Icahn
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Translational & Molecular Imaging Institute

Summer 2017
Issue 12

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Message from the Director

We are more than half way into the Summer which I am sure a lot of you are enjoying with some outdoors activities, rest, family time, and rejuvenation. We at TMII have had a very active and successful year so far with many scholarly and personal achievements some of them outlined below in the News and Updates section. This makes me very proud of all of you and I look forward to further achievements and progress for the rest of 2017. In this issue you will find information on a very unique collaboration in Psychiatry, Neuroimaging, Cardiovascular imaging, Nanomedicine in the area of Psychological chronic stress, Immunology and Cardiovascular disease which started this summer part of a large NIH Program Project Grant which takes advantage of a lot

of the state-of-the-art facilities we have at TMII. You will also find in this newsletter, very exciting work being presented in the areas of PET/MR and PET/CT imaging that demonstrate the possibility of more quantitative molecular assessment of disease. I am very thrilled to share with you photos of the TMII 2017 7th Annual Symposium and the Windows to OUR BODY medical Art Exhibition which demonstrated the artistic talent of our faculty, staff, trainees and collaborators. We are busy organizing the TMII 2018 8th Annual Symposium (April 27, 2018) which will have a amongst other things a focus on big data/machine learning with top notch speakers such as Yann LeCun from Facebook. This is a very important area in our field and to some

of our ongoing initiative such as the Imaging Research Warehouse which you can read about in this issue. Finally, I am thrilled to announce the installation by the end of the summer in our Small Animal Imaging Center in Hess SC1 a microPET/CT system from Mediso which will supplement the other imaging resources at TMII. I am certain we will feature work from this new resource in the upcoming newsletter. I you wish all a great read of the TMII Newsletter and a great end of the Summer!

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WHAT'S NEW?

TMII News & Updates

TMII faculty and trainees have been busy these past months getting new grants...

- Octavia Bane (Taouli Lab) received an F32 Postdoctoral Fellowship for her study of "Multiparametric MRI for the Assessment of Renal Transplant Dysfunction".
- Stefanie Hectors (Taouli Lab) was awarded a 3 year Prostate Cancer Foundation Young Investigator Award.
- Venkatesh Mani (Fayad Lab) received a 2 year AHA grant to study "Cardiovascular Safety of E-Cigarettes assessed by PET/MRI"
- Max Senders (Mulder Lab) recently received an AHA AWRP Predoctoral Fellowship to study, "Integration of classical and contemporary views on atherosclerosis using highly innovative

PET/MR plaque phenotyping.
- Joo-won Kim (Xu lab) was awarded National MS Society Fellowship for "Assessing Microstructural Integrity of Cervical Spinal Cord Gray and White Matter with Ultra-High Field Diffusion MRI for Progressive MS"

... And writing papers...

- Judy Alper (Balchandani Lab) "Is There an MRI-Discernible Etiology for Trigeminal Neuralgia? A Structured Review" World Neurosurgery
- Marc Dweck (Fayad Lab) "Hybrid Magnetic Resonance Imaging and Positron Emission Tomography With Fluorodeoxyglucose to Diagnose Active Cardiac Sarcoidosis" JACC: Cardiovascular Imaging

- Stefanie Hectors (Taouli Lab) "Quantification of hepatocellular carcinoma heterogeneity with multiparametric magnetic resonance imaging" Scientific Reports
- Amr Alaarg (Mulder Lab) "Applying nanomedicine in maladaptive inflammation and angiogenesis" Advanced Drug Delivery Reviews

TMII also welcomes new post doc Gaurav Verma to the Balchandani High Field Imaging Lab

Lastly, summer marks the return for TMII Summer Science Camp. This year 11 campers are at TMII from July 11 to August 16th, learning about imaging acquisition and processing along with experimental design and anatomy.

