

## FACILITIES & OTHER RESOURCES - OVERALL

### USC MARK AND MARY STEVENS NEUROIMAGING AND INFORMATICS INSTITUTE

In September, 2013, the University of Southern California (USC) in Los Angeles created the Institute for Neuroimaging and Informatics (INI), a world-class facility in which all the techniques for modern ultra-high-field and standard-field MRI brain scanning, image analysis, databasing, mathematics, genomic analysis, computation and medical imaging will be housed under one roof. Dr. Arthur Toga was recruited to USC along with 8 other faculty that previously had formed the Laboratory of Neuro Imaging (LONI) at UCLA to found this new Institute. In March, 2015, the university received a \$50M transformative gift from Mark and Mary Stevens, changing the name of the institute to the USC Mark and Mary Stevens Neuroimaging and Informatics Institute.

USC is remodeling a legacy building and building new facilities to house office, lab space, an MRI suite, and computational resources at the Keck School of Medicine. The overall academic environment will be a remarkable specially designed modern building of 35,000 gross sq ft. While the Raulston building is being remodeled, temporary space is allocated within the Soto 1 building (**Figures 1 and 2**) on the Health Sciences Campus. The allocation of significant campus funding to create this Institute, and its facilities, creates the opportunity to establish a broad and rich multidisciplinary expertise. The Keck School of Medicine has dedicated significant campus resources, capital infrastructure and space, to LONI and the Stevens Neuroimaging and Informatics Institute.



**Figure 1.** The Soto Street Building on the USC Health Sciences Campus in Los Angeles, CA.

The new Institute provides an extensive infrastructure designed and operated to facilitate modern informatics research and support for hundreds of projects including several multi-site national and global efforts. We have redundancies built in to all equipment, and a completely secure facility to protect equipment and data. The resources described below provide networking, storage and computational capabilities that will ensure a stable, secure and robust environment. It is an unprecedented test bed to create and validate big data solutions. Because these resources have been designed, built and continuously upgraded over the years by our systems administration team, we have the appropriate expertise and operating procedures in place to use these resources to their maximum benefit.

**Physical Infrastructure of the Soto Building at USC.** The Stevens Neuroimaging and Informatics Institute is physically located in the Soto Street Building (**Figures 1 and 2**) on the USC Health Sciences Campus, occupying two suites of the building's ground floor. The space is comprised of a reception area, two Director's Offices area, faculty offices, a modern data center, a user area and conference rooms. The data center contains a 300 KVa UPS/PDU capable of providing uninterruptible power to mission-critical equipment housed in the room, dual 150KVva connections to building power, an 800kW Caterpillar C27 diesel backup generator, three Data Aire computer room air conditioning (CRAC) units, humidity control and a Cosco fire suppression and preaction system. A sophisticated event notification system is integrated in this space to automatically notify appropriate personnel of any detrimental power and HVAC issues that arise.

**Data Center Security.** The datacenter is secured by two levels of physical access, to ensure HIPAA compliance for data security. The main facility is secured 24/7 with access control devices. Only authorized personnel are allowed in, and guests are permitted only after checking in, and only during business hours. The datacenter itself is additionally secured by a second layer of proximity card access. Only authorized staff are permitted to enter the datacenter facility. Individual racks containing HIPAA data are secured by lock and key to prevent cross access.



**Figure 2.** Architectural design of the temporary office space in the Soto building at USC. The Institute spans suites 101 and 102 of the first floor.

**Computational and Storage Resources.** Rapid advancements in imaging and genetics technology have provided researchers with the ability to produce very high-resolution, time-varying, multidimensional data sets of the brain. The complexity of the new data, however, requires immense computing capabilities.

The compute infrastructure within the datacenter boasts 3,328 cores and 26 terabytes of aggregate memory space. This highly available, redundant system is designed for demanding big data applications. Blades in the Cisco UCS environment are easy to replace. A failing blade sends an alert to Cisco where a replacement ticket is generated automatically. Upon arrival, the new blade can go from the shipping box to being fully provisioned and in production in as little as 5 minutes.

Institutions and scientists worldwide rely on the Institute's resources to conduct research. The Stevens Neuroimaging and Informatics Institute is architected using a fault-tolerant, high-availability systems design to ensure 24/7 functionality. The primary storage cluster is 33 EMC Isilon nodes with 3.8 usable petabytes of highly available, high performance storage. Data in these clusters moves exclusively over 10g links excepting node to node communication in the Isilon cluster which is handled by QDR Infiniband, providing 40 gigabit bidirectional throughput on each of the Isilon cluster's 66 links. Fault tolerance is as important as speed in the design of this datacenter. The Isilon storage cluster can gracefully lose multiple nodes simultaneously without noticeably affecting throughput or introducing errors. An EMC VNX 15 terabyte SAN cluster with tiered solid state disk storage complements the storage environment, providing another avenue of redundant storage offered across differentiated networking to provide another layer of resilience for the data and virtualization infrastructure.

External services are load balanced across four F5 BIG-IP 2200S load balancers. The F5 load balancers provide balancing services for web sites, applications, as well as ICSA-certified firewall services. The core network is entirely Cisco Nexus hardware. Each of the two Cisco Nexus 5596s supports 1.92 terabits per second of throughput. Immediately adjacent to this machine room is a user space with twelve individual stations separated by office partitions. These workspaces are manned by staff who constantly monitor the health of the data center as well as plan for future improvements. Each space is also equipped with a networked workstation for image processing, visualization and statistical analysis.

**Network Resources.** Service continuity, deterministic performance and security were fundamental objectives that governed the design of the network infrastructure. The Institute's intranet is architected using separate edge, core and distribution layers, with redundant switches in the edge and core for high availability, and with Open Shortest Path First (OSPF) layer 3 routing, instead of a traditional flat layer 2 design, to leverage the fault tolerance offered by packet routing and to minimize network chatter. While ground network connectivity is entirely Gigabit, server data connectivity is nearly all 10 Gigabit fiber and Twinax connected to a core of 2 Cisco Nexus 5596 switches, 10 Cisco Nexus 6628 switches, and 6 Cisco Nexus 2248 fabric extenders. For Internet access, the Institute is connected to the vBNS of Internet2 via quad fiber optic Gigabit lines using different route paths to ensure that the facility's external connectivity will be maintained in the case of a single path failure.

The facility has two Cisco Adaptive Security Appliances providing network security and deep packet inspections. The Stevens Neuroimaging and Informatics Institute has also implemented virtual private network (VPN) services using SSLVPN and IPsec services to facilitate access to internal resources by authorized users. A VPN connection establishes an encrypted tunnel over the Internet between client and server, ensuring that communications over the Web are secure.

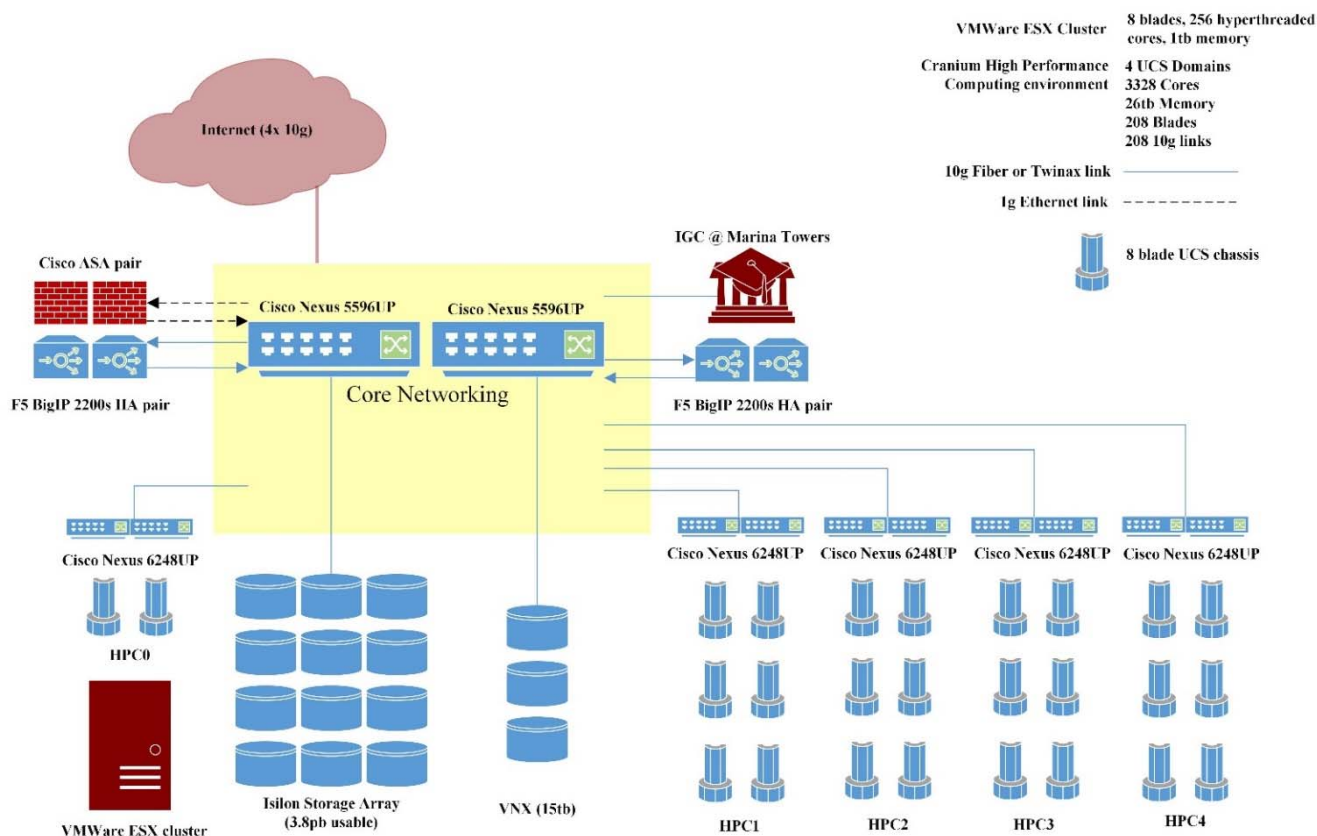
Furthermore, the Institute has an extensive library of communications software for transmitting data and for recording transaction logs. The library includes software for monitoring network processes, automatically warning system operators of potential problems, restarting processes that have failed, or migrating network services to an available server. For instance, the laboratory has configured multiple web servers with Linux Virtual Server (LVS) software for high-availability web, application and database service provisioning as well as load balancing. A round-robin balancing algorithm is currently used such that if the processing load on one server is heavy, incoming requests, be it HTTP, JSP or MySQL, are forwarded to the next available server by the LVS software layer. Listeners on one virtual server monitor the status and responsiveness of the others. If a failure is detected, an available server is elected as master and it assumes control and request forwarding for the entire LVS environment.

**Offsite and Onsite Backup Resources.** All critical system data and source code is backed up regularly to local nearline storage and cloned to LTO6 magnetic tape for offsite archival with Iron Mountain. Offsite backup data is kept in current within one week to enable rapid redeployment of all services with a view of operations and data as of a reasonable time frame. The EMC Isilon nodes retain snapshots of one month's worth of data to offer the most rapid, but least disaster-resilient restoration. Snapshot retention allows rapid restoration of unintentionally overwritten or deleted data and does not require retrieval from archived tape. Nearline-stored backup data provides similarly rapid restoration of the prior year's on-site data. Offsite archived magnetic media, while the last resort, can be recalled the same day and offers retrieval of data from a date range as recent as the prior week to as old as the initial archival series of tapes over one year old. Onsite datasets grow rapidly, constantly and require a flexible tape backup solution. Clones are pushed to tape by way of a pair of EMC backup accelerators to an expandable 10 LTO6 drive Quantum i500 tape array. The array provides the backup parallelism the expansive data collection requires for offsite archival on such an aggressive schedule.

**Virtualized Resources.** Due to the rate that new servers need to be provisioned for scientific research, the Institute deploys a sophisticated high availability virtualized environment. This environment allows systems administrators to deploy new compute resources (virtual machines or VM's) in a matter of minutes rather than hours or days. Furthermore, once deployed these virtualized resources can float uninhibitedly between all the physical servers within the cluster. This is advantageous because the virtualization cluster can intelligently balance virtual machines amongst all the physical servers, which permits resource failover if a virtual machine becomes I/O starved or a physical server becomes unavailable. The net benefit for the Institute is more software

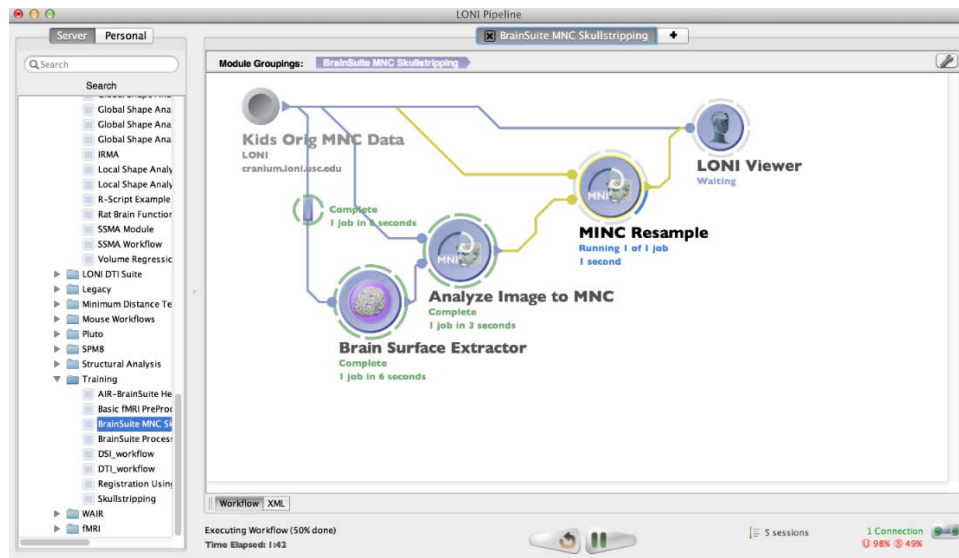
resources are being efficiently deployed on a smaller hardware footprint, which results in a savings in hardware purchases, rack space and heat expulsion.

