning-Based Neural Tissue Segmentation of MRI in Multiple Sclerosis*
Ponnada Narayana, UT Health Science Center Houston

11:40 Poster Data Blitz

11:50 Lunch, Networking, and Poster Presentations
Poster Presentations 12:10 - 12:50

Convener: Robia Pautler, Baylor College of Medicine

1:20 *Keynote: Deep Learning Approaches in Spectral CT*
Cristian Badea, Duke University

Convener: Omid Veiseh, Rice University

Session 2: Featured Speakers

1:55 *From Pixels to Models: An Introduction to Image Analysis with MATLAB*
Brett Shoelson, Matlab

2:15 *Imaging Informed Machine Learning Models for The Local Grading of Glioma*

Agenda

David Fuentes, UT MD Anderson Cancer Center

2:35 *Machine Intelligence in Medical Imaging: Breast Cancer and COVID-19*
Maryellen Giger, University of Chicago

2:55 Break

Convener: Massoud Motamedi, UT Medical Branch at Galveston

Session 3: Selected Trainee Abstracts

3:05 *Clinical Applications of Convolutional Neural Networks for COVID-19 Chest X-Ray Screening*
Daniel Bao, UT Medical Branch at Galveston

Computer Vision Exhibits Entropy Similar to Prostate Cancer Physicians: A Computational Observer Study
Jeremiah Sanders, UT MD Anderson Cancer Center

Using Deep Learning to Quantify Bacterial Self-organization Patterns
Jiangguo Zhang, Rice University

Convener: Jim Bankson, UT MD Anderson Cancer Center

Session 4: Rapid Fire Talks

3:45 Rapid Fire Talks

4:30 Virtual Networking

Speakers in order of appearance

Jia Wu, PhD
Assistant Professor
Imaging Physics

Artificial Intelligence 101 in Medical Imaging: Open The Door to Discover Clinically Meaningful Imaging Markers in Precision Oncology

Dr. Jia Wu received his Ph.D. from the University of Pittsburgh in 2013. He did his postdoctoral training at the University of Pennsylvania and Stanford University. Since 2018, he was promoted to Instructor at Stanford University. At MD Anderson, Dr. Wu will focus on addressing unmet clinical challenges of precision oncology through leveraging multidisciplinary knowledge, including artificial intelligence, medical image analysis, bioinformatics and more. His research will be centered on developing useful imaging markers with three general aims, with Aim 1 to discover clinically relevant imaging patterns to assist cancer diagnosis, prognosis, and optimize treatment; Aim 2 to identify biological underpinnings of putative imaging patterns through integrating with 'omic' and pathologic data; Aim 3 to validate and translate the newly discovered imaging markers into clinical practice to improve cancer patient management.

Abstract: Biomarkers that stratify patients with clinical relevance are critically needed for precision medicine in the cancer field. Medical imaging captures a comprehensive macroscopic picture of tumor phenotype and its environment. Though imaging is used daily in oncology, e.g., clinical TNM stage, studies of intrinsic phenotypes are needed to explore rich imaging descriptors. In this talk, Dr. Wu will cover using artificial intelligence tools to extract meaningful and clinically actionable features. More importantly, he will introduce the challenges and opportunities to evaluate and potentially translate these imaging biomarkers in the clinical environment. In the future, we expect the synergy among imaging, clinicopathological, and molecular biomarkers will result in robust surrogate markers to advance precision medicine.

Shella D. Keilholz, PhD
Professor
Biomedical Engineering

Learning Brain States from Resting State fMRI

Shella D. Keilholz received her B.S. degree in physics from the University of Missouri Rolla (now Missouri University of Science and Technology) and her Ph.D. degree in engineering physics at the University in Virginia. Her thesis focused on quantitative measurements of perfusion with arterial spin labeling MRI. After graduation, she went to Dr. Alan Koretsky's lab at the NIH as a Postdoctoral Researcher to learn functional neuroimaging. She is currently a Professor in the joint Emory/Georgia Tech Biomedical Engineering Department, Atlanta, GA, USA and Program Director for the 9.4 T MRI. Her research seeks to elucidate the neurophysiological processes that underlie the BOLD signal and develop analytical techniques that leverage spatial and temporal information to separate contributions from different sources.

Abstract: Resting state fMRI captures intrinsic activity across the whole brain, which is typically summarized into functional networks using time-averaged metrics like correlation. To gain a deeper understanding of how intrinsic macroscale activity both arises from and constrains local neural activity, we must move beyond time-averaged metrics to new methods that can characterize the complex dynamics of brain activity. Using tools from machine learning, we show that brain activity can be described in terms of states and trajectories, with features that are common across individuals. Moreover, we can use machine learning to identify the best generative models of brain activity along with their parameterizations. The ability to synchronize these models with measured resting state fMRI data opens up new possibilities in terms of model validation, and paves the way for individualized models of brain function that can be used for personalized treatment of neurological and psychiatric disorders.

Ananth Annapragada, PhD
Professor and Vice-Chief for Research
E.B.Singleton Department of Radiology

Translating AI's in Pediatric Radiology

Ananth Annapragada is Professor of Radiology, Director of Basic Research and Vice-Chief of Research in the Edward B. Singleton Department of Radiology at Texas Childrens Hospital and Baylor College of Medicine. Previously, he was the Robert Graham Professor of Entrepreneurial Biomedical Informatics and Bioengineering at the School of Biomedical Informatics at the University of Texas, Health Sciences Center at Houston. He holds additional positions at the Keck Institute and The University of Houston.

An engineer by training, Ananth received his Ph.D. in Chemical Engineering from The University of Michigan in 1989. After Post-Doctoral Fellowships at the University of Minnesota and MIT, he joined Abbott Laboratories as a Research Scientist in 1991. In 1996, he joined SEQUUS Pharmaceuticals, Menlo Park, CA. He stayed with SEQUUS through its merger with ALZA, and when ALZA was acquired by Johnson and Johnson, he left for his first Academic position in 2000, at the Cleveland State University and Cleveland Clinic Foundation. In 2003, he moved to UT. He moved to TCH in June 2011.

Ananth's research interests are in the development of nanomaterial based solutions to medical and imaging problems. Some examples of his work in the field are the development of novel nanoparticle contrast agents for both CT and MR, "Intelligent" nanostructures for glucose responsive insulin delivery, and targeted nanostructures for imaging and therapy.

Ananth is a co-founder of several biotech companies based on research originating in his laboratory, including Marval Inc., Sensulin LLC (Oklahoma City, OK) and Alzeca Inc. (Houston, TX). He serves on the Board and the Scientific Advisory Board of Alzeca, in his role as Chief Scientist. He is also on the Scientific Advisory Board of Sante Ventures a VC firm based in Austin TX, with ~$2B under management.