UPCOMING EVENTS

Cure Frontiers in Research Semianr Series

> September 14, 2017 11am-12pm Davis Auditorium - Jullie Pan, MD PhD University of Pittsburg "Imaging the pathophysiology of epilepsy"

3rd Annual Medical Imaging and Bioengineering Lecture

> December 8, 2017 3pm - 4pm - Hess Center - Room 8-101 Frank Preiswerk, PhD - Brigham & Women's Hospital

For more information on these and other events go to: http://tmii.mssm.edu/events

Mount Sinai receives $13 million NIH grant to study link between stress-associated brain activity and cardiovascular risk

Zahi Fayad, PhD

Researchers at the Icahn School of Medicine at Mount Sinai have been awarded $13 million from the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) for a five-year research program that aims to uncover the mechanisms by which stress contributes to cardiovascular risk. The program aims to improve our understanding of how the effect of stress on the brain can directly impact the immune system and cardiovascular disease, and to provide a scientific platform for clinicians and researchers to integrate this knowledge into patient care.
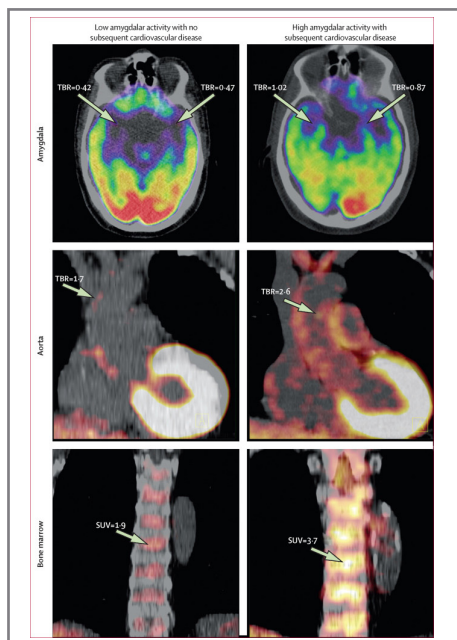
Amygdalar, arterial, and bone-marrow uptake of 18F-FDG in individuals with and without subsequent cardiovascular disease events. The Lancet, 2017

While abundant epidemiological data exists describing severe chronic stress as a risk factor for cardiovascular disease, the mechanism by which stress contributes to cardiovascular events is not fully understood. Preclinical preliminary data from the program's investigators describe a direct causal link between psychosocial stress, neural signals, and atherosclerosis, the chronic inflammatory disease that is the underlying cause of heart attacks and strokes. To better characterize risk of future cardiovascular events as affected by psychosocial stress, researchers will study the levels of macrophages—key immune cells contributing to the inflammation that characterizes atherosclerosis—within the arteries, blood, and organs of the immune system.

The program consists of three distinct studies. The first will use mouse models to explore how the brain reacts to stress and affects the immune system to increase cardiovascular disease risk.   The second study will translate discoveries from the first to develop non-invasive imaging methodologies, such as combined MRI and PET scans, in order to study these same processes in larger mammals and humans. The third study will then use these imaging technologies to examine the link between increased emotional stress and increased cardiovascular risk in human subjects diagnosed with post-traumatic stress disorder.

"A better understanding of non-traditional risk factors to cardiovascular disease, such as psychosocial stress, allows for a more comprehensive risk assessment in patients," says Zahi A. Fayad, PhD, Mount Sinai Endowed Chair in Medical Imaging and Bioengineering, Professor of Radiology and Medicine (Cardiology), and Director of the Translational and Molecular Imaging Institute (TMII) at the Icahn School of Medicine at Mount Sinai, and the Principal Investigator of the study. "The development of non-invasive imaging technology to assess cardiovascular risk in relationship to brain and immune system activation opens new opportunities for early diagnosis and treatment of cardiovascular disease."

"The findings from this pioneering study will have significant impact on current and future research in cardiovascular disease, psychiatry, and imaging,"
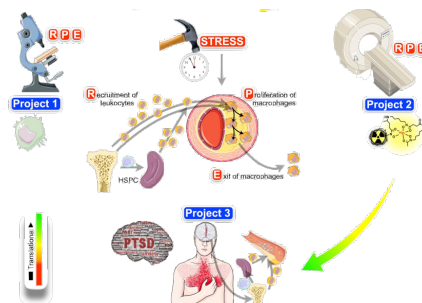
says Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean, Icahn School of Medicine at Mount Sinai, and President for Academic Affairs, Mount Sinai Health System. "We appreciate the NIH recognition of our efforts and are excited to be part of this groundbreaking endeavor."

The research team from the Icahn School of Medicine at Mount Sinai is composed of Dr. Fayad (overall PI, PI Project 3 and Administration/data Core); Willem Mulder, PhD, Professor, (PI Project 2); Venkatesh Mani, PhD, Assistant Professor (PI Imaging Core); Cheuk Tang, PhD, Associate Professor; Claudia Calcagno, MD, PhD; James Murrough, MD, Assistant Professor; Dr. Charney; Valentin Fuster, MD, PhD, Director, Mount Sinai Heart; Emilia Bagiella, PhD, Professor; and Helena Chang, MS, Senior Biostatistician. Other institutions involved in this program include New York University and Massachusetts General Hospital. The research team includes multidisciplinary investigators in cardiac and neuroimaging, psychiatry, psychology, neuroscience, neurology, cardiology, immunology, and nanotechnology.

