G. OVERALL BENEFIT

The Martinos Center and its Core imaging facilities have a proven track record as an effective outreach mechanism, as hundreds of trained and certified users currently employ our MRI systems in their research projects. Our records show 300+ unique users have logged in to our scanners in the past 18 months. Of the 60+ MGB Core facilities, the Martinos Core is the third largest (the two larger Cores both provide genomics services), with greater than 10% of the more than $1 billion in research activity at the MGH utilizing the broad imaging services provided by the Martinos Core. These include the NIBIB-funded CTSA Harvard Catalyst Biomedical Imaging Core, the Mass General Neuroscience Institute, the MGH Stroke Center, the NIA-funded Massachusetts Alzheimer's Disease Research Center, the Mass General Institute for Neurodegenerative Disease, the NIH P01-funded Center for Integrative Pain Neuroimaging, the MGH Morphometric Analysis Center, the Center for the Neuroscience of Psychedelics, and the Psychiatric Neuroimaging Program. The Martinos Center is actively supported by federal and other funding agencies including ten Institutes and Centers of the NIH and the National Science Foundation. The Center is home to more than 120 (mostly NIH-funded) research faculty members and over 100 postdoctoral trainees and graduate students, and provides its biomedical imaging facilities for well over 100 additional affiliated investigators from other MGH departments and from institutions around the Boston area and the country. The broad range of biomedical imaging needs of this exceptionally large and diverse user community drives the continuing technological advancement of the Martinos Center's state-of-the-art imaging facilities. The Martinos Center Core also provides advanced biomedical imaging resources for researchers from other institutions across the Boston area and the northeastern United States, including MIT, Harvard University, Boston University, Tufts University, and Harvard and MIT-affiliated research hospitals and institutes, including BWH, Beth Israel Deaconess Medical Center, and Boston Children's Hospital. These researchers are actively supported by federal and other funding agencies, including many Institutes and Centers of the NIH, the National Science Foundation, and several private foundations.

Even more broadly, the Martinos Center Core has a strong track record of serving as a national resource as an NIBIB P41 National Center for Biomedical Imaging and Bioengineering to clinical/translational and basic scientists who represent, in addition to the MGH, many other institutions across the nation and world. This success has been possible because the Martinos Center has a highly user-oriented focus; the tools at the Center are intended not just for our own internal use, but for use by many scientists and clinicians locally, nationally, and internationally. Dissemination of technology has been a central priority of the NIBIB P41 National Center for Biomedical Imaging and Bioengineering, and mechanisms are in place to assist with disseminating any technology that is enabled by the proposed new instrument. Not only does the Martinos Center support active software dissemination (such as the FreeSurfer software package) and several ongoing seminars and focused workshops, it also has in place—in collaboration with Siemens Healthcare—a process developed by Siemens to distribute pulse sequence and image reconstruction software for the Siemens MRI platform to other Siemens customers through the "C2P" program. Even hardware developments have been disseminated through the rotating training internship in the RF Coil Laboratory and through licensing coil designs to MRI manufacturers—including the 32-channel head and the 64-channel head-neck coil arrays developed at the Center, which are now commercialized by several vendors and have become the standard coils for applications ranging from clinical care to basic research.

Realistically, the proposed new instrument has the potential to benefit dozens more NIH-funded investigators within the first few years of use, as existing projects migrate from older 3T MRI scanners and new projects come to the fore. Also, because this system will be the next-generation product 3T scanner, it is poised to set the trend for future 3T system capabilities and will effectively serve as a new resource for researchers at Martinos and the regional community. Key benefits of the new system include the significance advance in gradient performance, system architecture and software, enabling improved workflow and ease-of-use for researchers and technicians operating the scanner. This streamlined and standardized workflow, together with the advanced gradient capabilities and state-of-the-art hardware and software platform, will also likely enable the first large-scale multi-site studies of advanced imaging studies leveraging high gradient strengths and slew rates across large populations of patients.

The overall benefits of the proposed new 3T whole-body scanner can be seen in terms of both its immediate and long-term impact. Presently, 3T MRI systems are the workhorses at the Martinos Center, and the more modern systems have very high utilization rates and schedule congestion, while the obsolete systems, chiefly the one slated to be replaced by the proposed upgrade, are no longer able to offer state-of-the-art functionality to our user base. The new whole-body 3T scanner would represent the first of its generation at the Martinos Center, enabling our hardware and software developers to translate their tools to the newest platform so we can serve our community at the Center, the local research community and globally better.