Abstract: The advent of readily available convolutional neural networks and high-powered GPU's has triggered a revolution in AI applications, and the field of Radiology, with its reliance on image recognition, has become the perfect target for powerful AI's. The FDA has in turn rapidly rolled out guidance for the development of Radiology AI's, and a large number of companies have populated the space: the 2019 RSNA meeting featured ~180 companies exhibiting Radiology AI products, and the 2020 meeting is anticipated to double the size of that roster. Showcased products include tools for patient positioning, image acquisition parameter optimization, probe positioning, image reconstruction, dose reduction, image interpretation and tentative diagnosis.

Paralleling these rapid developments is the increasing recognition of the importance of valid data to train AI's. Factors of local relevance need to be incorporated, a particularly difficult task when training algorithms for broad general applicability across the country or the globe. One therefore anticipates the need for local training and optimization of pre-trained algorithms. The critical nature of both the algorithm and the training data raises the question of who actually owns the final trained algorithm.

In this presentation, I will describe the development and testing of several home-built algorithms, and explore the issues involved in deploying hybrid home-built and commercially sourced algorithms in a clinical environment.

Kristy K. Brock, PhD
Professor
Imaging Physics

Harnessing the Power of AI for Image Guided Cancer Therapy

Kristy Brock is a Professor with tenure in the Department of Imaging Physics at the University of Texas MD Anderson Cancer Center, where she is the Executive Director for the Image-Guided Cancer Therapy Research Program. Her research has focused on image guided therapy, where she has developed a biomechanical model-based deformable image registration algorithm to integrate imaging into treatment planning, delivery, and response assessment as well as to understand an validate imaging signals through correlative pathology. Her algorithm, Morfeus, was licensed by RaySearch Laboratories and was incorporated into their commercially available radiation therapy treatment planning system. She is board certified by the American Board of Radiology in Therapeutic Medical Physics. Dr. Brock has published over 100 papers in peer-reviewed journals and is the Editor of the book ‘Image Processing in Radiation Therapy’.

Abstract: Imaging is a critical component in the detection, characterization and treatment of cancer. The rich information content of advanced imaging methods, combined with the growing capacity to collect multiple types of images from various sources and time points during therapy creates an exciting opportunity for image-based guidance and assessment of interventions for radiation oncology, surgery, and interventional radiology. However, several obstacles prevent the full exploitation of this paradigm including understanding and validating the imaging signals to enable high precision treatment intents tailored for a patient’s tumor and normal tissue profiles, resolving the natural deformations in anatomy between imaging events or between imaging and intervention events, and engaging these advanced imaging techniques to assess the patient’s response to treatment. Recent advances in artificial intelligence, specifically in deep learning, has accelerated methods to address these challenges. This presentation will illustrate recent advances in image guided cancer therapy that leverage deep learning for segmentation, registration, and outcomes prediction.

Ponnada Narayana, PhD; DABR
Diagnostic and Interventional Imaging, Vice-Chair for Research and the Director of Magnetic Resonance Research

Effect of Training Size on Deep-Learning-Based Neural Tissue Segmentation of MRI in Multiple Sclerosis

Dr. Narayana is a Professor of Diagnostic and Interventional Imaging, Vice-Chair for Research and the Director of Magnetic Resonance Research at McGovern Medical School at The University of Texas Health Science Center at Houston (UTHealth). He also holds an Endowed Chair in Biomedical Engineering at UTHealth.

He served on numerous NIH Study Sections. He served on the Editorial Board of a number of major journals.

Dr. Narayana's major research interests include Quantitative Magnetic Resonance of Central Nervous System, Development of Advanced Magnetic Resonance Techniques, and Image Processing with an emphasis on automatic analysis. His current research interests include patient-adaptive, real time MRI, and application of AI to image analysis.

Dr. Narayana directs a state-of-the-art 3T whole body MRI scanner and 7T animal-dedicated MRI scanner.

He has been continuously funded by NIH for the last 35+ years. He directs the MRI Analysis Center that is involved in analyzing multi-center MRI data.

He served as thesis advisor for more than 18 MS, PhD, and MD/PhD students. He trained more than 20 post-doctoral fellows and mentored 10 junior faculty members. He has authored/coauthored 300 publications in peer-reviewed journals and numerous book chapters. He is a Diplomate of the American Board of Radiology in Radiological Physics.

Abstract: **Purpose**: To determine the required training size for a desired accuracy in brain MRI segmentation in multiple sclerosis (MS) using deep learning (DL).

Methods: Magnetic resonance images on 1008 clinically definite relapsing-remitting MS patients who participated in a multi-center, double-blinded, phase III clinical trial

were included in this study. Images were acquired on 1.5T and 3T scanners manufactured by GE, Philips, and Siemens. Images were acquired using dual turbo spin echo, FLAIR, and T1-weighted turbo spin echo sequences. Images segmented using an automated analysis pipeline1,2 and validated by two neuroimaging experts served as the ground truth. A DL model, based on a fully convolutional neural network3, was trained separately using 16 different training sizes. The segmentation accuracy as a function of the training size was determined. These data were fitted to the learning curve4, based on an inverse power law, for estimating the required training size for desired accuracy. The performance of the network was evaluated by calculating the Dice similarity coefficient (DSC), and lesion true-positive and false-positive rates.

Results: The DSC for lesions showed much stronger dependency on the sample size than gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). When the training size was increased from 10 to 800 the DSC values varied from 0.00 to 0.86 ± 0.016 for T2 lesions, 0.87 ± 009 to 0.94 ± 0.004 for GM, 0.86 ± 0.08 to 0.94 ± 0.005 for WM, and 0.91 ± 0.009 to 0.96 ± 0.003 for CSF. The training size needed for a given accuracy strongly depended on the lesion volume. For lesion volumes of 500 µl, an accuracy of 0.8 was achieved with a small training set of 30. In contrast, even with a training size of 800, the accuracy was only 0.5 for lesion size smaller than 70 µl.

Conclusion: Excellent segmentation was achieved with a training size as small as 10 image volumes for GM, WM, and CSF. In contrast, a training size of at least 50 image volumes was necessary for adequate lesion segmentation. The inverse power law dependence allows prediction of the minimum training size needed for a given DSC target.

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Cristian Badea, PhD
Professor
Radiology

Deep Learning Approaches in Spectral CT

Dr. Cristian Badea is a Professor in the Department of Radiology and faculty in the Departments of Biomedical Engineering and Medical Physics at Duke University. His research interests are in the physics and biomedical applications of computed tomography (CT), micro-CT, tomosynthesis, and image reconstruction algorithms. Currently, Dr. Badea is the co-director of the Quantitative Imaging and Analysis Lab with a mission to develop, optimize and apply novel CT and MRI quantitative imaging at both preclinical and clinical levels.