Courtesy of Mount Sinai Press Office

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SAVE THE DATE

8TH Annual TMII Symposium   April 27, 2018

Keynote Speaker: Yann LeCun, Facebook

Neuroimaging: Russell Poldrack, Stanford University
Cardiovascular: Dorin Comaniciu, Siemens Healthineers

Cancer & Body: Olivier Gevaert, Stanford Medicine
Nanomedicine: James Moon, University of Michigan

Icahn School of Medicine at Mount Sinai | Translational & Molecular Imaging Institute | 1470 Madison Avenue | New York, NY 10029-6574 | tmii.mssm.edu

Multi-Parametric PET Imaging: Advancing PET/MRI and PET/CT Methods
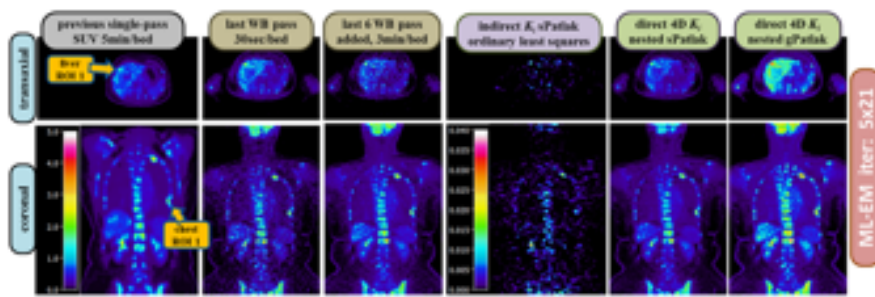## Nicolas (Nikolaos) A Karakatsanis, PhD

Dr. Nicolas A. Karakatsanis is a postdoctoral research scientist at the Cardiovascular Imaging Lab of Prof. Zahi A. Fayad at TMII since summer 2015. Nicolas is certified by the American Board of Science in Nuclear Medicine (ABSNM). He has been elected as the 2017-2019 intern of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) Computer and Instrumentation Council (CaIC) and is a Senior Member of the Institute of Electrical and Electronic Engineers (IEEE).

Whole-body PET 4D parametric ML-EM iterative reconstruction by indirectly and directly applying on dynamic PET sinograms standard and generalized (sPatlak and gPatlak respectively) Patlak graphical analysis

Nicolas current and future research interests involve developing and translating into clinic a series of novel PET multi-parametric imaging methods aiming at progress quantification of a spectrum of molecular mechanisms underlying cardiovascular, oncologic or neurodegenerative diseases. For that purpose Nicolas has been focusing on the efficient utilization of data synergies identified between molecular PET and anatomical MRI and/or CT images when both acquired within the same clinical exam session, thanks to the advent of integrated PET/CT and more recently PET/MR scanners.

After successfully defending his PhD thesis on performance validation and optimization of preclinical and clinical PET systems using Monte-Carlo simulations at the School of Electrical and Computer Engineering at the National Technical University of Athens, Greece, and the Crump Institute for Molecular Imaging at UCLA, Nicolas moved in 2011 as a postdoctoral research fellow at Johns Hopkins University to undertake the challenge of introducing for the first time a clinically feasible dynamic PET/CT imaging method, capable of producing advanced parametric whole-body (WB) PET/CT images for the quantitative metabolic assessment of metastatic oncologic diseases and their response to therapy. Until then, parametric PET imaging has been limited to single-bed scans and mainly for neuroimaging PET research studies. At the beginning of 2014 Nicolas moved to University of Geneva, Switzerland, to further advance his active research in WB parametric P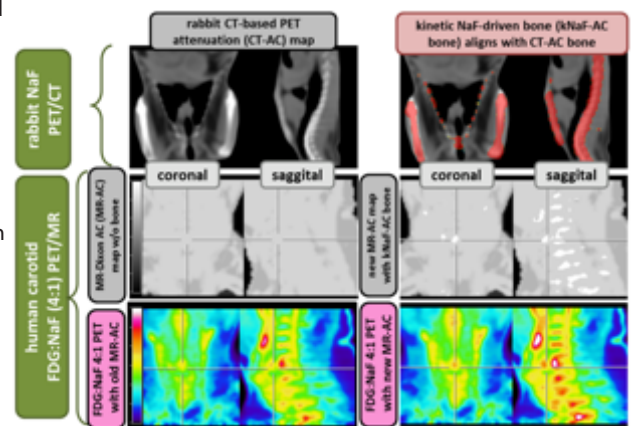ET/CT by exploiting the unique features of continuous bed motion (CBM) PET scan technology for enhanced uniformity in PET image quality between and across the multiple bed positions.