The software powering the virtualized environment is VMware's ESX 5. The ESX 5 is deployed on eight Cisco UCS B200 M3 servers, each with sixteen 2.6/3.3 GHz CPU cores and 128GB of DDR3 RAM. These eight servers reside within a Cisco UCS 5108 blade chassis with dual 8x10 Gigabit mezzanine cards providing a total of 160 Gigabits of available external bandwidth. Storage for the virtualization cluster is housed on the 23 nodes of Isilon storage. The primary bottleneck for the majority of virtualization solutions is disk I/O and the Isilon cluster more than meets the demands of creating a highly available virtualized infrastructure whose capabilities and efficiency meet or greatly exceed those of a physical infrastructure. A single six rack unit (6RU), eight blade chassis can easily replicate the resources of a 600+ server physical infrastructure when paired with the appropriate storage solution such as the Isilon storage cluster.



**Figure 3.** Stevens Neuroimaging and Informatics Institute network infrastructure and supercomputing environment.

**Workflow Processing.** To facilitate the submission and execution of compute jobs in this compute environment, various batch-queuing systems such as SGE (<https://arc.liv.ac.uk/trac/SGE>) can be used to virtualize the resources above into a compute service. A grid layer sits atop the compute resources and submits jobs to available resources according to user-defined criteria such as CPU type, processor count, memory requirements, etc. The laboratory has successfully integrated the latest version of the LONI Pipeline (<http://pipeline.loni.usc.edu>) with SGE using DRMAA and JGDI interface bindings. The bindings allow jobs to be submitted natively from the LONI Pipeline to the grid without the need for external scripts. Furthermore, the LONI Pipeline can directly control the grid with those interfaces, significantly increasing the operating environment's versatility and efficacy, and improving overall end-user experience. See **Figure 4** for a screenshot of the latest version of the pipeline.



**New Facility.** The new construction in the Raulston Memorial Research Building will be the permanent home of the Stevens Neuroimaging and Informatics Institute. This new facility represents a significant investment on the part of the university. The Raulston renovations are projected to cost nearly \$50M and take 18 months to complete. The entire façade as well as interior of the building will be upgraded to complement the science being conducted at the Institute. The new facility will house a data center, a state-of-the art theater and workspaces.

The data center will be approximately 3,000 square feet and is being designed using cutting edge high density cooling solutions and high density blade compute solutions. A total of 48 racks will be installed and dedicated to research use. Of the 48, 10 racks will be reserved for core services. The core services are on separate, dedicated, redundant power to ensure continuous operation. The current design of the data center includes a Powerware 9395 UPS system providing two 750kW/825kVA UPSs in an N+1 configuration for non-core racks and two 225kW/250kVA in a 2N configuration for core services racks. The UPS sends conditioned power to 300kVA Power Distribution Units (PDUs) located inside the data center. The PDUs feed 400A rated Track Power Busways mounted above rows of racks providing an "A" bus and a "B" bus for flexible overhead power distribution to the racks. The design calls for the use of VRLA batteries with 9 minutes of battery run time for the core services UPS and 6 minutes of battery run time for the non-core UPS (note that the generator requires less than 2 minutes of battery run time in order to fully take over the load in the event of an outage). A 750kW/938kVA diesel emergency generator located in a weatherproof sound attenuated enclosure adjacent to the building will provide at least 8 hours of operation before needing to be refueled.

The Cisco UCS blade solution described above allows the Institute to run the services of a much larger physical infrastructure in a much smaller footprint without sacrificing availability or flexibility. Each Cisco chassis hosts 8 server blades and has 160 gigabits of external bandwidth available per chassis. Each of the 48 racks can hold up to 6 chassis plus requisite networking equipment (4 fabric extenders). Thus, the new data center has adequate rack space to accommodate this project.

In addition to a new data center, the new space in Raulston will house a 50-seat high definition theater – the Data Immersive Visualization Environment (DIVE). The prominent feature of the DIVE is a large curved display that can present highly detailed images, video, interactive graphics and rich media generated by specialized research data. The DIVE display will feature a dominant image area, with consistent brightness across the entire display surface, high contrast, and 150° horizontal viewing angle. The display resolution target is 4k Ultra HD, 3840x2160 (8.3 megapixels), in a 16:9 aspect ratio. Due to the ceiling height requirements, the DIVE will require two floors of the building. The DIVE is designed to facilitate research communication, dissemination, training and high levels of interaction.

Adjoining the Raulston Memorial Research Building on the north side is a brand new MRI facility. The Center for Image Acquisition (CIA) will house a Siemens Magnetom Prisma, a new 3 Tesla MRI scanner, and a Siemens Magnetom 7T MRI scanner. The MAGNETOM Prisma 3T includes unparalleled simultaneous 80mT/m @



200T/m/s gradients, a new, high end gradient system that delivers high gradient amplitudes and fast switching capabilities in a combination that is currently truly innovative. The Siemens Magnetom 7T MRI system is an investigational device. Both MRI scanners are at the leading edge for neuroimaging

The Raulston building will house upwards of 90 faculty, postdocs, students and staff in a variety of seating configurations from private offices to shared offices to open workspaces designed for collaboration. Great care was taken to design the people space to facilitate ongoing discussion and collaboration while providing a peaceful work environment for all.

A rendering of the new building included below (**Figure 5**). The Raulston building is scheduled to open in 2016.



**Figure 5.** Future home of the Stevens Neuroimaging and Informatics Institute showing the data center (south side), DIVE, and the Center for Image Acquisition (north side).

**Additional Office Spaces.** Additional office spaces for faculty, staff and students is available in Suite 400 of the Marina Towers in Marina Del Rey, CA. This building houses other high tech research groups like the Information Sciences Institute and serves as a West LA hub for the Stevens Neuroimaging and Informatics Institute. Suite 400 is nearly 5,200 sq ft with 14 faculty and shared offices, 2 director's offices, 2 conference rooms, a student workroom with 8 workstations and a large kitchen.

### **ALBERT EINSTEIN COLLEGE OF MEDICINE (EINSTEIN)**

**Scientific Environment:** The research team of the Laboratory of Developmental Epilepsy, led by Drs. Galanopoulou and Moshé, is fully qualified to successfully conduct the proposed research. Their research group has developed and characterized models of adult and early life epilepsies and have extensively utilized chronic models of epilepsies for the preclinical screening of new therapeutics. Drs. Galanopoulou and Moshé are Board Certified clinical epileptologists as well as basic science researchers and are qualified to design, perform, and interpret findings with an ultimate goal to translate them eventually to the clinical arena. Dr Galanopoulou was a co-organizer of an international effort (ILAE, AES supported; in collaboration with NINDS)

to optimize preclinical epilepsy research so that it is more predictive of clinically relevant discoveries. The research team led by Drs. Galanopoulou and Moshé consists of three post-doctoral research fellows, one graduate student and 2 research technicians who are fully qualified to conduct the proposed experiments. The Pls' laboratory is fully equipped to carry on all aspects of this study, including stereotactic surgery, drug administration, seizure and video EEG monitoring of immature and adult rodents, behavioral studies, histology, molecular biology, in vitro and in vivo electrophysiology, and statistical analysis.

Dr. Wenzhu Mowrey is an Instructor at the Department of Biostatistics at the Albert Einstein College of Medicine and has been collaborating with Drs. Moshé and Galanopoulou on projects related to identifying new treatments for infantile spasms, funded by NINDS, the Department of Defense, and CURE. Dr. Mowrey has all the expertise to address the statistical aspects of the data analysis in the current project.

Dr. Craig Branch is Associate Professor at the Department of Physiology & Biophysics, Albert Einstein College of Medicine, and Director of the Integrated Imaging Program, Gruss MRI Imaging Center, and Blaufox PET/CT/SPECT Imaging Facility, Einstein COM. Dr. Branch has experience with MRI methodology, including rodent MRI and will offer his expertise and leadership at the Gruss MRI center for the purpose of this project.

**Laboratory:** The laboratory available to the Pls and their associates is in the modern Rose F. Kennedy Center and consists of nine laboratory and seven office space rooms (totaling 167 m<sup>2</sup>.) completely equipped for stereotactic surgeries, electrographic recordings (in vivo and in vitro), seizure and behavioral testing, histology and histochemistry, molecular biology and has four fume hoods.

**Clinical:** N/A

**Animal:** Rose F. Kennedy Center contains animal housing colony rooms (for rats and mice), fully equipped with a supporting staff, including three full-time institutional veterinarians. These facilities and staff are 100% available to the PI.

<http://einstein.yu.edu/research/shared-facilities/cores/52/animal-housing-and-studies/>

**Computer:** Office computers (Windows or Mac OsX) with appropriate software (MS Office, Adobe Acrobat, Photoshop, Kaleidagraph, SigmaPlot, MATLAB, Endnote, SAS, Statview, geNorm, ABI 7000 sds v1.2.3, StepOne software, Image J, JMP10 statistical software; Stellate, Sirenia and XLTEK software for EEG recording and analysis; Cheetah software for in vivo recordings) and a scanner are available for every member of the team. Computers with digital cameras or A/D converters are available for electrophysiology and histology. Internet access is available to all laboratory members.

**Office:** Office space is available for the Pls and each of their associates, including post-doctoral research associates.

**Other:** A Core facility on Cellular and Molecular Neuroimaging (Director Dr. K. Dobrenis) is available to all investigators at the Kennedy Center for imaging of biological specimens, including confocal imaging, Neurolucida/Stereoinvestigator microscope for cell counts and neurite tracing, electron microscope, and state of the art image processing and analysis software.

<http://einstein.yu.edu/research/shared-facilities/cores/47/cellular-and-molecular-neuroimaging/>

A Rodent Behavioral Evaluation Core Facility (Director Dr. Maria Guillinello) is available to the investigators at Kennedy that provides the possibility to perform a variety of behavioral and functional assays on rodents.

<http://einstein.yu.edu/research/shared-facilities/cores/49/rodent-behavioral-evaluation/>

**Gruss MRRC Equipment.** MRI laboratories (floor 1): A magnetic/RF shielded room housing the 9.4 T, 21 cm Varian Direct Drive MRI/MRS system. Adjacent to the MRI laboratories are the following supporting areas; a machine shop, electronics and coil fabrication laboratory, a wet laboratory, a physiology instrumentation laboratory and an animal physiological laboratory including housing for barrier and non-barrier animals.

Animal MRI (9.4 Tesla laboratory):

A 9.4 T 21 cm ID Agilent Direct Drive MRI, running VNMRJ 3.2. This system is equipped with 2 channel Transmit / 4 channel Receive capability. A 12 cm ID gradient set (60 G/cm, 180 us rise-time) with integral 14 channel shim set is installed, and driven by a Copley 266 gradient amplifier (Analogic, MA) and a 14 channel, 10 amp / channel shim power supply (Resonance Research Inc., Billerica, MA). RF Coils: Three double tuned transmit body coils (tuned to proton and either 19-F, 13-C or 31-P, M2M Imaging Corp., Cleveland, OH) and receive only surface coils for 1-H, P-31, 19-F and 13-C (Doty Scientific, Columbia, SC) are available for brain and body rodent applications along with mouse and rat brain 4-channel array coils for SENSE imaging. All coils are actively decoupled from surface coils using an M2M coil control unit and fiber optic communications.

Adjacent to the 9.4 Tesla MRI laboratory is a 14 m<sup>2</sup> fully equipped surgical facility, general surgery tools, an operating light and autoclave. Physiological monitoring in the 9.4 Tesla MRI is achieved using either a BioPac

Systems (Goleta, CA) MP150 Data acquisition system or an SA Instruments (Bayshore, NY) model 1025 monitoring and gating system.

### **Computer Resources**

**Imaging Analysis Hardware:** All MRRC data processing is done transparently through the Einstein-Yeshiva High-Performance Supercomputing Cluster (HPSC or “the Cluster”). The Cluster consists of 120 computing “nodes” for a grand total of over 2,000 processor cores supported by 8 gigabytes and 4 terabytes of RAM memory per node and a total 800 terabytes of raw storage. General Image Analysis/Scientific Software: Managed software access is provided to all users. Supported software includes AFNI, FSL, SPM, AEDES, ImageJ, FreeSurfer, MRICro/n, and several MATLAB toolboxes for functional MRI analyses; LCMModel, MRUI, and LUIS for spectroscopy and ASL; and MedINRIA, Slicer, TrackVis, CATNAP, and CAMINO for diffusion and tractography analyses. Other computing and statistical software is available through the University including SPSS. Specialized Image Analysis Software: Image analysis software is also developed in-house for a variety of purposes. The code is written in C++, MATLAB, or IDL.

## **JOHNS HOPKINS UNIVERSITY**

**Scientific Environment:** Johns Hopkins University is a premier biomedical research institution, with extraordinary opportunities for collaborations with faculty possessing a broad range of expertise. There is a collegial atmosphere, allowing for interdisciplinary collaboration and for obtaining scientific advice as needed for research projects.

**Departmental Environment:** The Department of Anesthesiology and Critical Care Medicine at Johns Hopkins University has a rich history of research into mechanisms and pathobiology of brain injury, in both clinical and animal studies. Over the last 20 years, the department has supported laboratory research in cerebrovascular physiology and brain damage from traumatic brain injury, perinatal brain injury, stroke and cardiac arrest, using multiple small and large animal models. The department has over 180 faculty members to support operating rooms and critical care units (pediatric intensive care unit, neurocritical care unit, surgical intensive care units). There is a large residency program and clinical fellowships in pediatric critical care and pediatric anesthesiology. Basic and clinical researchers have extramural funding in cerebrovascular disease, neuroscience, pain, and vascular biology. There is a departmental Research Division, providing support for grant submissions, budget preparation, and financial management. There is also support for internal grant review, and editorial and administrative support.

