INSTRUMENTATION PLAN

This application seeks support from the High-End Instrumentation Grant Program to fund a new Siemens 3 Tesla (3T) whole-body human MRI system equipped with high-performance gradients to be used for clinical, translational, and basic science research at the Athinoula A. Martinos Center for Biomedical Imaging, the institutional core biomedical imaging facility at the Massachusetts General Hospital (MGH) and the largest human imaging research facility in the greater Boston area. This system will replace an existing 16-year-old obsolete 3T MRI scanner and will provide a **substantial increase in performance with next-generation whole-body gradient technology featuring a *maximum gradient strength (G_{max}) of 200 mT/m, the highest value achieved to date in a commercially available whole-body 3 Tesla system, and maximum slew rate of 200 T/m/s***. This next-generation 3T MRI scanner will exceed the acquisition capabilities of other state-of-the-art systems to meet the diverse scientific needs of our users, including cutting-edge clinical and translational neuroimaging, body, oncology and cardiovascular imaging studies; cognitive and basic neuroscience research; and novel instrumentation development. While the 3T research program at the Martinos Center has been very successful, **the 3T Tim Trio MRI scanner to be replaced is obsolete and no longer capable of serving the diverse and advanced technological needs of our user community, nor are our other systems capable of meeting our users' growing needs for advanced instrumentation. The development of the hardware and software platform for this ancient scanner by the vendor ended years ago, and even another full upgrade would only bring us to a platform that has reached the end of its development. *The urgency of replacing the 3T Tim Trio is compounded by the imminent end-of-support status of this system, which will occur at the end of 2023 and will significantly curtail the availability of spare parts and qualified service engineers to repair and maintain this obsolete system. Therefore, it is imperative that we replace the system soon,* and the best candidate is the newest generation 3T platform described in this proposal.**

The proposed *next-generation 3T human MRI scanner* will be built on Siemens' latest 3T platform, the Vida scanner, and offer new gradient capabilities and improved system performance that will greatly enhance ongoing NIH-funded imaging research at the MGH and leverage our Center's expertise in developing next-generation MRI technology for clinical, translational, and basic science research, thereby preparing our investigators to lead the next generation of multi-site studies targeting precision imaging of the human brain and body. Based on discussions with the scanner manufacturers and the broader MRI community, an active push is being made to integrate stronger gradients into state-of-the-art clinical and research scanners for improved image quality and encoding speed, as evidenced by the considerable investment by Siemens into the technology built into this new 3T whole-body scanner. Equipped with high-performance *whole-body* gradients and featuring the latest hardware, software, and physiological monitoring tools, the next-generation 3T Vida will be an essential and valuable addition to our existing fleet of 3T scanners, which are more than a decade old. Situated within the vibrant research environment of the Martinos Center and MGH, the new 3T Vida instrument will future-proof our users against the rising tide of MR technology development and enable existing and newly funded studies to migrate to this new platform, supported by a strong team of technical users who will take advantage of the new platform to disseminate cutting-edge imaging techniques developed at the Martinos Center for broader use.

To support our selection of the proposed instrument, we compare the performance of the requested next-generation 3T human MRI scanner with other similar instruments available on the market. The current generation of commercially available 3T scanners such as the Siemens Prisma, GE Premier, and Philips Achieva 3T X-series (Quasar Dual gradient system) scanners feature integrated whole-body gradient systems with a G_{max} of 80 mT/m and slew rates of 200, 200 and 100 T/m/s, respectively. *Compared to the more widely available GE Premier, the GE Signa Ultra High Performance (UHP) 3T whole-body 60 cm bore MRI scanner is only available at a limited number of research sites and includes a modest improvement in G_{max} up to 115 mT/m and slew rates up to 240 T/m/s. The next-generation Siemens 3T Vida MRI scanner will feature much higher G_{max} of 200 mT/m, up to 2-5x the current industry standard for clinical MRI systems, and slew rates up to 200 T/m/s, on a commercially available platform that will be widely distributed and released at RSNA 2022. The next-generation Siemens 3T Vida thus represents a significant advance in gradient capabilities over other whole-body scanners and paves the way toward the greater adoption of high-performance gradients for research and clinical studies.*

With respect to dedicated built-to-order research scanners equipped with high-performance gradients, the GE MAGNUS head gradient coil offers 200 mT/m maximum gradient amplitude and slew rates of up to 500 T/m/s per axis within a 37-cm final patient bore diameter using clinically available gradient power amplifiers (1). However, the head gradient coil design precludes use by our growing number of body, cardiovascular and fetal MRI users, who seek the improved signal-to-noise (SNR) ratio and encoding speed afforded by high-performance gradients for an array of structural, functional and metabolic imaging studies. Similarly, the Siemens 3T Connectome scanner at MGH offers ultra-high gradient strengths up to 300 mT/m and fast slew rates up to 200 T/m/s on a whole-body platform, but due to safety reasons cannot be used for imaging outside the brain. Thus, the proposed Siemens 3T whole-body human MRI scanner strikes the best balance between gradient capabilities, system performance, and field of view to satisfy the broad range of users seeking imaging time at the Martinos 3T Core Imaging Facility. The fact that Siemens is the manufacturer of the proposed instrument only serves to build on the strength of our long-standing partnership with the vendor to develop clinically useable protocols on their latest commercial scanners and establish new standards for clinical and translational imaging.

