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Overview

The Radiology Department has a number of shared resources, including a research computer network based on Ethernet and running both DECnet and TCP/IP protocols on optical fiber and thick coaxial cables. On this network are: All clinical and research MR systems (10 systems); a General Electric (GE) single photon emission computer tomography (SPECT) system; two GE PET systems; and all digital X-ray systems. Digital image data from any of these systems can be sent over the research network.

The Radiology Department's networks are connected to the Longwood Medical Area Network that connects networks at five institutions affiliated with Harvard Medical School. This provides a gateway to the Harvard University network and the national and international wide area networks such as Bitnet, NSFnet, and the Internet. All computers are connected throughout the Department's Ethernet/TCP-IP network.

General MRI Facilities

The MR Division has five clinical areas within the Longwood hospital campus: 1) The main hospital site at 75 Francis Street, L1 level of the main hospital building; 2) The main hospital site at 45 Francis street, the "Pike"; 3) the Lee Bell Center for Breast Imaging; 4) The Longwood Medical Research Center at 221 Longwood Avenue (LMRC Building); and the 5) Carl J. and Ruth Shapiro Cardiovascular Center. All MRI systems are fully supported with inpatient and outpatient facilities, including nursing and technologist staff. A full-time clinical PhD MR Physicist provides clinical MRI protocol development and QA and implementation support. Imaging results are interpreted at electronic reading stations over a clinical PACS with interconnectivity with advanced Radiology and Hospital Information Systems.

Main Clinical and Research MR Imaging Facilities

On the L1 level at 75 Francis Street there is a 9,000 square-foot area in the Ambulatory II Building to support patient and research activities. Housed in this facility are secretarial areas, scheduling rooms, reading rooms, darkrooms, waiting and nursing rooms, a crash area, and a physics and biological support area. This area houses 6 images devices (3 MRI/3 CT), a clinical facility with patient care waiting rooms, inpatient and outpatient facilities, and a six-bed recovery area, all of which support both the diagnostic and interventional programs.

All imaging systems are fully supported inpatient and outpatient facilities with nursing and technologist staff. Imaging results are interpreted at electronic as well as film reading stations, and the systems are connected to the Ethernet, enabling transfer of images and raw data locally and over computer network systems.

Clinical and research MR imaging are performed on three systems – all of which are 70cm wide-bore systems. We have recently modernized the MR facilities, and, as part of this effort, have installed a Siemens 3T Verio, for interventional procedures, a 1.5T Siemens Aera dedicated to in-patient care that is staffed around the clock, and a GE 3T MR750W magnet. The 3T GE system (located on L1 level of the main hospital building) is dedicated to 3T focused ultrasound and is the center of clinical and research programs in FUS.

MRI-guided focused ultrasound systems (ExAblate 2000) with MRI-compatible positioning and sonication systems for single transducer use are integrated with the 3T GE MR. This device was developed through collaboration with InSightec and is used for clinical treatments within the MR Imager. In addition, we have a separate in-house constructed system for the testing of the phased array applicators. The research system has been integrated with 128-channel RF driving systems for phased array testing.

Hospital Main "Pike"

One 1.5T GE Signa Excite MRI resides in this area. The system is connected to the Ethernet, enabling transfer of images and raw data locally and over computer network systems. Although available for research, this primarily an outpatient imaging facility dedicated to clinical use.

Lee Bell Center for Breast Imaging

The Lee Bell Center for Breast Imaging is a 6,850 sq. ft. facility within the main building of the Brigham and Women's Hospital that provides the hospital's screening mammography. This area provides office and clinical space for the provision of mammography and other clinical/research services and contains a conference room with a smart board in one of the radiology reading rooms. The Center is equipped with a GE Centricity PACS (picture archiving communication software) system and has several PCs connected to the Hospital's computer network that includes Internet access. One 3T Siemens Trio MRI system is located in this area, equipped with open breast coils with vacuum-assist biopsy targeting equipment. A breast system from Robin Medical with active tracking has been installed. In addition to the 3T MRI system, the Center has 5 GE digital mammography units, 3 Philips ultrasound units, 1 Hologic stereotactic biopsy unit, and Hologic CAD (computer aided detection) software. This equipment allows for the provision of the following clinical services: screening and diagnostic digital mammography, breast ultrasound, magnetic resonance (MRI) of the breast, stereotactic percutaneous core biopsy, MRI-guided percutaneous core biopsy, ultrasound-guided percutaneous core biopsy, preoperative image-guided lesion localization prior to surgical biopsy, galactography (ductography), and cyst aspiration.

