BioMedical Engineering and Imaging Institute

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Message from the Director

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In so many ways this year has been unlike any other in recent memory. I am inspired by and grateful for the commitment of our frontline healthcare workers and Mount Sinai's leadership in caring for both patients and the healthcare workforce and in safely restarting research. At BMEII, our work and our institute continue to expand to novel territory, with exciting developments in trained immunity, neuroimaging, COVID-19 research, and our facility offerings. I am pleased to welcome new faculty and staff to BMEII to enhance our research and institutional operations, and to announce our new podcast, ImagingNation. Please enjoy this fall 2020 edition of the BMEII newsletter. Wishing you all continued health and safety.

BMEII News & Updates

Catch Our New Podcast, ImagingNation

This past summer, BMEII launched a podcast called ImagingNation. Hosted by Jazz Munitz, Associate Researcher of Nanoimmunotherapeutics and Manager of Preclinical Nuclear Imaging, the podcast aims to provide insight into imaging, medicine, and bioengineering for a wide variety of audiences. The first episode features Zahi Fayad, PhD and Rob Hirten, MD on the Warrior Watch study and the promise of wearable technology. In the second episode, Drs. Yang Yang, Adam Bernheim, and Michael Chung discuss their pioneering work using clinical data, chest CT images, and artificial intelligence (AI) to rapidly diagnose COVID-19 and the impact of AI on the field of radiology. Stay tuned for new episodes this fall!

You can find ImagingNation on Apple Podcasts, Spotify, and on our website at bmeiisinai.org.

Welcome, New BMEII Staff

Valentin Fauveau, a data scientist and biomedical engineer, joined BMEII as a Programmer Analyst and supports re-searchers through data management, data analysis, and predictive modeling. Valentin holds a BS in Biomedical Engineering from Universidad de los Andes (Bogota, Colombia) and masters degrees in Medical Imaging and Artificial Intelligence (Télécom Paristech, Paris, France) and Computational Bioengineering (Columbia University, New York, US).

Jenna Korotkin is a Clinical Research Coordinator in the Taouli Lab. She graduated in May 2019 from Cornell University with a BS in Human Biology, Health & Society, and double minors in Human Development, and Policy Analysis & Management. After working at Massachusetts General Hospital, Jenna joined the BMEII team and is responsible for recruitment and regulatory compliance for various imaging studies.

As a Program Manager at BMEII, Mallory Stellato handles patient coordination and operations for Dr. Zahi Fayad's stress and atherosclerosis study and supports communications and business development for the Institute. She completed her MPH in 2020 at Columbia University's Mailman School of Public Health and holds a BS in Biology & Society from Cornell University with a minor in Global Health.

Congratulations to the Radiology Retreat Winners!

Presenter	Talk Title
Shingo Kihira	Association of COVID-19 with Large Vessel Occlusion Strokes: A Case-Control Study
Mark Finkelstein	Value of Chest Radiographs in COVID-19: Analysis of Clinical and Imaging Features in Relation to Patient Outcomes in Young Adults.
Timothy Carlon	Sources of Revenue Loss and Recovery in Radiology Practices During the Coronavirus Disease 2019

Scientists Engineer New Cancer Immunotherapy to Train Immune System in Cancer Fight

Nanobiologic immunotherapy uses tiny, bioengineered material to harness immune system

A groundbreaking new type of cancer immunotherapy developed at the Icahn School of Medicine at Mount Sinai trains the innate immune system to help it eliminate tumor cells through the use of nanobiologics, tiny materials bioengineered from natural molecules that are paired with a therapeutic component, according to a study published in *Cell* in October.

This nanobiologic immuno-therapy targets the bone marrow, where part of the immune system is formed, and activates a process called trained immunity. This process reprograms bone marrow progenitor cells to produce "trained" innate immune cells that halt the growth of cancer, which is normally able to protect itself from the immune system with the help of other types of cells, called immunosuppressive cells.

This work for the first time demonstrates that trained immunity can be successfully and safely induced for the treatment of cancer. The research was performed in animal models, including a mouse model with melanoma, and the researchers said it is being developed for clinical testing.

Immunotherapies that are already part of standard cancer care, such as the drug that eliminated former President Jimmy Carter's metastatic melanoma, are also able to unmask cancer to the immune system, but they have limitations. The type of immunotherapy used for former President Carter, called a checkpoint inhibitor, fully benefits only a small number of patients and can have severe side effects.