The proposed instrument will serve as key enabling technology that will complement and bridge the diverse research being performed on the range of conventional and custom MRI scanners at the Martinos Center and across Mass General Brigham, including two P41 National Centers for Biomedical Imaging and Bioengineering (NCBIB), the Center for Mesoscale Mapping at MGH and the Advanced Technologies – National Center for Image Guided Therapy (AT-NCIGT) at Brigham and Women's Hospital (BWH), as well as numerous recently funded projects across Mass General Brigham and the greater Boston research community that rely on high-performance gradient systems to push the limits of speed and imaging resolution for detailed structural and functional characterization of the central nervous system, pediatric, body and cardiovascular pathophysiology. The features and benefits provided by this upgrade over our existing system are summarized as follows: (1) ***next-generation whole-body gradient technology featuring unmatched, commercially available G_{max} = 200 mT/m and high slew rate = 200 T/m/s*** that will significantly boost SNR and enable higher resolution and faster imaging across a range of applications; (2) streamlined and standardized workflows for greater ease of use, enabling a broader user base as well as robustness and consistency across sessions using the newest Numaris X Syngo software platform; (3) standardized hardware and software for compatibility with other sites, enabling the Martinos Center's technological developments to be readily translated to the newest platform and integrated into new, collaborative multi-site trials; (4) improved manufacturer support and maintenance for a product system moving forward, reducing the burden of in-house modifications to the old system; (5) **enhanced system performance including 128 RF receiver channels, local BioMatrix shims, integrated BioMatrix high-temporal-resolution physiological monitoring, a faster image reconstruction computer, *a new Open Recon platform for on-scanner integration of research and third-party image reconstruction algorithms*, and new sequence and application packages compatible with the latest Siemens platform**; and (6) an up-to-date testbed for the unique instrumentation and technology research and development performed at the Martinos Center, including advanced imaging sequences and reconstruction, higher-density receive coil arrays, and shim-RF multi-coil arrays to be shared with our collaborators and freely disseminated to the MRI community.

Of these new features and benefits, the improved gradient capabilities, enhanced system architecture including higher RF channel count and BioMatrix technology, and new Open Recon platform and accelerated image acquisition techniques are most impactful to our users. The higher G_{max} and slew rate will translate directly into better image quality by boosting SNR, reducing echo spacing and image distortions, and enabling higher in-plane resolution, thinner slices, and/or overall shorter acquisition times. The increased gradient performance will benefit a wide range of imaging sequences and applications, including fast imaging techniques such as echo planar imaging (EPI) and turbo spin echo (TSE), the workhorse of functional, perfusion and anatomical MRI, and provide transparent benefits to diffusion MRI. The higher density coil arrays enabled by this hardware upgrade along with the enhanced system architecture will further improve the SNR of the images and enable even higher spatial resolution imaging than what is currently available. The combined improvements in gradient technology and higher RF channel count, combined with vendor-supported software packages for accelerated imaging including simultaneous multislice imaging, compressed sensing, Wave-CAIPI and deep learning will translate into shorter scan times for high-resolution anatomical imaging, which is a key target for clinical 3T MRI and will make the new 3T scanner even more accessible to clinical research studies beyond those shown in our Research Projects described below. Furthermore, the whole-body gradient design will make the new 3T scanner accessible to clinical research studies across a wide range of organ systems outside the brain, including the heart, lung, liver, prostate, spine and knee, as represented in our diverse base of Major and Minor Users. We previously demonstrated that higher gradient strengths and slew rates available on the Siemens 3T Prisma system, the previous-generation 3T research MRI platform, could provide better sensitivity and imaging speed for both clinical and research studies (2). With this next-generation 3T MRI scanner, we will similarly achieve a significant boost in imaging speed and quality, further increasing interest amongst investigators and motivating the transition of studies from the 3T Prisma to the next-generation 3T Vida. By increasing the performance, usability, and long-term stability of the existing 3T scanner, we expect to distribute studies more evenly between our 3T scanners. *This new scanner will help address the exceedingly high demand for 3T MRI scan time at our Center and resolve the imminent end-of-support status of the current 3T Tim Trio, which is currently vastly underutilized due to the limited availability of spare parts and service engineers capable of repairing the system.*

By serving a highly productive interdisciplinary group of NIH-funded investigators, the proposed instrument will enhance existing research programs while encouraging new projects and collaborations to emerge and flourish. The proposed instrument will also offer a unique opportunity to help develop new supporting technology on a commercially available next-generation 3T system that will not only benefit the Martinos Center but will also pave the way for this technology to be deployed to many other 3T MRI sites worldwide.

A. JUSTIFICATION OF NEED

A.1 Background

The Athinoula A. Martinos Center for Biomedical Imaging runs the institutional biomedical imaging research core facility of the Massachusetts General Hospital and provides cutting-edge tools and expertise across all domains of image acquisition and analysis to support a large and diverse community of investigators. The Martinos Center is the third largest of the 60+ Mass General Brigham Cores, with more than 10% of the $1+ billion in research activity at the MGH utilizing its broad imaging services. The Martinos Center also provides advanced biomedical imaging resources for researchers from other Boston area universities and hospitals, including Harvard and MIT-affiliated research hospitals and institutes. These researchers are actively supported by federal and other funding agencies including the NIH, National Science Foundation, Department of Defense, and many private foundations. Research at the Martinos Center has a twofold mission: to advance the development of imaging technologies and to apply these technologies to support basic science and translational research, driven by an overarching interest in the continuous improvement of clinical care. Martinos Center investigators are innovating in anatomical, diffusion and functional MRI and spectroscopy, as well as cutting-edge tools for computational image analysis. These innovations are in turn used by the Center to support over 200 NIH-funded research projects at the MGH and other Boston-area institutions in fields ranging from neurovascular, neurologic, and psychiatric disorders to cognitive neuroscience, cancer, and cardiovascular function.

