
**The Athinoula A. Martinos Center
for Functional and Structural Biomedical Imaging**

First Annual Report
June, 2000

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THE MARTINOS CENTER FOR BIOMEDICAL IMAGING

The Martinos family has a vision of establishing a biomedical imaging center for the purpose of fostering translational neuroscience research, research that spans disciplines from basic to clinical investigation, to the development and medical application of new technologies. In the past year, that vision has taken its first steps toward becoming a reality. This is a summary of those first steps, from the formation of a partnership between the Harvard-MIT Division of Health Sciences & Technology (HST) and the Massachusetts General Hospital (MGH), to the numerous other scientific and educational collaborations and initiatives that are taking shape as a result of the Martinos family's vision.

HST has invited the MGH to participate in founding the new Athinoula A. Martinos Center for Functional and Structural Biomedical Imaging (MCBI). This partnership will unite the clinical and imaging expertise and equipment base of the MGH-Nuclear Magnetic Resonance Center (NMR) with HST's strengths in engineering and basic neuroscience and the resources represented by the Martinos family gift. Many of the details of the partnership have been agreed to in principle, including the governance and management structure for the Center, its leadership, location and initial participants.

Vision and Mission

The MCBI will be a world-leading biomedical imaging center that combines, under one roof, the principal strengths of the HST community (i.e. the communities of MIT and Harvard, including the affiliated teaching hospitals):

- Engineering and physical sciences
- Computation sciences and informatics
- Neurological and cognitive sciences
- Basic and applied biological science
- Imaging and radiological sciences
- Clinical sciences

Its mission is to build the next generation of functional imaging tools, to apply these tools to biologically, neurologically and clinically relevant problems, to provide training for physical, biological and clinical scientists, and to provide a hub for interdisciplinary collaborations across Harvard and MIT, and other institutions worldwide.

Leadership, Governance, and Participation

An international search for the founding director of MCBI was launched in late spring of 1999. After calling leaders internationally, we gathered a list of approximately 20 individuals who had been recommended. We asked each of those individuals if they were interested, and encouraged them to forward their CV to us. We also received inquiries from a number of individuals, whom we also encouraged to send in their CV. We narrowed the list to 7 individuals.

We then solicited input from leaders in biomedical imaging, asking them to rank these candidates relative to one another, and encouraging them to suggest other candidates whom we should consider. From those comments, two candidates emerged as the clear leading candidates,

with Dr. Rosen having an edge over the other highly-rated candidate. The search committee met to review these candidates and the vote was overwhelmingly in favor of working aggressively to recruit Bruce Rosen.

A brief biography of Dr. Rosen will make it clear why the search committee was so excited by the prospect of having him become the founding director of MCBI. Over the last 15 years, Dr. Rosen's research effort has demonstrated several attributes that make him uniquely suited to direct the new Martinos Center. He has made many pioneering research contributions; he has a clear understanding of relevant basic science, technology and clinical implication with a unique ability to unite and build on those three elements; and he has an outstanding track record of anticipating the next wave of important technological and scientific avenues. While the unifying theme for Dr. Rosen's research has been the use of magnetic resonance methods for elucidating the function of biological tissues and organs, Dr. Rosen has also been increasingly active in research utilizing other imaging modalities. In his work, he has demonstrated an unusual ability to appreciate and make connections among MR physics, biology and biochemistry, and clinical physiology. His work has been well-focused on important problems and has had considerable clinical and basic science impact.

The recruitment effort was thus launched and involved the HST directors, faculty, and search committee. The vision of the MCBI was compelling to Dr. Rosen; however the grand challenge was to launch the vision in a way that embraced the community, rather than provide an unconnected element to the community. Over the course of the next 6 months we shaped an implementation of the vision that would be seeded by a partnership between MGH and MIT-Harvard (HST). It is with strong help, support, and visionary leadership from many quarters that we have reached agreement, in principle, to establish the MCBI as outlined in this report. A partial list includes:

- Prof. James Thrall, chief of Radiology, MGH
- MGH NMR Center faculty, especially Professors Bruce Rosen and Gregory Sorensen
- Prof. Dennis Ausiello, chief of Medicine, MGH and past chair of the Executive Committee on Research at MGH.
- Prof. John Parrish, Director of the Center for Minimally Invasive Technologies and present chair of the Executive Committee on Research at MGH
- Dr. Ronald Newbower, Vice President for Research, Partners Health Care System and MGH
- John Fini, Financial Director of Research Management, MGH

- Provost Robert Brown, MIT
- Julie Norris, Director Office of Sponsored Programs, MIT
- Patrick Fitzgerald, Director of Cost Analysis, Office of Sponsored Programs, MIT
- Prof. Eric Grimson, Associate Director, Artificial Intelligence Laboratory, MIT
- Prof. Mriganka Sur, Head, Department of Brain and Cognitive Science, MIT

- Dean Joseph Martin, Dean of Harvard Medical School, HMS
- Dean Dennis Kasper, Senior Academic Dean, HMS

Through many discussions with the group of individuals listed above, we have established that the guiding principles for the Governance and Management of MCBI are to:

- 1) Creatively marshal and grow the expertise in basic, preclinical and clinical biomedical imaging in a collaborative manner across institutional and departmental boundaries in a way that pushes and is pulled by clinical biological and neurological opportunities in biomedical imaging
- 2) Build upon the resources for management at the founding institutions, rather than establishing a wholly independent entity
- 3) Provide incentives and minimize disincentives for participation while maintaining accountability to the founding partners and sponsors

The legal documents specifying the governance and financial agreements for the MCBI are being drafted presently. In rough outline we expect the following components. MCBI will be an inter-institutional resource shared by researchers in the MIT, Partners Health Care System, and Harvard community. The center director will be an HST primary faculty member, with HST being the lead academic unit responsible for this MCBI consortium. Oversight will be the responsibility of an Executive Board composed of leaders in the MIT and Harvard communities. Administratively, the MCBI will be an official center established and with financial oversight by the usual MIT center mechanisms. In the future, an External Advisory Committee will be established to provide advice and recommendations regarding strategic directions of the center. The management structure will include an internal management committee to help establish and implement policies and procedures for allocation of instrument time, award seed grants and student assistantships, and manage funds for operations.

An essential element of the governance and financial structure is explicit expectation that the faculty participating in the center will be derived from the the large community described in the Vision and Mission section.

Location and Resources

Plans for the permanent home of the MCBI call for it to be physically located adjacent to the new McGovern Institute for Brain Research (MIBR). This entirely new facility will allow the co-location of the MCBI with an important new institution whose mission complements our own. The McGovern Institute is designed to focus on the investigations of the molecular and cellular neurobiology of the brain using animal models, while the MCBI will be dedicated to translating these and other basic science research into better treatment, prevention, and understanding of human disease using bioimaging technologies. The estimated date for completion of this all-new shared facility is 2004.

The two sites currently under consideration for the MCBI/MIBR are both in the Kendall Square area. One site is on Carlton Street, opposite the Whitaker Health Sciences Building (which houses HST, the Department of Brain and Cognitive Sciences, and an animal facility). The other site is adjacent to the Whithead Institute for Biomedical Research, and the Stata Center currently being constructed to house Computer Science, Information Systems, and Cognitive Science. MIT is currently soliciting proposals from site planners to evaluate the facilities programming for each of these sites. We expect to make a final site determination by fall 2000.

Until the new facility is constructed, current plans call for the MCBI to reside in the research space presently occupied by the MGH-NMR Center, located in the Charlestown Navy Yard, with a satellite computational facility located on the MIT campus.

The Navy Yard facility currently houses two human MRI systems (1.5 Tesla and 3 Tesla) equipped with newly renovated psychophysical testing facilities, three animal research magnets and an animal surgery lab, computational facilities, an education center and office space. Construction has already begun to expand this facility to twice its current footprint to house the MCBI. New facilities will include: two new human magnet systems (3 Tesla and 7 Tesla systems) located on site, and an additional 3 Tesla human research system to be housed in the MGH Neurology intensive care unit, two additional high-field animal MRI systems, and a state-of-the-art 306 channel magnetoencephalography (MEG) suite. Future plans include a Positron Emission Tomography (PET) imaging facility, an optical imaging laboratory, a dedicated behavioral testing laboratory, and additional office and workspace that will bring investigators from several departments and institutions together in one centralized location.