**Laboratory:** N/A

**Animal:** N/A

**Computer:** Dr. Robertson has computers with capacity for basic word processing, spreadsheets, graphic and statistical analysis. Campus resources provide specialized software at reduced rates. Campus internet access provides access to additional software (e.g., Reference Manager) and access to electronic journals through the Welch Medical Library. There is also computer support through departmental staff.

**Office:** Dr. Robertson has private office space with computers, color printing, fax, scanning, and other standard office equipment. Administrative support is provided for both research and clinical purposes. The department provides a full-time editor for editing manuscripts, grants and other documents.

**Clinical:** The Pediatric Intensive Care Unit in the Bloomberg Children’s Center at Johns Hopkins University is a 40 bed ICU, with over 2,000 patient admissions per year. On average, about 40% of the admitted patients are admitted for neurological disorders or following neurosurgical procedures. The Bloomberg Children’s Center is the designated Level 1 Pediatric Trauma Center for the state of Maryland, with approximately 15-20 patients/year admitted to the PICU with severe traumatic brain injury. Dr. Robertson is the co-director of the Pediatric Neurocritical Care program, and collaborates regularly with a multidisciplinary team from Pediatric Neurology, Pediatric Neurosurgery and Pediatric Neuroradiology. In addition, the team has close contact with clinicians involved in pediatric brain injury rehabilitation at the Kennedy Krieger Institution.

## **MASSACHUSETTS GENERAL HOSPITAL**

### **Clinical Resources**

MGH is the oldest and largest hospital in New England. Each year, the MGH and its 4 health centers, admit approximately 47,000 inpatients and handle almost 1.5 million visits in its extensive outpatient programs. In 2011 alone, the Massachusetts General Physicians Organization and the clinics located on the main campus only had approximately 1,224,269 ambulatory visits.



The Partners Research Patient Database Registry (RPDR) provides clinical information for the inpatient and outpatient population at MGH and Brigham and Women's Hospital to researchers with appropriate IRB approval. The database contains inpatients and outpatients for whom care has been billed through hospital billing systems. The RPDR population includes 90-98% of the total patient population at MGH from 1993 to present. Data included in the RPDR includes comprehensive patient demographics, diagnoses, procedures, medications, provider information and encounter information. RPDR data acquisition engine allows investigators to query over 50 million medical records with defined parameters. The program then generates a list of patients including their primary care provider information that match our parameters.

#### **Division of Neurocritical Care and Emergency Neurology, and MGH Stroke Service**

The Neurocritical Care Neurology Service includes 11 faculty in addition to a physiatrist. The Neurocritical Care team consists of a neurocritical care or stroke fellow, and a neurocritical care attending. A neurocritical care fellow and neurology resident take call in-house, guaranteeing that at least two members of the team are in the hospital at all times. Two attending neurocritical care physicians take call at any given time. One of these is the neurocritical care attending for the Acute Neurotrauma Service, staffed by a multidisciplinary team of neurocritical care neurology, trauma neurosurgery, and trauma general service, with 24-hour per day coverage of the emergency department and Neurosciences ICU throughout the year. The Neurotrauma Neurocritical Care Service additionally provides a year-round consult service to other units throughout the hospital. The MGH also runs a robust Acute Stroke Service, to which patients with undifferentiated acute neurologic emergencies are referred from the broad New England area and beyond for further care. This program also includes a robust telemedicine program for pre-hospital screening at approximately 30 hospitals throughout Maine, New Hampshire, and Massachusetts. The Acute Stroke Team consists of an acute stroke attending, a stroke fellow, a dedicated neurology resident, and a vascular neurology attending who staffs the Stroke Inpatient Unit. Outpatient neurology services include both a Neurocritical Care Neurorecovery Clinic and a Stroke Clinic. The Neurocritical Care Neurorecovery Clinic consists of four providers meeting one half-day every 2 weeks and seeing patients discharged from the Neurosciences Intensive Care Unit with traumatic brain injury and subarachnoid hemorrhage following. The Stroke Clinic meets four half-days per week and are divided among two Stroke Prevention Clinics, a Hemorrhage Prevention Clinic, and a Cardio-neurology Clinic. Neurocritical Care Neurology Service personnel include 15 staff neurologists, 13 fellows, and a dozen acute neurology research coordinators. More than 300 patients with traumatic brain injury and more than 360 patients with intracerebral hemorrhage (ICH) have been admitted to the MGH neuroscience services over the past three years.

#### **Neurosciences Intensive Care Unit**

The 21,854 ft<sup>2</sup> MGH Neurosciences Intensive Care Unit contains 22 patient rooms and is staffed by over 100 Neurointensive Care Nurses, a Clinical Nurse Specialist, and a Nursing Director. Physician coverage is provided by two teams of fellows and residents and board-certified Neurointensive Care attending physicians. Coverage is provided 24 hours per day/7 days per week by fellows and residents. Each bed is supported by a GE Bedside vitals monitor with continuous waveform capture of physiological data, databased through the Excel Medical BedMaster system. The Unit is, in addition, equipped with a portable CT scanner, 22 built-in bedside XLTEK continuous EEG machines with video monitoring, central viewing stations and Neuroworks EEG viewing software, 2 transcranial Doppler ultrasound machines, a GE Logiq e Ultrasound machine, Licox brain tissue oxygenation monitoring supplies, AdTech and PMT depth electrode supplies, Ives, Inc., MRI-compatible scalp electrodes, Persyst, Inc. quantitative EEG software, Hemedex cerebral blood flow perfusion probes, microdialysis, two Arctic Sun cooling units, three Vigileo non-invasive cardiac output monitors, 40 computers and 5 private offices. Directly adjacent to the NeuroICU are 1) a radiology suite with a 3-Tesla Siemens Skyra MRI scanner and a General Electric CT-PET scanner, 2) a wet lab space with centrifuge and - 20C freezer storage for processing biological samples, and 3) a Neurophysiology Lab for computational processing of critical care EEG monitoring data. The Neurocritical Care fellowship training program at MGH is the oldest and largest such program in the country, with between 10 and 12 fellows per year.

#### **Clinical Neurophysiology and Epilepsy Services**

The MGH Neurology Clinical Neurophysiology and Epilepsy Services includes 13 neurology faculty and 7 fellows who see patients with adult epilepsy syndromes, and perform and interpret scalp-derived and intracranial EEG recordings. Over 10 technologists perform studies including 24-hour daily call for emergencies. Specialized expertise among faculty include multiple faculty each with experience performing continuous and critical care EEG, intracranial electrophysiology monitoring including continuous EEG/EECoG evaluation and management of seizures, ischemia following subarachnoid

hemorrhage, and cortical spreading depolarizations including quantitative trending, analysis, and source localization. Additional expertise within the service includes psychiatrists, neuropsychologists, neuroradiologists performing advanced neuroimaging (fMRI, MEG, CT-PET), and functional neurosurgeons. The service meets for clinic at least 3 half-days per week in addition to 4 weekly conferences: a combined multidisciplinary surgical epilepsy conference, an EEG review conference, a pediatric epilepsy conference, and an adult epilepsy clinic conference in which all clinic patients are reviewed comprehensively for diagnosis and management. Over 4 clinical researchers help lead epilepsy clinical trials and research programs involving medication interventions, seizure localization, critical care neuromonitoring, clinical outcomes, and seizure-related complications. Database storage for thousands of electrophysiology studies provides a library of normative historical waveform data, including multimodality monitoring synchronized with additional physiologic waveform recordings, managed by a data manager, and available to a number of data analysts and research staff. Dedicated laboratory space and two weekly research conferences are held: a computational neurophysiology conference and a quantitative critical care electrophysiology conference reviewing project progress.

### **Neuroradiology**

Neuroradiology is staffed 24/7 by neuroradiology fellows and attendings. The emergency department has a 1.5T MRI, two CT scanners staffed 24/7 with in-house CT technicians, specifically designed for use with brain CT perfusion, capable of 4 cm, rather than 2 cm, of coverage during a single cine rotation. A 3-D reconstruction lab generates perfusion images and CT angiography images for clinical service. The emergency scanners also produce automatic thick slices in the axial, coronal and sagittal plane that enable rapid assessment of major vessel occlusion on the source images without the need for computational processing. In addition to the CT scanners located within the emergency department, there are 5 GE Lightspeed CT scanners located one floor above, and the additional PET-CT scanner located adjacent to the Neurosciences Intensive Care Unit. There is also one portable CereTom CT scanner that images patients in their Neurosciences Intensive Care Unit room.

## **PHOENIX CHILDREN'S HOSPITAL, PHOENIX, AZ**

Phoenix Children's Hospital (PCH) is a tertiary care center which provides comprehensive inpatient, outpatient specialty and primary care, urgent care, emergency and level one pediatric trauma services. Phoenix Children's Hospital is a free standing children's hospital in the fifth largest metropolitan region in the country and the only facility dedicated solely to the needs of children in the state. In its first ten years as a free standing hospital, it rapidly became one of the largest in the country being easily in the top 10 in volume (355 licensed beds) and major disease conditions (for example, PCH is with the top 5-6 for cardiovascular and neurological procedures). PCH is an American College of Surgeon's Level I trauma center seeing about 2100 patients/yr. In 2011, a new patient tower opened (over \$500 million in construction costs). In 2014, Phoenix Children's had 18,286 admissions; 78,612 visits to the Emergency Department; 216,241 outpatient visits; and 16,227 surgical procedures in the primary facility and 4 major outreach locations. Phoenix Children's offers care in more than 70 subspecialty fields of pediatric medicine including 6 centers of excellence. Nine of Phoenix Children's divisions—Cancer; Cardiology and Heart Surgery; Diabetes and Endocrinology; Gastroenterology and GI Surgery; Nephrology; Neurosurgery/Neurology; Orthopedics; Pulmonology; and Urology—were ranked in the 2015-16 edition of U.S. News & World Report Best Children's Hospitals.

The overall clinical program at PCH includes over 220 employed medical staff, over 800 medical staff with privileges, and transplant programs in blood, kidney, heart, and liver. The staff of PCH is the primary pediatric staff of the University of Arizona, College of Medicine – Phoenix, a school which is less than 10 years old and has preliminary LCME accreditation as a separate and distinct school from the Tucson campus. The research areas are also new but growing rapidly and include wet bench research at the University of Arizona College of Medicine - Phoenix, Arizona State University, and the Translational Genomics Research Institute (TGen). Internally, PCH has over 340 IRB approved active research protocols. In addition to these collaborators, clinical research collaboration also includes the University of Arizona College of Public Health and Arizona State University.

Phoenix Children's Hospital is a freestanding hospital licensed to care for pediatric patients 18 years of age and younger. There are circumstances where it may be in the best interests of those patients older than 18 to be admitted to this facility. These patients may include patients with complex medical conditions that are either congenital (e.g., congenital heart disease, spina bifida, cystic fibrosis), began in childhood or would be considered

to be a pediatric disease process. In these cases, providers at Phoenix Children's Hospital may be uniquely qualified to provide care for these patients that are not otherwise available in adult hospitals.

In the Fall of 2014, Phoenix Children's Hospital announced the development of a joint venture with Nanthealth, LLC and the Chan Soon-Shiong Foundation, resulting in the planned creation of the Chan Soon-Shiong Children's Institute for Precision Medicine at Phoenix Children's Hospital (CSSCIPM). For PCH, the creation of this venture will allow researchers, clinicians, and patients unprecedented access to whole genome sequencing, transcriptomics and proteomics capabilities with a rapid turnaround time frame offered in a CLIA laboratory setting. The molecular profiling capabilities of the CSSCIPM at PCH will include access to high speed computers and state-of-the-art bioinformatics algorithms that will allow rapid and accurate analysis of the high volumes of data generated for each patient. The access to a high quality, clinical grade pediatric database that houses the molecular profiling information of large numbers of pediatric patients will allow the meaningful interpretation, reporting, and investigational research of 3 – 4 million variants that are uncovered with the sequencing of each pediatric patient. More importantly, a pediatric focused approach using these next generation sequencing technologies will enable rapid discovery of new genes and new pathogenic variants leading to an unprecedented rate of knowledge expansion for pediatric diseases. Currently, our knowledge of the genes involved in pediatric diseases is very limited and thus in today's medical setting, care that is delivered based on the child's molecular profile is almost non-existent. The care is therefore not personalized to the patient's genetics and is focused more on traditional approaches based on protocols and checklists arising out of observational studies for care management. The genomics, transcriptomics and proteomics research within the CSSCIPM will enable cutting edge research for pediatric diseases that include cancer and inherited Mendelian diseases as well as common, complex genetic diseases such as autism, type 2 diabetes, obesity and autoimmune diseases. Because the focus of PCRI is translational research, the discoveries within the CSSCIPM is expected to guide decision-making concerning standard of care and/or investigational treatment within a rapid time frame. PCRI will provide operational and administrative oversight for research activities undertaken by the CSSCIPM and will oversee the biorepository operations required to support such an initiative.

#### **Computers:**

The clinical staff for each division is provided offices within the clinic space. Each office is approximately 100 square feet in size. Each office includes a PC computer, phone, and network capabilities. Support staff has access to workstations which include computer, phone, and network capabilities. Additionally the hospital has work stations in each of the clinical inpatient and surgical areas where staff can access electronic medical records for patients. Offsite clinics are networked into the main systems to provide electronic access.