The Martinos Center is a vital part of the vibrant biomedical research community of the MGH Charlestown research campus, which comprises over a million square feet of research space across the many departments that actively utilize the Martinos Center's imaging resources for their research (see ***Section G: Overall Benefit*** for more details). The user base of our existing 3T scanners has grown rapidly over the last decade, attracting researchers from within the Martinos Center, MGH, BWH and the greater Boston research community. In particular, our conventional and custom 3T MRI systems *represent key technology available at the Martinos Center*. Over the past 23 years, the Martinos Center has built up deep expertise in 3T MRI, with several major research efforts pushing the limits of gradient technology for high-sensitivity and high-resolution MRI. We are now poised to apply this experience to enable, support and design current and future studies that will be performed by our users on the proposed next-generation 3T scanner. Building on its strong track-record in developing cutting-edge MRI techniques, the Martinos Center has been actively involved in integrating such techniques into many large-scale imaging studies, including the multi-site Adolescent Brain Cognitive Development (ABCD) study conducted at 3T. We envision that the proposed next-generation 3T Vida will serve as the central platform for conducting the next generation of multi-site imaging studies incorporating high-performance gradient technology. As the first whole-body 3T MRI equipped with G_{max} = 200 mT/m and slew rates of 200 T/m/s, this new system will be the first to enable large-scale imaging trials across sites using such technology, which will be a key feature for Martinos investigators to innovate upon and establish as the standard for broader dissemination in large-scale imaging studies like the ABCD, thereby ensuring that the instrument will serve as an important local, regional and national resource for years to come.

As high-fidelity 3T MRI sequences have become the workhorse for state-of-the-art clinical and research studies, with methodological developments in these fields showing no signs of slowing down, we are seeing a greater number of basic and clinical neuroscience as well as pediatric, oncological, body and cardiovascular imaging studies conducted at 3T using the best available gradient technology, thereby rapidly increasing demand to a critical mass for the next-generation whole-body 3T human MRI system. The proposed *next-generation whole-body 3T MRI* replacement of one of our oldest 3T MRI systems will thus support and enhance already funded research studies as well as enable new clinical and translational studies. <u>This application focuses on the immediate needs of new and existing users for the 3T system as well as enhancements to the instrument that are enabling the design of new projects and already attracting new 3T users from the large community of investigators at the Martinos Center and within the greater Boston area</u>. In the following sections, we describe the proposed upgrade, configuration of the existing 3T instruments at the Martinos Center and their limitations for addressing the needs of our clinical/translational research community, and highlight how this upgrade will address the specialized needs of our users that drive our request for this High-End Instrumentation Grant.

A.2 Inventory of Similar Instruments

Out of the Martinos Center's eight available human MRI systems, six are currently 3T MRI. All of them are manufactured by Siemens. In partnership with the scanner manufacturer, the Martinos Center has a long history of developing specialized MRI systems for human imaging, and three of the six 3T MRI scanners at the Martinos Center are initial prototypes of now commercially available systems that are marketed and distributed worldwide.

Among the specialized 3T instruments installed at the Martinos Center, the Connectom A 3T MRI system is the most recent. Equipped with ultra-high gradient strengths (300 mT/m peak gradient strength, 200 T/m/s slew rate), the MGH Connectome scanner was developed as part of the MGH-USC Human Connectome Project, and its advances in gradient technology were incorporated into the commercially successful Siemens MAGNETOM Prisma scanner. The Connectome scanner has been used to demonstrate the benefits of 300 mT/m gradients for diffusion MRI, but for safety reasons cannot be used for imaging outside the brain. As such, the ultra-high gradient 3T Connectome MRI scanner is practically limited to supporting brain imaging studies only, and while serving a critical role in advancing technology development for diffusion MRI, has in practice catered to a small group of specialized users who are experienced in the methods required for generating high-quality data. Due to the fundamental design limitations of the current Connectome scanner, we are now embarking on a significant upgrade of the system through an NIH BRAIN Initiative U01 project to develop the next-generation Connectome scanner ("Connectome 2.0") with maximum gradient strength of 500 mT/m and slew rate of 600 T/m/s. To meet these aggressive target specifications, the one-of-a-kind Connectome 2.0 scanner will feature an asymmetric head-only gradient coil, thereby precluding its use for studies in other organs.

In addition, the Martinos Center provides a head-only 3T PET/MRI system based on a Tim Trio and offers two 7T MRI scanners to high-field users, including the world's first 7T MRI scanner with a clinical console and an FDA-approved 7T MRI system for clinical and translational research. Beyond these specialized systems that are not suitable for whole-body imaging, the Martinos Center has four whole-body 3T human MRI systems. Since one of the whole-body systems is an integrated PET/MRI system (Biograph mMR), only three are presently available as general-purpose, commercially available whole-body MRI systems *(see **Table 1** for a summary of usage of these 3T scanners).* One of those systems is the first (oldest) whole-body 3T by Siemens in the United States, which has been upgraded several times, mostly recently to the 4G platform (Prisma Fit). It offers a 60 cm patient bore, 64 RF channels with the associated coils, and a high-performance XR gradient set with a peak gradient performance of 80 mT/m. Since the system runs the most recent Siemens software platform available at the Martinos Center (VE11C) and houses a high-performance gradient coil, *it is in very high demand to the point of being oversubscribed (projected at 2400 hours in 2022)* (see ***Figure 1***). The Center is **not** able to accommodate all NIH-funded users requesting time here.

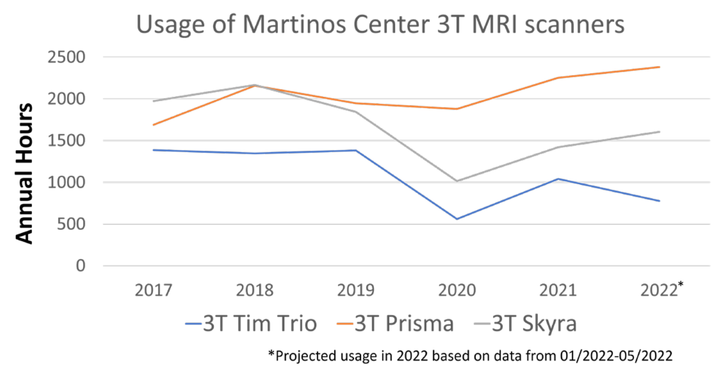

Table 1. Usage of similar Martinos Center 3T MRI scanners to the 3T Tim Trio (the instrument to be replaced) over the last 5 years. Usage was calculated from billing hours summaries for the calendar years indicated above. For 2022, annual hours were projected based on data from January to May 2022.