Abstract: We are now at the cusp of major CT imaging advancements provided by the addition of spectral information. Spectral CT can be performed using either energy integrating detectors, as in dual energy CT, or with a photon counting detector (PCD). Our group has advanced preclinical spectral CT by building a few prototype systems and demonstrating their value in cancer and cardiac preclinical studies. However, the full potential of spectral CT has not yet been realized, especially when using photon counting technology. In this talk, we illustrate some of the challenges and the deep learning (DL)-based solutions to improve spectral CT both at preclinical and clinical levels. We present DL strategies applied to preclinical spectral CT for corrections of artifacts, noise reduction and material decomposition. Finally, we show a DL-based spectral extrapolation method for extending the field of view on clinical dual source CT systems. Even with a moderate amount of training data, DL methods are capable of improving spectral CT, leading to increased imaging performance.

Duke University

Brett Shoelson, PhD
Principal Application Engineer

From Pixels to Models: An Introduction to Image Analysis with MATLAB

Brett holds a B.A. degree in anthropology from the University of Florida, a B.S. in biomedical engineering from Mercer University (Macon, GA), and an M.S. and Ph.D. in biomedical engineering from Tulane University. Brett owned and operated a publishing company before returning to school for a second round of education focusing on engineering. Following his doctoral work, he did post-doctoral research at Harvard Medical School, and was a fellow at the National Institutes of Health for five years. The 13 years prior to his employment at The MathWorks were spent focused on process automation with MATLAB in the biomedical arena. Currently, Brett is a Principal Engineer at MathWorks, and focuses on image and vision processing, and on machine and deep learning.

Abstract: Analyzing images efficiently requires selecting the best approach for the job. Some challenges are best solved with pixel-based analyses; some are best solved using features; and others necessitate aggregating information from multiple images in machine- and deep-learning workflows. In this overview session, we will discuss how your image analysis requirements inform the tools you should consider bringing to bear.

David Fuentes, PhD
Associate Professor
Imaging Physics

Imaging Informed Machine Learning Models for The Local Grading of Glioma

David Fuentes was born in Galveston, Texas, in 1981. He received the B.S. degree in aerospace engineering from the University of Texas at Austin, in 2002, and the M.S. and Ph.D. degrees in computational and applied mathematics from the University of Texas at Austin, in 2005 and 2008, respectively. In 2008, he joined the Department of Imaging Physics at The University of Texas MD Anderson as a Postdoctoral Fellow. He achieved the rank of Instructor in 2010, Assistant Professor in 2013, and became an Associate Professor in 2019. His research interests focuses on the development, implementation, and validation of high performance human assisted computational tools for image-guided interventions. These efforts span the fields of: Machine learning, Uncertainty Quantification, Optimization, Parallel Computing, Image Processing, Fluid Mechanics, and Solid Mechanics.

Abstract: The value of imaging in patients with brain tumor can be enhanced if pathologic data can be estimated from imaging input using predictive models. The purpose of this work was to estimate the local glioma grade using a machine learning model trained on preoperative image data and spatially specific tumor samples. MR imaging was performed with anatomic, diffusion, permeability, and perfusion sequences, followed by image-guided stereotactic biopsy before resection. An imaging description was developed for each biopsy, and multiclass machine learning models were built to predict the World Health Organization grade. Models were assessed on classification accuracy, precision, and recall. The developed models are evaluated for the potential to improve patient survival by guiding resection. Results suggest that patients with highly proliferative regions removed showed better outcomes, supporting the use of the model to guide surgical intervention.

University of Texas MD Anderson Cancer Center

Maryellen Giger, PhD
Professor
Radiology

Machine Intelligence in Medical Imaging: Breast Cancer and COVID-19

Maryellen Giger, Ph.D. is the A.N. Pritzker Professor of Radiology / Medical Physics at the University of Chicago. She has been working, for multiple decades, on computer-aided diagnosis /machine learning/deep learning in medical imaging and cancer diagnosis / management. Her AI research in breast cancer for risk assessment, diagnosis, prognosis, and therapeutic response has yielded various translated components, and she is using these "virtual biopsies" in imaging-genomics association studies. She has now extended her AI in medical imaging research to include the analysis of COVID-19 on CT and chest radiographs, and is PI on the NIBIB-funded Medical Imaging and Data Resource Center (MIDRC). Giger is a former president of AAPM and of SPIE; and is the Editor-in-Chief of the Journal of Medical Imaging. She is a member of the National Academy of Engineering; Fellow of AAPM, AIMBE, SPIE, SBMR, IEEE, IAMBE; and was cofounder, equity holder, and scientific advisor of Quantitative Insights [now Qlarity Imaging], which produces QuantX, the first FDA-cleared, machine-learning driven CADx system.

Abstract: Artificial Intelligence in medical imaging involves research in task-based discovery, predictive modeling, and robust clinical translation. Quantitative radiomic analyses, an extension of computer-aided detection (CADe) and computer-aided diagnosis (CADx) methods, are yielding novel image-based tumor characteristics, i.e., signatures that may ultimately contribute to the design of patient-specific cancer diagnostics and treatments. Beyond human-engineered features, deep convolutional neural networks (CNN) are being investigated in the diagnosis of disease on radiography, ultrasound, and MRI. The method of extracting characteristic radiomic features of a lesion and/or background can be referred to as "virtual biopsies". Various AI methods are evolving as aids to radiologists as a second reader or a concurrent reader, or as a primary autonomous reader. This presentation will discuss the development, validation, database needs, and ultimate future implementation of AI in the clinical radiology workflow including examples from breast cancer and COVID-19.

University of Chicago

Daniel Z. Bao
Medical Student

Clinical Applications of Convolutional Neural Networks for COVID-19 Chest X-Ray Screening

Daniel is a 2nd year Medical Student at UTMB and likes to follow advanced applications of ML in the Computer Vision field. He first started using neural networks for protein binding predictions, but has found other interests in medical imaging with COVID-19 under the pathology informatics field with Dr. Peter McCaffrey. He is a Houston local from Pearland and graduated from the University of Houston in 2020 with a B.S in Biomedical Sciences and a minor in Chemistry. In his free time he enjoys playing cool music and reading sci-fi novels.