221 Longwood Advanced Imaging Center

The LMRC Advanced Imaging Center at 221 Longwood consists of offices for research staff, laboratories and three MRI magnets – one 3T Siemens Skyra MRI, one 3T GE magnet HDxt MRI system, and a 7T Bruker animal imaging system. The 3T GE scanner is equipped with a commercialized focused ultrasound system (FUS) system. The hospital also has its own in-house FUS systems for animal experiments that can move among the magnets at the 221 Longwood facility.

The Carl J. and Ruth Shapiro Cardiovascular Center

This facility has a Siemens 3T MRI for use within radiology research and clinical uses. The Shapiro Center also has the first 320-slice CT scanner in New England and a hybrid 64-detector CT/PET scanner.

Small Animal Imaging Laboratory (SAIL)

The SAIL is comprised of the 7T Bruker BioSpec and the IVIS Lumina LT Series III In Vivo Optical Imaging system. Services include study design, scanning, optimization of scanning protocols, training for independent scanner operation and advice on image analysis. The core facility is available to all public research institutions and industrial partners.

The 7T Bruker scanner system includes a 2 channel MRI Cryoprobe for mouse brain imaging, a 4-channel mouse cardiac/abdomen coil, a Tx/Rx 72mm circularly polarized volume coil, an 86mm volume coil, double tuned 1H/31P and 1H/13C surface coils, and 3 1H receive only surface coils (10, 20 and 30mm sizes). The system is also equipped with a specialized mouse bed for Magnetic Resonance Elastography imaging, which includes a shear wave transducer, fitting for the 20mm surface coil and LEDs for visual stimulation. For in vivo imaging, a mouse and rat bed are available with integrated warming base and nose cones for anesthesia delivery, SA instruments for ECG, respiration and temperature monitoring which also allows for respiration and cardiac gating and a Harvard Apparatus MRI-compatible injection pump. Two anesthesia machines with oxygen and isoflurane are accessible in the MRI suite as well.

The IVIS Lumina LT is capable of both in vivo and in vitro bioluminescence and fluorescence imaging, with a highly sensitive CCD camera, light tight imaging chamber and complete automation, and offers full spectrum imaging with 30nm tunability. The IVIS is also equipped for delivery of anesthesia for up to three mice at a time. The IVIS is located in the procedure room directly adjacent to the satellite animal vivarium with the SAIL suite and includes a biosafety cabinet, anesthesia machine, and CO2 chamber for pre and post imaging procedures.

Software for the Bruker 7T: ParaVision v5.1 which includes a parallel imaging package, diffusion tensor imaging license, spectroscopy package, IntraGate retrospective cardiac gating and susceptibility weighted imaging.

Software for the IVIS Lumina LT: Living Image Software with advanced cataloging, browsing, and analysis tools.

SAIL Satellite Vivarium:
Within the SAIL suite is an animal vivarium overseen by HCCM which includes veterinary care for both short term and longitudinal studies of mice and rats. The vivarium is adjacent to the procedure room and within the two spaces are two biosafety cabinets for pre and post imaging procedures and animal prep areas with anesthesia and CO2 capabilities. Animals may be housed here for the duration of both IVIS and MRI studies.

MRI-Related Facilities

Center for Clinical Spectroscopy

Laboratory and Clinical: The Center resides at the Harvard Institute of Medicine on the 8th floor with three offices for the key personnel, shared office for research fellows, four cubicles for students, as well as dedicated lab space for chemistry and phantom construction. We also share laboratory space with the NMR research core.

Computer: The Center for Clinical Spectroscopy has several computer systems dedicated for MR spectroscopy data analysis. Four workstations are available for data processing all of which can access an HP Proliant ML350 server system equipped with HIPAA-compliant RAID-5 data storage and hosts the software using a multiplatform virtual computing environment. Additional laptops are all encrypted with SafeBoot drive encryption. All systems have access to a dedicated file area that is stored on Partners servers and is backed-up daily with the last two revisions kept in storage at any time. Raw MRI and MRS data will be transferred by exporting the data to a 256-bit AES encrypted and password protected portable hard drive (Lenovo USB Portable Secure Hard Drive model# 57Y4400) or military-grade rugged and 256 AES-bit hardware-based password and encrypted USB flash drives (IronKey model# D200).