The proposed instrumentation upgrade will bring to the Center the most advanced commercially available 3T MRI scanner with significantly improved gradient performance beyond the current state-of-the-art at just the right time. Research collaborations between the MGH and BWH, the academic flagships of the Mass General

Brigham (MGB) integrated health system, have become closer in the last year as MGB has sought to form one of the nation's leading biomedical research organizations with the Harvard Medical School teaching hospitals under its umbrella. This strategic initiative has increased cross-institutional collaborations between investigators at the Department of Radiology at MGH and BWH, especially as the two departments are now under the common leadership of Dr. James Brink, Chief of Enterprise Radiology at MGB and also Radiologist-in-Chief and Chair of the Departments of Radiology at MGH and BWH, respectively. As the latest whole-body 3 Tesla instrument featuring high-end gradients (Gmax=200 mT/m and slew rate 200 T/m/s), the next-generation 3T Vida is poised to serve as a premier research platform to serve leading investigators at both institutions, as exemplified by the two P41 National Centers for Biomedical Imaging and Bioengineering that are serving as major users of this instrument. The P41 Center for Mesoscale Mapping at the Martinos Center (**Major User Project 1, led by Dr. Rosen**) is focused on imaging brain structure and function at the critical mesoscopic scale, bridging the gap between traditional human brain mapping at the macroscale using noninvasive imaging and the wealth of information that is being unleashed from large-scale microscopic imaging studies of the brain as part of the NIH BRAIN Initiative 2.0's vision of mapping the brain at multiple scales. The P41 Advanced Technologies – National Center for Image Guided Therapy (**Major User Project 2, led by Dr. Tempany**) serves as a national resource for all aspects of into medical procedures enhanced by imaging, with a focus on imaging cancer heterogeneity for personalized minimally-invasive image-guided therapy in the brain, prostate and other organs. The next generation 3T Vida with its high performance gradients represents a vital platform for developing, validating and translating the technology being developed by each P41 Center and disseminating the new methods to the greater neuroscientific and cancer research communities to advance their broader missions. Finally, and perhaps most importantly, the next generation Vida platform will increase the spectrum of applications that can be translated to the clinic and to large-scale multi-site imaging studies, not just in the brain but throughout the whole body, in keeping with the "bench-to-bedside" philosophy of MGB.

At the Martinos Center, a leader in MRI technology development for over 30 years, researchers have developed new acquisition strategies such as Simultaneous MultiSlice (SMS) echo-planar imaging, which are now standard for fMRI and diffusion acquisition. The same group of researchers is currently working in a collaboration project with Siemens on much accelerated structural 3D imaging for clinical purposes (Wave-CAIPI MRI), for which dissemination and commercialization with Siemens has already begun on the newest Siemens MRI platform. Furthermore, the group of technical development investigators is expanding to develop and disseminate new high-resolution diffusion, fMRI, deep learning and motion-correction techniques for pushing the limits of MR acquisition technology, as seen in **Major User Projects 1, 5, 9, 12 & 15, led by Drs. Rosen, Guerin, Bilgic, Stockmann, Barry & Rathi** and **Minor User Projects 1 & 3, led by Drs. Liu & Frost.** A fully integrated implementation plan for translating and disseminating the products of this research to the scientific community will make full use of the new research capabilities of the proposed new 3 Tesla MRI, including the Open Recon interface and availability of the Syngo Numaris X software platform.

One of the most exciting prospects of the proposed new instrument is its combination of high-performance whole-body gradients and the high channel count RF receive system. This allows, for the first time at the Martinos Center, the implementation of new high-performance cardiac imaging techniques and their application to patients with cardiovascular disease. At the Martinos Center, which has traditionally been predominantly neuroimaging focused, a strong cardiac MR imaging program is taking root, catalyzed by the arrival of key cardiology users from the Department of Medicine and supported by the recruitment of junior and senior investigators who are integrating new cardiac MRI techniques into their research programs. **Major User Projects 10, 17 & 22, led by Drs. Das, Malhotra and Rosenzweig**, cardiologists at the MGH with strong research programs in cardiometabolic disease and heart failure, propose clinical trials and basic research studies that require not only special cardiac MRI techniques such as quantitative T1, T2, and T2* mapping and diffusion MRI, but also benefit greatly from the ability to utilize modern imaging techniques to image the heart faster. Currently, cardiovascular imaging subjects currently scanned at the Martinos Center often get scanned on two different 3T scanners at the Martinos Center during the same visit as no one system currently provides all the techniques utilized in their trials. The new whole-body 3T system will not only offer all the techniques required in one system, it outperforms both systems currently utilized, enabling a smoother workflow and ultimately accommodating more patients.

Another key cardiac project led by Dr. Sosnovik and described in **Major User Project 6** focuses on diffusion imaging of the heart, a technique that can only be successfully accomplished by the use of very powerful gradients, which the proposed new instrument provides, and the ability to utilize modern accelerated imaging techniques in combination with large channel count cardiac coils, such as the Siemens Body 30-channel coil and dedicated 64- and 128-channel cardiac array coils, all of which are available at the Martinos Center and can be used with the new proposed instrument. This project is also focused on the development of new cardiac imaging techniques that will be disseminated to the greater community. **Major User Project 26, led by Dr. Nezafat**, a leading cardiovascular imager at the Beth Israel Deaconess Medical Center, is an example of a cardiac project that will directly benefit from free-breathing advanced diffusion imaging coupled with the advanced physiological

monitoring capabilities on the new scanner and horizontal integration with other modalities such as stress cardiac MRI to understand the pathophysiology of cardiac remodeling in heart failure.

