

Icahn Medicine at *Institute* Mount Sinai

Translational and School of Molecular Imaging



Our mission is centered around development, validation, translation and education of innovative technology in biomedical imaging to address both basic and clinical research problems and therefore improve human health.

The Translational and Molecular Imaging Institute (TMII) is a state of the art research facility housed in ~20,000 square feet in the Center of Science and Medicine (CSM). TMII (Director, Zahi A. Fayad, PhD) is comprised of faculty, staff and trainees responsible for coordinating and executing all research projects performed in these facilities. Currently TMII has over 50 members with expertise in all aspects of translational imaging research. The faculty consists of Biomedical and Electrical Engineers and Radiologists who are leading experts in neuroimaging, cardiovascular imaging, body/cancer imaging, and nanomedicine. Highly skilled staff provides a full suite of support services for image acquisition, image analysis, scheduling and performance of the proposed experiments.

Access to the TMII facility is based on a fee for service schedule (https://tmii.mssm.edu/imagingcore/resource-fees/). These user fees are calculated to cover the operating and maintenance costs of the instruments and related Core expenses. These rates are determined and periodically reviewed by the Dean's Office and adjusted to reflect the actual costs. User fees include technical support for operation of imaging equipment.

For internal Mount Sinai users, resource usage time is compiled from the web-based scheduling system and charged directly to your account on a monthly basis. Any questions on the charges should be addressed to the TMII Director.

The user fee includes support for:

Study Start-up	Study design/ IRB review & consultations
	Maintenance self-scheduling system
Scan Protocol	Scan parameter Implementation/ Optimization (Hi Res Structural, DTI, EPI
)
	Adaptation of C2P sequences to our scanners
fMRI Task Protocol	fMRI Software administration (Eprime, PsychToolBox, PschoPy(thon),
	Matlab, Cogent)
	Basic task modifications (Triggering, Physio monitoring control, etc)
fMRI Stimulus	Visual (LCD, 3D goggles)
Equipment	Audio (Headphones, ear buds)
	Eye-tracking equipment (not software control support
Physiological	Set up (SpO2, Heart rate, Respiration, ECG, GSR, EMG, Skin Temperature)
Monitoring	
Data Handling	Long-term online image archive (XNAT)
	Burn anonymized data to CD for external sites
Data Processing	Computer Lab with preloaded analysis software (BV, SPM, FSL, Osirix,
	Custom In House tools, Matlab and Python)
PET isotopes	Standard tracers: FDG, NaF
	Advanced tracers: Contact TMII for up-to-date options
Report	Radiological read and report of incidental findings

1. MR/PET (3T) Siemens mMR.



The 3T MR/PET is a fully integrated and capable of simultaneous whole body PET and MRI scanning. This allows more precisely coregistered functional and structural acquisition while r educing the radiation dose in PET imaging by replacing the CT scans with an MRI scan. True simultaneous acquisition of MR and PET data by the hybrid system merges the highly sensitive PET metabolic information with the highly specific MR anatomical and functional information. The 3T MRI system is a whole body imaging system, capable of routine

as well as advanced imaging of all body regions. The PET scanner will be fully integrated into the MR, utilizing state of the art solid-state technology for simultaneous PET imaging during MR image or spectrum acquisition. The 3T MR-PET is designed for the purposes of oncological and neurological diagnostic imaging. The highly integrated nature of these systems provides the capability for full spatial and temporal correlation between both modalities. The maximum gradient amplitude will be approximately 40 mT/m per axis, with a maximum gradient slew rate of about 200 T/m/s per axis. The system's magnet has an integrated cooling system and active shielding. The shimming capabilities include: Active (with 3 electric and 5 electric nonlinear linear shim channels) and Passive shims for maintaining very high homogeneity and excellent image quality over a wide range of applications. Online shimming is performed in less to then 20 seconds in order to optimize homogeneity. The RF transmit and receive system include: compact, air cooled tube RF amplifier providing 35 kW peak power; integrated electronics with cabinet water cooling; integrated circularly polarized whole body RF coil; up to 32 receive channels. The PET system include: adaptation to a work environment within high magnetic fields including APD and LSO based detector technology; adaptation and optimization of numerous MR components to an integrated PET imaging unit; high-resolution, highcount rate, positron emission tomography (PET) imaging of metabolic and physiologic processes; high quality metabolic and anatomic image registration and fusion for optimal lesion detection and identification within the body; state-of-the-art 3D PET data acquisition and analysis tools; state-of-the-art 3D PET reconstruction, attenuation and scatter correction software. Expected PET performance specifications: spatial resolution: <6.5mm; timing resolution: < 4.5 ns; sensitivity: > 0.5%; axial FOV: > 19 cm; transaxial FOV: up to 45 cm. The system also supports MR and PET gated scan acquisition; support for list mode acquisition, offline histogramming and reconstruction; special calibration. Alignment and quality control sources including shielding; multimodality workplace; 3D iterative reconstruction.