Abstract: **Background**
Nearly all patients who are suspected of having pneumonia (including COVID-19 pneumonia) undergo thoracic imaging via Chest X-ray. For COVID-19 positive patients, these images can offer preliminary glimpse into the extent of infection and may even provide prognostic insight apart from a simple positive or negative PCR result. Properly trained image classification algorithms have the potential to quickly identify COVID-positive chest x-rays (CXRs) and may even serve as a bridging tool for COVID-19 tests that are pending results. Importantly, prior work has described accurate classification of public COVID-19-positive CXRs trained with publicly available datasets from RSNA and NIH as a baseline comparison which raises important questions about the extent to which such models—or their results—are transferrable to specific institutions who which to deploy such models.
Hypothesis/Goals
In this work, we aim to replicate a high COVID-19 classification accuracy using a model trained on publicly available images and then to transfer that model performance to an institutional dataset of COVID-positive CXRs. We hypothesize that performance will depend upon combination of public and institutional images in early phases of training. Such a model would aid in the classification and triage of COVID-positive patients and would lay the foundations for model-guided prognosis. Importantly, this work will help to establish best practice in translating publicly-trained models to specific healthcare setting.
Methods
AP/PA CXRs from the RSNA Kaggle Pneumonia Challenge and NIH's

were used as baseline images and as a pneumonia/consolidation data set. Further, public COVID-19 chest x-rays updated on April 2020 were downloaded as COVID-19 baseline images. To avoid duplication and overfitting, only the last image for each patient that was most indicative of an active infection was used for subsequent model training. Only the “No Opacity” images were chosen from Kaggle’s dataset to represent “Normal” CXRs along with the “consolidation” class from the NIH dataset as “Pneumonia.” DICOMs were converted to PNG format to create the initial validation set of around 460 COVID-19 images and 500 images from the other classes (Normal & Pneumonia) were used to balance the total dataset. These images were loaded into a Convolutional Neural Network using Tensorflow 2.0/Keras libraries with a 512x512 input and trained for 15 epochs for around 30 minutes using an 80/20 train-validation split. The DICOM images were alternatively combined for the non-transfer learning model.

Results

Reasonable performance (>80% categorical accuracy) was achieved using a balanced selection from RSNA and NIH datasets combined with images from UTMB, and limited transferability (~50% categorical accuracy) when using the clinical COVID-19 images as a validation set.

Conclusion

This work demonstrated that publicly-trained models can be improved by introducing institutional data--and its unique variation—into training and illustrates best practices in applying public data to the institutional healthcare setting. It also highlights the lack of replicability among publicized models with higher reported classification accuracies, which may be due to overfitting or closed-source architecture advantages.

Acknowledgements-Dr. Walser from the UTMB Department of Radiology for obtaining CXR images.

Jeremiah Sanders, PhD
Medical Physics Fellow

Computer Vision Exhibits Entropy Similar to Prostate Cancer Physicians: A Computational Observer Study

Jeremiah Sanders was born in Dallas, TX. He received the BS degree in Aerospace Engineering from the University of Texas at Arlington in 2014. He received the MS degree in Medical Physics from Duke University in 2016 after being introduced to medical imaging. He received the PhD degree in Medical Physics from The University of Texas MD Anderson Cancer Center (UT MDACC) UTHealth GSBS in 2020. His doctoral research focused on MRI pulse sequence development and ML applications development for MRI-assisted radiosurgery (MARS) of prostate cancer. He also has experience developing ML applications for brain MRI including brain metastasis detection and segmentation, multi-compartment whole-brain segmentation, and brain perfusion mapping. He spent the summers of his doctoral research developing satellite detection algorithms at the Maui Optical and Supercomputing Site. He is currently a Medical Physics Fellow in the Department of Imaging Physics, UT MDACC and a member of the Steven J. Frank Lab, Department of Radiation Oncology, UT MDACC where he supports the MRI and ML development efforts for prostate MARS.

Abstract: **Background:** Quantitative techniques for characterizing modern computer vision (CV) algorithms are necessary to inform their clinical application, use, and quality assurance. Furthermore, predictions from CV models should be understood in the context of human predictions for the same clinical tasks if they are expected to assist or substitute humans in clinical decision making. **Hypothesis/Goals:** To introduce computational observer studies (COS) and spatial entropy mapping for characterizing CV algorithms and to evaluate them on a clinical MRI task that informs the treatment and management of prostate cancer patients.

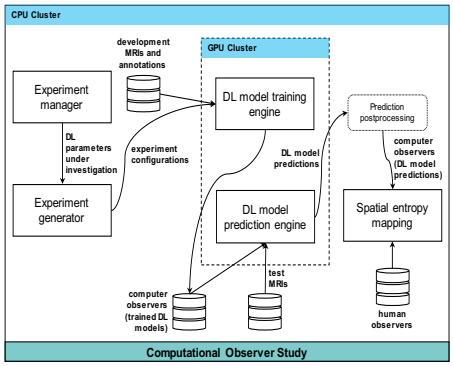

Figure 1. The computational observer study performed in this work. Computer observers were produced by training FCNs to perform the same segmentation task that the human analysts performed.

Specifically, we analyze the task of prostate and periprostatic anatomy segmentation in prostate MRI and compare human and computer observer populations against one another.

Methods: An observer study comprising 7 human analysts was conducted. The analysts included 4 radiation oncologists, 1 abdominal radiologist, 1 medical dosimetrist, and 1 imaging physicist. Several techniques to minimize human observer bias were implemented in the study. The analysts contoured the prostate, external urinary sphincter (EUS), seminal vesicles (SV), rectum, and bladder for post-treatment quality assessment (QA) of 25 patients. The 25 patients underwent prostate MRI-assisted radiosurgery (MARS) and were scanned with fully balanced steady state free precession MRI without an endorectal coil.

A COS was conducted on an NVIDIA DGX-1 workstation (FIGURE 1). An experiment generator was written to train 18 CV algorithms, created from 18 deep learning (DL) models, in succession. 250 3D prostate MRIs acquired with 2 pulse sequences that yielded T2w and T2/T1w image contrast, respectively, were used for developing the DL models (225/25 training/cross validation). The MRIs were acquired for treatment planning and post-treatment QA of prostate MARS. 18 computer observers were constructed from the 18 DL models (fully convolutional networks, FCNs) developed with unique convolution pathways and supervised training techniques. This yielded 18 unique DL models to perform the segmentation task, each of which had convolution kernels with unique characteristics and were produced as an attempt to replicate the natural variation in the experience of human observers. Spatial distributions of the entropy of the segmentation masks for observer populations were computed and compared across human and computer populations for the 25 patients. Spatial distributions of the entropy of the segmentation masks for observer populations were computed and compared across human and computer populations for the 25 patients. The entropy of the segmentation masks H for an observer population was computed voxel-wise; $H(x,y,z) = -\sum p(x_i, y_j, z_k) \log\left(p(x_i, y_j, z_k)\right)$, where $p(x_i, y_j, z_k)$ is the probability distribution of the tissue class of voxel (i,j,k). All 7 human analysts were included in the human observer population. All 18 computer observers were included in the computer observer population.