Software: MR spectroscopy data processing using software developed by Dr. Lin and his group as well as LCmodel, jMRUI, and other spectroscopy quantitation software packages are available at the Center. 2D Correlated Spectroscopy data will be processed using Felix 2007 (FelixNMR, San Diego, CA) and Matlab for custom data processing routines. 2D data analysis packages are also available include matNMR and PROfit. Finally, for multinuclear studies, JAUYANG is a semi-automated analysis of 13C data. 31P MRS data is analyzed using in-house developed software. Statistical packages such as SPSS are available for statistical analysis.

Equipment: The MR Division has several clinical areas within the hospital campus: 1) the L1 level of the main hospital building; 2) Brigham and Women's MRI Research Center (BWMRC) at 221 3) the Lee Bell Center for Breast Imaging; 4.) the Pike at 45 and 75 Francis Street; and 4.) the Carl J. and Ruth Shapiro Cardiovascular Center. All MR systems are fully supported with inpatient and outpatient facilities, nursing and technologist staff. A full-time clinical PhD MR Physicist provides clinical MRI protocol development, and QA and implementation support. Imaging results are interpreted at electronic reading stations over a clinical PACS with interconnectivity with advanced Radiology and Hospital Information Systems.

The BWMRC located in the Eugene Braunwald Research Center at 221 Longwood Ave., provides research MRI services to scientists affiliated with BWH, Harvard Medical School and the research community at-large. It was recently renovated under a grant from the American Recovery and Reinvestment Act which now includes the widebore 3T Siemens Skyra that is multinuclear equipped. The Harvard Catalyst Clinical Center is located on the 3rd floor of the same building allowing for rapid handoff of blood samples acquired in this study. Similarly the inpatient MRI scanners at the main hospital, a widebore 3T Siemens Verio that is also multinuclear equipped. The HCCC also has facilities in the main hospital for blood sample storage and processing.

The Radiology Department has a number of other shared resources, including a research computer network based on Ethernet and running both DECnet and TCP/IP protocols on optical fiber and thick coaxial cables. On this network are: All clinical and research MR systems, both GE and Siemens (10 systems); a General Electric (GE) single photon emission computer tomography (SPECT) system; two GE PET systems; and all digital X-ray systems. Digital image data from any of these systems can be sent over the research network.

Additionally, the Center has relationships with the Boston Children's Hospital, Dana Farber Cancer Center and the Massachusetts General Hospital with access to a several 3T MRI scanners, and a human 7T Siemens.

Neuroimaging and fMRI Services

FACILITIES AND OTHER RESOURCES

Scanning Facilities

Brigham and Women's MRI Research Center (BWMRC). In April, 2010, BWH was awarded a $6.1M ARRA G20 construction grant "Brigham and Women's MRI Research Center (BWMRC)" to completely renovate the institution's MRI research facilities at 221 Longwood Ave. This translational research imaging facility houses two 3T MRI scanners (both fully equipped with NordicNeuroLab fMRI Hardware and Software Systems (NNL fMRI Systems) to perform fMRI studies), one 1.5T MRI scanner, and one 20cm 7T animal MRI scanner with cryoprobe technology. In addition, there is one fully equipped subject examination room and one interview room, both designed for use before, during, and/or after imaging experiments; an electronics and coil development laboratory; a polarizer laboratory to produce hyperpolarized gases for specialized MRI experiments; swing space for investigators to use during experiments; a conference room; a radiology reading room; a break room; and a fully equipped small animal imaging suite (including an on-site Biosafety Level 2 vivarium to facilitate longitudinal studies, and an animal handling laboratory).

Additional fMRI Scanning Sites

Two additional Siemens 3T MRI scanners, located in the main hospital, are also fully equipped with NordicNeuroLab fMRI stimulus delivery and behavioral recording systems, as well as physiological recording equipment, to perform fMRI studies.

fMRI Stimulus Delivery, Response Recording Hardware and Software Systems

Comprehensive solutions for MRI-compatible stimulus delivery and behavioral recording are available at all scanners that perform fMRI. This includes four complete fMRI systems (NordicNeuroLab, Norway, http://www.nordicneurolab.com) for visual (goggle and LCD) and auditory (headphones and earbuds) stimulus delivery, behavioral response recording and integrated eye-tracking. The NNL MR-compatible headphones have electrostatic transducers and provide a flat frequency response up to 35 kHz. Paradigm controlling and presentation software packages such as NNL Aktiva, Presentation (http://www.neurobs.com) and E-Prime Pro (http://www.pstnet.com) are available and synchronized with the scanner logic signal.