This is an ultrahigh field 7.0 Tesla actively shielded whole body MRI scanner. The super-conducting magnet is selfshielded, reducing its overall footprint and making it compact and lightweight by 7T standards, weighing 24-tons. The (warm) inner bore of the magnet is 82 cm, which houses the 60 CM inner patient bore. The dimensions of the magnet without covers is approximately 2.5 m in length, 2.6 m in width, and 2.65 m in height. The 5-Gauss line extends slightly further than for a 3T scanner with 5.6 m radial and 7.8 m axial dimension. A whole-body gradient system provides gradient amplitude of up to 70 mT/m per axis,

and a maximum slew rate of up to 200 T/m/s. The RF transmit system comes with 8 parallel transmit channels; 8 individually shaped RF pulses can be prescribed simultaneously and independently in amplitude and phase. The multi-nuclei package allows for imaging and spectroscopy at non-proton frequencies, i.e. detection of e.g. 19F, 31P, 7Li, 23Na, 13C, 17O. Our 7T/820AS is configured to accommodate an 8-channel Tx-array and 48-channel Rx receivers. Several coils are currently available such as the 1- channel Tx and 32-channel Rx head coil and the 8-channel Tx and 8-channel Rx head coil.

3. 3T Siemens MAGNETOM Skyra.

Th is is an FDA approved 3 Tesla human MRI scanner. Its wide bore design (173 cm system length with 70



cm) can accommodate subjects with larger body compositions compared to the 60 cm bore of a typical clinical 1.5T & 3T. A newly deigned RF system and coil architecture integrates (Tim 4G) with all digital-in/digital-out technology. The scanner has an actively shielded water-cooled gradient system and zero helium boil-off. Specialized RF distribution increases uniformity in all body regions. Onboard software is available for: neuro, angio, cardiac, body, onco applications. A variety of coils for all body parts and configuration is available.

4 PET/CT Siemens Biograph mCT. The PET/CT is equipped with a 40 slices multidetector CT and LSO PET crystals. Utilizing timing information (time-of-flight) between the two PET coincidence events, coupled with high definition resolution recovery, the system provides improved image signal-to-noise which can be used to either enhance image quality and/or reduce acquisition time. With a system timing resolution of 555 ps, image quality is clearer with more defined images and provides distortion-free image quality for the entire of the field of view. Specialized image processing techniques utilizing more accurate point spread

functions produces higher quality 3D iterative reconstruction with enhanced contrast and higher resolution. Supported image matrices include 128x128, 200x200, 256x256, 400x400, and 512x512.

5 Multidetector CT (MDCT) Siemens Somatom Definition Flash. This Dual Source CT, uses two Xray sources and two detectors simultaneously, to cover the entire thorax in less than a second. A 2 meter scan requires only 5 seconds, enhancing the efficiency of perfusion or dynamic vascular imaging and reduction the dose for all scans, resulting, e.g. in dose down to sub-mSv for cardiac imaging. Dual Energy automatically provides a second contrast for without any extra dose. Advance software efficiently manages the reduction in dose allowing for: limited exposure to radiation-sensitive organs and increases tissue contrast with no sacrifice to image quality.

6 (2) **1.5T Siemens MR MAGNETOM Aera**. Short and open appearance (145 cm system length with 70 cm Open Bore Design) can accommodate subjects with larger body compositions compared to the 60 cm bore of a typical clinical 1.5T & 3T. Newly deigned RF system and coil architecture integrates with all digital-in/digital-out technology, one system use standard gradients (33 mT/m @125 T/m/s) and the second system has advanced gradients (45 mT/m @ 200 T/m/s). Actively shielded water-cooled gradient system with zero helium boil-off. Inline software is specially designed for: neuro, angio, cardiac, body, onco, breast, ortho, pediatric and scientific specialties such as Magnetic Resonance Elastography; a technique that measures the stiffness of tissues by introducing shear waves and imaging their propagation.