Electronic medical records systems, computerized order entry and all support information needed for this project can be easily obtained in a secure fashion via the hospital's integrated IT system. PCs, printers, scanners, and fax machines are located all throughout the hospital. Personnel can easily obtain, in a secure fashion, electronic medical records systems, computerized order entry, and all support information needed for this project via the Phoenix Children's integrated IT system.

#### **BARROW NEUROLOGICAL INSTITUTE at PHOENIX CHILDREN'S HOSPITAL**

Barrow Neurological Institute at Phoenix Children's Hospital (Barrow at PCH) is a Center of Excellence at Phoenix Children's Hospital (PCH) and is affiliated with the University of Arizona, College of Medicine - Phoenix (U of A COM- PHX). Barrow at PCH, under the leadership of Director P. David Adelson, MD, FACS, FAAP, has developed a comprehensive and integrated neuroscience program and serves as the administrative umbrella for all of the "neuro" divisions at Phoenix Children's Hospital including its core divisions; Neurosurgery, Neurology, Psychology, Neuropsychology, Psychiatry, and Physical Medicine and Rehabilitation, as well as the collaborative divisions of Neuroimaging, Neurocritical Care, Neuro Neonatal Intensive Care, Neuropathology, Neuro-Oncology, and Neuro-Otology, with approximately 50 faculty and 80 support staff.

Barrow at PCH is housed in its own building on the PCH Medical Center and consists of 2.25 floors and over 30,000 square feet of office, clinical/ clinic, and rehabilitation space as well as dedicated clinical research space consisting of 8 offices, 1 conference room and 1 consult room for the Neuroscience Research Division that includes Research Coordination, Bioinformatics, Biostatistics, Biorepository, Neuroimaging, and Neurophysiology. The Director, Dr. Adelson, has ample administrative office space including 6 offices for staff, 1 boardroom, and is individually supported by a full-time administrator, administrative executive assistant, and clinical administrative assistant, along with clinical staff and a full-time research staff. There are presently over 20 research staff including research scientists, research coordinators, biostatistician, research associates, biomedical engineers, administrators, and support staff dedicated to the Neuroscience Research Division.

Barrow at Phoenix Children's has very active fellowship and residency programs. With the alliance between Barrow Neurological Institute at St. Joseph's Hospital and Medical Center and Phoenix Children's Hospital, the Child Neurology Residency Program moved to Barrow at Phoenix Children's in June 2011. Child Neurology is classified as a "dependent residency" and is linked to the Adult Neurology Residency Program at Barrow at St. Joseph's. The Child Neurology Residency Program is a three year program which follows two years of general pediatric preliminary training. With the alliance, a five year combined program was launched at Barrow at Phoenix Children's. The program has successfully matched two years in a row with the establishment of the new five year combined program. Starting in July 2014 the program will have a full complement of six residents. The Institute has fellowship program in Neurosurgery starting in July 2013 and a Neuropsychology Post-Doctoral Fellowship that started in 2012

Barrow at PCH places a large emphasis on teaching and research activities. Each division participates in training PCH pediatric residents as well as the Neurology, Neurosurgery, and Psychiatry residents from Mayo Clinic Arizona and St. Joseph's Hospital. In addition, many of the faculty are involved in teaching and mentoring medical, graduate, and undergraduate students from the University of Arizona College of Medicine (COM)-Phoenix, Creighton University, and Arizona State University.

#### **Clinical:**

##### Neurotrauma/ Concussion Program

Through an interdisciplinary collaboration of Neurosurgery, Neurology, Neurocritical Care, Sports Medicine, Neuropsychology, Neuroimaging, Injury Prevention, and Neurorehabilitative Services, the program provides improved communication, clinical care, research, education, and patient- and family- centered care to children who have suffered from a concussion or traumatic brain injury.

##### Stroke Program

Under the direction of Dr. John Condie, the multidisciplinary Pediatric Stroke Program is focused solely on providing comprehensive care in the evaluation, management and treatment for infants, children, and teens who have suffered a stroke, or children who may be at risk for stroke due to other medical conditions. The dedicated pediatric stroke team has the appropriate expertise and resources for the diagnosis and treatment of pediatric stroke and pediatric stroke prevention. Early recognition and diagnosis is critical for stroke patients, as delays in seeking treatment can lead to permanent disability and stroke recurrence.

##### Inpatient Rehabilitation Program

The Frances H. McClelland Rehabilitation Program at Phoenix Children's Hospital is made up of a comprehensive team of pediatric trained physicians, nurses, and therapists who care only for growing children. Among the specialties of our rehab program for kids is the Inpatient Rehabilitation Program - offering services tailored specifically to the needs of each child. Our inpatient rehabilitation program -- the only one just for children in Arizona -- has been caring for hospitalized patients for more than 15 years. We help children ages 8 months to 17 years. The goal is to serve the comprehensive needs of our patients and return them to their home, school, and community as quickly and safely as possible. The inpatient rehabilitation program provides a comprehensive, multidisciplinary approach provided by a team of experienced pediatric professionals to maximize the recovery of children conditions such as traumatic brain injury, spinal cord injury, stroke, neuromuscular diseases, orthopedic conditions, burns, deconditioning, and respiratory/cardiac conditions.

##### The Neuromuscular Program

The Neuromuscular Program at Barrow Neurological Institute at Phoenix Children's Hospital is led by Saunder Bernes, MD, and is a designated Muscular Dystrophy Clinic site by the Muscular Dystrophy Association. It is the only MDA Clinic in Arizona that sees pediatric patients. The program strives to provide consistent, coordinated, and multi-disciplinary collaborative care for children with neuromuscular disorders, a model that fosters positive outcomes. The divisions of Neurology, Physical Medicine and Rehabilitation (PM&R), Orthopedics, Pulmonology, Cardiology, Endocrinology, Gastroenterology, and Palliative Care join together to create a multidisciplinary medical team in this program. Support services from dedicated, specially trained health care professionals, such as nurses, social workers, and physical therapists, complete the comprehensive neuromuscular team.

##### Deep Brain Stimulation Program

The Deep Brain Stimulation program at Barrow Neurological Institute at Phoenix Children's Hospital is a multidisciplinary program designed to care for children with rare and complex movement disorders. Pediatric neurologist, neurosurgeon, psychiatrist, psychologist, physiatrist and rehabilitation specialists collaborate to provide comprehensive treatments for each child. Our goal is to provide support for the family, individualized care for children with movement disorders, and to foster positive outcomes.



Deep Brain Stimulation treatment involves two neurosurgical operations. The first surgery utilizes a state of the art brain lab neuro-navigation system which frames the head for precision, chooses an optimal safe trajectory and allows the neurosurgeon to place two electrodes in precise locations of the brain for the best possible outcome. Correct placement of the electrodes is paramount to the success of the procedure.

#### Comprehensive Epilepsy Program

Dr. John Kerrigan directs the Phoenix Children's Hospital (PCH) Comprehensive Epilepsy Program, which is staffed by 5 pediatric epileptologists. This program includes a 12-bed state of the art pediatric epilepsy monitoring unit (PEMU), structural and functional neuro-imaging, and psychiatric and neuropsychological evaluations. For those patients whose seizures are not controlled with medications, epilepsy surgery, ketogenic diet, and vagal nerve stimulation are also offered. In addition, there are 7 portable video-EEG machines utilized for recording in the Pediatric and Neonatal Intensive Care Units. There are 9 EEG technologists with 2 dedicated to the epilepsy monitoring unit at any time.

#### Headache Program

Since Up to 90 percent of school-age children report having headache pain with the most common disorder being migraine, Barrow at PCH has developed a comprehensive headache program. Drs. Marcy Yonker and Kara Lewis are co-directors of this program. The program has an out-patient Headache Clinic where Drs. Yonker and Lewis, along with a highly skilled medical team, see children for a full evaluation to determine the source of the child's headache and develop the best treatment course to help children return to their normal lives. Drs. Yonker and Lewis also collaborate with a team of specialists in the hospital to create treatment plans that address the physical and emotional needs of children hospitalized with migraines.

#### Autism Diagnostic Clinic

The Autism Diagnostic Clinic at Phoenix Children's Hospital is the only comprehensive program in a freestanding children's hospital in the state of Arizona. Children are seen by specialists; including neurology, gastroenterology, speech, and occupational therapy. The focus of this program is on family-centered care. The goal is to diagnose early, provide the most comprehensive assessment and treatment plan, and provide families with the support to best take care of their child. The comprehensive team under the leadership of Dr. Robin Blitz works with the child and family to implement effective learning and behavioral interventions to help the child grow and develop to the best of their ability. The Autism Diagnostic Clinic also helps identify medical diagnoses often associated with autism spectrum disorders (ASD), such as seizures, gastrointestinal disorders, sleep disorders, and behavioral disorders.

#### Fragile X Clinic

The Fragile X Clinic at Barrow Neurological Institute at Phoenix Children's Hospital is a comprehensive, multi-disciplinary clinic focused on the coordinated care and management of children with Fragile X Syndrome and their affected family members. Developmental Pediatrics is joined by Genetics, Physical therapy, Occupational therapy and Speech therapy to provide a holistic and comprehensive evaluation of each patient. The Fragile X Clinic is an established Fragile X Regional Center with the National Fragile X Foundation (NFXF). Through a grant with the CDC, the NFXF has developed the Fragile X Clinical and Research Consortium (FXCRC). The Fragile X Clinic at Barrow at PCH is an active participant in providing registry information to FXCRC with the ultimate goal of being able to foster the dissemination of scientific and clinical data among researchers and providers.

#### Pediatric Comprehensive Sleep Medicine Program

The innovative Sleep Medicine Program at Barrow Neurological Institute at Phoenix Children's Hospital is possible through a coordinated effort of multiple divisions with the same goal in mind: to provide the best possible care to children who suffer from a variety of sleep disorders. Founded in 2009 and accredited by the American Academy of Sleep Medicine (AASM), the Sleep Medicine Program is led by Rupali Drewek, MD, a pediatric pulmonologist and Matt Troester, DO, a neurologist with Barrow at Phoenix Children's. The Sleep Medicine Program is one of just seven exclusively pediatric accredited sleep centers in the entire western United States. Dr. Drewek, Co-Director of the Sleep Laboratory, is one of two pediatric pulmonologists in Arizona triple board certified in Pediatrics, Pediatric Pulmonology and Sleep Medicine. Dr. Troester is the only pediatric neurologist in Arizona quadruple board certified in Child Neurology, Clinical Neurophysiology, Epilepsy and Sleep Medicine. He serves as Co-Director of the Comprehensive Sleep Medicine Program with Dr. Drewek.

The four bed, state of the art, neurodiagnostic sleep laboratory has had tremendous growth since its inception. In 2009, there were approximately 100 studies performed compared with nearly 500 in 2013.

Only half way through 2014, we are on track to nearly double study volume by year end. The Sleep Program within Barrow at Phoenix Children's works collaboratively with other divisions to treat the whole child. Sleep

Medicine works in concert with the Concussion Program, managing lingering sleeping difficulties in those with mild to severe traumatic brain injuries. We also work with the surgeons in cases of central sleep apnea related to various central nervous system malformations. The Sleep Program also works with the Cardiometabolic Risk Assessment, Research, and Education (CARE) Program and collaborates with multidisciplinary clinics across the campus including management of sleep related breathing problems in children with obesity. Children and families have access to all of the specialists they may need including: GI, neurology, psychology, hepatology, cardiology, pulmonary, genetics and social work.

#### Neuro Oncology Program

The Jaydie Lynn King Neuro-Oncology Program at Phoenix Children's Hospital is the only comprehensive pediatric program of its kind in Arizona, offering multidisciplinary, personalized care for children and adolescents with primary brain and spinal cord tumors. The Program combines the expertise of subspecialists in the Barrow Neurological Institute at Phoenix Children's and the Center for Cancer and Blood Disorders (CCBD).

Led by Michael Etzl, MD, and Amy Rosenfeld, MD, Phoenix Children's Jaydie Lynn King Neuro-Oncology Program provides the highest quality patient care through a team approach using the latest evidence based treatments, innovative research, and psychosocial support to continually try to improve the chances for cure and minimize tumor and treatment related side effects. We pride ourselves on making a significant difference in the quality of life for our patients.

### **CRITICAL CARE**

#### **Clinical:**

The 48 bed Pediatric ICU has an annual patient volume of 2500-3,000, with multidisciplinary care of all patients from 0-21 years of age. This family centered and cutting-edge design resulted in the PICU at PCH receiving the Honorable Mention (2<sup>nd</sup> place) designation for the ICU design award given by the Society of Critical Care Medicine, American Association of Critical Care Nurses and the American Institute of Architects in 2013. The PICU at PCH has a mortality rate of 2% and a standardized mortality ratio of 0.58 as compared with 42 other ICU's within the PHIS network.

The average length of stay within the ICU at PCH is also 1 day less than other PHIS PICU's despite the fact that the Case Mix Index is similar to other centers. The ICU environment is also completely electronic, with all orders, documents and records maintained in the EMR. All rooms have Phillips M70 or 90 monitors which are slaved to a central monitoring site and also have displays which can be seen from the small nursing stations located between each 2 rooms. Safety alarms are automatically routed to personal communication devices according to severity and such devices provide instant communication between physicians, nurses, RT's and ancillary staff. State of the art neurologic monitoring in the form of INVOS near infrared spectroscopy, continuous video EEG, Licox brain oxygenation and intracranial pressure monitoring is readily available. Immediate support of patients undergoing cardiac arrest or sudden deterioration is available with extracorporeal life support and on site surgical expertise for such events is also available. The PICU serves as the major tertiary-quaternary program in the region and also receives patients from as far away as Montana, New Mexico, Idaho, Nevada and other areas of the Southwest. PCH has the only Level 1 ACS approved Pediatric Trauma Center, hosts the only dialysis program, liver transplant, bone marrow, renal and heart transplant program in the region.