Another new capability that has so far not been available at the Martinos Center is fully integrated local shim. The Martinos Center has done pioneering work on local shim arrays and will continue to do so, aided in the development and dissemination of such technology by the availability of the proposed instrument, as exemplified by **Major User Project 9, led by Drs. Bilgic and Stockmann**. In addition, the proposed Siemens Vida is the first commercially available MRI system that features local shim channels integrated into the head-neck coil to allow for improved shimming of the C-spine and other areas of the head and neck. **Major User Project 12, led by Dr. Barry**, focuses on spinal cord fMRI and will directly benefit from these new capabilities at the Martinos Center, as well **Dr. Andronesi's** (**Major User 11**) spectroscopic studies of mutant IDH and wild-type gliomas.

The impact of having access to the newest MRI software platform and higher performance compute resources cannot be understated. Many investigators at the Martinos Center perform their research using the newest state-of-the-art acquisition and analysis techniques. As new software development for the system being replaced ended years ago, the new instrument will finally bring the newest acquisition packages and the requisite compute power for the associated image reconstruction to our users. Prime examples of users heavily utilizing aggressively accelerated imaging to gain higher spatial resolution and/or model out the effects of physiological noise from their functional MRI data include **Major User Projects 3, 4, 6-8, 10-12, 17 & 26**. **Drs. Simonyan, Napadow, Montesi, Lewis, Bianciardi and Barry** have been funded users at the Martinos Center for many years, playing a critical role in new methods development as early adopters of the new acquisition technologies.

An often overlooked, but for some applications critical feature is the new integrated B_0 tracking feature in the Magnetom Vida, that all but eliminates noticeable effects of drift in the main magnetic field during data acquisition. This feature, not present in the early generation 3T systems, has been much improved in the newest generation 3T system proposed here and will have a significant impact on **Major User Project 11, led by Dr. Andronesi,** and involving spectroscopic markers for a mutant type of malignant intracranial glioma, another example of technology developed at the Martinos Center that has significant potential impact on clinical populations.

Finally, the high-performance gradient package will provide transparent benefits to the many users using diffusion MRI as a key tool (**Major User Projects 1-2, 6, 9, 11, 13, 16, 18-21 & 24-26 and Minor User Project 2**). To highlight a few key projects, Dr. Maier will leverage the new system to push the limits of high b-value dMRI in the prostate for the detection of prostate cancer. Dr. Lee will utilize the strong gradients to explore diffusion time dependence in the aging brain, using the new Vida to facilitate multi-site validation studies of how water exchange is altered in Alzheimer's disease. Dr. Huang will use the new system to translate imaging markers of axonal pathology using diffusion microstructural modeling and pave the way for multi-site clinical imaging trials of neuroprotective therapies in multiple sclerosis. Dr. Takahashi will take advantage of the high gradient strengths to boost the SNR of diffusion tractography in the developing human brain and investigate neuroscientific links between white matter development and gyrification in patients with lissencephaly and agenesis of the corpus callosum. Drs. Gholipour at Boston Children's Hospital will use the strong gradients to overcome the challenges of delineating fetal brain microstructure using dMRI, and Dr. Afacan will develop motion and distortion robust dMRI sequences for detection of subtle microstructural changes in pediatric epilepsy.

Overall, the proposed replacement of an obsolete 3T MRI system with the newest generation Siemens 3T Vida benefits research performed across MGB immediately, while creating venues for exciting new research that will ultimately lead to a better understanding of how the human brain and body functions in health and in disease. The proposed instrument supports the important long-term research strategy and investment in cutting-edge instrumentation at MGH and the Martinos Center, which has laid the groundwork for defining the standards for many large-scale imaging studies, as exemplified through the Martinos Center's involvement in developing the imaging protocols and scanning procedures for the multi-site Adolescent Brain Cognitive Development (ABCD) study and several disease-based Human Connectome Project studies (e.g., the HCP-Lifespan and Boston Adolescent Neuroimaging of Depression and Anxiety projects). Research performed at MGH in MR imaging techniques and MR instrumentation is about 5–10 years ahead of the medical device industry and has given Martinos Center investigators a well-deserved technological edge upon which they have innovated and developed, providing imaging technologies that have had a meaningful and lasting impact on how large-scale research studies and clinical imaging is performed worldwide. MGH, BWH and the Martinos Center both have a proven track record of bringing their research from the bench to the bedside, and the proposed instrument will carry on this tradition of driving forward technological development in the service of improving health care.

Providing exceptional imaging equipment—together with key expertise to operate the equipment and innovative technology development to fully exploit the power of the equipment—has always been integral to the Martinos Center operational model and its mode of attracting users. Upgrading the 3T MRI system from the existing 16-year-old prototype to the next-generation system is important for the medium-/long-term strategy of the Center and will serve as a continuation of efforts to provide the most powerful imaging equipment, ultimately giving our investigators – and NIH-funded researchers nationwide – the technological edge needed for innovative clinical, translational, and basic research.