

## **HENRY H. WHEELER Jr. BRAIN IMAGING CENTER (BIC)**

**January, 2019**

### **History and Current Status**

The Henry H. Wheeler Jr. Brain Imaging Center (BIC), originally established in 2000, is predominately dedicated to basic and clinical neuroscience using MRI methods. Dr. Mark D'Esposito, Professor of Neuroscience and Psychology, has been the Director since its inception after being recruited from the University of Pennsylvania School of Medicine to create the BIC. UC Berkeley neuroscientists have made numerous contributions to the field of systems and cognitive neuroscience using MRI methods (predominantly fMRI) through the study of normal and disordered neural processes. Over the past 18 years since the arrival of the first MRI scanner at UC Berkeley, over 35 different labs from many different departments and schools across campus have utilized the BIC. In addition, the BIC has provided MRI imaging for scientists and clinicians from many outside institutions in the Bay Area and across the country.

In 2001, a Varian 4T MRI scanner was installed and dedicated 100% to brain imaging research, predominantly for fMRI. Berkeley's decision to create a BIC was novel at the time in many respects. For instance, this MRI scanner was installed on a campus without a medical school and outside a clinical or hospital environment. In this way, the BIC could prioritize research without compromising clinical workload. Following our successful lead, the approach set by UC Berkeley was subsequently replicated at many other top-tier universities in the United States. The cost of the Varian scanner was entirely funded by a \$5 million donation from Mr. Henry H. Wheeler Jr. In 2008, a new Siemens Trio Tims 3T scanner was purchased and installed through funding from a grant from the National Science Foundation (PI: Dr. D'Esposito), and a loan from the University (50% of cost), which remains in operation today. In 2012, this scanner was moved from a temporary facility to the Li Ka Shing Center for Biomedical and Health Sciences.

### **Type of BIC research activities and faculty makeup**

The type of research being performed at the UC Berkeley BIC is broad and covers many areas within systems and cognitive neuroscience as well as MRI methodological development. It should be noted that the BIC is not a "research center", but rather a "technology center". Thus, the type of research performed at the BIC is entirely dictated by its users. In addition to basic neuroscience, a particular strength of our users is clinical neuroscience research studying patients with neurological, psychiatric and developmental disorders. BIC investigators have received funding from numerous sources such as the National Science Foundation, the National Institute for Health, the Department of Defense and the Veterans Administration Research Service, to name a few. Berkeley BIC users are from many different departments and schools including: Anthropology, Bioengineering, Business, Electrical Engineering/Computer Science, Psychology, Molecular & Cellular Biology, Public Health, and Vision Science/Optomety. Outside BIC users, which have all be cultivated by Dr. D'Esposito and Dr. Inglis, have come from UC San Francisco, Lawrence Berkeley National Laboratories, Kaiser Permanente, the Northern California VA Healthcare System, The Marine Mammal Center (Sausalito, CA) and Emory University, to name a few. An example of the BIC's success as a regional and national resource is our participation in the NIH CARDIA study (The Coronary Artery Risk Development in Young Adults), which studies the development and determinants of clinical and subclinical cardiovascular disease and its risk factors. This study began in 1985 with a group of 5115 black and white men and women aged 18-30 years, from Birmingham, Chicago, and Oakland, CA. These same participants have had follow-up examinations every 5 years, for the past 30 years. In Years 25 and 30, the CARDIA study began collecting MRI scans, and UC Berkeley BIC was chosen over Stanford and UCSF as the MRI imaging site for their Oakland cohort if individuals in the study. Thus, the BIC staff scanned a total of 600 individuals during those time periods.

## **Ancillary research activity supported by the BIC**

The BIC has been integrally involved in the development of ultralow field MRI in collaboration with Professor John Clarke's group in Physics. This novel technology uses a superconducting sensor called a SQUID, the mainstay of commercial MEG machines, to provide unique views of brain tissue.

Although the BIC predominantly supports human research, BIC staff work closely with investigators studying animals. For example, Professor Terry Deacon in Anthropology, and the Museum of Vertebrate Zoology image rare, valuable, post mortem brain specimens of sei and fin whales, and white-sided and Amazon river dolphins. Professor Berns at Emory University performed fMRI scanning on 50 service dogs in training at the Canine Companions for Independence (Santa Rosa, CA), to predict whether a particular dog was likely to complete training and be suitable for placement for assistance work with a disabled human. Recently, BIC staff scanned anesthetized sea lions and post mortem sea lion brains from The Marine Mammal Center (Sausalito, CA), to study domoic acid toxicity in California sea lions, which is produced in certain harmful algae blooms (HABs) in the Pacific Ocean, causing illness and deaths in marine mammals.