MR-compatible Physiological Monitoring Equipment.

MR-compatible heart and respiratory rate monitoring equipment (Siemens; GE Medical), O2SAT monitors, and a portable blood pressure monitor (Omron HEM-608, Japan) are available. In addition, a dedicated MR-compatible physiological monitoring system (Magnitude, InVivo MDE, FL) that is capable of monitoring pulse oximetry, skin conductance, ECG, and heart rate, is linked with a data acquisition board (Powerlab 8/30, ADInstrument) to record and archive physiologic data.

Technical Assistance

The fMRI Service is responsible for maintaining and troubleshooting all of the stimulus delivery and behavioral/physiological recording hardware and software systems, as well as the computational infrastructure needed for fMRI studies. The Service is available for assistance with all aspects of fMRI, including the development and implementation of in-scanner neuropsychological paradigms; assistance with specific behavioral response and physiological recording needs; development and implementation of specialized fMRI pulse sequences, acquisition methods and image reconstruction; assistance with data acquisition; data processing and analysis; and administrative needs (e.g. IRB/grant questions) In addition, the Service is available, via email, for troubleshooting and questions. The Service is also continually working to upgrade and improve existing systems. Please see fmri-service.bwh.harvard.edu for additional information.

MAJOR EQUIPMENT

MRI: fMRI research is conducted on four human scanners and one animal scanner on the BWH campus.

BWMRC at 221 Longwood Avenue:

- Siemens 3T Skyra, 70cm bore, 64 channel receiver, with multinuclear capability
- GE 3.0 T HDx short-bore scanner; this instrument also has focused ultrasound capability
- Bruker 7T, 20cm animal MR with cryoprobe technology

At the main hospital site:

- Siemens 3T Trio, 60cm bore, 12 channel receiver; Lee Bell Imaging Center
- Siemens 3T Verio, 70cm bore, up to 32 channel receiver, multinuclear capability; L1 Imaging suite

Center for Pulmonary Functioning Imaging/Hyperpolarized MRI

Laboratory: The Center for Pulmonary Functional Imaging has two 400 sq ft laboratories; one is located at the Longwood Medical Research Center (LMRC), 221 Longwood Ave. and the second one is located at 1249 Boylston Street, Boston, MA. The laboratory located at 221 Longwood Avenue is used for activities that require direct access to the MRI scanners and is used for the design and fabrication of custom RF coils. The Department of Radiology at Brigham and Women's Hospital has 12 clinical scanners operating at both 1.5T and 3.0T. Two of these scanners are located at 221 Longwood Avenue in the Advanced MRI Center. A new Siemens Skyra 3T scanner, to be installed in the summer of 2012, will be equipped with the multi-nuclear option so that 129Xe research can easily be performed on this scanner. A 32 channel 129Xe chest coil for the Siemens platform is being developed to be housed at BWH permanently for research. The Siemens 3T scanner together with the lab's custom 32 channel RF coil will be used for specific studies that require optimal signal to noise ratio, i.e. 3D single breath XTC. The lab also utilizes a 1.5T GE scanner located at the Advanced MRI Center that is not multi-nuclear and, therefore, funds are allocated to allow operation at the 129Xe Larmor frequency as well as to build a RF coil and T/R switch. A subcontractor Mirtech is building (a) an “up/down” converter to enable its use at the 129Xe frequency, (b) a transmit/receive RF coil and (c) a T/R switch for this GE 1.5T system. The Advanced MRI Center occupies over 7000 square feet at 221 Longwood Avenue and comprises physician reading rooms, a patient reception area, examination rooms, waiting rooms, three MR scanners, laboratories and offices for personnel.

Office: Substantial start-up funds have been made available to establish additional infrastructure both at the LMRC (~1100 sq ft) and at office space at 1249 Boylston Street. Dr. Patz has an office both at 221 Longwood Ave. and at 1249 Boylston. Dr. Hatabu has an office at BWH in the Peter Bent Brigham building. Note that a very important design feature of our space both at 221 Longwood Ave as well as at 1249 Boylston is that we have allocated several “touch down” locations for visiting collaborators. These locations are either located within an office with a door or in a cubicle and always have full Internet access and desk space. This is specific feature we have designed into our space for our multiple interdisciplinary collaborators/investigators/consultants.