7 Siemens ACUSAN S3000 ARFI Ultrasound - The ultrasound system automatically produces an acoustic 'push' pulse that generates shear-waves, which propagate into the tissue. Using image-based localization and a proprietary implementation of acoustic radiation force impulse (ARFI) technology, shear wave speed may be quantified, in a precise anatomical region, focused on a region of interest, with a predefined size, provided by the system. Measurement value and depth are also reported, and the results of the elasticity are expressed in m/s. This system provides new method for the evaluation of the elastic properties of tissues is now available in the Cancer/Body Core. Clinical applications of ARFI imaging include: liver fibrosis quantification, breast, colorectal and prostate tumor imaging.

8 Siemens Force CT. The Force is the third iteration of Siemens' dual-source CT design which features two sets of x-ray tubes and detectors for enhanced imaging of all patients, including young children, patients with renal insufficiency, and those who cannot hold their breath. Due to its low-kV imaging technique, Force broadens CT's application for patients with renal insufficiency and offers an acquisition speed of 737 mm/sec, so an entire adult chest, abdomen, and pelvis study can be done in one second with no breath-holds. In cardiac imaging, Force can obtain an entire study within one-quarter of a heart beat at a temporal resolution of 66 msec, which is the speed required to freeze the fastest-moving anatomy, such as the right coronary artery.

9 "Mock" MR PSTNet.

The MRI simulator will allow researchers to acclimatize the subjects to the 'enclosed' and loud MRI environment before they actually go into a real scanner. This is especially important for studies involving children.

10 **fMRI peripherals** All the MRI scanners will be fully



equipped with the latest state of the art peripherals for functional imaging including LCD goggles, integrated eye-tracking, fiber optic subject response gloves, pneumatic computerized headphones with microphones as well as a full spectrum of physiological recording probes for ECG, GSR, pulse-Ox etc. There is also a specialized MRI compatible computerized olfacto-meter.

11 Neuro Testing room

A sound proofed and independent temperature controlled neuro testing room is located near the 3T MRI for physiological testing such as EEG, ERP and other modalities. This room is also equipped with large monitors for paradigm training and testing.



1 9.4T MR Bruker.



This is a high-resolution rodent only MRI scanner allowing for high-resolution *in-vivo* imaging of mice and smaller specimens. It is 9.4 Tesla 89-mm bore MRI system operating at a proton frequency of 400 MHz (Bruker, Billerica, MA). The 9.4T is equipped with a mouse respiratory and cardiac sensor connected to a monitoring and gating system (SA Instruments, Inc., Stony Brook, NY). Sedation is administered by an Isoflurane/O₂ gas mixture delivered through a nose cone and placed in a 30 mm birdcage coil with an animal handling system. Additionally, a temperature controller is available in the bore of the magnet, to maintain the animal in the RF coil at a selected temperature. Recent upgrades (Bruker Paravision 4)

have enabled the use of navigator pulses to allow for cardiac and/or respiratory gating without the use of electrodes.

2 7.0T MR Bruker Biospec 70/30.

This is a high-resolution MR scanner for small animals. The maximum bore diameter for imaging is 15.4cm. This system is equipped with two gradient choices, a large built-in gradient system with up to 200 mt/m and a slew rate of 640 T/m/s. This gradient in combination with a large circular polarized coil will allow imaging of animals up to 15.4cm in diameter. The system is also equipped with a high performance gradient insert with 440mT/m and slew rate of 3,440 T/m/s for high-resolution imaging. The system



has 2 transmit and 4 receive channels. There is a 35mm ID circular polarized coil for in-vivo mouse imaging as well as a 4-channel phased array for mouse brain and a 4 channel phased array for mouse cardiac imaging. There are also 3 other dual tuned 20mm surface coils for 31P, 13C and 19F. The 7T Bruker is equipped with the Autopac system, a fully integrated animal handling, laser guided positioning system. Animal warming holders are available for rats and mice as well as a full spectrum of monitoring peripherals for ECG, triggering and respiratory monitoring etc.