Nicolas current primary mission at TMII is to facilitate the development of clinically adoptable cardiovascular PET/MR imaging methods equipped with advanced cardiorespiratory motion and attenuation correction methods to detect as well as quantitate the molecular processes of inflammation and micro-calcification in carotid, aortic and coronary atherosclerotic human plaques using 18F-FDG and 18F-NaF PET tracers respectively. In addition, Nicolas has utilized his expertise in dynamic PET imaging to enhance the clinical evaluation of cardiac metabolism as assessed by 18F-FDG and 18F-NaF PET/MR scans in cardiac sarcoidosis and amyloidosis TMII studies respectively. Dynamic PET analysis and subsequent extraction of tracer uptake additional parameters may facilitate more accurate diagnosis and avoid false-positive PET findings due to inadequate suppression of the physiological non-specific PET myocardial signal. Furthermore, Nicolas is leading a dual-tracer 18F-FDG:18F-NaF carotid PET/MR imaging study in TMII targeting the combined multi-parametric imaging of both inflammation and micro-calcification in human atherosclerotic plaques within a single clinical exam session. The PET/MR study exploits a carefully designed delayed injection scheme to enable robust discrimination of the two different PET tracer signals from the same scan thereby allowing for investigation of potential

Dual-tracer 18F-FDG:18F-NaF PET/MR with PET kinetics-driven bone segmentation

temporal correlations in the progress and treatment response of two of the most critical molecular mechanisms considered to be associated with atherosclerosis progress and plaque rupture risk. Finally, Nicolas is continuing his previous research work in WB parametric oncologic PET/CT imaging with Dr Lale Kostakoglu and the Division of Nuclear Medicine at Mount Sinai Hospital.

Nicolas current work is primarily supported by NIH R01 grants acquired by the Cardiovascular Imaging Lab. His latest work on direct 4D WB 18F-FDG PET parametric imaging has been receiving the attention of the PET research community as a promising molecular imaging framework combining the benefits of quantitative imaging with those of extended multi-bed imaging at clinically acceptable noise levels. Thus, his related article on the topic has been ranked in the Top-10 of the most popular Physics in Medicine and Biology journal article for 2016 and included in the journal's list of highlighted articles for that year.

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7th Annual TMII Symposium
April 7, 2017

Held at the Davis Conference Center in the Hess Center for Science and Medicine at the Icahn School of Medicine at Mount Sinai, the 7th Annual TMII Symposium welcomed renowned scientists from around the world to speak on the topics of cardiovascular imaging, neuroimaging, cancer & body imaging, and nanomedicine. Attendees came from around the Mount Sinai Health System including, Beth Israel, MS West and St. Luke's as well as neighboring institutions,
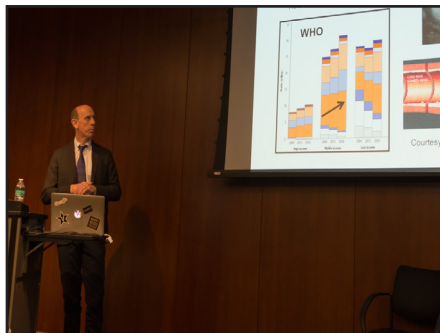
Keynote speaker Dr. Michael McConnell - Verily Sciences/Alphabet -

In addition to the invited speakers, 4 abstracts were selected for oral presentations in each session. The full program book and photos can be found at http://tmii.mssm.edu/tmii2017/ Additionally, videos of all the exceptional presentations can be found at https://www.youtube.com/playlist?list=PLqLDR0CTP9_otAZpwEy3EgOStthPo7V9f


Dr. Kendall Lee - Mayo Clinic - discusses Neuromodulation in the Neuorimaging Session

Out for the 50 abstracts that were presented one abstract in each program was selected for best poster:

Cancer/body Imaging

Stefanie Hectors (ISMMS): "Advanced diffusion-weighted imaging modeling for prostate cancer characterization: correlation with quantitative histopathologic tumor tissue composition."
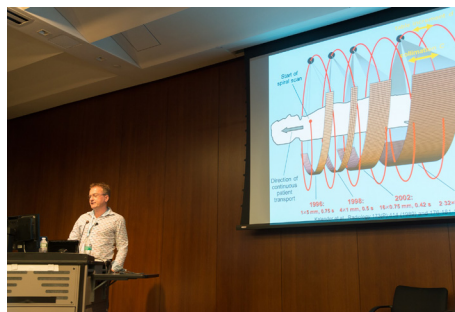
Dr. Marc Kachelrieß explains advances in Cardia CT during the Cardiovascular Session

Cardiovascular Imaging

Amit Dey (NHLBI): "Increased Vascular Inflammation Relates to Increased Prevalence of High Risk Coronary Plaque in Psoriasis Patients."
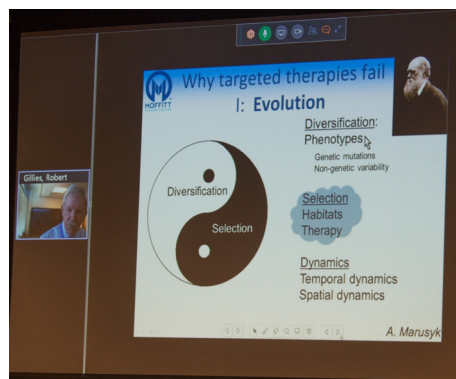

Nanomedicine

Yiming Zhao (ISMMS): "Real-time monitoring of nanoparticle formation via FRET imaging"

Neuroimaging

Joo-won Kim (ISMMS): "Clinically Feasible Optic Nerve Diffusion Basis Spectrum Imaging at 3T:

Dr. Robert Gillies - Moffitt Cancer Center presents (virtually) on Tumor Habitats in the Cancer/Body Session

Dr Michael McMahon - Johns Hopkins School of Medicine speaks on Molecular Imaging in the Nanomedicine section

This year's welcome reception was held at the Grady Alexis Gallery at El Taller and coincided with opening of the "Windows to Our Body" Art Exhibition. They exhibition featured original works by the imaging scientist at TMII. The gallery showcases how the state-of-the-art in medical imaging can, not only peer into the body with unprecedented precision, but reveal dynamic and captivating patterns and symmetry in the process.

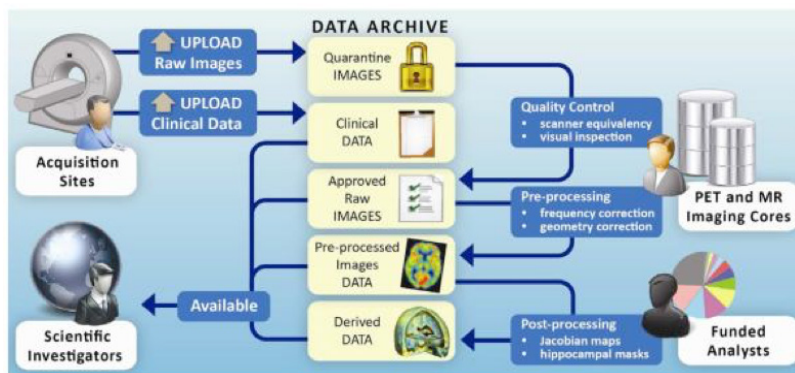# TMII and Radiology Develops Imaging Research Warehouse
Zahi Fayad, PhD & David Mendelson, MD

The Mount Sinai Health System has announced the creation of the Imaging Research Warehouse (IRW). This massive image database, developed by the Mount Sinai Translational and Molecular Imaging Institute (TMII), is the first of its kind in New York City. The IRW integrates clinical imaging with electronic health records, and as it expands it will give researchers new access to information about more than 1 million Mount Sinai patients. The IRW will revolutionize clinical care and translational research to ultimately improve human health.

"This imaging warehouse is uncharted territory for our scientists, and we are excited to give our imaginations free rein to explore imaging for the first time and think without boundaries," said Zahi Fayad, PhD, Director, TMII, Professor, Medical Imaging and Bioengineering, Radiology, and Medicine (Cardiology), Icahn School of Medicine at Mount Sinai. "By having this imaging data available, we can find new patterns of disease and new ways to diagnose and develop new treatments."