One unique aspect of the ICU at PCH is its large population of Hispanic and Native American patients to which we provide care. These patients have a plethora of rare and undiagnosed diseases and unexplained reactions to common diseases which would benefit from more investigation. Another unique aspect of Critical Care at PCH is the fact that several clinicians also provide patient care support to the Alaskan Native Health Center in Anchorage—which offers another unique population which is often underrepresented in research studies. The Division was accredited as a Pediatric Critical Care Fellowship training site in 2011 and has successfully recruited 2-3fellows/year (with an eventual goal to 4/year), some of whom have already received grant funding. The division holds monthly research, educational, quality improvement and journal club meetings. The Division also supports the newly established Pediatric Stroke Team at PCH, which is composed of 3 Critical Care Members (2 physicians and 1 Nurse Practitioner), in addition to our Neurology-based Neurocritical care physician. This team saw 93 patient referrals in its first 2 years. Neurocritical Care board certification was achieved by 3 members of PCH (Buttram and Liu, Critical Care and Condie, Neurology) in 2013. Critical Care also provides an Extracorporeal Life Support Resource Team, which helps cover patients on Extracorporeal Support within the Neonatal ICU, Cardiovascular ICU and PICU. ECLS care was provided for 297 days in 2012 and 260 days in 2013. Critical Care medicine manages all ICU patients, in collaboration with the primary service of record.

### **IT AND DATA MANAGEMENT**

Phoenix Children's Hospital (PCH) has a fully functioning data warehouse that combines data from over 43 discrete systems used throughout the organization. This data warehouse is complete, mature and used daily by hundreds of staff at PCH to make real-time clinical decisions that affect patient care. PCH has been able to define and utilize linking between all the data from the clinical, financial, and operational systems to discover relationships between data that are not immediately obvious to someone focused on traditional, specific, clinical datasets. This capability has supported many research initiatives through the use of not just the core clinical dataset for a patient but also all the ancillary data to help describe the patient's complete case. This ability to report in real-time and across a broad with a complete array of datasets, places PCH in a unique position to derive a complete clinical picture of the patient often outside the thinking of traditional data capture methods. This strategy has been so successful that PCH is now widening the scope of clinical data gathering to include clinical data from our affiliated community physicians with the implementation of a privately managed health information exchange between its networks of providers. This initiative allows the analysis of clinical data from a broader continuum of care for each patient and leverages PCH's data management skills in both a shared data/cloud storage solution while controlling the security and management of identifiable patient data. Phoenix Children's Hospital has a specialized skill in predictive analytics by leveraging the opportunity to analyze big data mined from our very large datasets to predict future outcomes based on past history. Using techniques and personnel from the banking and retail industry, PCH has been successful in utilizing predictive analysts to better position its resources to meet patient demand in its clinics. These same tools are now being used to analyze historical patient data to predict future patterns or events in very focused and specific scenarios. PCH classifies data work into three broad categories as defined in the figure below; data architecture, data analysis and data consumption. The data architecture role describes the collection and normalization of the data from the source systems into the data warehouse and is a core competency at Phoenix Children's. The data analysts are individuals with both data manipulation skills (SQL) and subject matter expertise of the data being analyzed. They then transform the data into meaningful information for consumption. The final role of data consumption uses an array of data visualization tools. It is focused on the subject matter expert and allows that person to quickly ask different questions of the derived dataset prepared by the analyst.

#### **SCIENTIFIC ENVIRONMENT**

Barrow at PCH places a large emphasis on teaching and research activities. There are presently over 20 research staff including research scientists, research coordinators, biostatistician, research associates, biomedical engineers, administrators, and support staff dedicated to the Neuroscience Research Division. Each division participates in training PCH pediatric residents as well as the Neurology, Neurosurgery, and Psychiatry residents from Mayo Clinic Arizona and St. Joseph's Hospital. In addition, many of the faculty are involved in teaching and mentoring medical, graduate, and undergraduate students from the University of Arizona College Of Medicine (COM)-Phoenix, Creighton University, and Arizona State University.

#### ***UNIVERSITY OF MINNESOTA, CENTER FOR ORPHAN DRUG RESEARCH (CODR)***

Major equipment in the analytical laboratory includes a Hewlett Packard series 1100 LC/MSD Mass Selective Detector system, Perkin Elmer Series 200 HPLC system with UV/Visible detector, Agilent 1100 Series HPLC system with variable wavelength detector (190-600 nm), and equipped with an 80-sample automatic injector, API-electrospray source, quaternary pump, column heater, micro flow cell, and nitrogen gas generator. The laboratory also has a state of the art ultra-sensitive Agilent 1260 Infinity HPLC system with fraction collector and three detectors; fluorescence, diode array, and UV/Visible detectors. Also available in the laboratory are a Barnstead Nanopure Diamond water purification system, Scientech SM124D analytical balance, Orion Cahn C-35 microbalance that can weigh a 250 mg sample to 1 µg or a 25 mg sample to 0.1 µg, Caliper TurboVap LV Concentration Evaporator Workstation, Branson B8510 and 1510 sonicators, Lab Companion BS-06 Waterbath, Marvel division explosion-proof refrigerator, Hettich Rotanta 460RS temperature control centrifuge, Accumet AB15 pH meter, Incubator with maximum temp for 60°C, -20°C and a -80°C freezer, refrigerator/freezer, a microcentrifuge, automatic pipettes, vortex mixers, Sentry safe to secure controlled substances and glassware.

Dr. Cloyd's laboratory has a 9 m<sup>2</sup> cell culture facility with a Forma CO<sub>2</sub> cell culture Incubator and a high performance state-of-the-art Baker SterilGARD® III Advance Class II Type A/B3 Biosafety Cabinet and Forma Scientific Cryomed tank for storage with liquid nitrogen. The molecular biology lab is equipped with a -20°C and a -80°C freezer, refrigerator/ freezer, BioTek Synergy 2 Multi-Detection Microplate Reader with Luminescence and UV-Visible Absorbance, Gen5™ Data Analysis Software, and a Take 3 Multi-Volume Plate

for nucleic acid quantitation, tabletop refrigerated centrifuge (Eppendorf 5430R) air-cooled centrifuge, max rcf = 30,130 x g (17,500 rpm), with 3 rotors; 24 x 1.5/2.0, MTP for two multi-well plates, 6 x 15 mL/50 mL, New Brunswick Innova 4230 refrigerated incubator shaker: temperature range from 20°C below ambient to 80°C, Agitation = 25 - 400 rpm, Orbit - 3/4" or 1" (1.9 or 2.54 cm) diameter orbits, Nunc plate washer, Biorad electrophoresis apparatus with dual access power source, orbital plate stirrers, automatic pipettors and chemical/fume hood.

## **COLUMBIA UNIVERSITY**

### **NEW YORK-PRESBYTERIAN HEALTHCARE SYSTEM**

The NewYork-Presbyterian Hospital (NYPH) is a 2,224 bed university teaching hospital based in New York City, jointly serving Weill Cornell Medical College and Columbia University College of Physicians and Surgeons. The Hospital provides state-of-the-art inpatient, ambulatory and preventive care in all areas of medicine at five major centers: Weill Cornell Medical College (WCMC), Columbia University Medical Center (CUMC) in Northern Manhattan, Morgan Stanley Children's Hospital of NewYork-Presbyterian in Washington Heights and on the Upper East Side, the Allen Pavilion in the community of Inwood Manhattan, and the Westchester Division in White Plains, NY. NYPH is the largest hospital in New York and employs over 5,080 physicians holding faculty appointments at one or both medical schools and more than 14,700 non-physician healthcare providers and hospital employees. NYPH is one of the most comprehensive health care institutions in the world and is internationally recognized for its outstanding comprehensive services, offering the latest advances in medical, surgical and computer technology to help ensure high quality, efficient, and cost-effective healthcare.

NYPH is also the flagship hospital of an extensive healthcare network, which consists of more than 150 participating organizations including 32 hospitals, 6 long-term care facilities, 12 home health agencies, 3 specialty institutes, and 97 ambulatory care centers. Through the NYPH Healthcare Network, the Hospital and its affiliates provide the most comprehensive, high quality services to residents of Manhattan, Brooklyn, Queens, and the Bronx, as well as Westchester, Long Island, New Jersey, Connecticut and several upstate New York counties. More than 12,000 attending physicians provide care in the System. Each System member is an affiliate of either Weill Cornell Medical College or Columbia University College of Physicians and Surgeons.

NYPH regularly ranks in the top 10 medical centers in the United States. As part of the Hospital's commitment to the total well-being of each patient, it offers a range of specialized services, as well as special health care programs for neighboring communities. Specifically, NYPH ranks fourth in the strength of its neurology programs. The clinical resources available at NYPH are outstanding, with access to expert consultants in all clinical specialties and advanced and experimental technologies in many fields of medicine. This ensures that patients with stroke enrolled in our study will receive a thorough evaluation and optimal treatment during the study period. The patient population includes a mix of both Manhattan residents and commuters admitted directly through the Emergency Department and patients transferred from adjacent municipalities, thus ensuring a highly diverse mix of racial, ethnic, and socioeconomic groups.

Research also plays an important role at NYPH. Remarkable advances have emerged from both laboratory studies and the investigations of new therapies or medicines in the clinical phase. These investigations make it possible for the physicians, surgeons, and other healthcare professionals of NYPH to offer patients more options for life-saving care and improved health than ever before at no cost. NYPH provides an optimal environment to conduct the proposed study with its clinical excellence in the management and treatment of subarachnoid hemorrhage patients and its rich academic environment promoting multi-disciplinary collaboration in clinical research to advance medical care.

### **COLUMBIA UNIVERSITY MEDICAL CENTER**

Columbia University Medical Center (formerly Columbia-Presbyterian Medical Center) is staffed by more than 1,100 attending physicians, 400 residents, and 100 visiting fellows. Each year the Center admits 45,000 inpatients to over 970 beds and handles close to 700,000 visits to its outpatient clinics, doctors' offices, and emergency rooms. The medical center functions as a level 2 trauma center, and as a community hospital for the ethnically-diverse Washington Heights section of northern Manhattan, which provides a population base for clinical studies.

Columbia University Medical Center is an internationally recognized leader in the creation of new knowledge and therapies to improve health in individuals and populations. With sponsored research totaling more than \$600 million annually, our faculty has the opportunity to pursue research that encompasses all areas of contemporary biomedical investigation and public health.



CUMC's tradition of innovation has led to significant achievements, including the first successful heart transplant in a child; Nobel-winning developments in cardiac catheterization, isolation of the first known odor receptors in the nose, and discoveries about how memory is stored in the brain; the first use of dilantin to treat epilepsy; development of the antibiotic bacitracin; creation of the Apgar score to assess newborns; identification of cystic fibrosis; design of the first significant programs to reduce maternal mortality in resource-poor countries; and the oldest program in nurse midwifery.

### **Department of Neurology; Neurocritical Care Division**

CUMC is a NYS Department of Health designated stroke center with 24 hour/day neurology and neurosurgery consultation services provided by in-house residents, and ACGME Neurovascular and UCNS Neurocritical Care Fellows. Neuro-emergency patients (stroke, TBI, cardiac arrest and status epilepticus) are admitted to an 18-bed neuro-ICU located on the 8th floor of the Milstein Hospital Building. The Neuro-ICU is staffed by a team of three attending neurointensivists and seven full-time UCNC neurocritical care fellows. Two attending intensivists and two fellows are available every day for NICU coverage and to provide urgent ED consultations. The division is also supported 3 PhD faculty members, 5 full-time research associates, and 1 international visiting scientist. The neuro-ICU has an embedded 64-slice helical CT scanner and 3.0 Tesla MR scanner, and continuous EEG and brain multimodality monitoring capability in all rooms. There are several ongoing research projects in the neuro-ICU funded with federal, private and foundation support including: the Neurological Emergency Treatment Trials (NETT), the Columbia University SAH Outcomes Project, the Brain Multimodality Monitoring Project, and programs devoted to hypothermia, systemic metabolism, and brain imaging in coma.

### **EEG**

All beds in the Neuro ICU are equipped for on-line EEG monitoring. Continuous EEG data is recorded digitally using 21 standard scalp disk electrodes placed according to the international 10-20 system affixed with collodion. In some patients, sterile sub dermal needle electrodes may be used around surgical sites, when standard scalp electrodes cannot be placed in that location. EEG is recorded using XLTEC® (Oakville, Ontario, CA) Connex™ acquisition system and software. The system records up to 32 channels of EEG, sampled at 200 Hz/channel, plus simultaneous, time-synchronized digital video. EEG electrode maintenance is performed at least twice daily by EEG technologists. Raw EEG is read at least twice daily as part of routine clinical care by an electroencephalographer. Data is processed in real-time by Xltek and Persyst (Prescott, Az) using MagicMarker™. MagicMarker™ generates displays and stores user-definable metrics based on Fast Fourier transform of the EEG signal, such as alpha/delta ratio, spectral edge, and coherence.

EEG data are stored on a central sever, with 4 terabytes of available disk memory; it is accessible for real-time review throughout the Medical Center, as well as remotely via Citrix. Processed EEG data are automatically stored in an SQL database along with time stamps, permitting correlation with logged data from other devices and monitors. As a back-up all study EEG files are also saved on a dedicated external 4 terabyte hard drive located in the PI's office.