3 Mediso nanoScan Micro PET/CT

The newest acquisition to the Small Animal Imaging Center, **nanoScan Micro PET/CT** has the highest PET resolution using the industry's most advanced pixelated modular LYSO detectors. It has an exceptionally high-count rate tolerance supporting high activity studies of multiple animals or short half-life isotopes. The system has easy access to the animal from both the front and the back of the PET/CT gantry and state-of-the-art Tera-TomoTM 3D PET image reconstruction engine. High imaging throughput can be obtained by large bore size and large field-of-view in both axial and transaxial directions in addition to multiCell



imaging chambers for mice, rats and rabbits and a PrepaCell Preparation station

4. Biophotonic IVIS-Spectrum.

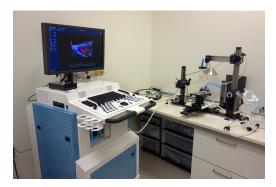


The **IVIS Spectrum** in vivo imaging system uses a novel patented optical imaging technology to facilitate non-invasive longitudinal monitoring of disease progression, cell trafficking and gene expression patterns in living animals. The IVIS Spectrum is a versatile and advanced in vivo imaging system. An optimized set of high efficiency filters and spectral unmixing algorithms lets you take full advantage of bioluminescent and fluorescent reporters across the blue to

near infrared wavelength region. It also offers single-view 3D tomography for both fluorescent and bioluminescent reporters that can be analyzed in an anatomical context using our Digital Mouse Atlasor. For advanced fluorescence pre-clinical imaging, the IVIS Spectrum has the capability to use either transillumination (from the bottom) or epi-illumination (from the top) to illuminate in vivo fluorescent sources. 3D diffuse fluorescence tomography can be performed to determine source localization and concentration using the combination of structured light and trans illumination fluorescent images. The instrument is equipped with 10 narrow band excitation filters (30nm bandwidth) and 18 narrow band emission filters (20nm bandwidth) that assist in significantly reducing autofluorescence by the spectral scanning of filters and the use of spectral unmixing algorithms. In addition, the spectral unmixing tools allow the researcher to separate signals from multiple fluorescent reporters within the same animal. http://www.perkinelmer.com/Catalog/Product/ID/IVISSPE

5 Micro Ultrasound Vevo 2100 VisualSonics.

This is dedicated Ultrasound system for small animal models (mice to rabbits) of disease. This scanner is capable of all imaging modes found in clinical US scanners such as color Doppler, M-mode, 3D imaging and volume analysis but at much higher spatial resolution. It allows for rapid animal screening of tumor and other models. The higher resolution of this system will also allow for image-guided injection. **B-Mode (2D)** imaging for anatomical visualization and quantification, with enhanced



temporal resolution with frame rates up to 740 fps (in 2D for a 4x4 mm FOV), and enhanced image uniformity with multiple focal zones. M-Mode is for visualization and quantification of wall motion in cardiovascular research, single line acquisition allows for the very high-temporal (1000 fps) resolution necessary for analysis of LV function. Anatomical M-Mode is for adjustable anatomical orientation in reconstructed M-Mode imaging; software automatically optimizes field of view for maximum frame rate. Pulsed-Wave Doppler Mode (PW) is for quantification of blood flow. Color Doppler Mode is used for detection of blood vessels including flow directional information and mean velocities; as well as for identification of small vessels not visible in B-Mode. Power Doppler Mode is for detection and quantification of blood flow in small vessels not visible in B-Mode; increased frame rates allow for significantly faster data acquisition. Tissue Doppler Mode for quantification of myocardial tissue movement; for example in assessing diastolic dysfunction. Vevo MicroMarker[®] Nonlinear Contrast Agent Imaging can be used for quantification of relative perfusion & molecular expression of endothelial cell surface markers; enhanced sensitivity to Vevo MicroMarker contrast agents as linear tissue signal is suppressed. **3D-Mode** Imaging is for anatomical and vascular visualization, when combined with either B-Mode, Power Doppler Mode or Nonlinear Contrast Imaging; allows for quantification of volume and vascularity within a defined anatomical structure. Digital RF-Mode is for the acquisition and exportation of radio frequency (RF) data in digital format for further analysis; full screen acquisition provides a complete data set for more comprehensive analysis and tissue characterization. ECG and Respiration Gating is used to suppress imaging artifacts due to respiration and cardiac movements. Both are important in cardiac and abdominal imaging for both 2D and 3D data sets. **Transducers:** * MS-200 12.5 or 21 MHz, Depth from 2mm to 36mm *MS-250 16 or 21 MHz, Depth from 2mm to 30mm *MS-400 24 or 30 MHz, Depth from 2mm to 20mm *MS-550D 32 or 40 MHz, Depth from 1mm to 15mm http://www.visualsonics.com/vevo2100

6 Near IR Frangioni imager. This rodent scanner is designed to visualize cellular probes that fluoresce in the Near IR region which provides much better tissue penetration than traditional Green Fluorescent Proteins.