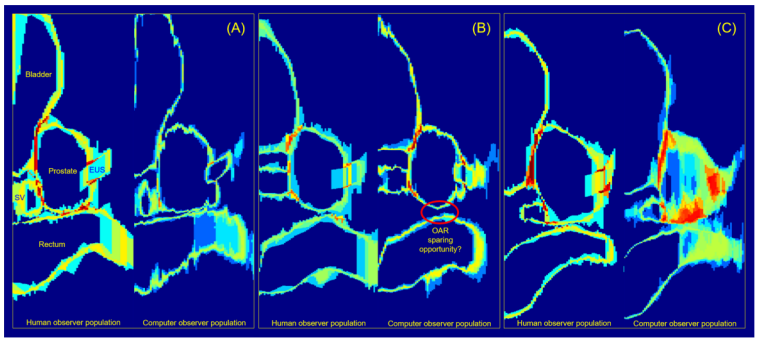

Figure 2A-C. Spatial entropy maps for 3 patients. The horizontal axis is the craniocaudal dimension and the vertical axis is the anteroposterior dimension. (A) Computer observers exhibited less entropy than human observers. (B) Human and computer observers exhibited similar entropy. Note the separation between the prostate and rectum, which is an organ at risk (OAR). (C) Computer observers exhibited higher entropy than human observers.

Results: Spatial entropy maps for 3 patients compared between the human and computer observer populations revealed patterns of clustering in specific anatomic regions of the MRIs (FIGURE 2). The clusters with the highest entropy were located around the circumference of the target organ (prostate), especially at junctions between the target and surrounding organs at risk. Across all of the patients observed, the most common regions of high entropy clusters were observed at the bladder neck, the junction between the prostate and SV, the region along the prostate and anterior rectal wall, and the circumferential region around the junction between the prostate apex and EUS.

Conclusions: Computational observer studies offer the potential to investigate the performance of modern CV algorithms on specific clinical tasks, and provide avenues for further investigations to characterize these complex algorithms. In the case study presented, we demonstrated that a population of CV algorithms produced patterns similar in the spatial entropy of tissue classes as a group of analysts involved in the MARS clinical workflow. We also presented examples where the spatial entropy of the CV observers produced patterns of lower and higher spatial entropy, respectively, than the human observer population. These findings have several implications for the management of prostate cancer patients with MARS and the advancement of MARS with CV.

Jiangguo Zhang
Graduate Student
Bioengineering

Using Deep Learning to Transform Between Conventional and Fluorescent Microscopic Images of Myxococcus xanthus

Jiangguo Zhang is a third-year Ph.D. student in the Department of Bioengineering at Rice University under Oleg Igoshin. His current research focusing on extracting aggregation features of fruiting bodies with the assistance of a deep neural network.

Abstract: **Background:** Under nutritional stress, the *Myxococcus xanthus* initiates a developmental program to self-organize into fruiting bodies, large mounds in which cells differentiate into metabolically inert spores. Under microcinematography (time-lapse microscopy), swarms of cells are coalescing into aggregates of different sizes, shapes, and cell densities. However, the quantification of conventional microscopic images is impeded by certain artifacts (reflections, debris, etc) (Fig.1A). As a result, the grey-scale intensity of these images does not exactly represent the underlying cell density, and the cell movement among aggregates is untraceable. A better estimation of cell density is possible from fluorescence microscopy(Fig. 1B) but these images require fluorescent labeling of cells and are more labor-intensive.

Hypothesis: The conventional and fluorescent microscopic images of *M.xanthus* contain the same information related to cell aggregation and cell movement. Recent advances in the application of DL for image style transfer can be adapted to transfer the image from the conventional microscopic view to the fluorescent microscopic view, and vice versa.

Methods: Using the microscopes capable of alternating between conventional and fluorescence microscopy, we can observe the developmental patterns in both channels. We then use this data to develop and train an image transformation model: the phase-contrast images are fed to a neural network to generate effective "fluorescent" images approximating cell density maps(Fig. 1C). We further use the histogram equalization method to enhance the contrast in the area among aggregates to visualize the cell streams connecting different aggregates. This model is also trained in the opposite direction to generate "phase-contrast" images from computer-synthesized fluorescent images, which can be generated by our agent-based models.

Rice University

Results: The generated images uncover the aggregation pattern as well as the cell stream information from conventional microscopic images. The similarity between the synthesized image and the real image is comparable to two images taken less than 60 minutes apart.

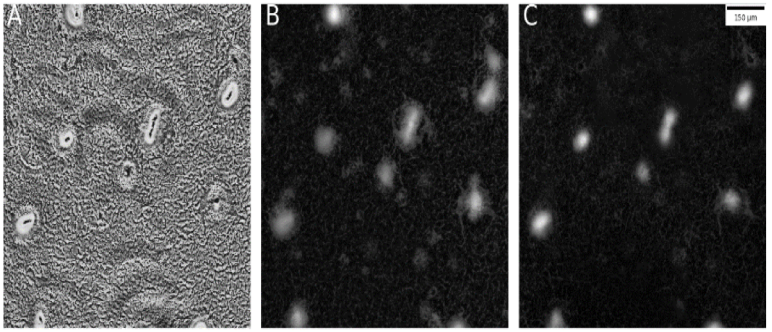

Figure 1 Aggregation images: (A) Input phase-contrast image; (B) tdTomato fluorescent image; (C) Model-generated "fluorescent" image from panel A.

Conclusions: This work applies recent advances in DL image analysis to understanding the system biology of bacterial self-organization. Our methodologies could be applicable to image transformation and feature extraction problems to study emergent patterns in other cellular systems.

Acknowledgments: This work is funded by NSF IOS-1856742 award.

Poster Presenters

First Name	Last Name	Institution	Poster Title
Bryan	Antonio	RU	*Decoding Brain Networks Associated with Tongue Motor Control Generated via an MRI-compatible Brain Computer Interface using Support Vector Machines and Multilayer Perceptrons*
Nickolas	Fularczyk	UH	*Segregation of Cytoskeleton Alterations in Neurons from Schizophrenia Patients in Response to Inhibition of the GSK3/SGK-1 Signaling Pathway*
Rasoul	Hekmati	BCM	*Individualized Brain Computer Interface in the MRI environment Increases Signal-to-noise-ratio in Bilateral Somatomotor, Attention, and Proprioceptive Awareness Networks*
Duong	Huynh	BCM	*Increased Support Vector Machine-Generated Consistency of Motor, Attention, and Sensory Networks via Individualized Real-Time fMRI Neurofeedback*
Rahul	Kadakia	UT	*Redox Responsive 19F MRI Probes for Detecting Cellular Hypoxia*
Vi	Ly	UTHSCH	*Deep Learning Segmentation of Diffusely Abnormal White Matter (DAWM) In Multiple Sclerosis*
Rob	Raphael	RU	*Optical Coherence Tomography Imaging of the Murine Vestibular System*
Nianchao	Wang	TAMU	*Automated Cell Segmentation and Classification of Autofluorescence Microscopy Images*

Poster Abstracts

Decoding Brain Networks Associated with Tongue Motor Control Generated via an MRI-compatible Brain Computer Interface using Support Vector Machines and Multilayer Perceptrons

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Background and Significance: The development of brain-computer interfaces (BCI) has attracted significant attention in neuroscience research. BCIs, outside the MRI environment offer neuro-rehabilitative function to patients with motor and sensory impairments by decoding brain activity with the goal to operate external devices, such as prosthetics. The Papageorgiou lab has developed an MRI-compatible BCI, referred to as individualized real-time fMRI neurofeedback (iRTfMRI-nFb) for the neurorehabilitation of motor disorders, which affect speech, swallowing, and eating. Current BCI research focuses on increasing the sensitivity of decoding cortical networks using machine learning algorithms.