### **3Tesla-MRI scanner**

All MRIs will be obtained on the General Electric MRI 3.0 Tesla scanner (Fairfield, CT; 16 channel receiver, 8-channel head coil for brain imaging) located on the 8th floor of the Milstein Hospital Building, inside the Neurological ICU. Vital signs including heart rate, arterial or non-invasive blood pressure, oxygen saturation and intracranial pressure of all ICU patients are continuously monitored while undergoing MR scanning. The imaging data will then be transferred through an intranet connection for analysis to the Program for Imaging and Cognitive Sciences (PICS), which is located in the basement of the Neurological Institute at Columbia University for processing. In the PICS a centralized computer network allows analysis structural and of functional imaging data. The fMRI Research Center incorporates a variety of systems with image acquisition for these purposes including the fully equipped GE workstation with tools for 3-D volume measures of anatomical structures, and functional tools for real time image reconstruction processing. Both FSL (<http://www.fmrib.ox.ac.uk/fsl/fsl/list.html>) as well as SPM (<http://www.fil.ion.ucl.ac.uk/spm/>) are routinely used for data analysis in the center. All computers are password protected.

### **Freezer**

We will be storing all patient biological samples (i.e., plasma) in our Fisher Scientific 17.3 cubic feet, -80 degree Celsius freezer (IU1786A). Included within the budget and justification are the accessories that will be needed for the current proposal: Eppendorf centrifuge tubes, freezer boxes, and labeling material. The freezer is housed in the Neurological ICU in Milstein Hospital Building, 8th floor in close proximity to where the samples are obtained in order to facilitate maintenance of protein and sample integrity.

### **Information Technology and Computing Resources**

The Department of Neurology maintains an independent, fire-walled computer intranet which provides networked services and mass data storage with automated daily tape back-up. Network traffic is monitored for security purposes. The network also provides access to the Columbia University Computing Center, which maintains a mainframe computer and statistical programs (SAS). Non-multimodality data that is collected from patients will be entered into a custom, password-protected computerized database that will be stored on the network servers. The added security and regular data backup in this internal network makes it possible to maintain a high degree of data integrity, patient confidentiality, and data loss prevention.

### **Clinical Information Systems**

The General Electric Medical Systems Information Technologies' Unity Network® is a hospital communication link for the sharing of clinical information between cardiology, patient monitoring, hospital information, and laboratory equipment. The Unity Network offers convenience and flexibility for acquiring, reviewing, and managing patient information from patient monitoring devices. The BedMasterEx system, developed by Excel Medical Electronics, uses this open architecture to acquire vital signs, alarm, and waveform data from any patient monitoring device on the Unity Network. BedMasterEx allows researchers to update a SQL database automatically and in real-time. All multimodality data (except EEG data) is stored on the BedMasterEx system.

### **Data Server**

MS SQL database running on an independent server, with 2.0 TB SCSI RAID disk storage. These data will be backed up to a 2 TB SATA disk storage device on the same server and an enterprise-wide archival tape storage system is also available. As an additional level of security all monitoring data including the digital EEG files will be backed up bi-weekly on a completely separate RAID server located in the PIs office.

### **Data Time Synchronization**

BedMasterEx can communicate with the Unity Network's Time Master and ensure the correct synchronized time on the Unity Network by using a Network Time Protocol (NTP) server to update its own system clock. NTP is a protocol that accurately synchronizes the time on computers around the world.

### **Data Sampling Rates**

Digital data is acquired and stored every five seconds, waveform data is acquired every two seconds, and 'pointers' to binary files of waveforms data are stored providing a maximum resolution of 240 Hz.

### **Office**

The PI of the study has his own office located on the same floor as the Neuro-ICU at Milstein Hospital 8 Center, Room 300, 177 Fort Washington Avenue, New York, NY 10032.

### **Computer**

Dr. Claassen has a personal computer in his office (OptiPlex 755 Minitower, equipped with an Apple cinema 30" high resolution monitor for image and multimodality monitoring analysis and EVGA e-GeForce monitor graphics card). He also has access to word processing and basic statistical analysis software needed for the completion of the project including Microsoft Office, End-Note, SPSS, SAS, and SQL. Should he receive funding, he will purchase MATLAB. Statistical analysis is usually performed in SPSS or SAS. Daily incremental backups are done to insure that there is no accidental loss of data.

The Irving Institute for Clinical and Translational Science The Irving Institute for Clinical and Translational Science (CTSA) aims to transform the culture of research to hasten the discovery and implementation of new treatments and prevention strategies. The core objective is to move the CUMC research community to a more multi- and interdisciplinary scientific mindset by removing barriers and creating incentives for interactions among investigators from different disciplines. The resources provided by the Irving Institute offer support in biomedical informatics, study design and biostatistics, bioethics, regulatory issues, core laboratory facilities and a fully-staffed Clinical Research Center for investigators across campus. Core resources relevant to this submission include the Biomedical Informatics Resource, Design and Biostatistics Resource. The Irving Institute's headquarters occupies the entire 10th floor of two connected buildings, the Presbyterian Hospital and the Harkness Pavilion. The total space occupied is approximately 25,000 square feet. The administrative center occupies 1,211 square feet at the center of the overall space.

Additional resources of relevance to this submission at CUMC include The Mailman School of Public Health, which provides training and resources devoted to research methodology and statistics (see below); The Neurological Institute of New York, a clinical alliance between neurology, neurosurgery, and neuroradiology; and the Gertrude Sergievsky Center for Epidemiology. All these facilities actively participate in the design and implementation of laboratory-based and clinical neuroscience research studies. Between these entities there are a total of 115 faculty members who participate in clinical research.

### **Library**

The Hammer Health Sciences library is located across from the Neurological Institute of New York and houses a large collection of books and journals relevant to the neurosciences.

### **THE UNIVERSITY OF MELBOURNE (UM)**

The University of Melbourne is the #1 ranked Australian institution on the Times Higher Education Ranking (33rd worldwide) and the Shanghai Jiao Tong rankings (43rd worldwide). The University of Melbourne Parkville Precinct is one of the largest and most productive neuroscience hubs worldwide. The O'Brien's laboratory is located at the University of Melbourne's new state-of-the-art Neuroscience building, the Melbourne Brain Centre. The research environment at the Melbourne Brain Centre is both ideal and necessary for this project as it offers full access to advanced in vivo neuroimaging, behavioral testing, EEG, immunohistochemical, and molecular facilities.

**Epilepsy and Neuropharmacology Laboratory:** This laboratory (~100 sqm) has successfully developed and optimized a facility for studying a variety of rodent models of epilepsy (e.g. amygdala kindling, GAERS, post-kainic acid status epilepticus, post-traumatic, post-stroke, cerebral tumor-associated epilepsy) and traumatic brain injury (fluid percussion injury, cortical contusion, weight drop and repeated concussions). The laboratory has extensive published experience in discovery and drug development research using these models. The laboratory has the capacity for prolonged video-EEG monitoring of up to 60 rats/mice simultaneously, as well for chronic drug administration via a variety of routes (icv/iv/sc) including capacity for continuous or intermittent dosing regimens. There are also electrophysiology rigs for in vivo and ex vivo single cellular and optical studies, a full range of histological and immunohistochemistry facilities, stereological microscopy, confocal microscopy and molecular biology including rtPCR, Western Blotting, in-situ hybridization.

**The Small Animal MR Facility:** The Small Animal MR facility in the Florey Neuroscience Institutes, University of Melbourne, is equipped with a 4.7 Telsa Bruker BioSpin magnet upgraded to the *Avance III™* platform. The system consists of two broadband transmitter channels and eight broadband receiver channels for multi-coil phased array coil imaging applications. In addition to volume and single surface coils for rat brain imaging, a 4-channel phased array receive-only coil with geometrical shape adapted to the rat head is available for an optimal homogeneity and sensitivity of the radiofrequency excitation field. The system is configured with Paravision 6 software including packages for parallel imaging, spiral imaging, echo planar diffusion imaging, and susceptibility weighted imaging. Physiological monitoring of animals is carried out using a PowerLab 8-channel recording system to measure ECG, arterial blood parameters, and temperature. Rat models can be ventilated using a Columbus CIV-101 ventilator and anesthesia can be delivered via inspired gases, intravenous, intramuscular or intra-peritoneal routes. Rat models are monitored continuously throughout experiments with core temperature maintained using a heated water pad placed under the animal. Comprehensive image analysis software is available for post-processing including Matlab and Paravision analysis tools, and most commonly used open research based software packages (eg. Mricro, FSL, SPM, MRtrix, MRStudio).

### **UNIVERSITY OF MARYLAND**

#### **Clinical Facility**

The R Adams Cowley Shock Trauma Center (RAC STC), located at the University of Maryland Medical Center in downtown Baltimore, cares for over 8,500 injured patients each year. By Maryland State legislation, RAC STC is "is the core element of the state's emergency medical system" and serves "...as the state's primary adult trauma clinical resource center." RAC STC is a free-standing dedicated trauma hospital and provides the highest level of care for critically ill and injured patients in the state. RAC STC is also the Specialty Referral Center for the State of Maryland for Neurotrauma and Hyperbaric Medicine. Trauma Center has several unique facilities through which our core mission is accomplished:

The University of Maryland School Epilepsy Center is the clinical site that will perform the EEGs for this project. This center provides care to adults and children with epilepsy and seizures and serves approximately 2,000 individuals annually with epilepsy, seizures, and related neurological disorders. The

Maryland Epilepsy Center at the University of Maryland is one of only two major centers in the Central Maryland region providing comprehensive care to people with epilepsy and seizures and support to their families. Among the center's member staff are 7 physicians (Jennifer Hopp, MD, Acting Director of the Division, Allan Krumholz, MD, Elizabeth Barry, MD, Tricia Ting, MD, Cha Min Tang, MD, Ana Sanchez, MD, and Arif Kabir, MD), with special expertise in adult clinical epilepsy, two Research Nurse

Coordinators (Karen Callison, RN and Virginia Ganley, RN), Epilepsy Clinical Nurse Coordinator (Helga Matausch, RN), a Neuropsychologist (Lynn Grattan, PhD), and a Research Assistant and Database Manager (Jing Zhu, MS). Our Database Manager supervises the input, analysis and retrieval of data for our clinical and research databases. Our Division also includes a Neurosurgeon with expertise in Epilepsy Surgery (Howard Eisenberg, MD), Pediatric Neurology Faculty (Alpa Vashist, MD), 11 EEG Technicians, and 3 Clinical Neurophysiology and Epilepsy Fellows.

### **Research**

The Shock, Trauma and Anesthesiology Research organized research center (STAR-ORC), is a worldclass, multi-disciplinary research and educational center focusing on brain injuries, critical care and organ support, resuscitation, surgical outcomes, patient safety, and injury prevention. It is the first research center in the nation dedicated to exclusively to the study of trauma, its complications, and prevention. Originally established by Congress as the Charles "McC" Mathias, Jr., National Study Center for Trauma and Emergency Medical Systems, the center was designated an organized research center at the University of Maryland School of Medicine in 2007. The Shock, Trauma and Anesthesiology Research Center serves as a research umbrella for the program in Trauma and the Department of Anesthesiology. Many of the researchers working in the new research center are doctors who care for trauma patients at the University of Maryland's R Adams Cowley Shock Trauma Center. The STAR-ORC mission is to facilitate translational research in areas related to trauma, tissue injury, critical care and anesthesiology. The Shock Trauma research program aims to become the benchmark for national and international trauma research that addresses fundamental and major issues of injury in its broadest sense affecting prevention, patient care, delivery of care issues, public policy and financing of trauma care and systems of care. The Shock Trauma Research Committee reviews all research protocols for scientific merit and feasibility prior to Institutional Review Board (IRB) submission. Each trial must be approved by the IRB prior to implementation. The research program centers around the following:

- clinical research trials
- serving as a testbed for emerging technologies
- developing collaboration with the Air Force through its C-STARS-MD (Center for the Sustainment of Trauma And Readiness Skills) program based at the Shock Trauma Center (and other branches of the military)
- collaboration with the National Study Center on public policy initiatives.

Clinical research trials center on prospective and retrospective studies on resuscitation and treatment of the injured. The Shock Trauma Center serves as a testbed for emerging technologies such as telemedicine initiatives and military field testing of resuscitation and other clinical technology. The RAC STC also utilizes a 24/7 clinical research staff that screens all admissions to the Shock Trauma Center for eligibility into UMB IRB approved, on-going studies. This staff is composed of clinical research assistants and clinical research coordinators. They work in concert in university investigators in conducting clinical research at RAC STC and are responsible for screening, determining eligibility, consenting and enrolling participants, and data capture and collection.

The Epilepsy Clinical Research Center was developed and expanded recently to evaluate the treatment and outcomes of all the patients admitted to our center. A comprehensive computer database includes approximately 2,000 patients dating from 1989 to the present and currently is being utilized for research projects to assess clinical outcomes in epilepsy surgery patients as well as psychogenic seizure patients, among other ongoing investigations. Our database manager, Jing Zhu, MS, supervises the input and analysis of clinical and research data, and has basic knowledge in statistical analysis. She has a joint appointment with epidemiology as well as neurology and has expertise in database information systems in both fields.

## **UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES**

All of the facilities and major equipment needed to carry out this project are available in the Department of Anatomy, Physiology and Genetics at USUHS. The PI's lab consists of two rooms, 420 sq ft each, and adjacent core facilities including a dedicated cell culture lab (200 sq ft), radioisotope lab (200 sq ft), large equipment lab (200 sq ft), computer/data analysis lab (200 sq ft) and a large walk in cold room/freezer. Collectively, these labs are equipped with all of the routine instrumentation necessary for carrying out research in biochemistry and cell and molecular biology. This includes: electrophoresis equipment and power supplies for Western blot and isoelectric focusing (Novex & Pharmacia), precision temperature circulating water bath,



standard water baths, pH meter, polytron homogenizer, sonicator, table top microcentrifuges, 4oC chromatography chamber, -20oC freezers, -70oC freezers, dissecting microscopes, standard and inverted microscopes, balances, McIlwain tissue chopper, laminar flow hood, tissue culture incubators, a multi reagent dispenser/reader system (Dynes Technology, VA) for automated enzyme assay, Speedvac Concentrator, Table Centrifuges, Heater Block, Ultra Pure Water Purification System, Sonicator, Olympus IX71 Microscope with Fluorescent Filters and Objectives attached to Spot Digital Camera, Microscope Light Sources, Balances, Perkin-Elmer 1420 Victor2 Multilabel Counter for Fluorescence and Luminescence, iBlot Invitrogen gel transfer system, Star Life Sciences Mouse OX Small Animal Oximeter, computers, workstations, monitors.