COLLABORATIONS AND INITIATIVES

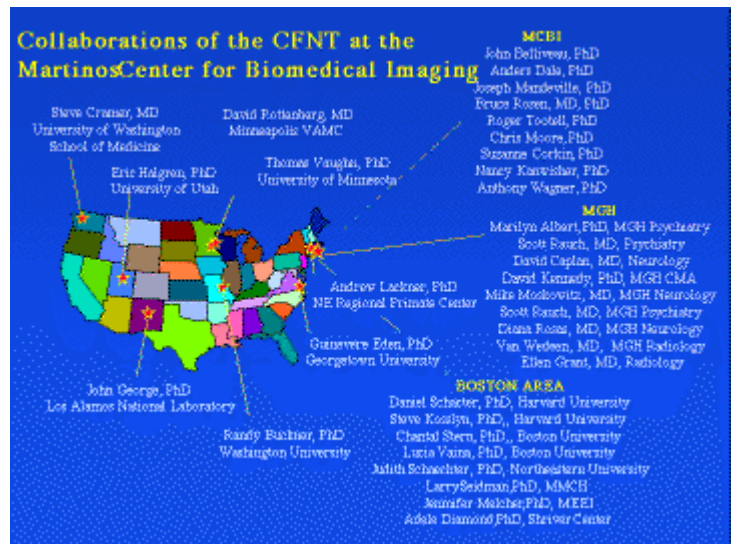
Accomplishing the goals of the Martinos vision - to push the spatial and temporal limits of imaging technologies, to apply these technologies in innovative ways to new problems and questions concerning human health, and to use this new knowledge to impact the current and future treatment of human disease - will require the best and brightest cohort of engineers, and basic and clinical scientists that can be assembled. These individuals will possess different skills, expertise and perspectives, and will be working in a variety of disciplines and settings. This is why the MCBI is all about partnerships.

In the past year, the vision for the MCBI has enabled many fruitful and productive partnerships - partnerships that we expect to be formally in the MCBI portfolio, once the MCBI has been formally launched. For the purposes of this document, we use the term "pre-MCBI" in recognition of the dual facts that the MCBI vision has stimulated significant activity but, as yet, the MCBI does not exist as a legal entity.

Four major alliances were established - with the US Government, with leaders in the biomedical imaging industry, and with a private foundation whose mission complements our own. These major initiatives have become the springboard for many additional collaborations between the pre-MCBI and academic and clinical institutions both locally and nationally.

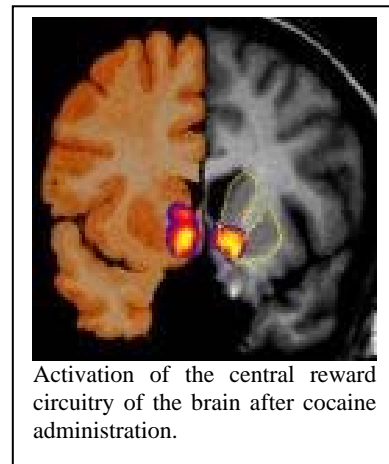
The Center for Functional Neuroimaging Technologies at the MCBI - Multimodal Brain Imaging

We have been awarded five years of funding (~\$5M) from the National Center for Research Resources of the National Institute of Health (NIH) to establish the pre-Martinos Center as an international resource for advancing functional neuroimaging technology. Core technical development of the resource is centered around four interrelated projects whose collective goal is to significantly impact the field of brain mapping through the development and dissemination of innovative MR-based, multimodal neuroimaging techniques and technologies. In addition to MRI, these technologies include Diffuse Optical Tomography (DOT), Magnetoencephalography (MEG) and Electroencephalography (EEG). While the four core projects of the center represent collaborative efforts across labs and departments within the pre-MCBI, the Regional Resource already has established a network of more than twenty collaborators that extends across the country.