Goal: Our aim was to assess the performance of linear, radial basis function (RBF) support vector machines (SVMs) and multilayer perceptrons (MLPs) to classify: i. the task- versus the baseline-associated time series blood-oxygen-level-dependent (BOLD) brain signal and ii. the neurofeedback- versus the control-condition-generated BOLD signal.

Hypothesis: RBF-SVM and MLPs will achieve higher performance for both classifications compared to linear SVM.

Methods: We decoded participants' motor, sensory, attention, and reward brain networks generated by tongue-motor-control in four directions (up; down; left; right) using SVMs and MLPs. To classify tongue-motor-control versus baseline, we trained the models to distinguish brain activity during the performance of tongue-motor-control versus tongue at rest. For iRTfMRI-nFb versus control conditions, the models were trained to distinguish between brain activity occurring during the presence of either the control or the iRTfMRI-nFb conditions. We determined classification accuracies using a leave-one-subject-out cross-validation procedure: in each iteration, the models were trained on brain data from 29 participants and predictive accuracy was evaluated on data from one participant not included in the training dataset.

Results: For neurofeedback vs control classification, the performances of RBF-SVM and MLPs were statistically different from the linear SVM's performance. However, for task vs rest classification, there were no statistical differences between the linear and nonlinear algorithms.

Conclusion: The optimization machine learning algorithms for decoding brain activity is of utmost importance in iRTfMRI-nFb for the effective neuro-rehabilitation of cortical motor lesions.

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Segregation of Cytoskeleton Alterations in Neurons from Schizophrenia Patients in Response to Inhibition of the GSK3/SGK-1 Signaling Pathway

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Background. Human induced pluripotent stem cells (hiPSCs) allow for the establishment of brain cellular models of psychiatric disorders that account for a patient's genetic background and provide a unique source for interrogating cellular signaling perturbations associated with the disease. On the basis of RNA sequencing profiling of hiPSC-derived neurons from a genetically homogenous family of schizophrenia (SCZ) subjects, our team identified 454 differentially expressed genes enriched in pathways converging to phosphoinositide 3-kinase (PI3K)/glycogen synthase kinase 3 (GSK3) signaling and its upstream regulator, Serum/Glucocorticoid Regulated Kinase 1 (SGK-1). Using single-cell image analysis we found that these gene expression changes correlate with cell cytoskeleton alterations that were rescued by inhibiting the GSK3 pathway and SGK-1.

Hypothesis/Goals. We hypothesize that alterations of neuronal morphology correlate with disruption of the GSK3/SGK-1 pathway and to SCZ diagnosis. Through this information, we aim to generate hypotheses about disease mechanisms that will be testable in SCZ disease models.

Methods. We applied an array of supervised machine learning methods trained on image-based features associated with the beta-III tubulin marker to test if image-based features of cytoskeleton alterations are predictors of the disruption of the GSK3/SGK-1 signaling pathway.

Results. We were able to successfully and reliably segregate morphological alterations of hiPSC-derived neurons in response to disruption of the GSK3/SGK-1 pathway and to SCZ diagnosis.

Conclusions. By identifying potential image-based phenotypes associated with the disruption of the GSK3/SGK-1 signaling pathway identified on the basis of RNA sequencing profiling , our results will advance the understanding of how information from signaling pathways and other regulatory factors are integrated to regulate disease-related gene expression.

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Individualized Brain Computer Interface in the MRI environment Increases Signal-to-noise-ratio in Bilateral Somatomotor, Attention, and Proprioceptive Awareness Networks

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Background: Tongue movement control is accomplished by the glossopharyngeal (CNIX) and hypoglossal (CNXII) cranial nerves. Injury to these nerves can be supra- or infra-nuclear to the brainstem's medulla oblongata, following stroke, brain, or head and neck tumors. The sequelae of CN IX and/or XII injuries can result in neuropathic tongue and oral pain, partial paralysis of the tongue, swallowing, mastication, and speech impairment. The prevalence of cranial nerve neuropathy varies and can be as high as 48% following head and neck cancer radiotherapy treatment. In this study, we applied an fMRI-based brain computer interface with the goal to enhance voluntary tongue movement selectivity in each direction in a consistent fashion. This method aims to induce upregulation of the Blood-Oxygen-Level-Dependent (BOLD) signal via individualized real-time fMRI neurofeedback (iRTfMRI nFb). Our method is based on bypassing the lesioned pathway and providing nFb to individualized networks that are intact and can become functionally associated to the lesioned one.

Hypothesis/Goals: The overall goal is to quantify the BOLD neuromodulation generated by iRTfMRI nFb for its use in the neuro-rehabilitation of lower cranial nerve injury. The immediate goal of this study is to enhance consistency of voluntary tongue movement in four directions in healthy subjects. Our long-term goal is to apply this method as a therapeutic modality to patients following sustenance of lower cranial nerve injury. We hypothesize that nFb in comparison to control-no nFb will: (i) increase the area under the curve (AUC), generated by the BOLD's percent signal change in somatomotor and attention areas for each of the tongue movements, and (ii) decrease the BOLD variance in these same networks.

Methods: Healthy subjects (n=30) participated in a two-day iRTfMRI nFb study. On day one, we decoded the individualized cortical patterns generated by tongue movement in four directions (up; down; left; right). On study-day two, each subject's individualized network for tongue movement direction selectivity was upregulated using iRTfMRI nFb. The AUC generated by the BOLD's PSC between nFb and control-no nFb, was computed using a sensitivity index D prime across networks, as a function of time. We measured the difference in the BOLD's variance for the nFb versus the control across subjects using the euclidian distance. We visualized the difference in the nFb and control's variances using t-SNE, a dimensionality reduction technique, which shows that when points are closer together in the 2D graph then, their data is more similar to one another.

Results: iRTfMRI nFb is characterized by a somatosensory and somatomotor (intraparietal lobule, basal ganglia, thalamus), attention (middle and inferior frontal gyri) and proprioceptive awareness (insula) bilateral networks. These areas are significantly activated 16 secs after onset of tongue movement for a total of 20 secs, as denoted by D prime. To quantify t-SNE variances in each of these networks as a function of time, we used the euclidian distance for each nFb-generated network across subjects, which showed a significant decrease in variance when compared to the control's networks for each direction (45% decrease for left; 66% for right; 21% for up; 34% for down; $p<0.0001$).