**Office:** The PI has a private office (100 sq. ft.). The department employs four full time secretaries who provide support within the department.

## **UNIVERSITY OF BRITISH COLUMBIA (UBC)**

### **Resources and Environment**

The lab environment consists of ~ 3,500 sq.ft of wet lab space including separate rooms for tissue culture (2 hoods), whole cell and brain slice electrophysiology (4 rigs) and light microscopy. The main lab space consists of 5 twin wet benches with a desk at each for trainees to work on their notes, computer, etc. Other shared benches include equipment for qRT-PCR (2 instruments), DNA sequencing (Illumina), and protein and molecular biology manipulations. There are 3 chemical fume hoods including a 1.5-person glovebox equipped with a parallel synthesizer. Other chemical synthesis resources include an Agilent 6100 series of Single Quadrupole LC/MS system, a Beckman Coulter P/ACE MDQ Capillary Electrophoresis instrument, high-pressure reactions vessels, and a Biotage Isolera One automated flash column chromatography instrument. Current personnel include three Research Associates each with between 6 to 10 years of experience after their PhDs, two lab technicians, three graduate students, one postdoctoral fellow and three undergraduate/coop students.

### **Shared and Fee-for Service Analytical Facilities**

The Department of Chemistry offers a number of analytical services for compound purity and structural characterizations. These include:

Capillary electrophoresis chromatograph, Circular dichroism/optical rotary dispersion (CD/ORD) spectrophotometer, Fluorometer, Fourier transform infrared spectrometer (FTIR) with attenuated total reflectance (ATR), Gas chromatograph (GC) with flame ionization detector (FID) and thermal conductivity detector (TCD), Gas chromatograph-mass spectrometer (GC-MS), Laser-induced resonance-enhanced multiphoton ionization-TOF-mass spectrometer (REMPI-TOF-MS), Liquid chromatograph-mass spectrometer (LC-MS), Nuclear magnetic resonance spectrometer, Polarimeter, Thermogravimetric analyzer/differential scanning calorimeter (TGA/ DSC), Ultra-high-performance liquid chromatograph (uHPLC), and three UV/Vis spectrophotometers – one with NIR capabilities.

## **UNIVERSITY OF CALGARY**

### **Scientific environment**

The Project Coordinating Committee (PCC) co-led by Dr. Jetté is fully qualified to successfully conduct the proposed research designed to advance participatory action research and accelerate knowledge transfer in civilian and non civilian (veterans) patients with Traumatic Brain Injury (TBI) at risk to develop epilepsy or after epilepsy has occurred. The PCC will oversee and drive the activities of the Core, organize working groups and supervise the student and research assistant in accomplishing the proposed tasks. The partners in the Core will work together toward the goals, contribute to ongoing adjudication of the project's progress, provide feedback and critical assessment to accomplish the aims and assessing the implementation of identified knowledge transfer strategies with the ultimate goal to successfully design and complete clinical trial of prevention therapy or disease modification in TBI and epilepsy.

Jointly, the Departments of Community Health Sciences (CHS) and Clinical Neurosciences (along with the University of Calgary Hotchkiss Brain Institute and Institute of Public Health) have a number of training opportunities and seminars delivered by expert researchers that can be accessed by the graduate student/postdoctoral fellow, research assistant and even made available to the PCC and working group members via webinars held through the University of Calgary. Examples include effective methods for patient engaged research and knowledge translation strategies. Furthermore, the team can capitalize on the resources and

expertise made available through the newly created SPOR Unit (Supporting Patient Oriented Research) at the University of Calgary.

Another important resource Dr. Jetté and her team can access is the Ward of the 21<sup>st</sup> Century (W21C), a “not-for-profit research and innovation initiative based at the University of Calgary and the Calgary zone of Alberta Health Services. W21C serves as a research and beta-test-site for prototypical hospital design, novel approaches to health care delivery, human factors research and innovative medical technologies.”

Dr. Jetté’s team has extensive experience with the proposed methodology included in the Public Core Engagement Proposal (participatory action research, survey design and administration, usability testing, focus groups, etc.).

### **Computers**

Equipment includes office computers (Windows and Mac OsX) with appropriate software (MS Office, Adobe Acrobat, Photoshop, Endnote, SAS, Stata, Stat Transfer etc.), available for every member of the team. Access to internet is available to all members of the team.

### **Offices**

Each investigator has a fully equipped office in their respective institution. Office space is available for the student in Dr. Jetté’s laboratory.

## **UNIVERSITY OF CALIFORNIA, LOS ANGELES (UCLA)**

**Seizure Disorder Center Animal Laboratories:** Animal study areas are located in RNRC rooms 2253 (12 m<sup>2</sup>), 2253A (10 m<sup>2</sup>), and 2253B (17 m<sup>2</sup>) that form a three room suite with an adjoining interior door to room 2243 (19 m<sup>2</sup>) with an adjacent storage room (5 m<sup>2</sup>). Hallway access is limited to rooms 2253 and 2243 so that experimental isolation is available for the two interior recording rooms (2253A & B). Room 2253 contains a digital video review station and EEG data analysis and is the office to Mr. Joyel Almajano, Staff Research Associate III. In addition, room 2136 (28 m<sup>2</sup>) is used for both chronic and acute in vivo experiments. Room 2243 is used as a surgery room and contains facilities for animal care, as well as a workbench with dissecting scope for microelectrode preparation. We currently have seven setups each with 16-channel capacity for chronic electrophysiological experiments, one dedicated setup for intracellular recordings on anesthetized rodents with ability to label recorded cell with neurobiotin, and another setup for whole cell intracellular recordings in living tissue slices. Animals are maintained in the vivarium on the 6th Floor of the Brain Research Institute where there is a second 24-hour infrared video monitoring system. Here we are currently capable of monitoring 16 rats housed in individual cages using a 4-channel, high-storage capacity DVR.

**Offices:** Key personnel directly involved with this research are located in RNRC as follows: Richard Staba, PhD in room 2155, Anatol Bragin, PhD in room 2147, and Jerome Engel, Jr., MD, PhD in room 1250. Offices for postdoctoral students are located in 2144 directly across the hall from Drs. Staba’s and Bragin’s offices.

**UCLA Brain Mapping Center:** Located in the David Geffen School of Medicine at UCLA the Brain Mapping Center houses a Bruker Biospin a 7.0 Tesla magnetic resonance imaging/spectroscopy instrument with a clear bore diameter of 30 cm and is staffed by a full time lab manager. Three gradient systems are included: (1) BGA-20: 200 mm inner diameter with a maximum gradient strength of 200 mT/m. (2) BGA-12: 116 mm inner diameter with a maximum gradient strength of 400 mT/m (3) BGA-6: 60 mm inner diameter with a maximum gradient strength of 950 mT/m. A range of radiofrequency receive and transmit volume quadrature coils and receive-only or receive-transmit surface coils are available for use with these systems. A mouse 4-channel phased array coil is also available. These options support the full spectrum of modern neuroimaging techniques including structural MRI, functional MRI, perfusion MRI, diffusion tensor MRI, and multinuclear MR spectroscopy for imaging rats and mice. The system runs off a Linux-based consoles running Paravision v6.0 or v5.3. While the instrument is optimized for neuroimaging studies it is also be capable of imaging other body areas in rodents, including the heart and visceral organs. Full physiological monitoring is possible including core temperature control, heart and ventilation rate, end-tidal PCO<sub>2</sub> and non-invasive blood pressure. The instrument is installed in a space occupying 50 m<sup>2</sup> located in the Brain Mapping Center. A full surgical suite is available in the adjoining room with a surgical microscope and downdraft air exhaust table. Both surgery and magnet rooms are equipped with isoflurane gas anesthesia equipment. Offline image processing is achieved on a dedicated Linux workstation with 0.75Tb of raid 5 storage space and 2GB of RAM and on Macintosh computers within the Brain mapping Center. The MR unit is available for use by UCLA-affiliated investigators who have research studies that require imaging of animals.

**Computers:** A 12-core/24-CPU Linux workstation with 48G of RAM and 12TB disk memory and 30TB backup is used for all neuroimaging analysis and is administered by Dr. Harris. It is equipped with all standard imaging

and statistics software (FSL, SPM, AFNI, MATLAB, R) as well as a grid-engine, job submission queue for parallel, high through-put analysis. Supercomputing resources are also available through the UCLA Hoffman Cluster which has 256 nodes for general campus computing but many more nodes available for special jobs.

**Harris Laboratory:** Dr. Harris shares laboratory space within the UCLA Brain Injury Research Center (BIRC), which has developed a core basic laboratory facility for use by all BIRC investigators (Drs. Giza, Glenn, Harris, Hovda, Prins, Sutton). The BIRC laboratories are within the Department of Neurosurgery and consists of multiple rooms totaling 279 m<sup>2</sup>, including separate lab space for the following procedures: Animal surgery with two surgical areas, each equipped for isoflurane anesthesia and a surgical microscope; Necropsy/perfusions with equipment for tissue harvesting, a perfusion hood and two cryostats; A wet lab equipped for studies on molecular biology (protein and RNA analysis, ELISA or spectroscopy); Two histology rooms, one with a fume hood; Two rooms for microscopy/image analysis, one containing a Leica upright vertical and Zeiss M2.

Axiomager (both interfaced with MicroBrightfield Stereology Software System) and one containing a Zeiss confocal microscope; Two rooms for behavioral testing with tracking software; A darkroom, with developer for X-ray films.

## UNIVERSITY OF CAMBRIDGE

The Acute Brain Injury (ABI) Program at the University of Cambridge is based in the Neurosciences Critical Care Unit (NCCU) and the Wolfson Brain Imaging Centre (WBIC; <http://www.wbic.cam.ac.uk/>). The WBIC provides a 3T and a 7T research MR system and a PET-MR scanner adjacent to a state-of-the-art 23-bedded neurocritical care unit (NCCU), which has over 900 admissions a year, and is the ICU for a single Major Trauma Centre covering a population of over 3 million. Patients in the NCCU are cared for using protocol driven therapy, which is guided by multimodality monitoring including intracranial pressure monitoring, brain oximetry, and cerebral microdialysis. We are currently in the process of integrating EEG monitoring into this setup.

Our research is funded by the European Commission FP 7 Program, National Institute for Health Research (UK), Wellcome Trust, and Medical Research Council; and addresses acute and chronic TBI, coma, and the vegetative state, using PET and MR (including Diffusion Tensor Imaging, MR spectroscopy and functional MRI) and to explore regional heterogeneity in pathophysiology in the injured brain, and examine its outcome impact in terms of tissue fate (<http://www.medschl.cam.ac.uk/anaesthetics/research/acute-brain-injury/>). Our research focuses on characterizing pathophysiology and relating it to outcome. A complementary theme of work employs multimodality bedside monitoring, and provides the substrate for a research program, embodied in an innovative software platform (ICM+; <http://www.neurosurg.cam.ac.uk/pages/ICM/about.php>). Derived indices of cerebrovascular physiology developed by the ICM+ collaborators are now being used globally to personalize therapy in patients with intracranial hypertension. In a closely allied program of research, a group in Computational Critical Care Physiology (C3P), aims to use non-linear signal processing to explore pathophysiology and drug effects. Members of our group have leadership roles in large international projects such as CENTER-TBI (a €30 million European comparative effectiveness and precision medicine study; [www.center-tbi.eu](http://www.center-tbi.eu)), and randomised controlled trials such as an international trial of decompressive craniectomy in acute subdural haematoma (<http://www.rescueasdh.org/>), which is nearing completion. Since 2000, the ABI Group have published over 500 indexed publications, and been lead applicants or co-applicants on successful research grant applications exceeding \$50 million.

## UNIVERSITY OF CINCINNATI MEDICAL CENTER

### **Clinical Facilities**

The University of Cincinnati Medical Center is the only Level 1 Trauma Center in the Greater Cincinnati area. Treatment of head trauma occurs under the direction of the Neurotrauma service, directed by Dr. Norberto Andaluz, and the Neurocritical Care Service, staffed with 8 dedicated Neurointensivists along with a team of Neurointensive Care Fellows and specially trained critical care nurses and respiratory specialists. The Neuroscience Intensive Care Unit has over 20 beds and we treat over 350 brain trauma patients in the intensive care unit each year. A new 3T MRI scanner is available for use to perform necessary MRI studies along with certified radiology technologists with experience in MRI techniques.

The standard of care in the Neuroscience Intensive Care Unit includes 24/7 continuous EEG monitoring, multimodality monitoring featuring intracranial pressure monitoring along with brain tissue oxygen, regional cerebral blood flow, and depth EEG recordings. Advanced neuromonitoring is time-locked with standard physiologic measurements and interpreted by board-certified Neurointensivists. All waveform and discrete physiologic data is stored on a University network drive.

The Department of Neurosurgery has a Division of Clinical Trials, with 4 full-time clinical study coordinators and 2 full-time administrative and regulatory assistants. Presently the Department participates in ~17 ongoing clinical trials, in addition to ~20 other clinical studies (e.g. retrospective chart reviews). The Department also has a Division of Medical Communications, with 3 full-time medical illustrators and 1 full-time editor. Professional journal subscriptions, computers and office supplies, and administrative and secretarial support are also provided.

### ***Office & Data Handling***

Dr. Foreman has dedicated office space (150 sq ft) that is fully networked, equipped with a telephone line, computer, and printing equipment and space for small meetings. A library in the department's space can accommodate large meetings of 6 and 20 persons, respectively. Laboratory space is available via Dr. Jed Hartings within the Department of Neurosurgery, and are located in the Medical Science Building and near administrative supplies, personnel and equipment. Moreover, the Medical Science Building is connected to the Medical Center, so that Department of Neurosurgery offices are a 3-min walk to the Neuroscience Intensive Care Unit.