C. Nanomedicine and Radiochemistry Laboratories.

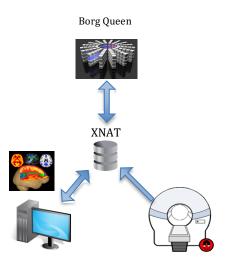
The Nanomedicine laboratory has 2 modules: the synthetic lab and the analytical/biochemistry/biology lab. We are able to synthesize established imaging reagents for supply and distribution. In the synthetic lab, there are 2 large synthetic chemistry hoods that can accommodate 4 synthetic chemists working simultaneously. Each scientist has individual bench space for work-up and for storing samples, reagents, buffers and the like. The analytical/biochemistry/biology lab has 2 smaller hoods for doing wet chemistry work. Both facilities have been equipped with state-of-the-art instruments to support the work. The synthetic lab is well equipped for investigators to perform small-scale syntheses of organic, inorganic and organometallic compounds for use in a multitude of imaging modalities as well as drug delivery nanoparticles. In addition, we are also capable of labeling peptides and antibodies with commercially available optical dyes, CT, or MR contrast agents.

The Radiochemistry laboratory is equipped with gamma counters, dose calibrators.

D. Bioinformatics and Data Processing - CSM- 1st Floor.

One of the main functions of TMII is to provide the infrastructure for access to research imaging. A comprehensive set of Image modalities are supported for both human as well as animal work. Scheduling support for access to the different scanners consist of web-based online calendars as well as live telephone scheduling support. TMII also provides a central hub for image distribution and archival. There are 32TB of online storage where all imaging data is pushed to and distributed from. The capacity will be expanded annually as needed.

1. **Image Analysis Support.** TMII provides image analysis analysis for cardiovascular, body/oncological and neuro imaging. The image analysis for specific projects needs to be discussed directly with the TMII core (contact TMII Director Dr. Zahi Fayad.) This core consists of IT personnel, software engineers, imaging physicists, research assistants and other support personnel. Expert consultation for research projects including protocol design, specialized pulse sequences, special image acquisition hardware (coils), custom made functional MRI stimulus hardware are all supported. Comprehensive project based image analysis support is also provided. Modalities supported include PET, MRI, fMRI, DTI and its variants, resting state fMRI. Image analysis training is also supported for those researchers who want to learn more about image analysis in general. Training range from regular classroom based graduate course taught by TMII faculty to hands on training on the use of specific software packages such as FSL, SPM, Brainvoyager and TMII's own in house developed software packages in all areas (neuro, body, oncology and cardiovascular). The data center has a dedicated servers room which houses a larger Mac Server Cluster with 2 x 16TB of initial online storage with direct connectivity to all the imaging modalities in CSM. In addition, there is also an image analysis room equipped with large viewing display and high performance workstations open for the researcher to learn or perform image analysis.



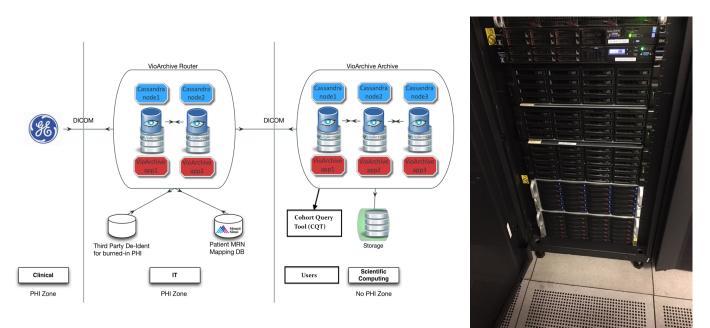
2. TMII XNAT. TMII XNAT serves as the central point for research data transfer, archive, and sharing. TMII XNAT is built upon a secure database, supports automated pipelines for processing managed data, and provides tools for exploring the data. Only users authorized by the study investigators can access their data. TMII XNAT is fully HIPAA compliant. The TMII XNAT team provides support for data migration between various DICOM repositories, HIPAA de-identification, image preprocessing, image quality control, and other customized services. Currently TMII XNAT runs on two mirrored Linux servers with 60TB storage space on each. It can host more than 15,000 image sessions with backups. TMII XNAT user training, documentation, and imaging data management consultations are available by request (https://tmii.mssm.edu/xnat). A yearly service support contract

has been established with the XNAT developer group from Radiologics Inc.