Another system in high demand is the Siemens Skyra wide bore whole-body 3T MRI. It offers the same software platform (VE11C) and compute power as our Prisma Fit and a 70 cm patient bore. However, being a first-generation wide-bore 3T MRI system, its performance specifications are compromised for the gradients (40 mT/m peak, but limited duty cycle) and RF transmit performance. Furthermore, it suffers other imperfections common for older era wide-bore MRI systems that are perfectly acceptable for clinical applications but limit research applications, including high-resolution and high-speed structural, functional and anatomical MRI. Despite its performance limitations, the system continues to have high utilization (*projected to be 1600 hours in 2022*) owing to the large bore for patient comfort and the availability of modern acquisition and reconstruction methods. In a survey of the major users of the Skyra, if given the choice, our current clinical research users, including projects focused on brain, pediatric, cardiac and body imaging, would opt for improved system performance and image quality over the wide-bore configuration of the current Skyra 3T scanner.

The last available whole-body 3T MRI is the one to be replaced with this application, a Siemens Tim Trio that was installed in 2006. It features a 60 cm patient bore, TQ engine gradients (40 mT/m peak), 32 receive channels and VB17SP4 software. While the gradient performance that is critical for many high-speed/high-performance imaging applications is marginally better than that of the wide-bore Skyra, the lack of many modern pulse sequences and the limited compute power makes the system unattractive to many users looking to use state-of-the-art techniques for their studies. We have tried to enhance the system with custom in-house built image-reconstruction computers and various upgrades. *However, many of the latest acquisition technologies developed at the Martinos Center and/or offered more recently by Siemens, including Wave-CAIPI, compressed sensing, and deep learning-enabled reconstruction, are not adaptable to this very old software version. As a result, we have seen a steady decline in the number of new and existing users on the Tim Trio, which is now significantly under-utilized; for reference, the projected usage in 2022 is only 776 hours).* In short, the demand for newer techniques and better hardware has outpaced our ability to recreate such technologies in-house. As a result, we have struggled to maintain utilization of the system. This has forced the few remaining users to compromise on the techniques they use and accept less than optimal data quality. The current situation has placed significant constraints on our investigators seeking to use cutting-edge acquisition technologies that are actively developed at our Center for higher resolution, accelerated imaging for human studies – a true missed opportunity for direct translation and adoption of these technologies. *The urgency of replacing this system is underscored by the imminent end-of-support by Siemens at the end of 2023 (see end-of-support letter signed by Martin Silverman of Siemens in the **Letters of Support**).*

Thus far, our 3T MRI systems have been largely used for structural and functional MRI of the human brain, but with the active development of new scanning methodologies and institutional initiatives supporting imaging research across organ systems, an increasing number of body imaging applications at 3T have come to the fore, especially in cardiac and oncologic imaging, which now comprise nearly 1/3 of our major NIH-funded users. While increased susceptibility artifacts around the lung pose a disadvantage for imaging the heart at a higher field-strength, the increased sensitivity at 3T enables advanced MR techniques such as diffusion and spectroscopic imaging to be brought to the heart. The upgrade would thus provide a next-generation whole-body high-performance 3T MRI with up-to-date hardware and software for seamless physiological monitoring and new capabilities to enable free-breathing cardiac and body imaging exams.

A.3 Description of the Proposed Instrument

The proposed instrument is a next-generation Siemens MAGNETOM 3T Vida MRI scanner featuring the latest generation gradient hardware and software for research and clinical imaging. *The next-generation 3T Vida system is being debuted at the Technical Exhibition of the Radiological Society of North America's (RSNA) Scientific Assembly and Annual Meeting in 2022. We have received a first-hand demonstration of the system's capabilities on-site at the Siemens factory in Erlangen, Germany, where the scanner is being manufactured, as part of our close collaboration with Siemens in developing key aspects of the gradient technology incorporated into this system. The choice of Siemens as the vendor for the replacement of our outdated 3T Tim Trio was therefore straightforward* and in fact builds upon the strength of our Center's decades-long partnership with Siemens in developing and translating cutting-edge MRI technology for a wide range of clinical and research applications. As such, the instrument will be the first of its kind at MGH.

The advanced 3T MRI system is built on the Vida platform incorporating an innovative wide-bore magnet design with excellent magnetic field homogeneity. This next-generation system is installed with a high-performance whole-body gradient with G_{max}=200 mT/m and 200 T/m/s slew rate on a 60 cm patient bore size (**Figure 1**), achieving a combination of gradient specifications that are not commercially available from any other MRI scanner manufacturer. *This gradient coil features the latest high-efficiency technology including directly cooled conductors to enable high current density without incurring excessive heating (3). The gradient system is driven by two high-performance gradient power amplifiers (GPA's) with peak current of 1200 A and peak voltage of 2250 V per axis and features sophisticated dual-GPA control, which has been developed in concert with the latest generation of high-performance gradients at Siemens.*

Siemens is commercializing the next-generation high-performance gradient option on the Vida platform, in keeping with the precedent established at Siemens for embedding the latest gradient technology into state-of-the-art wide-bore systems. The gradient upgrade package provided by Siemens and built into the wide bore of the original 3T Vida system will result in a bore size of 60 cm, which is the same width as the previous generation high-gradient performance Siemens 3T Prisma MRI. Based on our experience with the Prisma, the 60 cm bore size accommodates the vast majority of our research subjects, including those participating in body, cardiac, and fetal MRI studies, and will provide better magnetic field homogeneity over our existing wide-bore 3T scanner, which is important to our growing set of cardiac MRI users. Of note, these subjects are usually scanned clinically on the 1.5T Avanto scanner at the MGH main campus, which also has a 60-cm bore diameter. Therefore, the slightly narrower bore size of the new 3T Vida scanner will not be a significant limiting factor in accommodating body/cardiac MRI users, whose research studies will benefit from the improved magnetic field homogeneity and gradient performance provided by the proposed instrument, as detailed in ***Section C***.