Office of National Drug Control Policy - 7 Tesla ultra high field human imaging

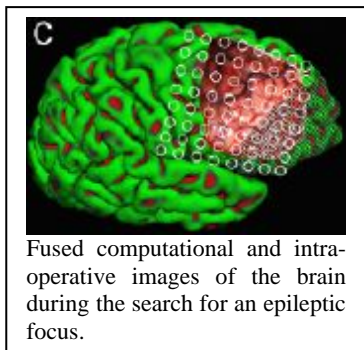
Based on our success in studying substance addiction, the Office of National Drug Control Policy (ONDCP) has agreed to an alliance to build next generation of functional imaging tools to study the basic brain mechanisms of human motivation and reward. With almost \$7 million in support from the ONDCP and the installation of a new 7 Tesla human magnet (one of only 3 such MRI systems in the world), we will be able to image the brain with unprecedented spatial and temporal resolution and chemical sensitivity. This ultra-high field system will allow MCBI scientists to better understand in what ways the brain of an addict, a compulsive gambler, or in individual suffering from depression may function abnormally, and to perform studies that will eventually lead to new treatments for addiction and other disorders of human motivation.



National Foundation for Functional Brain Imaging - MEG Technology and Mental Health

Through a partnership with the National Foundation for Functional Brain Imaging, whose mission is to study the neurobiology of mental health, the pre-Martinos Center will be acquiring

a state of the art \$2 million 306 channel magnetoencephalography (MEG) system this summer. In addition, we are very fortunate that Eric Halgren, Ph.D., a leading clinical investigator from the University of Utah, will be joining the MCBI faculty to head the MEG Core. Dr. Halgren's experience in the application of MEG to the study of epilepsy and to electrophysiological presurgical mapping assures that this effort will get off to a strong start.



Clinicians including Drs. Caplan and West (Neurology), Dr. Kuperberg (Psychiatry), and Drs. Grant and Sorensen (Neuroradiology) will be applying MEG technology to their clinical research efforts regarding language disorders, schizophrenia, and presurgical evaluation of epilepsy. Because of the greatly improved temporal resolution that MEG can contribute to neuroimaging studies, wide interest also has been expressed by the basic neuroscience community. Investigators like Nancy Kanwisher in Brain and Cognitive Sciences at MIT plan to incorporate this technology in their research programs.

Industrial Partnership with Siemens

The pre-MCBI will be equipped with state-of-the-art Siemens MRI systems. Our recently negotiated research partnership with Siemens will bring five completely new human scanners to the MCBI, (two of which have already been installed), including a 1.5T Siemens Sonata whole-body system, two 3.0T Siemens Allegra head scanners (one of these systems will reside in the Neurological Intensive Care Unit for inpatient research), a 3.0T whole-body scanner for brain, heart, and other whole body studies, and a 7T whole-body human imaging system.

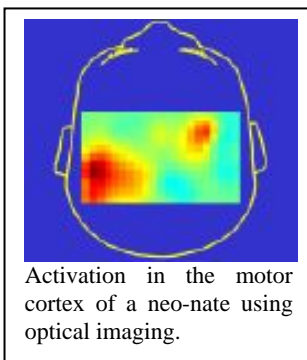
In addition to these commitments, Siemens will be siting two full-time scientists at the MCBI to facilitate our imaging research efforts. These include Franz Schmidt, an internationally respected MR hardware designer, and Jim Moore, a full time software/pulse programmer. In addition, Dr. Doug Kelly has joined the MCBI to lead the 7T systems engineering program. Doug comes to us with over five years of industrial experience leading high-field systems integration and development efforts. Finally, along with hardware and personnel, our relationship with Siemens will provide a continuous stream of upgrades to our systems, keeping them at the "state of the art" for the duration of our agreement (initially five years). The estimated value of the relationship with Siemens is over \$14 million dollars.

Cross-Institutional Research Partnerships – Technology Development, Basic and Clinical Science

All of these major alliances, enabled by the partnership between HST and the MGH that is at the core of the Martinos Center itself, have led to numerous local affiliations. Described below are three examples of MCBI-sponsored multi-institutional collaborations that particularly reflect the mission of the MCBI - to develop biomedical imaging technology and utilize this technology for basic science and clinical research applications.