## **Ancillary non-research activities supported by the BIC**

BIC staff organize a Bay Area-wide meeting of Siemens users: the Northern California Siemens Neuro User Group (NorCal SNUG), which has met annually since 2014. Several local and regional problems and efforts have resulted from this meeting. Inspired by the NorCal SNUG, a nationwide SNUG was created, with the goal of giving a more coherent voice from neuroscience research customers to Siemens. A similar user group was run by BIC staff when BIC had a Varian 4 T scanner.

BIC regularly engages in outreach activities, in particular hosting local school group tours. The Academic Talent and Development Program in cognitive neuroscience, a UC summer school for high school students, has visited BIC every year since 2007. BIC also hosted the Sees the Day summer camp for 6-11 year olds every year for a decade. In early 2019, we have a first time visit from an Oakland charter school, and a return visit from an east bay high school maths/stats class which last year led to two senior girls working at BIC for a month as part of their internship activities.

## **MRI usage**

The BIC's MRI scanner have been used an average of 70 hours per week over the last 10 years. It is available for human brain research all year, 24 hours a day, 7 days a week. There are approximately 50 qualified scanner users and 10 users in training at any one time.

## **User Support**

BIC staff comprises two MRI physicists (Dr. Ben Inglis, hired 18 years ago; Dr. Daniel Sheltraw, hired 13 years ago), two MRI engineers (Mr. Rick Redfern, hired 17 years ago; Mr. Miguel Perez; hired 12 years ago). The BIC staff has been a stable, dedicated and cohesive group for many years, without turnover, which has supported users in many diverse areas. Unlike many scanning centers, BIC's philosophy is to train users to run the scanner and peripheral devices themselves and for users to conduct their own experiments, without a MRI technician, based on the belief that scientists using brain imaging, like scientists in other disciplines, need the insights and experiences of running their own experiments to maximize their potential. Furthermore, we have observed that data quality improves when the user is responsible for data acquisition. BIC staff provide weekly one-on-one assistance to users wanting to establish new protocols, and occasionally BIC staff offer informal classes or journal clubs to introduce new capabilities to the user

community. The BIC staff also write publicly-available blogs such as *practiCalfMRI* (>6000 followers), *mathematiCalfMRI*, and *techniCalfMRI*, which cover MRI physics, MRI theory and peripheral equipment, respectively, to provide continuing education to the community. These blogs also serve as conduits for BIC staff to receive useful information and ideas from other BICs, providing further benefit to the local BIC community. BIC physicists work directly with users to define their experimental parameters, obtain and install custom pulse sequences, establish pilot scanning protocols, and determine the reasons behind any limitations found in data.

BIC engineers work with users to install peripheral equipment and modify custom equipment for use in the MRI environment. Over the BIC's 18 year history, about 50 different forms of equipment have been interfaced to the scanner, which all required some degree of customization to meet a user's needs. The BIC staff also involved in many new methodological developments. For example, the BIC staff played an integral role in the prototyping of printed head restraints, and BIC engineers have fabricated phantoms, peripheral equipment holders such as mirror mounts and TMS coil holders, screens and other devices that are not available commercially. A big strength of the BIC scanner setup is that it supports a wide array of experiment types - from vision science to gaming to force feedback to high fidelity audio - in such a way that all experiments can be performed optimally, with no performance compromise. BIC staff have also always played a vital role in the validation and optimization of new pulse sequences for neuroscience research. For example, BIC staff created an advanced EPI sequence that offered a range of parameter options not available on the commercial EPI sequence; were integral to the international effort to test and optimize multiband EPI for fMRI, leading to several important blog posts advising users on acceptable parameter settings and usage criteria; the development and implementation of arterial spin labeling (ASL) methods for neuroimaging; the deployment of routine MR spectroscopy methods for quantifying neurotransmitters such as GABA, and the development of new MRS methods for the study of metabolism, including a way to measure glucose in brain tissue without isotopic labeling. A summary of BIC staff activities can be found in the annual reports page of the BIC website: <http://bic.berkeley.edu/node/21>

## **Training environment**

The BIC provides an important training experience for undergraduates, graduate students and post-doctoral fellows to learn MRI methods. We generally train new users at a rate of about 20-25 per year, but about 75 individuals per year take our safety training course. In 2017, we had our 800th person pass the BIC safety quiz, and our 200th person pass the 3 T user quiz.