As a MAGNETOM 3T Vida MRI scanner, the instrument will feature all the advantages of the current state-of-the-art Vida platform with 128 receive channels, TrueShape 2-channel parallel transmit, a full set of head,

Figure 1. Photographs of the next-generation Siemens 3T Vida MRI system equipped with a high-performance whole-body gradient coil (Gmax=200 mT/m, slew rate 200 T/m/s). Front (left) and back views (right) of the scanner show the gradient set integrated into the bore of the magnet and driven by two gradient power amplifiers.

neck and body imaging coils including the BioMatrix sensorized 72-channel spine coil, 30-channel body coil, 32-channel head coil and 64-channel head-neck coil with integrated shims. The system is equipped with the highest performance compute option for the fastest image reconstruction available with modern accelerated imaging techniques. It comes with the latest state-of-the-art Numaris X software platform and a suite of software packages required for neuro, body and cardiovascular imaging, including fMRI, ASL, advanced diffusion MRI and cardiac applications. *The system also introduces new research capabilities through the Open Recon interface, which is designed to enable third party image reconstruction and post-processing solutions to be integrated directly in the reconstruction pipeline. The Open Recon platform effectively eliminates the need to export the images or raw data to a separate device and makes custom reconstructions and processed images directly available on the scanner console.* The new 3T system electronics will be based on those offered by Siemens in the current state-of-the-art Vida. This includes a modern 4G DaVinci generation console and a high-end "MARS" image reconstruction computer equipped with a high-capacity RAID for temporary data storage and multiple GPU accelerators for fast image reconstruction. The magnet will be the newest generation Siemens zero-boil-off 3T Magnet. This new 3T system will be fully warrantied and maintained by Siemens with a standard service contract.

A.4 Need for the Proposed Instrument

The proposed instrument seeks to extend the 3T MRI program at the Martinos Center by replacing our existing system with a modern system equipped with the latest gradient hardware, coil technology, and software interface, providing enhanced performance that will last for years to come. As shown in the **Section C: Research Projects**, there are many active, ongoing studies utilizing the 3T scanners at the Martinos Center that will take advantage of the new 3T Vida's unique capabilities. Specific needs are summarized below.

A.4.1. Our current 3T whole-body MRI is obsolete and no longer serves the needs of the user community

The existing 3T whole-body MRI scanner that will be replaced with the proposed new scanner is a Siemens Tim Trio that was installed at the Martinos Center in 2006. After over 16 productive years of operation, this scanner has become obsolete to the point that we can no longer effectively use it to serve our community of investigators. Due to the outdated software (VB17A) and limitations in RF hardware, many state-of-the art anatomical, functional and structural MRI techniques cannot be made available on that system. In parallel, the need for a new state-of-the-art platform with better hardware, software and development capabilities has arisen due to the demand from our technical users to advance their developments on the latest system (e.g., see ***Major User Projects 1, 2, 5, 9, 12 & 16*** and ***Minor User Projects 1 & 3***) as well as new users that are performing advanced neurological, body and cardiovascular imaging techniques (e.g., see ***Major User Projects 3, 4, 6-8, 10, 11, 13-15, 17-26*** and ***Minor User Project 2***).

As the number of NIH-funded technical development and human MRI projects have increased in the last few years (see Major and Minor Users), the Prisma and Skyra 3T MRI scanners are typically booked back-to-back for weeks on end, making it challenging for NIH-funded studies to reserve imaging slots. As such, the progress toward achieving the aims of many projects becomes unnecessarily delayed by the chronic shortage of available scan time. The next-generation Vida will provide a much-needed and forward-looking alternative to the Prisma and Skyra scanners as the latest commercially available Siemens 3T system equipped with cutting-edge gradient and RF technology and up-to-date software for sequence development.

A.4.2. The new 3T whole-body MRI enables state-of-the-art technology development and dissemination

The next-generation 3T Vida MRI system with high-performance gradients will not only benefit research across the wide range of neuroimaging, body, pediatric, oncologic and cardiovascular MRI projects being carried out by our users, but also will help fulfill the central mission of the two P41 NCBIB's utilizing the instrument: to develop new technologies for dissemination. New key features of the next-generation Vida include the Open Recon platform for custom image reconstruction directly on the scanner and the latest Syngo Numaris X software, which will facilitate the translation of technical developments in MRI hardware and software being performed by Mass General Brigham investigators to users across the country and world. Currently, the Martinos Center has no system of the newest software generation, making it very difficult to disseminate developments in MR acquisition and reconstruction technology. Tremendous progress has been made over the last decade in accelerated brain MRI – areas in which our investigators have played a significant role (4, 5). However, much of this technology remains unavailable for application and further development on our current 3T systems due to the older software. The next-generation Vida will bring our developers and users back to the forefront of cutting-edge image acquisition on the latest technology platform, thereby providing a direct route for state-of-the-art technology development and dissemination, supported by and serving active large-scale research efforts such as the Center for Mesoscale Mapping and the Human Connectome Project.