Computer: All investigators have several computers in their offices and have access to other computers and printers throughout BWH. These computers are all connected to a GB local network. In addition, the MRI Division’s computational resources are based on the very substantial infrastructure of BWH's SPL, which provides a UNIX-based application environment, including high bandwidth access to large-scale file and computer servers, and which maintains the division’s research computer network.

Equipment: A new open-source, academic-built Xe polarizer has recently been installed on L1 at BWH.

Focused Ultrasound Surgery (FUS) Laboratory

The Focused Ultrasound Laboratory is housed in 4,500 sf research and office space on the fifth floor of the LMRC (Longwood Medical Research Center). The laboratory is well equipped to perform all requisite tasks involved with MRI-guided focused ultrasound research: transducer and phased array construction, matching, tuning and characterization, computer simulations, ultrasound measurements, small animal experiments, and nonhuman primate tests.

Mechanical and electronic facilities: The laboratory contains equipment to fabricate custom ultrasound transducer arrays, including a diamond wire saw, a precision dicing saw, and evacuation chambers for forming backing layers. The lab's machine shop features a CNC micro-router, lathe, band saw, table saw, and drill press. The laboratory also has a computer-controlled laser cutting system to make transducer housings and prototype devices. The laboratory's electronic facility contains a considerable variety of electronic components and test equipment used to not only troubleshoot and repair components, but also to build customized equipment. The facility includes several 4-channel digital oscilloscopes, a network analyzer, a vector impedance meter, multiple PC-based data acquisition systems, PC-based frequency and signal generators, a spectrum analyzer, arbitrary waveform generators, high voltage fixed and variable capacitors, broad and narrow band preamplifiers, and equipment to design and print its own circuit boards.

Ultrasound characterization and measurement: Five 3D computerized high resolution positioning and beam plotting systems are available, each with integrated data acquisition equipment for acoustic characterization, and with all basic equipment required for ultrasound laboratory experiments (test tanks, RF-amplifiers, arbitrary waveform generators, oscilloscopes, voltmeters, hydrophones, and cavitation detectors). A degasser and radiation-force balance are available for general use. The laboratory is equipped with a 128 channel and a 256 channel VeraSonics ultrasound system, both of which allow custom control of a transmitted ultrasound signal and record full RF time-traces received from individual channels. The lab also has access to the department's clinical ultrasound imaging systems. An assortment of ultrasound transducers and transducer arrays are available for tests and clinical studies. These transducers range from interstitial needle applicators to intracavitary probes to external phased arrays. A 12-bit, four-channel high-speed digitizer system along with programmable filter and pre-amplifier are available to acquire acoustic signals produced during sonication. This system is driven with custom software written in Matlab that controls both the digital acquisition and the ultrasound driving system. We also have a large collection of formalin-fixed human calvaria to perform transcranial ultrasound measurements.

Computer Facilities: The laboratory has six high-end PC workstations, access to the MGH/BWH High Performance Computing Cluster (over 600 cores, 7 Tflops of computing power, 1.5TB memory and 32 TB of extremely high performance storage), and is additionally affiliated with the department's Surgical Planning Lab (SPL), which provides considerable support and expertise in the fields of networking and computer science. The SPL is a computation-oriented lab, specialized in the processing and display of medical images. The SPL network, servers, and valuable software such as Matlab, are available through SPL. Additional technical software (e.g. Mathematica) is also available to the laboratory through Harvard Medical School's site license. The laboratory has theoretical models that can predict the ultrasound field distribution and the absorbed energy deposition in three-dimensional tissue volumes with irregularly shaped tissue interfaces. Simple models used to simulate the ultrasound field in a homogenous medium are also available as are simulation programs for prediction of the temperature elevation generated by the ultrasound beams in the tissue.

MRI: The laboratory has research access to the department's clinical MRI and CT facilities, including systems a 1.5T and a 3T scanners (GE Healthcare and Siemens) located on the ground floor of the LMRC that can be used for animal studies. Additional scanners are available for researchers at the main hospital building at 75 Francis St. for non-animal studies. In addition, we have access to a 33 cm diameter Bruker Biospec 7 T MRI scanner (Bruker Biospin, Ettlingen, Germany) equipped with a 12-cm actively shielded gradient. Rat experiments in this proposal will be performed on this scanner. We have multiple MRI coils available to us as well as facilities to construct our own coils.