Conclusions: This study shows that the purposeful induction of upregulation via iRTfMRI nFb can achieve enhanced control of voluntary tongue movement in each of the four directions by increasing the AUC and decreasing the variance of the BOLD signal. Our quantified findings can lead to clinical applications for the neuro-rehabilitation of patients who have sustained lower cranial CNIX and CNXII injury.

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Increased Support Vector Machine-Generated Consistency of Motor, Attention, and Sensory Networks via Individualized Real-Time fMRI Neurofeedback

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Background: The glossopharyngeal (CNIX) and hypoglossal (CNXII) cranial nerves control tongue movement along with pharyngeal and laryngeal function. Supranuclear or infranuclear injury to these nerves as a result of neurological insults, such as stroke, brain, or head and neck tumors, or following radio- and chemo-therapy is associated with neuropathic tongue and oral pain as well as partial paralysis of the tongue, swallowing, mastication, and speech articulation difficulties. The prevalence of cranial nerve neuropathy can be as high as 48% following head and neck cancer radiotherapy treatment. In this study, we applied an innovative brain computer interface approach with the goal to enhance voluntary movement of the tongue in a consistent fashion in healthy subjects. This approach is based on the induction of neuromodulation via individualized, real-time functional MRI neurofeedback (rt-fMRI nFb) training. The principle of our innovative method, as a treatment regimen is to bypass the lesioned pathway and capitalize on others that are intact and can become functionally associated to the lesioned one, as a result of neurofeedback.

Goal and Hypothesis: The overall goal is to develop, optimize, and apply individualized rt-fMRI nFb therapeutics to neuro-rehabilitate lower cranial nerve injury. The immediate goal of our study is to enhance consistency of voluntary tongue movement in healthy subjects. The long-term goal is to apply this method as a therapeutic modality to patients following lower cranial nerve injury associated with oral neuropathic pain. Our hypothesis was that nFb in comparison to control-no nFb would increase: (i) the activity of spatial patterns that control voluntary tongue movement as evidenced by enhanced classification accuracies generated by machine learning approaches, and (ii) the magnitude of the blood-oxygen-level-dependent (BOLD) signal in somatosensory and somatomotor regions which control tongue movement.

Methods: Thirty healthy volunteers participated in a two-day rt-fMRI nFb study. On day one, we decoded the cortical spatial patterns generated by voluntary tongue activations in four directions (up; down; left; right), which were interleaved with periods of tongue-rest. The individualized networks associated with each participant's tongue movement were extracted and used for nFb delivery. On study-day two, we delivered nFb to each subject's individualized network. Linear support vector machine (SVM) was used to classify brain patterns associated to each tongue movement generated during nFb and control scans.

Results: Neurofeedback-generated tongue movement is characterized by a somatosensory and somatomotor bilateral network, such as the thalamus, basal ganglia, precentral gyrus, insula, as well as attention and proprioceptive awareness networks, such as the middle frontal, inferior (opercular) frontal and inferior parietal lobule. SVM nFb-generated classification accuracy is higher than control-no nFb (93.94% vs. 88.1%, $p<0.001$). Our findings show that nFb generates greater consistency of controlled tongue motor movement in healthy participants.

Conclusions: This study suggests that the purposeful induction of neuromodulation via individualized nFb can achieve enhanced control of voluntary tongue movement. This finding has significant implications as a neuro-rehabilitation method for patients who have sustained lower cranial CNIX and CNXII injury.

Acknowledgements: This study is funded by grants to T.D. Papageorgiou: McNair Medial Institute, Robert and Janice McNair Foundation, TIRR/Mission Connect, Junior Faculty Award, NIH-T32.

Redox Responsive ^{19}F MRI Probes for Detecting Cellular Hypoxia

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Magnetic resonance imaging (MRI) is a well-established imaging modality that has been used for *in vivo* human diagnostics for over 30 years. ^{19}F MRI, as an emerging technique, allows non-invasive imaging of whole organisms with negligible background signal. ^{19}F has favorable NMR properties, including a nuclear spin of ½, a Larmor frequency that differs only 6% from ^{1}H, and an 83% sensitivity relative to ^{1}H. In a biological context, there is minimal endogenous fluorine MR signal in the body, since all fluorine is present in solid ionic form in bones and teeth. This makes this modality especially promising for sensing applications as all the observed signal will come from exogenous imaging agents. Further, paramagnetic metals can be used to modulate the relaxation and chemical shift properties of interacting fluorine nuclei via paramagnetic relaxation enhancement (PRE) and pseudocontact shift (PCS) effects.[1] My research focuses on exploiting both metal redox chemistry and coordination changes to design ^{19}F MR-based sensors to detect a variety of biological disturbances.

Previous work in the Que Lab focused on using Cu^{2+}ATSM, a small molecule that functions *via* selective intracellular accumulation in hypoxic cells following reduction of Cu^{2+}ATSM to [Cu^{+}ATSM] and subsequent ligand dissociation. **CuATSMF$_3$-Fl**,[2] a trifluorinated and fluorescent derivative of CuATSM, retained hypoxia selectivity ($E_{1/2}$ = -0.56 V vs SCE), displayed no initial ^{19}F NMR signal, and exhibited minimal fluorescence due to quenching effects of Cu^{2+}. Upon reduction, an increase in signal in both modalities was observed. These studies were further validated with hypoxic HeLa cells incubated with **CuATSMF$_3$-Fl.** Second generation fluorinated CuATSM probes focused on increasing the fluorine content per agent to allow for higher MR signal intensity. Encapsulating the modified fluorinated CuATSM probe (**CuL$_1$**)[3] in a nanoemulsion allowed the complex to maintain high fluorine density while staying miscible in the aqueous environments. Cell culture studies demonstrated that **CuL$_1$** nanoemulsion was not cytotoxic and hypoxic cells incubated with the nanoemulsion showed a robust ^{19}F NMR peak while no ^{19}F peak was observed in the normoxic cells. Ongoing work with fluorinated CuATSM probes includes synthesizing a highly fluorinated scaffold with water solubilizing linkers for *in vivo* studies.

Fluorine's broad chemical shift range allows us to synthesize multicolor imaging probes as the chemical shift depends directly on the adjacent atom bound to the fluorine. Thus, a probe with a -CF_3 moiety is expected to give a signal considerably different than a fluorine bound to boron (-BF_3) or sulfur (-SF_5). This drastic change in chemical shift can help identify different biological environments by using multiple imaging agents in tandem, each of which contains a unique fluorine moiety and responds to a specific biological environment. Ongoing work utilizes a Fe^{3+} containing MRI probe with an -SF_5 moiety that initially shows no signal; however, upon reduction, the Fe^{2+} probe displays a strong signal at a chemical shift greater than 100 ppm away from a typical -CF_3 agent. Additional work with -SF_5 containing moieties includes synthesizing a Co^{2+}/Co^{3+} MRI probe that shows pH dependence with signals greater than 25 ppm away from one another at acidic and basic pH.