New Technology with Clinical Potential

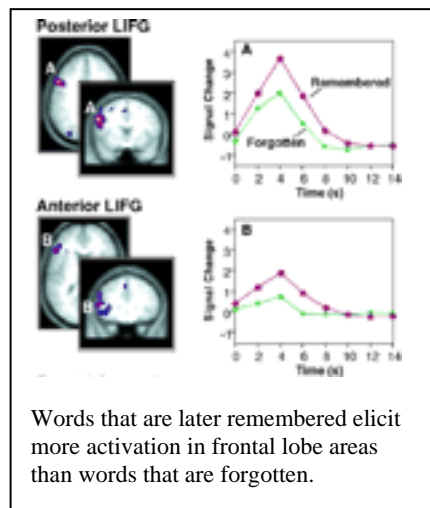
The pre-MCBI has teamed up with the multi-institutional Center for Innovative Minimally Invasive Therapies (CIMIT) to establish a laboratory for the study and application of Diffuse Optical Tomography (DOT). The head of this laboratory is Dr. David Boas, a physicist whose goal is to bring his expertise in the theoretical aspects of optical imaging into the realm of healthcare. DOT uses properties of scattering light to probe biological systems. Its potential medical uses include bedside monitoring of brain hematomas, diagnosis of ischemic versus bleeding strokes, imaging of tissue blood oxygen saturation and flow, and identification of cancerous lesions. DOT can also be applied to the study of cortical brain activation, as an alternative to MRI in magnet incompatible patients, or in conjunction with MRI to probe metabolic and vascular changes associated with disease states.



Dr. Boas brings his technological expertise to a collaboration with Dr. Ellen Grant, a radiologist, and Dr. Barry Kosofsky, a child neurologist. This interdisciplinary team of investigators aims to develop DOT as an imaging tool for monitoring and evaluating premature infants who are sometimes born with cerebral ischemia and other types of metabolic brain dysfunction.

Basic Neuroscience of Memory

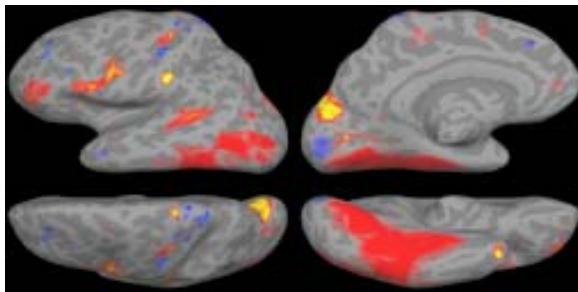
The ability to remember the past is critical to many aspects of human thought and behavior, from learning our first words, to developing complex social relationships to, remembering the events of our lifetime. Memory is so fundamental that many labs across the community study its relevance in normal learning, in the aging process and in neurological disorders such as Alzheimer's disease and other forms of amnesia. Many important breakthroughs in understanding how memory is organized and supported by the brain have come from the creative combination of current cognitive psychological theory and behavioral methods with the innovative functional neuroimaging technologies developed at the pre-MCBI.



Recently, Anthony Wagner, a young investigator from MIT's Department of Brain & Cognitive Sciences, and Daniel Schacter, the Chair of Harvard's Psychology department, used event-related functional MRI techniques developed at the MCBI to demonstrate that areas of the brain's frontal and temporal lobes jointly promote the formation of new verbal memories. This insight into normal memory systems lays an initial foundation for clinical applications to study Alzheimer's disease and other disorders of memory function.

Quantitative MRI in Clinical Neuroscience

The pre-MCBI provides a fertile common ground for investigators with common interests but different perspectives and expertise to get together in "Working Groups", to focus their collective attention on compelling scientific questions that cannot be answered by any one discipline. In addition to focusing resources, working groups also serve to facilitate the exchange and dissemination of information and technology across the participating departments and institutions.



A group-averaged, inflated representation of the cerebral cortex showing areas of cortical thinning in schizophrenic patients compared with healthy controls.