As an example of hardware development, one such project is being performed by ***Major User Project 9, led by Drs. Bilgic and Stockmann***. The design and implementation of a 32-channel head-neck array coil with integrated shims is expected to improve field inhomogeneity in difficult areas to image such as the cervical spine (see ***Major User Project 12, led by Dr. Barry***), and for applications demanding high field homogeneity and SNR, such as diffusion MRI and MR spectroscopy (see ***Major User Project 14 led by Dr. Andronesi***). Another such development project is being performed as part of the Center for Mesoscale Mapping (***Major User Project***

1, led by Dr. Rosen), featuring work on the high-resolution diffusion imaging technique called gSlider (6). gSlider allows diffusion imaging of the brain and heart to be performed at unprecedented spatial resolution. The next-generation Vida provides the ideal platform for a technology like gSlider, as it brings high gradient strength for efficient diffusion encoding and spatial readout, 64-channel RF head coils that are required for accelerated imaging underlying a technique like gSlider, and sufficient compute power and speed to perform the image reconstruction for gSlider online on the scanner.

A.4.3. The new 3T whole-body MRI system provides a direct translational pathway for clinical and research applications of high-performance gradient technology

The delivery of the high-performance gradient package upgrade on the 3T Vida platform with G_{max} = 200 mT/m and maximum slew rate = 200 T/m/s will present a unique opportunity for our users to translate and apply high *b*-value diffusion imaging and microstructural imaging methods to the clinical arena. Our work with the Connectome gradient set over the past decade has shown us that high-performance gradient systems can be applied to provide many additional types of diffusion measurements beyond tractography, with the potential to serve as an "*in vivo* microscope" for interrogating tissue microstructure in states of health and disease (7-10). This knowledge has motivated ongoing efforts in the recently established P41 Center for Mesoscale Mapping to develop cutting-edge diffusion MRI techniques that image down to the mesoscale not only within the adult and pediatric brain but notably outside of it, particularly in the prostate and cardiovascular system, where a strong group of cardiologists and body imagers stand poised to utilize the powerful whole-body gradient embedded in the next-generation 3T Vida. Knowledge gained from the CMM and our suite of neuro-, cardiovascular, and body imaging projects utilizing diffusion MRI (see ***Major Users 1, 2, 6, 9, 11, 13, 16-21, 24-26 & Minor User 2***) will certainly inform and motivate new and ongoing projects on the next-generation Vida scanner. At the same time, the peak gradient strength on the next-generation Vida, which is more than double that of the current state-of-the-art Siemens 3T Prisma scanner (G_{max}=80 mT/m), promises to bridge the gap between the known scientific advantages of higher gradient strengths and their viable use in the patients who stand to benefit most.

A.4.4. The new 3T whole-body MRI greatly improves body and cardiac imaging capabilities

The increased interest in advanced cardiac imaging at Mass General Brigham and other Harvard-affiliated hospitals in recent years has created an increasing demand for high-performance gradient technology on a whole body 3T MRI scanner. The high gradient strengths and slew rates available on the next-generation 3T Vida will enable advanced techniques such as prostate diffusion (see ***Major User Projects 2 & 13, led by Drs. Tempany and Maier***), cardiac diffusion (see ***Major User Projects 4 & 26, led by Drs. Sosnovik & Nezafat***), and fetal and pediatric brain microstructure (see ***Major User Projects 19 & 24, led by Drs. Gholipour and Afacan***) to be performed more effectively. The availability of integrated physiological monitoring via BioMatrix technology will also create a new resource covering the needs of a single modern, high-performance 3T whole-body MRI for advanced clinical trials and methodology development (see ***Major User Projects 3 & 7, led by Drs. Simonyan and Montesi***). Finally, the unique contrasts that will be used by cardiovascular imagers (see ***Major User Projects 10, 17 & 22, led by Drs. Malhotra, Das & Rosenzweig***), including quantitative T1, T2 and T2* mapping and diffusion, will all benefit from the updated software and sequences delivered on the system.

A.4.5. New technologies available on the next-generation Vida over existing 3T whole-body scanners

The next-generation 3T Vida system has been designed to include several enhancements over current 3T scanners that provide additional imaging performance to enable higher resolution and faster acquisitions, thereby

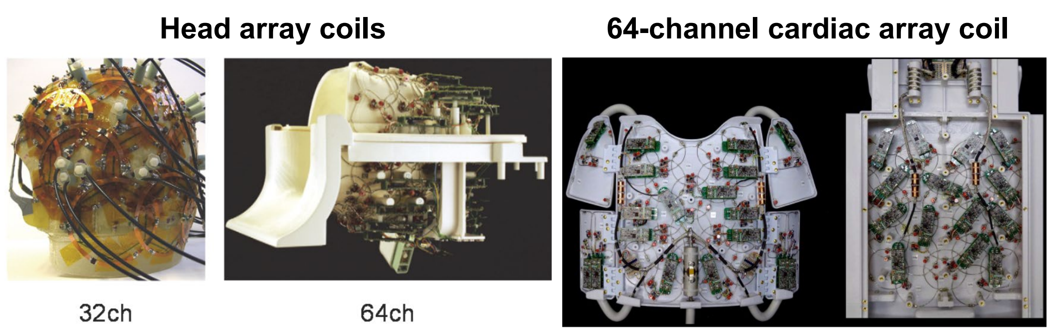

Figure 2. High-density array coils designed and supported by the RF Laboratory of the Martinos Center.

extending the reach of 3T MRI technology to explore new scientific frontiers and expand the range of patient populations who can be scanned with high fidelity. An abbreviated list of the performance enhancements that will have a direct impact on several of our active Research Projects is provided below.