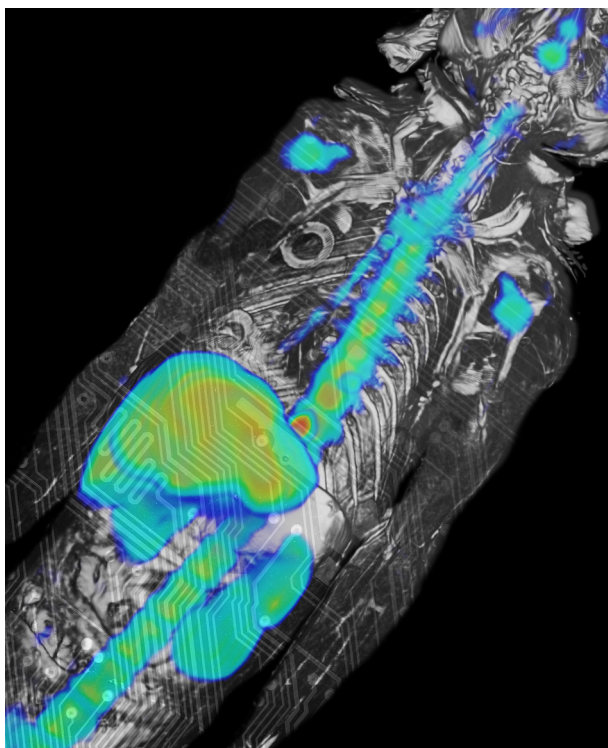Findings from this research demonstrate that the nanobiologic immunotherapy's trained

Figure. MTP-HDL nanobiologics were labelled with radioactive 89-Zr, and injected into two nonhuman primates. Using the Biograph Vision PET/MR in the BMEII radiation suite, Mulder and team visualized the biodistribution of the nanobiologics as they accumulated in the hematopoietic organs. This image is also overlaid with graphics of microchip wires to symbolize epigenetic rewiring that is the hallmark of trained immunity.

immunity approach could be used as a stand-alone anti-cancer therapy, potentially with fewer adverse reactions, or in conjunction with checkpoint inhibitor drugs, the scientists say.

"Not only have we observed very strong anti-cancer effects of our nanobiologic immunotherapy," said lead author Willem J. Mulder, PhD, Professor of Diagnostic, Molecular and Interventional Radiology and member of the Biomedical Engineering and Imaging Institute at the Icahn School of Medicine at Mount Sinai. "The work involves the development and preclinical evaluation of a novel immunotherapy based on highly biocompatible nanomaterials called nanobiologics. Our study is a significant advancement for both trained immunity and cancer treatment, with real potential to move quickly into use in patients."

This research was part of a large collaboration between the Icahn School of Medicine and multiple other institutes and universities in the United States and Europe.

"This study is a game changer in the field of immunotherapy," said Zahi A. Fayad, PhD, Director of the Biomedical Engineering and Imaging Institute, and another author on the paper. "We are continuing the exploration of the technology at Mount Sinai and with our international collaborators."

The publication is available here.

This article is courtesy of Mount Sinai Media Relations.

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Upcoming Lectures

All lectures will take place virtually. For links, please visit, visit https://bmeiisinai.org/lecture-series/.

Date	Event	Speaker	Title
Mon Nov 9th 1:00-2:00pm	BMEII-Radiology Seminar Series	Dan Ma, PhD Assistant Professor, Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH	"MR Fingerprinting: A New Path For Clinical Quantitative MR"
Thurs Dec 17th 9:00-10:00am	Lucy G. Moses Lecture in Medical Imaging and Bioengineering	W. Hong Yeo, PhD Assistant Professor, George W. Woodruff School of Mechanical Engineering, Wallace H. Coulter Department of Biomedical Engineering, Director of the IEN Center for Human-Centric Interfaces and Engineering, Georgia Institute of Technology	"Wearable biosensors and biolectronics"

Senior Scientist
Gaurav Verma, PhD

Dr. Gaurav Verma is a senior scientist at the Icahn School of Medicine at Mount Sinai specializing in the development of accelerated and highly-sensitive spectroscopy and imaging sequences for ultra-high field MRI. He has implemented these sequences in the study of human gliomas, psychiatric disorders such as major depression and schizophrenia, and neurological disorders including amyotrophic lateral sclerosis, multiple sclerosis and epilepsy. Dr. Verma's ongoing work explores novel imaging sequences to characterize highly sensitive imaging and metabolic biomarkers for neuropsychiatric disorders, and image processing techniques employing conventional and machine learning-based strategies to glean additional data from the acquired images.