The pre-MCBI's first such working group was established this year to study Schizophrenia. This group includes clinical investigators from MGH Psychiatry and Neurology, a neuropsychologist from the Beth Israel Hospital, and an imaging processing and analysis team from the MCBI. One early result of this effort has been the application of a new means to assess the gray matter thickness of patients with schizophrenia and compare them quantitatively with normals. Their

preliminary results indicate reduced cortical thickness in areas of the brain thought important for language and other higher functions.

FUTURE INITIATIVES

The coming year will be a particularly busy one for the MCBI. In addition to finalizing the governance and financial agreements, moving into our new space in the Charlestown Navy Yard, and setting up our three new MRI systems and the new MEG suite, we plan to initiate several additional partnerships across the MIT and Harvard systems. New collaborations are currently being discussed with our neighbors at the Whitehead Institute and with the Harvard Joint Program in Neurobiology across the river. Three additional scientific and educational initiatives are described below.

Advanced Computational Image Processing and Analysis Center

To be located on the MIT campus we are proposing an MCBI Advanced Computational Image Processing and Analysis Laboratory. We are working to establish this laboratory in collaboration with the MIT Artificial Intelligence (AI) lab. This initiative will bring the

theoretical expertise of the MIT visual computational students and faculty to the practical image processing and analysis issues relevant to biomedical imaging. This facility would provide the Martinos Center an immediate presence on the MIT campus and a direct avenue for MIT and HST students to become involved in biomedical imaging research.

Clinical Research Core

We plan to establish a Clinical Neuroimaging Research Core of the MCBI in collaboration with the joint MGH-MIT Clinical Research Centers (CRCs). This will be a unique Resource, devoted to promoting the application of imaging tools to the study and treatment of human disease. The Core will provide a variety of services to the clinical imaging community to support and facilitate integrative and innovative clinical research, and to educate and train present and future generations of clinical neuroscientists. Services provided by the Clinical Core will include administrative support, research and collaborations coordination, provision of developmental funding, colloquia and specialized training courses, consultation in research design, statistics and data analysis, and access to the MCBI imaging facilities, computational infrastructure, and expertise. The benefits of creating a consolidated Clinical Core include optimization of research teams, efficiency of resource allocation, improved technological product development, and integration of student education and services to the medical community.

Imaging in Primates

A great deal of systems neurobiology has been based on work in primates, in large measure because they are evolutionarily similar to humans. The monkey brain can also be studied with a broad range of both invasive and non-invasive techniques, and can therefore act as an important laboratory for determining the accuracy of noninvasive work that can be done in humans.

While there are many similarities between the brains of human and non-human primates, there are important differences in the physical requirements of an animal imaging facility. In collaboration with the McGovern Neurosciences Institute, we are working to establish a dedicated primate imaging facility on the MIT campus in the next several years. In the interim, we plan to begin our studies of primates within the MCBI Charlestown campus, to gain experience in these important biological models, and to aid us in the design specifications of a dedicated primate imaging system. These initial studies will allow us to make direct maps of the monkey cortical areas, to see how similar or different they are to corresponding areas in humans. Additionally, we will concentrate on technical developments which will clarify the enormous potential of monkey imaging.

Multidisciplinary, Cross-Institutional Training Program

Translating new imaging technologies into insights regarding human biology and disease, and reciprocally, using emerging biologic questions to drive the development of new technologies, will require a merging of perspectives from basic and clinical science, and increasingly from the physical sciences. Despite the enormous potential however, the scientific and medical community's ability to take advantage of this opportunity is today significantly limited by the

supply of scientists trained at the interface between the technologies of quantitative imaging and neurobiology. This limitation arises in part because training programs traditionally do not merge these disparate intellectual cultures. In response to this need, Harvard and MIT have jointly submitted a proposal to the Burroughs-Wellcome Foundation to establish an integrated, multidisciplinary biomedical imaging training program at the MCBI specifically designed to provide training spanning the quantitative and biological sciences.