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Deep Learning Segmentation of Diffusely Abnormal White Matter (DAWM) In Multiple Sclerosis

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Background:
Multiple sclerosis (MS) is one of the most common disabling neurological diseases in young adults. It is an immune-mediated disease that involves both demyelination and axonal damage in the central nervous system (CNS) (Kitzler, 2012), resulting in hyperintense lesions on (focal white matter lesions; FWML) on T2-weighted magnetic resonance images. In addition FWML, fuzzy-bordered areas of subtly increased signal intensity, referred to as diffusely abnormal white matter (DAWM) (Vrenken. 2010), are also. Based on histopathology and MRI different degrees of demyelination, axonal loss, and immune cell density that are between FWML and DAWM (Marazano, 2020). However, the task of manual segmentation of DAWM is challenging and time-consuming.

Purpose:
The purpose of this study is to develop a deep learning (DL) method that automatically identifies DAWM accuratelyusing multispectral MRI based on a state-of-art model.

Methods:
T1, T2, and PD weighted and FLAIR images were segmnted by an expert (ground truth). Since the manual segmentation is very time-consuming, in this pilot study, manual segmentation was performed on 5 patients The multispectral images served as input to a pre-trained U-net model, using transfer learning. The dataset was split for training, validation, and testing in a 60-20-20 ratio in a 5-fold cross-validation procedure. The weights in all the layers in the U-net were frozen except for the last layer in order to improve the learning process on such a small sample size and preserve the weights of the pre-trained model.

Results:
With the 5-fold cross-validation process, the mean mean of Dice index for all the tissues combined was 0.95 ±0.04. For DAWM, FWML, cerebrospinal fluid, gray matter, and white matter, the corresponding Dice indices were 0.64± 0.12 0.65 ± 0.24), 0.84 ±0.25, 0.82 ±0.17, 0.84 ±0.17, respectively.

Conclusions:
Despite small sample size, the initial DL result are very promising. We now plan to increase the sample size to 100 and these images will be segmented by two experts. Next, a new model will be retrained on top of the pre-trained Unet and and add an attention gate to improve the learning curve of our model.

Acknowledgements:
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Optical Coherence Tomography Imaging of the Murine Vestibular System

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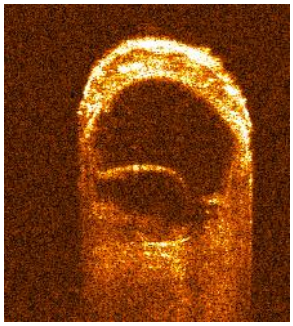
Background The vestibular system is responsible for our sense of orientation and balance. Disorders of the vestibular system can cause diseases such as Meniere's disease for which there are no effective clinical treatments. The vestibular semicircular canals and end-organs are contained within the temporal bone, and a major barrier to vestibular research is the inability to noninvasively image internal vestibular structures within the bony and membranous labyrinths and to study how these structures are perturbed in disease states.

Goals The goal of this research is to establish the ability of optical coherence tomography (OCT) to image the vestibular system in isolated and intact murine temporal bones.

Methods We have utilized optical coherence tomography (OCT) to image the vestibular system in isolated and intact murine temporal bones. OCT is a form of optical interferometry which enables imaging biological tissue at greater depths than optical or fluorescence microscopy. After sacrifice, murine temporal bones were rapidly removed and placed on the stage of a Thorlabs Ganymede Spectral Domain 620C OCT Imaging system. Images of vestibular compartments were acquired in 2D mode for cross-sectional imaging and 3D mode for volume imaging. The data were analyzed in ThorImage OCT software to obtain dimensions of internal structures and reconstruct vestibular anatomy. Our system has a theoretical lateral resolution of 4 μm and an axial resolution of 2.2 μm in water.

Results OCT imaging through the temporal bone readily permitted imaging of the semicircular canals located just beneath the bone. Imaging of a transverse cross section of the semicircular canal reveals distinct compartments delineating the boundaries between the perilymph and the endolymph, as shown at right. 3D imaging of the semicircular canals along the axis of curvature also revealed the presence of membranous structures and enabled imaging of connective tissue between the outer boundary of the duct and the bony labyrinth – structures previously only seen in electron microscopy. We have also demonstrated that OCT can image internal structures in the various vestibular end-organs: the ampulla, the saccule and the utricle.



Conclusions The results establish that OCT can non-invasively image through the murine temporal bone and visualize the internal structures of the vestibular system. The implementation of OCT introduces a powerful method for studying normal vestibular anatomy and physiology as well as testing hypotheses related to the causes and treatments of vestibular disorders.

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Automated Cell Segmentation and Classification of Autofluorescence Microscopy Images

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Background: Autofluorescence lifetime images provide morphological features and functional information about cellular metabolism. Single cell analysis of autofluorescence images allows quantification of heterogeneous cell populations. However, segmentation and classification of cells by functional state remain a challenge due to the low signal-to-noise ratio of autofluorescence images and close proximity of cells grown in 3-dimensional culture or tissues *in vivo*.

Hypothesis/Goals: Our goal is to develop algorithms for automated cell segmentation and functional classification of cells within autofluorescence lifetime images.

Methods: We compared automated cell segmentation programs using a customized watershed algorithm and a convolutional neural network in Python. To evaluate performance, we tested multiple 2D features (e.g. circularity, area, elongation, compactness, and FeretDiameter) and calculated Fisher's Discriminant Ratio (FDR) based on hand-segmentation results. We used machine learning methods to classify cell type within simulated cell populations of quiescent T cells, activated T cells, drug responsive cancer cells, and drug resistant cancer cells using the mean and standard deviation for 7 experimentally measured autofluorescence lifetime imaging endpoints (redox ratio NAD(P)H short lifetime, NAD(P)H long lifetime, fraction of free NAD(P)H, FAD short lifetime, FAD long lifetime, and fraction of bound FAD). The Uniform Manifold Approximation and Projection (UMAP) algorithm was used as a data-dimension reduction technique to visualize the multivariate separation of cell populations. Multiple machine learning algorithms, including Random Forest, Logistic Regression, and Multilayer Perceptron were used to quantify classification accuracy to predict cell type from simulated imaging data (Weka).

Results: Visual inspection of the UMAP graphs found significant separation between the T cells and cancer cells, and moderate separation between the activated and quiescent CD3+ T cells as well as the Trastuzumab-Responsive and Trastuzumab-Resistant Xenografts tumors. The same datasets were analyzed with various machine learning classifying algorithms. A Random Forest model consistently achieved the best classification, with a minimum accuracy of 94% for the dataset with all four different cell populations.

Conclusions: Classification algorithms based on various autofluorescence imaging features can be used to identify rare cell subpopulations within heterogenous mixtures of cells. These methods will enable robust imaging studies of heterogeneity in cancer.

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