Dr. Verma's ongoing spectroscopy research focuses on the development of very sensitive techniques for the detection of metabolites difficult to detect with conventional methods. This includes neurotransmitters like gamma-aminobutyric acid (GABA) and glutamate whose irregular activity has been implicated in depression. It also includes 2-hydroxyglutarate, an "oncometabolite"

An example of Dr. Verma's scientific art inspired by his work.

only detected in the presence of IDH-mutant tumor. Dr. Verma's imaging work focuses on combining information from multiple imaging modalities. This includes combining structural and connectomic data to perform automated segmentation of brain regions like the thalamus, and developing regression-based algorithms on structural imaging features to model normal and pathological brain aging.

Dr. Verma is passionate about sharing his research interests with the general public, including giving lectures and the development of scientific art. An example of this art, generated as a part of applying automated feature detection algorithms to high-resolution brain imaging is shown here.

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New Faculty
Xiang Xu, PhD

Dr. Xiang Xu recently joined the BMEII Neuroimaging Faculty. She holds a PhD in physical chemistry from New York University, with a focus on neuro magnetic resonance (NMR) spectroscopy. Before joining BMEII at Mount Sinai, Dr. Xu completed a postdoctoral fellowship and served as an Assistant Professor at the F. M. Kirby Center for Functional Brain Imaging and the Department of Radiology at Johns Hopkins University.

Her research as a graduate student focused on three major aspects: (1) to enhance NMR sensitivity using para-hydrogen (p-H$_2$) induced hyperpolarization, (2) to explore unique properties of ^{23}Na NMR and its biological applications, particularly the tensile strength of the cervical connective tissue matrix during pregnancy as well as the diffusion properties of Na$^+$ in optic nerves, and (3) chemical exchange saturation transfer (CEST). This branch of NMR bridges the chemical exchange properties of functional groups on molecules and enhanced signal detectability via water resonance, making it a suitable method for magnetic resonance imaging (MRI).

Dr. Xu's growing interest in MRI research led her to Dr. Peter van Zijl's research group at Johns Hopkins University, the first to utilize CEST principles for in vivo imaging. During her postdoctoral training, she learned how to perform MRI experiments on both pre-clinical and clinical systems. Building on her background in NMR, Dr. Xu incorporated MRI concepts into CEST spectrum acquisition and developed an ultrafast gradient encoded method to obtain a CEST spectrum with a 10-fold acceleration. As she gained more knowledge in MRI, she extended this method to acquire CEST images in an ultrafast fashion. Dr. Xu has also developed other techniques to improve CEST contrast on both preclinical and clinical scanner platforms. In addition to method development, her research also focuses on the study of the CEST effect of glucose (glucoCEST) in vivo. After observing reproducible glucoCEST enhancement in the tumor region of animal models, she translated the MRI protocol from a preclinical system to 7T and 3T human scanners and studied the glucoCEST effect in human brain tumor patients.

At BMEII, Dr. Xu will continue her efforts in using glucoCEST to study blood brain barrier disruptions in multiple sclerosis, brain tumors and other neurodegenerative diseases. In addition to translational research, she is interested in exploring the exchange properties of other molecules, and improving the sensitivity and reproducibility of CEST MRI. Unlike most conventional MRI, such as T1w or T2w images, where the contrast is generated during the image acquisition period, the contrast in CEST MRI is generated during a preparation period. Therefore, the goal of optimizing a CEST protocol is to prepare more efficient saturation during the preparation period while shortening the readout period. Leveraging the extensive expertise in pulse design and fast imaging at BMEII, Dr. Xu looks forward to many exciting collaborative projects in the coming years.

In her spare time, she enjoys traveling (currently on pause), nature, community gardening and playing with her toddler girls.

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International Society for Magnetic Resonance in Medicine (ISMRM) Presented Abstracts