Dr. Foreman and Dr. Hartings along with research staff have dedicated networked computers with extensive software installations for data analysis and manuscript preparation. In addition, several networked shared-use computers are available in the PI's laboratory space for data handling and manuscript preparation. Laboratory facilities include a network attached storage drive for digital storage of up to 3 terabytes of clinical monitoring files; this drive is backed up by a duplicate drive in a separate, second building. Support for hardware/software issues and networking problems is available during normal working hours.

### ***UNIVERSITY OF EASTERN FINLAND (UEF)***

The Pitkänen and Gröhn laboratories are located in the same building (3rd and 4th floor) at the A.I.Virtanen Institute for Molecular Sciences (AIVI) in the University of Eastern Finland, the 3<sup>rd</sup> largest University in Finland with neurosciences as a strategic focus area for research. AIVI is one of the five highly research-oriented biocenters in Finland, with teaching focus on post-graduate training. MRI facility is in the 1st floor of the same building as laboratories, and the underground tunnel connects the MRI unit with the animal facility where EEG monitoring laboratories are located. All facilities described are within 600 feet radius from each other.

**Functional Neuroanatomy Laboratory (Pitkänen lab):** Fully equipped histology and molecular biology laboratory (40 m<sup>2</sup>) with microtomes and cryostats. Three microscopy rooms (each 12 m<sup>2</sup>), including microscopes with brightfield, darkfield and fluorescence optics and analysis software; Zeiss microscope equipped with apotome. Confocal and multiphoton microscopes are available on-need basis. All facilities are available for the project full time.

**Animal Facility:** Separate laboratories for 1) surgical operations (8 m<sup>2</sup>), 2) video-EEG monitoring (two rooms, each 12 m<sup>2</sup>), including 5 video-EEG monitoring units (32 channels each), 4) behavioral testing (2 rooms, 12 m<sup>2</sup>), and 5) perfusion (8 m<sup>2</sup>). All these are located in the UEF Animal Center. Importantly, animals can be transferred from the animal center to imaging unit and back via underground tunnel, which is critical for chronic imaging follow-up studies to maintain the best possible animal well-being. Animals are taken care by the staff of Animal Center.

**Induction of TBI animal model, video-EEG analysis (Pitkänen lab):** Lateral-fluid percussion injury device, 5 video-EEG monitoring units (each can monitor 6 rats with 4 channels at a time), five licences for nervus EEG analysis software (installed on computers).

**MRI facility (Gröhn lab):** MRI systems are located in the Biomedical Imaging Unit (~60 m<sup>2</sup>) of the A.I.Virtanen Institute, which also serves as National Core Facility for experimental MRI (Grohn is the director of the facility). Imaging facility is part of the Animal Center which enables long term follow-up studies of experimental animals. There is a dedicated space for micro surgery of the rodents.

Three experimental MRI systems are located in the Biomedical Imaging Unit). Large bore horizontal 9.4T/31 cm magnet is currently interfaced to two different consoles: Bruker Biospec and Agilent DirectDrive and is equipped with two gradient sets, 4 receiver channels and large number of RF-coils including actively decoupled 4-channel receiver coil optimized for rat head. In addition we have horizontal 7T/16cm Bruker PharmaScan MRI system and a vertical 9.4 T/89 mm Varian DirectDrive micro-imaging system. All the pulse sequences and analysis software described in research plan have been implemented and either used in our previous studies or thoroughly tested.

The facility is equipped with microsurgery unit and extensive MRI compatible physiological monitoring instruments including respiratory and cardiac gating unit, blood pressure monitoring, pulse oximeter, capnograph, blood gas analyzer and MRI compatible EEG (Brainamp).

**Computer:** In Pitkänen lab: 16 computers for routine office work with all necessary software for word processing, image analysis and processing, preparation of presentations, and statistics (all bought within past 3 years); Five licences for nervous EEG-analysis software. In Gröhn lab more than 15 computers equipped with MRI analysis softwares (SPM, FSL, LC model, MATLAB), including a Linux server with 2 processors (6 cores/processor, 2 threads/core), with 96GB of memory. Access to several servers in the national supercomputing facility at Center for Scientific Computing (CSC) if large datasets or excessive computing recourses are needed.

**Data storage:** A secure private cloud will be installed and used as a temporary repository for all data acquisition. Six systems gathering EEG data in Lab Animal Centre will be connected to University of Eastern Finland (UEF) private cloud. All research group members will be able to store and access the data via UEF local area network (LAN) connection and perform the analysis on their personal computers. The data will remain in the private cloud as long as analysis is completed, after which the data will be moved into a long-term storage to CSC IDA service. Additionally, the data will be backed-up to magnetic tape cartridges to ensure data security. MRI data will be stored in an existing file server (Synology DS509+ NAS server with 10TB of space, 5 disks in a stack, RAID 6) that can be accessed via LAN connection from magnet consoles, computing servers, and personal computers. The data will be backed-up into magnetic tapes as a means of long-term storage after the project completion.

**Office:** In Pitkänen lab 6 office rooms (four 16 m<sup>2</sup>, two 20 m<sup>2</sup>). In Gröhn lab: 5 office rooms (16-20 m<sup>2</sup>each).

**Other:** University Computer Center (on need basis). Bioinformatics Center (on need basis). Library with Electronic Journal Collection (fully available)

## UNIVERSITY OF MIAMI

The University of Miami/ Jackson Memorial Medical Center ( UM/Jackson;approx. 70 acres) is ranked as one of the nation's top medical centers and the largest in the Southeastern United States.

UM/Jackson's 650 faculty physicians are involved with approximately one million patient visits annually in more than 30 specialty areas and primary care medicine. The medical center provides a regional resource for specialty care for transplantation, critically ill newborns, burn victims, trauma patients , patients needing comprehensive cancer care, and many other services. UM/Jackson houses a number of health care services that support and foster research and knowledge development. Among these are: The Bascom Palmer Eye Institute- world renowned for advanced patient care, research and education in ophthalmology; the Cerebral Vascular Disease Research Center- one of the top three research centers in the world and the longest funded program in the United States; and the Miami Project to Cure Paralysis- a multidisciplinary basic science and clinical research effort dedicated to finding the cure for paralysis resulting from spinal cord injury. The Miami Project found the first direct evidence of successful regeneration of adult human central nervous system tissue.

### Miller School of Medicine

The Miller School of Medicine is in the top third of medical schools in the country in terms of research and sponsored projects. Biomedical research is a top priority for the institution with more than \$ 126 million in research funding supporting close to 1,000 research projects. The medical Schools 1000-plus full time faculty members and an additional 400 research personnel conduct clinical and basic science research crossing all disciplines, from epidemiology and pediatrics to HIV- AIDS, psychiatry and the neurosciences. Jackson is the primary teaching hospital for the University of Miami School of Medicine and a major referral/ tertiary care center for south Florida.

### Department of Neurology

The Department of Neurology at the University of Miami's Miller School of Medicine is one of the largest clinical neuroscience departments in the nation. It is widely recognized as an international referral center where neurologists from Latin America, Florida and the rest of the United States turn to for expertise in solving complex neurological problems. The department is comprised of clinical and research laboratories and research centers such as the Kessinnich Family MDA ALS center which provides information and care to ALS patients and their families using a multidisciplinary approach. The department is also home to the neurovascular laboratory where researchers perform ultrasound studies in cerebral hemodynamics using ultrasound techniques. Furthermore, clinical and basic research of the human brain is conducted at the Brain Endowment Bank which studies Parkinson's disease, drug addiction and aging. The department's sleep disorders center provides a wide range of services to individuals with sleep related disturbances.

#### **Clinical Research Building**

The University of Miami's Clinical Research Building is comprised of 15 floors ( approx. 259,018 departmental gross sq. ft.) The building is organized with both research space and clinical core space designed for interactions with human research subjects. The core research team and Neurology faculty will occupy the 13<sup>th</sup> floor (approx. 17,500 sq. ft.). Three floors in the new building are dedicated to human subject research activities and each floor will contain a combination of space and exam/interview/consent rooms. A dedicated research pharmacy, a clinical laboratory, and a physiological evaluation/assessment suite are also part of the core research space. Equipment and furnishings in each of the core research floors can be customized depending on individual research needs. In total there will be over 130 direct encounter spaces within the core floors.

#### **Computer infrastructure**

Several computer work stations are available in the office space provided in the newly established clinical research building at the Miller School of Medicine. All principal investigators and coordinators have their own PC in addition dedicated printers are available to all research teams. The Biomedical Informatics department provides servers and data to center facilities with sophisticated firewall protections, hardware redundancy and back up storage of data. Personal and share directories are maintained in secured servers and allow researchers to exchange information in a secure environment.

#### **Neuroscience Intensive Care Unit:**

A 24 bed Neurointensive Care Unit, one of the largest in North America, is located in West Wing 8 of Jackson Memorial Hospital. It is staffed by four full time neurointensivists who lead a team of fellows and residents providing 24/7 on call coverage for the ICU. The neurocritical care team works closely with the neurosurgical and neurology teams to provide high quality clinical care and carry out clinical research. The ICU is equipped with a portable CT scanner, continuous EEG monitoring, brain oxygen monitoring, and cerebral microdialysis techniques.

#### **Major Equipment:**

EEG: The Neuroscience ICU has dedicated cEEG monitoring systems ( XLtech) which enables the routine use of cEEG monitoring for patients with traumatic brain injury.

### **YALE UNIVERSITY**

**Level 1 Trauma Center and Trauma Program:** Yale-New Haven Hospital is a Level 1 trauma center with an integrated trauma and neurocritical care service. Joint patient treatment occurs under the direction of Dr. Kevin Sheth (head of the Neurosciences ICU) and Dr. Kimberly Davis (head of Trauma Surgery). Our services see more than 1200 TBI related admissions a year of which more than 100 have moderate to severe TBI.

**Trauma-Surgical and Neuroscience Intensive Care Units:** Between our two services, we have 36 beds. Our state of the art Units feature continuous EEG monitoring capabilities at each bed, a high bandwidth data network with data capture routed via a data acquisition system using Moberg and Natus acquisition systems. A dedicated team of 110 Neuroscience ICU and TSICU nurses as well as fellows, resident and mid-level providers care for all TBI patients. Our facility has the ability to perform Multimodality monitoring using cEEG, depth EEG, cerebral microdialysis, Hemedex CBF, Brain tissue oxygen as standard of care with nursing documentation and nursing protocols derived to facilitate the monitoring.

**Continuous EEG Systems:** Each ICU bed is capable of performing 32 channel monitoring including scalp and depth data inputs. Permanent terabyte storage is located in on hospital maintained encrypted network servers. If we can finalize our protocol for strip electrode recordings for CSD, special amplifiers will be used for data acquisition (see Hartings 2009). We have a dedicated Critical Care EEG service that systematically reads the EEGs of all ICU patients using the ACNS nomenclature.



**Citrix Server Access:** All EEG and physiologic data collected by Moberg can be reviewed via our hospitals Citrix server, thus allowing each investigator to interface with the data repository.

**Biorepository:** Patients with acute brain injury are offered enrollment in our biorepository that not only aims at collecting early biologic specimens and clinical data, but also completes discharge and follow-up assessments on all patients enrolled.

## **UNIVERSITY OF PITTSBURGH**

### **Laboratory:**

Dr. Bell is an Associate Director of the Safar Center for Resuscitation Research (3434 Fifth Avenue, Pittsburgh, PA, a freestanding research building). The Center includes two floors and over 20,000 sq. ft. of laboratory–office–and animal research space. The first floor houses a fully equipped molecular biology laboratory which has been expanded this year to over 5,000 sq.ft. and is available for Dr. Bell's use.

### **Clinical:**

The Children's Hospital of Pittsburgh of UPMC is a newly renovated, state-of-the-art facility with 296 licensed beds (over 50 devoted to care of critically ill children). The facility is staffed by over 15 Pediatric Critical Care M.D. Specialists, over 200 Critical Care Nurses. The Pediatric Neurotrauma Center has 300 sq ft of office space available for data collection and analysis. Approximately 40 children with severe TBI are admitted to our institution per year and are available for clinical studies.

### **Animal:**

Dr. Bell has laboratory space within the Safar Center for Resuscitation Research. He has been allocated 500 sq feet of bench space and shares operating room space with the other investigators within the Center. There are multiple rooms within the Safar Center for rat and mouse breeding and housing within the Safar Center. There are shared equipment for microscopic analysis and tissue processing at the Center.

### **Computer:**

There are several computers for clinical research within the Pediatric Neurotrauma Center at CHP. Additionally, there are analytical computers within the Safar Center in Dr. Bell's laboratory for processing and image analysis of tissue sections.

### **Office:**

Office space is available for trainees within the Safar Center and at CHP of UPMC.

**MAJOR EQUIPMENT:** List the most important equipment items already available for this project, noting the location and pertinent capabilities of each

The Pediatric Neurotrauma Center utilizes all advanced neurological monitoring equipment that is currently commercially available, including externalized ventricular drains for CSF collection, catheters for monitoring interstitial pressures of brain oxygen (PbO<sub>2</sub>) and brain temperature (Licor, Integra), near infrared spectroscopy (NIRS) monitors of regional brain saturations (INVOS, Somanetics), continuous electroencephalograms (cEEG) and others. Additionally, an automated data collection system to integrate physiological monitoring systems has been installed for ease of data collection (Bedmaster EX, Excel Medical Systems) for all bedspaces within the Pediatric Intensive Care Unit. Freezers (-20 and -80) are available within CHP and the Safar Center for sample storage of relevant projects.