Animal Facilities: The Harvard Center for Comparative Medicine (HCCM) is responsible for the laboratory animal use program of the Harvard Medical School, Harvard School of Public Health, and the Brigham and Women's Hospital. Their services include routine and specialized animal husbandry of all common laboratory animal species, veterinary care, diagnostic pathology, infectious disease surveillance, quarantine.

AMIGO Suite

Laboratory and Clinical: The Advanced Multimodality Image Guided Operating (AMIGO) Suite is an extension of the BWH's IGT program, begun in 1991, which has since become an internationally recognized pioneer in real-time intra-operative MRI-guided therapy. Using the well-known "double-doughnut" system, BWH teams performed over 3,000 surgical and interventional procedures. By 1994 the BWH IGT Program introduced non-invasive MRI-guided focused ultrasound surgery. Opening in 2011, AMIGO continues these pioneering efforts with multimodal image guidance. As an innovative surgical and interventional environment that is the clinical translational test bed of the National Center for Image-Guided Therapy (NCIGT) at the Brigham and Women's Hospital and Harvard Medical School, the AMIGO comprises an integrated, 5,700 square foot area divided into three sterile procedure rooms in which a multidisciplinary team will treat patients with the benefit of intra-operative imaging using multiple modalities. In AMIGO, real-time anatomical imaging modalities like x-ray and ultrasound are combined with cross sectional digital imaging systems like CT, MRI, and PET. Molecular image-guided therapy will be pioneered with the use of multiple molecular probes, such as PET, optical imaging, and targeted mass spectrometry, to increase the sensitivity and specificity of cancer detection. Application of these technologies is expected to improve the ability to define tumor margins to more completely excise or thermally ablate tumors. In addition to multi-modality imaging, the AMIGO has various navigational devices, robotic devices, and therapy delivery systems that help physicians to localize and treat tumors and other targeted abnormalities. The AMIGO represents and encourages multidisciplinary cooperation and collaboration among teams of surgeons, interventional radiologists, imaging physicists, computer scientists, biomedical engineers, nurses and technologists to reach the common goal of delivering the safest and the most effective state-of-the-art therapy to patients in a technologically advanced but patient-friendly environment.

The AMIGO Layout

MRI Room

The Magnetic Resonance Imaging (MRI) room will be centered around a high-field (3 Tesla) wide bore (70 cm) MRI scanner integrated with video monitors, surgical lights, therapy delivery equipment, an MRI-compatible anesthesia machine, and vital signs monitor. Here, the clinical team will extend image-guidance principles from neurosurgery to many oncology applications. Initial procedures that will use the MRI in AMIGO include needle-based procedures such as soft tissue biopsy (liver, prostate, etc.), prostate brachytherapy, laser ablation of brain tumors, and percutaneous ablations of soft tissue tumors (liver, kidney, etc.). Catheter-based endo-vascular interventions, such cardiac ablations to treat arrhythmias, will utilize both MRI-guidance as well as angiography. The ceiling mounted MRI scanner can be moved out of the MR room and into the operating/angiography room. With this innovation, the patient does not need to be transferred into the operating/angiography table for MR imaging. The familiar "in-out" paradigm can also be used in which the patient is imaged and then withdrawn from the bore of the scanner for intervention. In some procedures, the doctor can reach into the scanner's short/wide bore to access the patient. These features enable flexibility in workflow to tailor procedures to the needs of the doctor and patient.

PET/CT Room

One of the most innovative features of the AMIGO is the inclusion of Positron Emission Tomography (PET), an invaluable molecular imaging modality that reveals functional and metabolic activity. The co-location of a PET/CT scanner in this suite will for the first time introduce molecular imaging into therapy and surgery. The integration of anatomical information from CT and MRI with the functional and metabolic information from PET will inform surgical decision making during tumor resections and percutaneous thermal ablations. Using this technology, we envision that physicians can localize and target viable tumor tissue before a procedure and verify the completeness of surgical removal or destruction of tumors by depicting any residual cancer tissue prior to the end of the procedure. Under research protocols, our team will develop image-guided procedures enabled by novel molecular imaging agents generated in the BWH's state-of-the-art cyclotron. Using integrated patient transfer technology, the patient, monitoring, and anesthesia delivery equipment can efficiently move from the PET/CT table to the operating/angiography room table. The marriage of a procedure room with a molecular imaging environment will accelerate the validation of new contrast agents as well as enhance clinical decision making.