| Session Name	Session Type	Abstract Title (Note: links are only active for registered attendees)	Presenter Name
Pancreas and Hepatobiliary	Digital Poster	Flow quantification with navigator-gated 4D flow MRI in portal hypertension	Octavia Bane, PhD Lab: Taouli
Diffuse Liver & Metabolism	Oral	Splenic T1ρ as a noninvasive biomarker for portal hypertension	Stefanie Hectors, PhD Lab: Taouli
Liver: Methods & Applications	Oral	Fully Automated Prediction of Liver Fibrosis using Deep Learning Analysis of Gadoxetic acid-enhanced MRI	Stefanie Hectors, PhD Lab: Taouli
Junior Fellows Symposium: The Environmental Impact of MRI	Weekday Course	Moderator	Stefanie Hectors, PhD Lab: Taouli
Elastography and Perfusion	Digital Poster	Comparison of multi-platform 2D and 3D MR elastography in vivo and in vitro	Paul Kennedy, PhD Lab: Taouli
Hepatobiliary and Pancreas	Digital Poster	Early Effect of 90Y locoregional therapy on tumor and liver parenchyma stiffness measured with MR elastography: initial experience	Paul Kennedy, PhD Lab: Taouli
Pancreaticohepatobilia	Power Pitch	Utility of magnetic resonance elastography and ultrasound shear wave elastography for assessment of portal hypertension	Paul Kennedy, PhD Lab: Taouli
MRA & Atherosclerosis	Oral	Self-gated dynamic contrast enhanced magnetic resonance imaging of the aortic root in atherosclerotic mice: a natural progression study	Claudia Calcagno, MD, PhD Lab: Fayad
Cardiovascular: Technical	Power Pitch	Moderator	Yang Yang, PhD Lab: Fayad
Novel Acquisitions & Reconstructions	Oral	High Spatiotemporal Resolution Motion-Resolved MRI using XD-GRASP-Pro	Li Feng, PhD Lab: Feng
Quantitative MRI: Reproducibility, Robustness, & New Directions	Power Pitch	Stack-of-Stars Inversion-Recovery MRI for Free-Breathing T1 Mapping and IR-Prepared Fat/Water Separation	Li Feng, PhD Lab: Feng
Machine Learning Reconstruction of Dynamic Acquisitions	Oral	Moderator	Li Feng, PhD Lab: Feng
RF Coils III	Digital Poster	Sensitivity Enhancement at 7T Brain MR imaging Using Wireless Coupled-Split-Ring-Resonators Array	Akbar Alipour, PhD Lab: Balchandani
Neuroimaging at High Field	Digital Poster	An MRI traumatic brain injury case study at 7 Tesla: pre- and post-injury structural network and volumetric reorganization and recovery	Stephanie Brown, PhD Lab: Balchandani
Psychoradiology & AI	Oral	Aberrant Functional Brain Network Topology for Classification between Major Depressive Disorder and Healthy Controls	Yael Jacob, PhD Lab: Balchandani
Image Analysis I	Digital Poster	Quantification of brain age using high-resolution 7T MR imaging and implications in major depressive disorder	Gaurav Verma, PhD Lab: Balchandani
Brain Tumour	Digital Poster	Multiparametric MRI Texture Analysis in Prediction of Genetic Biomarkers in Patients with Brain Glioma	Shingo Kihira, MD Lab: Nael
Beyond the Lumen: Vessel Wall Imaging in Cerebrovascular Diseases	Oral	Vessel Wall MRI in Assessment of Unruptured Intracranial Aneurysms: A Longitudinal Prospective Study	Kambiz Nael, MD Lab: Nael
Emerging Neuro Brain Imaging	Digital Poster	A Container and Detailed Preparation Protocol for Ex Vivo Whole Human Brain MRI	Alan Seifert, PhD Lab: Seifert
Spinal Cord: Cool MR Tools & How to Use Them	Oral	Spatial Specificity of BOLD Signal in the Spinal Cord at 7T Using a Noxious Thermal Stimulus	Alan Seifert, PhD Lab: Seifert
All Things Neurospectroscopy	Digital Poster	Comparison of three tissue sodium concentration quantification methods at 3T and 7T MRI	Lazar Fleysher, PhD Lab: Tang

Advanced Neuroimaging Research Program (ANRP) Continues to Grow

New areas of research at ANRP include 7T imaging of Alzheimer's Disease, multiple sclerosis, neurological manifestations of COVID-19, anxiety disorders, and Autism Spectrum Disorder. These are projects headed by ANRP PIs as well as investigators across departments, including Psychiatry, Neurology and Neuroscience. Projects have successfully received funding from NIA, NCI, NIMH, NSF and the ADRC core. Technical advancements include building MR elastography at 3T and 7T, development and safety testing of a dual tuned sodium/proton 7T head coil, development of parallel transmit (pTx) imaging protocols, and higher resolution fMRI, spectroscopic and arterial spin labeling (ASL) sequences for use in multi-modal imaging. We have invested in the Flywheel platform, a more secure and robust method to automate neuroimaging processing pipelines, which may be shared between sites to enable collaboration as well as standardization.

ANRP investigators are working on understanding the effects of COVID-19 on the brain. Dr. Balchandani and Dr.