a. Upgrade from 32- to 128-receive channels, and high-density plugs to enable 64-ch receive coil arrays. One of the most important practical features included in this upgrade is the increased number of RF receiver channels from the current standard of 32 channels to 128. Siemens provides a 64-channel head/neck coil and

72-channel spine coil with the new Vida, making full use of the available 128 receive channels on the system. This product is in part the result of a major research program at the Martinos Center involving the design and development of high-density coil arrays, including the prototype 1.5T and 3T 32-channel coil arrays (11) and three generations of 32- and 64-channel coil arrays at 7T as well as 64-channel and 96-channel arrays at 3T (11-14) (**Figure 2**). The new system supports 128 channels, inspiring new coil designs that will be tested and used extensively. This feature will enable the Martinos Center to continue designing high-density array coils. The system is also compatible with a wide range of Siemens 3T array coils such as the 60-channel body coil and 64- and 128-channel cardiac coils (15, 16), which are not part of the proposal but already present at the Martinos Center and will greatly benefit our cardiovascular MRI users (see ***Major User Projects 6, 10, 17, 22 & 26***).

b. Increased gradient performance from maximum gradient strength of 40 mT/m to 200 mT/m: The new 3T system will include a significant boost in gradient strength over the existing system, from 40 mT/m to 200 mT/m. The increased gradient strength will benefit ongoing and future advanced diffusion MRI, high-resolution fMRI studies, and fast anatomical imaging for clinical translational studies. Beyond improved sensitivity to tissue microstructure, the high-performance gradient set on the next-generation 3T Vida will enable the acquisition of diffusion MR images with shorter echo times than those achievable on any other commercially available research scanner to date, including the current state-of-the-art Siemens Prisma with G_{max}=80 mT/m. The higher gradient strengths on the next-generation Vida will provide a critical increase in SNR needed for acquiring sub-millimeter and/or high b-value diffusion data, as highlighted in our simulations in **Figure 3**. With a maximum gradient strength G_{max}=200 mT/m, the Vida platform has the potential to provide the same SNR level at b=10,000 s/mm^2 as our current Tim Trio scanner at a mere b=500 s/mm^2 and matches the SNR of the Prisma scanner at b=2000 s/mm^2. This dramatic gain is provided by the significant reduction in the minimum achievable TE, which can be as short as 77 ms at b=10,000 s/mm^2 (224 matrix, 1.25 mm resolution, 6/8 partial Fourier, $R_{inplane}$=2), rivaling the performance of the original MGH Connectome scanner. Diffusion MRI features prominently in more than half of our users' projects (***Major User Projects 1-2, 6, 9, 11, 13, 16, 18-21 & 24-26 and Minor User Project 2***), which will all benefit from the gain in sensitivity afforded by the new Vida.

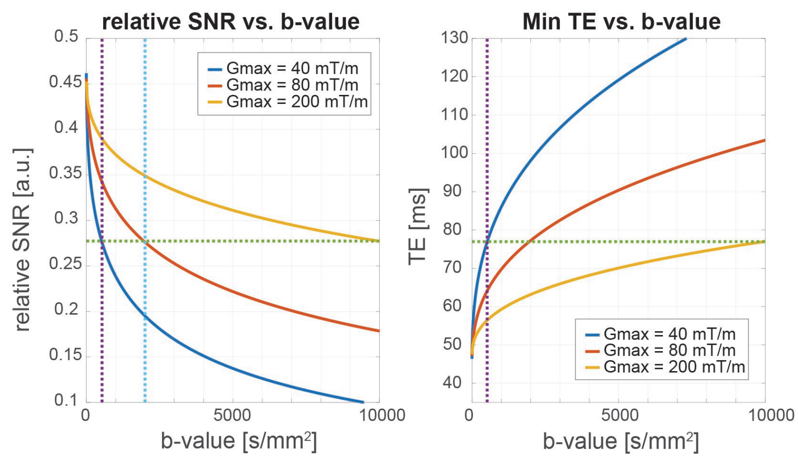

Figure 3. Relative SNR and TE comparisons between conventional scanner gradient strengths of G_{max}=40 mT/m and 80 mT/m and the next-generation Vida with G_{max}=200 mT/m. (left) The SNR gain is dramatic: Vida provides the same SNR (green horizontal line) at **b=10,000 s/mm²** as the G_{max}=40 mT/m scanner at only **b=500 s/mm²** (purple vertical line) and the G_{max}=80 mT/m scanner at **b=2000 s/mm²** (blue vertical line)**.** (right) Vida reduces the minimum TE to 56 ms for b=500 s/mm^2 compared to 77 ms at G_{max}=40 mT/m and 65 ms at G_{max}=80 mT/m (purple vertical line), enabling b=10,000 s/mm^2 at a TE of 77 ms (green horizontal line). T_2 of white matter ~60 ms is assumed.

The higher gradient strength on the next-generation Vida will also benefit high-resolution fMRI studies. In high-resolution fMRI, typically gradient slew rate is the specification of interest because faster slewing reduces the EPI echo spacing, which decreases image blurring and geometric distortion. However, for the large imaging encoding matrix sizes used in high-resolution EPI such as 256×256 and larger, the scan protocol becomes increasingly limited by the peak gradient strength—on our existing gradient coil, the peak gradient strength can be easily achieved by the image encoding pre-winders needed to reach high k_{max} samples in k-space. To achieve thin slice profiles for 2D imaging, the higher gradient strength will help to reduce the slice thickness. Gains in echo spacing and thinner slice profiles will enable faster and higher resolution fMRI to benefit our most sophisticated users (e.g., see ***Major User Projects 3, 4, 8, 11 & 12***).