The images along with the corresponding health records are free of patient identification. Mount Sinai investigators from all areas of medicine can delve into any group of images from anonymous Mount Sinai patients with

specific diseases or conditions to explore patterns and traits. By comparing thousands of similar images, they can find new features among those patient groups that they didn't know existed in hopes of identifying potential similarities in genetics or blood markers, that could lead to diagnostic techniques and cures.

Creating the IRW will bring significant advances to many diverse aspects of medicine, including mammography, prostate cancer, neuro-degenerative diseases, bowel disease, spine injuries, and genomics. The IRW also has the potential to transform the field of radiology, and streamline the way radiologists read and collect data in the future. Feeding this large data set into machine learning algorithms, for example, will allow radiologists to use specialized software to help evaluate images for known abnormalities. In turn, this may allow for new and more accurate imaging

techniques, such as shorter MRIs and CT scans, which will optimize imaging, streamline procedures, and elevate the patient experience.

"The Imaging Research Warehouse is a unique resource that will provide large volumes of de-identified images to the research community" said David Mendelson, MD, Vice Chair, Radiology, Mount Sinai Health System; Professor, Radiology, Icahn School of Medicine at Mount Sinai. "This model fills a gap in the new world of healthcare 'big data.' The data contained within patients' radiological images is hard to make use of, and this warehouse is the solution to expose this information for analysis."

The IRW is supported by a National Institute of Health pilot program.

Courtesy of Mount Sinai Press Office

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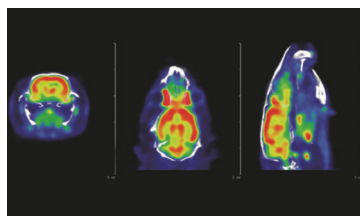Professor of Radiology
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nanoScan Micro PET/CT

The Small Animal Imaging Center will be installing a new nanoScan Micro PET/CT system from Mediso later this summer.

This PET system has:
- LYSO crystal full ring geometry
- up to 12cm transaxial FOV,
- a max apperture of 16cm
- 0.3 mm^3 PET spatial resolution.

The CT has a
- 80 W X-ray tube
- up to 1 mA of tube current
- 2-12 cm TFOV
- and ≤ 10 µm isotropic voxel size.

Stay in touch on social media for updates on installation and town-hall meeting.

The Brain Imaging Center, after the May Day torrential rain-out on May 5, was pleased to have nearly 30 runners join for our 2nd Annual BIC 10k run or walk through Central Park on May 16 2017. Thank you to all who helped bring another enjoyable run to a lovely spring day in the heart of New York. Some photos of runners before and after can be found at https://bic.mssm.edu/about/2017-bic-10k/. The run was also a bittersweet opportunity to begin saying goodbye to Dr. Rafael O'Halloran as he prepared to make the shift from Mount Sinai to what will surely be a wonderful career in commercial MRI development. Among his less-known contributions, Rafael was responsible for developing much of BIC's brain-centric artwork, including our 10k t-shirt designs. Their reappearance on smiling

runners as they finished the 10k course was a pleasant small tribute. Rafael's contributions to the development of the standard BIC protocol, imaging sequence optimizations and MR processing workflow, as well as his development of MSSM's potential for MR spectroscopy and high field imaging were outstanding and important to the Center. We now look forward to new opportunities for collaborating with him.

Registration is open, and the deadline for abstract submissions for the 4th Annual Brain Imaging Center Symposium has been extended until July 31 2017. Join BIC for what will be an outstanding day of speakers, presentations and discussions of progress in applications and techniques for functional and high resolution

Neuroimaging Throughout the Lifespan. This year's keynote address will focus on Imaging the Infant Brain, by MIT's Rebecca Saxe, for a day with talks by Vinod Menon (Stanford), Jack Gallant (Berkeley), Dan Schacter (Harvard) and our own Emily Stern and Sophia Frangou from the Icahn School of Medicine at Mount Sinai. Our popular Trainee Data Blitz will return, moderated by Melanie Boly (U. Wisconsin) and Lisa Feldman Barrett (Northeastern). Please submit an abstract and poster for consideration by the Oranizing Committee, and be sure to register for the October 19 2017 Symposium. Registration as well as abstract and poster submissions can be completed online at https://bic.mssm.edu/blog/bicday/bicdayregistration/

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