Bradley Delman are leading the effort to retrospectively analyze brain imaging data and prospectively study neurological manifestations of the disease at 7T. Close collaboration with Dr. Nathalie Jette in Neurology enables correlation with neurological symptom measures. Dr. Alan Seifert is performing very high-resolution
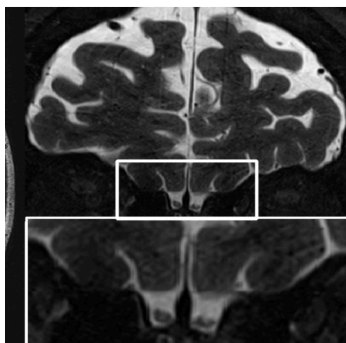
Using 7T brain and brainstem imaging to identify in vivo markers for neurotropism of the SARS-CoV-2 virus.

imaging studies of ex vivo brains of COVID-19 decedents and analyzing the imaging features and correlating to histology

in collaboration with Dr. Mary Fowkes in Pathology and a team of co-investigators.

The ANRP team is growing to include experts that both broaden and strengthen neuroimaging research at BMEII. We recently welcomed a new faculty member, Dr. Xiang Xu, and a new postdoctoral scholar, Dr. Oleksandr (Alex) Khegai. We continue to build strong collaborative ties with neighboring engineering schools. Dr. Mehmet Kurt, who holds an adjunct appointment at BMEII, is MPI on two new funded grants at ANRP from the NIH and NSF.

ANRP continues to provide a mechanism for junior investigators to generate preliminary imaging data for NIH grant submissions, through the ANRP Pilot Grant program. As an example, after receiving the ANRP pilot grant in 2019, Dr. Laurel Morris, Assistant Professor in Psychiatry, has since been awarded a NARSAD Young Investigator Award for the same project, and will be submitting grant applications to external funding agencies using the pilot data generated from the pilot grant.

Custom Radiofrequency Hardware Enables Advanced Imaging Methods

A radiofrequency (RF) coil is an essential component of an MRI scanner. An RF coil accomplishes two tasks in an MRI experiment: it excites atomic nuclei within the subject or object being imaged by transmitting a radiofrequency pulse 'on resonance' with the frequency of a given nucleus, and then receives the weak electromagnetic signals emitted by those nuclei. Unlike most scanner hardware components, RF coils can be easily changed between scans and can be custom-designed for optimized performance in specific applications.

The RF Coil Laboratory in BMEII was initially established in 2010, and is available for RF coil building and troubleshooting. The coil lab is equipped with a vector network analyzer, oscilloscopes, a circuit board printer, a 3D printer, a signal generator, DC power supplies, as well as other standard electronics equipment. BMEII core staff, trainees, and faculty have designed, prototyped, and tested numerous custom RF coils and components in this facility for basic and translational research projects.
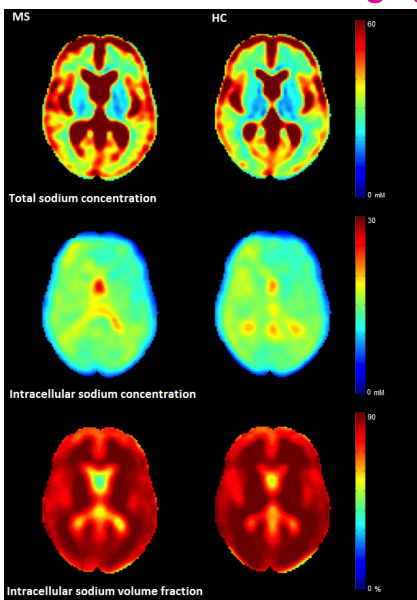
An example of the types of results we will be able to produce with this new sodium coil: maps of mean total sodium concentration, mean intracellular sodium concentration, and mean intracellular sodium volume fraction in subjects with multiple sclerosis and in healthy controls (from Petracca et al., Brain 2016:139;795-806).

These include coils for high resolution 7T MRI of the human cervical spinal cord, brainstem, carotid arteries, and body, as well as a passive wireless resonator array for enhancement of RF fields in the central nervous system and a dedicated coil for rabbit cardiac imaging. In addition to RF hardware, users have also developed mechanical and electronic accessories that are utilized for specific experiments in the high magnetic field environment of the MRI scanners.

BMEII recently partnered with Life Services, LLC to develop a dual-tuned hydrogen and sodium RF head coil for use at 7T. This device is essentially two RF coils, operating at different frequencies, in one housing: a hydrogen RF coil array for producing anatomical images, and a sodium array for mapping important properties of sodium in brain tissue. This 7T sodium head coil will enable new studies of sodium concentration and compartmentalization in diseases such as brain cancer and multiple sclerosis, and may also prove useful for imaging of sodium in skin and skeletal muscle.

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