Operating/Angiography Room (OAR)

The heart of the AMIGO suite, the operating/angiography room (OAR), is outfitted with a state-of-the-art, electronically controlled patient table surrounded by imaging modalities and therapy devices, including a ceiling-integrated navigation system, a fluoroscopy unit, 3D ultrasound, and a near-infrared imaging system. The patient table top can be changed to optimize the procedure for surgery or angiography. All images and data pertinent to the procedure are collected using video integration technology, prioritized, and then displayed on large LCD monitors at points of use in all three rooms in the suite. Procedures performed in this room will include open surgeries of the brain, skull base, spine, breast, chest, abdomen and pelvis as well as catheter-based cerebro-vascular, peripheral vascular, and cardiovascular interventions guided by both x-ray angiography and MR imaging. Endoscopic and robot-assisted procedures will for the first time be enhanced with the fusion of real-time endoscopic views and virtual endoscopic views constructed from MR or CT images. This novel approach will enable the clinician to see beyond the surface and should improve the safety and efficacy of these minimally invasive therapies. Above all, the AMIGO will provide a sophisticated, fully integrated image-guided therapy infrastructure that will lead to disruptive changes in procedural paradigms of surgery and interventional radiology.

Computer: Along with integrating high-field MRI, PET-CT, x-ray fluoroscope, and ultrasound, the AMIGO program leaders and its trainees are developing, using, and refining complementary technologies such as:

- 3D Slicer (www.slicer.org) open source software for medical image analysis and visualization;
- Computer systems that use 3D models for preoperative and intraoperative registration, planning, comparison of cases, and validation
- Robotic technologies; and

- Algorithms that allow for non-rigid registrations during operations.

These interventions represent multidisciplinary (i.e., combined work/input of radiologists, radiation therapists, surgeons, bioengineers, physicists, and computer scientists) efforts to integrate a variety of technologies; namely high-field MRI, computer-assisted fluoroscopy, endoscopy, and integrated and iterative navigational systems.

Equipment: The AMIGO suite will contain an intraoperative 3T MRI, a PET-CT, 3D ultrasound and an X-ray fluoroscopy system with navigational tools. The specific list of equipment planned for installation in the AMIGO location is as follows:

- A new 3.0T MR that moves along a ceiling track from the MRI room to the OR
- BrainLab and GE NAV surgical navigation systems
- A Surgical Table with MR-compatible materials and dedicated MR breast coil
- PET-CT (64 slice)
- A Diagnostic Ultrasound unit, including 3D ultrasound
- A C-arm Fluoroscope with Navigation Package
- A Patient Monitoring system for PET/CT room
- An MR-compatible Patient Monitoring system that is integrated with the above surgical table
- An MR-Compatible Anesthesia Unit for PET/CT room
- An MR-Compatible Anesthesia unit for MR Room
- An IT Server to work in conjunction with the AMIGO environment

Optical Imaging Laboratory

Laboratory

The Optical Imaging Laboratory has a total laboratory space of more than 1,000 sq. ft. at the Thorn Building of the BWH. The laboratory has equipment and tools for small animal handling, *in vivo* imaging, and surgery. The director has access to the animal housing facility managed by the hospital's veterinarian services. One full-time postdoctoral research fellow with experience in cell biology, biochemistry, neuropathology, oncology, and animal work support the director of the laboratory. Besides imaging, the lab can perform cell culture, create animal models of tumors including brain tumor, breast cancer, ovarian cancer, and melanoma, perform surgery, and conduct data analysis using commercial software and custom-written Matlab programs. The lab can also perform tissue harvests. For this, staff have access to the Harvard Medical School's Rodent Pathology Core for histopathology analysis.

Office

The director has a total office space of more than 200 sq. ft. at the BWH.

Computer

There are six Windows PCs and one Linux file server available for processing and archiving data. An image archive system at LMRC is available for us to back up and archive data. All the computers are connected via Internet II high-speed network. All the computers and internet connection are managed by a full- time system administrator.