MRI: Training begins with a comprehensive 2-hour safety seminar taught in by Dr. Inglis, supported by introductory videos and a 28-page document covering all procedures. The syllabus includes all hazards associated with high magnetic fields, electrical hazards, lab safety procedures, and fire, earthquake and other emergency procedures. Access to the BIC is granted only on successful completion of a safety training quiz. The trainee is then permitted to join an Introductory User Training class, in which the basic scanner procedures are demonstrated on phantoms. A comprehensive User Training Guide provides background to the common scanning procedures and parameter settings, designed to bridge the gap between theoretical knowledge and practical skills. Once the trainee has reached the point where he/she can perform a scan of a phantom without assistance, and has read a set of documents that constitute the user training syllabus (including institutional review board issues, contraindications, screening, background MRI and fMRI physics, and the User Training Guide, as well as the safety syllabus again), they take a user training quiz. A passing grade gives the newly minted user access to the scanner suite, at which point the new user generally schedules a meeting with Dr. Inglis to begin setting up a protocol for an experiment.

Peripheral equipment (e.g. stimulus computers, button response boxes, physiological monitoring, eye tracking) and the mock scanner: Training is accomplished by dedicated classes run by Mr. Miguel Perez. The classes are supported by extensive documentation and flow charts, and all devices in the BIC have attached to them laminated "cheat sheets" with the most common procedures listed, for quick reference.

Transcranial magnetic stimulation (TMS): The BIC also maintains a TMS lab, directed by Dr. Sheltraw, which includes four TMS systems (Magstim Super Rapid<sup>2</sup>, one MagVenture Magpro X100, Magstim 200, Magstim Bistim), a transcranial direct current stimulation system, and a EMG acquisition system. These systems allow for innovative TMS methods such as theta-burst and oscillatory TMS as well as simultaneous TMS and fMRI (we are one of few centers the world with this capability). BIC staff trains users through (1) safety training, including a TMS safety quiz, (2) introductory seminars on both TMS and transcranial electrical stimulation, and (3) hands on instruction for operating the TMS systems both online (inside the MRI scanner) and offline. BIC physicists have adapted commercial TMS equipment to work optimally in the MRI scanner, and have established the specifications for a next generation TMS device that will overcome the performance limitations of modern commercial TMS power supplies.

## **Budget**

Over the past five years, the annual cost to support the Berkeley BIC has been approximately \$900,000/year. This includes the salary costs for all of the BIC staff, annual MRI scanner warranty fees, supplies and equipment purchases, and equipment depreciation costs. Approximately \$700,000 per year is generated in recharge from users grants to support these annual costs. In addition, approximately \$325,000 per year has been provided by funds from the Institute of Cognitive and Brain Science, Department of Psychology and the Helen Wills Neuroscience Institute. In this way, the BIC, through recharge and University support has remained in positive balance throughout its 19 year history.

Over the past year, there have been dramatic cuts to the BIC budget. Beginning July, 2018, as decided by Chair Kring, all support from the Department of Psychology to the BIC (\$50,000/year), which had been in existence for 6 years, was completely eliminated. Beginning in July 2019, as decided by Director Isacoff, all support from the Helen Wills Neuroscience Institute to the BIC (\$227,000 per year), which had been in existence for 15 years, will be completely eliminated. Beginning December 2018, as decided by Directors Bunge and Ivry, all support from the Institute of Cognitive and Brain Science to the BIC (\$50,000 per year), which had been in existence for 18 years, was completely eliminated and re-directed towards pilot MRI grants for its members. Thus, in past year, the BIC budget has been cut by 36% (\$325,000/year). Since there is no plan in the near future for hiring any new faculty that uses brain imaging for their research, we do not anticipate any significant increase in funding for the BIC from recharge costs in future years. In fact, in the past 5 years we have seen a decline in grant funding from several of our key faculty that were originally hired as core brain imaging scientists (e.g. Drs. Bunge and Bishop in the Department of Psychology). The unanticipated decreased funding from these, and other faculty, had to be offset by increased efforts to obtain funding from funded users outside of Berkeley. Thus, our options for responding to these drastic cuts is limited and tenuous. Our plan to balance our budget over the next five years is twofold. First, we will have no choice but to terminate at least one BIC staff member in the next two years. This cut significantly reduce the services we previously provided to our users. Second, we will dip into the BIC endowment fund, generously provided by the Wheeler Family Foundation (\$250,000 per year from 2011-2020), to cover our deficit until annual BIC expenses have been reduced. Other solutions are possible. For example, grant funding to the University for projects that rely on the existence of the BIC, are typically at least that \$3 million per year in direct costs, which generates at least \$1.7 millions dollars per in indirect costs to the University. There has never been any recovery of these indirect costs directly back to the BIC.