3. Borg Queen Server. This server contains a total of 128 cores of AMD 2.0GHz CPU, 1TB of RAM (DDR4-2666), 3 x NVIDIA GTX 1080 Ti GPUs with 11GB memory each, and a total of 90TB of storage as of early 2018. Storage will be expanded to 450TB total before the end of 2018. The server will run Ubuntu 16.04 and can support other OS through either Linux containers or virtual machines. The most recent versions of image analysis software such as FSL, SPM, Matlab, and AFNI will be installed. A new flexible image analysis pipeline under development (SAPIENT) will also be deployed on Borg Queen to support neuroimage preprocessing before the end of 2018."

4. Image reconstruction tools for PET and fast MR imaging. TMII is equipped with a dedicated workstation for PET images reconstructions, such as the Siemens e7-tools and the open-source package STIR (http://stir.sourceforge.net/). The e7-tools are a collection of Microsoft Windows command line programs that allow the processing and reconstruction of Siemens PET emission data both using iterative and analytical algorithms. The software is capable of generating of other correction factors including attenuation, scatter and normalization. The software also allows for listmode histogramming and rebinning. The software is installed on an external computer to reconstruct PET images away from the scanners. STIR software on the other hand is an open source toolbox that offers the same functionalities as the e7tools, but is not limited to the analysis of Siemens PET emission data. Also available is a dedicated workstation housing PET-SORTEO (Simulation Of Realistic Tridimensional Emitting Objects), a simulation tool that uses Monte Carlo techniques to generate realistic PET data from voxelized descriptions of tracer distributions, in accordance with the scanner geometry and physical characteristics.

5. Mount Sinai Imaging Research Warehouse (IRW) The IRW is a platform intended to facilitate research by allowing researchers to gain open access to imaging data in the Mount Sinai Data Warehouse (MSDW). HIPAA compliance is handled by providing a mirror of the Mount Sinai PACS in a de-identified/pseudoanonymized state. Exams that are archived in Mount Sinai PACS, arising from an ORG that populates other data types to the MSDW, are sent to the IRW. All data in the IRW will use an alternative HIPAA-compliant identifier that could be cleanly referenced to its associated data in the MSDW. IRW images are archived on a NAS storage server with 250TB RAID6 space, which can host approximately more than 2 million exams. There are two servers that receive and de-identify images from PACS, followed by the forwarding of these images to three servers for archiving. There is a F5 load balancer that evenly distributes the archiving and querying loads among the archive servers.



Figures: IRW system design & IRW server in the datacenter

For the archive servers, VioArchive (by Vital Images) is used as the storage repository software for research images. De-identified DICOM files transferred to the VioArchive archive servers will be inspected by IRW personnel for quality assurance.

Researchers can use a DICOM client like OsiriX to query and retrieve images from the IRW to their local workstation. Researchers can also use VitreaView (http://vitrea.mssm.edu/vitrea-view/auth/login or http://view.mssm.edu/vitrea-view/auth/login) to view de-identified images. IRB approval is not required for Mount Sinai internal data usage.

As end of March 2018, the IRW has accumulated more than 120,000 studies including CT, MR, DX, PET, CR, MG, NM, and other modalities. Currently, the IRW team is providing datasets for several deep learning applications and projects.

More information is also available online@ <u>http://tmii.mssm.edu</u> & <u>http://icahn.mssm.edu/research/institutes/translational-and-molecular-imaging-institute/imaging-core/facilities-and-resources</u>

Contact: Zahi A. Fayad, PhD – Director, TMII Zahi.fayad@mssm.edu (212) 824-8452

Christopher J. Cannistraci, MS – Operations Manager Manager <u>Christopeher.cannistraci@mssm.edu</u> (212) 824-8466