c. Fully integrated parallel transmit system: Parallel transmit (pTx) overcomes transmit inhomogeneity artifacts in the body at 3T and is now an integrated standard feature on the Vida system. Early work in pTx technology was carried out by Martinos Center investigators (17-19). The new fully integrated system has solved prior limitations by overcoming the challenging workflow and integrating it transparently. The proposed 3T system provides automatic calibration/safety procedures to enable routine use of pTx, thereby ensuring optimal image quality and flip angle homogeneity for each patient. This is a major step forward for pTx and will significantly reduce the variability in image quality, which is important for longitudinal studies and clinical trials (see ***Major User Projects 2, 14-16 & 19***).

d. Integrated local shim coils: The proposed 3T Vida instrument is the first commercially available 3T MRI scanner to provide integrated local shim elements in the neck portion of the 64-channel head/neck coil. These additional channels allow our investigators to improve cervical spine imaging, a traditionally challenging area. This feature will offer significant benefits to image quality for ***Major User Project 12, led by Dr. Barry***. More importantly, the use of combined shim and receive coil arrays is also being pioneered by investigators at the Martinos Center (see ***Major User Project 9, led by Drs. Bilgic & Stockmann***) in a 32-channel head coil with integrated shim array for 3T (20). The new software platform and shim integration will enable users to make use of the 32-channel existing shim/RF coil for better image quality using local real-time shimming, which will dramatically reduce image distortions in techniques such as multi-shot EPI for diffusion and fMRI (***Major User Project 9, led by Dr. Bilgic***), high-resolution diffusion imaging with gSlider (***Major User Project 1***), improved spectroscopic resolution (***Major User Project 11, led by Dr. Andronesi***). The integrated CoilShim technology will also improve fat suppression in fetal and abdominal imaging (***Major Users 2, 13 & 19***).

e. New research capabilities with updated Numaris X software platform and Open Recon interface: The next-generation Vida offers the latest Syngo Numaris X software platform for pulse sequence development and the new Open Recon interface for implementation of custom reconstruction algorithms directly on the scanner. The Syngo Numaris X software will facilitate research collaborations and dissemination by enabling transfer of in-house developed pulse sequences and image reconstruction software to other sites and from the vendor directly. Open Recon will significantly advance our technical users' efforts to develop new approaches to image acquisition, reconstruction and harmonization on the latest 3T platform ***(Major Users 1, 2, 9, 16, 19, 24, 26; Minor Users 1 & 3)***. Open Recon makes use of the ISMRMD raw data format and state-of-the-art container technology, enabling custom reconstruction algorithms to run on the MARS hardware and display images on the scanner console in real-time, thereby eliminating the inefficient transfer of data off the scanner and greatly accelerating the pace of technical development. This will be a vast improvement over the current Tim Trio, which is running the obsolete VB17 software that is no longer supported by Siemens. More importantly, the new 3T scanner will provide users with access to the latest pulse sequence and image reconstruction works-in-progress (WIP) prototypes, offering critical functionality for our users' studies that are no longer supported on the Tim Trio.

g. Faster image reconstruction computer with GPU accelerators and increased RAM capacity. The new high-channel count RF coils motivate the push toward higher spatial and temporal resolution, and these high-performance imaging techniques often utilize computationally demanding parallel imaging reconstruction. The new 3T system ships with an advanced image reconstruction computer configured with multi-core CPUs, GPU accelerators, a larger RAID data buffer space, and additional RAM. The performance of the new image reconstruction machine is expected to be better than our current 3T Prisma scanner computer. Real-time reconstruction is critical for online quality control during experimental sessions. With the current system, image reconstruction is typically delayed by several minutes, making it impossible for the operator to detect image corruption, tying up the system and preventing new sessions from starting. Therefore, the faster reconstruction speeds will lead to improved image quality, scanner throughput and utilization and benefit all of our users.

f. Built-in physiological monitoring with faster sampling rate (for cardiac and respiratory measurements). Functional MRI users routinely record systemic physiological signals to remove physiological noise sources from the data, especially in resting-state fMRI. On the older Siemens scanners, including our current 3T MRI scanners, these physiological signals are not sampled sufficiently to be useful for fMRI data cleanup, so an additional set of sensors and analog-to-digital convertors with faster sampling are needed. Purchased separately from another vendor, the user must interface this external system with the MRI scanner to synchronize the physiological recordings with the MRI data, which is cumbersome at best. Starting with the latest generation of 3T scanners, Siemens has provided a physiological recording system—including faster sampling and integrated physiological data synchronization and storage—with the MRI scanner, which is available on the new 3T Vida. The built-in recording equipment integrated with the system greatly reduces experimental complexity, increases data quality, and eliminates the additional costs associated with purchasing and maintaining additional equipment, which will be a boon to many users (e.g., see ***Major User Projects 3, 4, 6-8, 10-12, 17 & 26***). The 72-ch spine coil also features built-in sensors that capture physiological waveforms, further increasing patient comfort and reducing time spent on positioning physiological sensors for capturing respiration, benefiting cardiovascular/body users.

In aggregate, these overall system performance upgrades will provide higher quality data for our users, more sensitive measurements, and may translate into fewer subjects required to complete a study.

A.5 Definition and Justification of Accessible User Time

The Accessible User Time for the requested instrument is projected to be 2400 hours per year. AUT is estimated from the time the instrument is available with all necessary support staff and medical coverage on-site, which is six days a week with 10-hour days from 8AM to 6PM, for 50 weeks a year. Accessibility to the instrument during these hours accounts for building access hours and safety regulations in place at the Martinos Center. During this time, two operators must attend to the scan session. All operators must have cleared safety training with the Center's MRI technologists. Of the 60 hours allotted each week, 10% will be used to regularly maintain the scanner and perform necessary safety measurements and adjustments for smooth scanner operation. This will include daily quality control checks of the scanner system. Subtracting an additional 10% of the available time for stability checks, hardware and software updates, and RF coil maintenance, yields 2400 hours/year available.