The proposed two-year fellowship program will implement several innovative multidisciplinary group training components, preparing pre and post-doctoral students from both quantitative and biological backgrounds for leadership in translational biomedical imaging research. Pre-doctoral trainees will be drawn from the Harvard Division of Engineering and Applied Science (DEAS), the engineering and physical science departments at MIT, HST's Ph.D. programs in Medical Engineering/Medical Physics and Radiological Sciences, the Departments of Brain and Cognitive Sciences (MIT), Neurobiology (HMS), Psychology (Harvard FAS), and HST-MD students. Post-doctoral fellows will be recruited and selected from an international search.

This program will be led by the new Director of the MCBI, Bruce Rosen, M.D., Ph.D., and Joseph Martin, M.D., Ph.D. Dean of the Harvard Medical School. Students will emerge from this program with the experience and intellectual background to work effectively in a multidisciplinary environment, able to develop and apply imaging technologies to scientifically compelling areas of biological research.

CONCLUSION

In summary, this first year has seen many important developments in establishing the groundwork for the Athinoula A. Martinos Center for Functional and Structural Biomedical Imaging - elaboration of a governance structure, selection of a Director, identification of a present and future site for the Center, and the formation of major alliances and collaborations. A sense of the progress can be derived from the time line on the next page. The joining of the MGH's substantial imaging and clinical resources and expertise, the strengths of MIT / HST in engineering and basic sciences, and the significant potential represented by the Martinos family gift provide a substantial foundation on which to build the new collaborations and new initiatives that will establish the MCBI as the world's foremost center for biomedical imaging in the years to come.

APPENDIX: TIMELINE

Mar-99	Martinos Visit
Apr-99	Initiate recruitment effort for director
May-99	
Jun-99	Formal gift agreement solicit written input evaluating potential director candidates
Jul-99	search committee recommends Rosen as Founding Director of MCBI meetings with Rosen to discuss candidacy and possible structures for MCBI determination of available sites on MIT campus or in close proximity to MIT evaluation of site at 28 Osborn Street for Martinos Center location
Aug-99	vibration and magnetic field measurements of 28 Osborn Street site
Sep-99	Meetings with Parrish, Ausiello, Thrall, and Newbower determination that 28 Osborn Street site can not accomodate MCBI initial business plan to establish financial implications for MGH and MIT
Oct-99	Meetings with Parrish, Ausiello, Thrall, and Newbower Draft Governance document, including financial arrangements Academic Review of Rosen case: Approved by HST Personnel Committee
Nov-99	Meetings with Brown and Newbower alternative site proposal for Carlton St. In Kendall Square
Dec-99	Financial and sponsored program officials (FASP group) from MIT and MGH meet to discuss financial arrangements
Jan-00	FASP group considers a variety of scenarios Obtain construction estimates for temporary site
Feb-00	Financial plan approved by FASP group and reviewed by Brown (MIT) and Newbower (MGH)
Mar-00	Announcement of gift to establish McGovern Institute for Brain Research FASP group revises plan so that costs of temporary location can be amortized over 4 years Small group meetings to discuss science of MCBI Working group meetings to plan educational program for submission to the Burroughs Wellcome Foundation
Apr-00	MIT legal and programs offices charged with drafting partnership agreement Small group meetings to discuss science of MCBI Submission of Burroughs Wellcome Proposal
May-00	Academic Review of Rosen case: Approved by Engineering Council Two "town meetings" of interested faculty to discuss science of the MCBI Academic Review of Rosen case: Approved by Academic Council Model partnership agreement between MGH and MIT approved for CIMIT Draft Preliminary report Small group meetings to discuss science of MCBI
Jun-00	Academic Review of Rosen case: Approved by MIT Corporation Small group meetings to discuss science of MCBI Submit first Annual Report to Martinos Family Draft governance document, including financial arrangements: review by MIT Draft governance document, including financial arrangements: review by MGH Plan submission to NSF Integrated Research and Training Program (IGERT) for training and center support Begin facility programming for site evaluation
Jul-00	Submit IGERT preproposal

Partnership agreement signed
Rosen offer accepted
Rosen formally appointed to MIT faculty

Aug-00
Sep-00 Site Evaluation completed
Oct-00
Nov-00 Celebrate Launch of MCBI
Dec-00