Equipment

The Optical Imaging Lab has the following major equipments: an IVIS 100 bioluminescence imaging station from Caliper Life Science Corp., NightOwl LB981 fluorescence imaging station from Berthold Technologies, Inc, and a CellVizio-Lab Fluorescence Microendoscope from Mauna Kea Technologies Inc. The first two stations can image small animals and well plates with high sensitivity, low background, and provide quantification results. The IVIS 100 station is highly automatic with a computer-controlled detector and imaging platform, and self-calibration. It is accompanied by Living Image software for image processing and quantification. The NightOwl fluorescence imaging station, with proper configuration of filters, can capture signals at wavelength ranging from green to near-infrared and quantify the results by using the normalize photon numbers. The CellVizio-Lab features a selection of miniature microprobes with an outer diameter ranging from 3 mm to 0.3 mm. The microprobes can be inserted into small animal as an endoscope to image brain, lungs, liver, kidney, colon, gastrointestinal tract, and other tissue/organs with minimal invasiveness. The microendoscopy image has a resolution of 2 um, approximating that of conventional microscopy, for in vivo diagnosis. A 3D Camera Ring–360 Degree Surface Profiling System for Small Animal Imaging, from Technest Holding Inc., will be installed at the Optical Imaging Lab that allows the obtaining of tomography images of fluorescence signals in a small animal for precise 3D localization and quantification. The lab also has a near-infrared vasculature viewer (IRIS) from Near-Infrared Imaging Systems, Inc. **The IRIS Vasculature Viewer uses near-infrared light to image blood vessels in both animals and human subjects without application of exogenous labeling agents. Some other equipment and tools in the lab include surgical microscopy, surgical tools, a stereotactic system, refrigerator, and a stand-alone anesthesia system.

Nuclear Medicine/PET

Laboratory

The Nuclear Medicine Division currently has three dual-head SPECT systems, two Dynamic cardiac SPECT (D-SPECT) systems, a SPECT/CT scanner (Symbia T6, Siemens Medical Solutions), a PET/CT 64 (DSTE-VCT, GE Healthcare), a PET/CT 64 (DRX-VCT, GE Healthcare), and another PET/CT system in the AMIGO suite (Biograph mCT, Siemens). The nuclear medicine clinic has a large hot lab for handling radiopharmaceutical doses, and a 400-SF dedicated reading room with extensive post-processing and image fusion capabilities. There is also a smaller hot lab used for nuclear medicine studies acquired in the Shapiro Building, which also has a reading room for cardiovascular studies. In addition, both imaging locations have rooms available for radiotracer uptake by the patients in preparation for SPECT or PET/CT imaging.

Office

The lead and junior researchers and support staff have offices in the Thorn Medical Research Building and within the Nuclear Medicine Division of the BWH. A common area is also available for graduate students and post-doctoral fellows outside the division director's office. All of these offices and both clinical nuclear medicine imaging areas are located within the main hospital complex.

Computer

In addition to the many computer systems that are used for acquiring nuclear medicine images on the SPECT and PET systems described above, our nuclear medicine division also contains: 5 Hermes Gold workstations which serve as local image archives and provide additional clinical and research image processing and review capabilities; 3 General Electric Centricity workstations; 2 General Electric AW workstations used for various image reading and processing applications; 2 General Electric Xeleris workstations used for PET and PET-CT image interpretation; and 2 Siemens E.Soft which are used mostly for SPECT image evaluation.

Cyclotron and Radiopharmaceutical Chemistry

Cyclotron/Radiochemistry Laboratory: The cyclotron and radiochemistry laboratory are housed in a new 2,400 SF building within the BWH campus. The facility is designed as cleanroom environment compatible with cGMP manufacturing procedures. The cyclotron is a General Electric PET-Trace dual particle accelerator (16.5 MeV protons and 8 MeV deuterons) equipped with 8 targets for production of C-11, N-13, O-15, and F-18 (both fluoride ion and molecular fluorine gas). This instrument is capable of irradiating eight targets (two simultaneously) with 16.5 MeV protons/deuterons. The cyclotron laboratory is equipped with computer controlled fully automated radiopharmaceutical production systems for producing routine positron emitting compounds and gaseous radioactive effluent monitoring systems.

The radiochemistry laboratory (approximately 1,000 SF) is adjacent to the cyclotron vault, and equipped with the necessary equipment needed to produce and develop PET radiopharmaceuticals for clinical and research use. It includes 6 Hot Cells (Comecer), and has a variety of automated radiochemistry equipment for remote-controlled synthesis, including General Electric FX (N), FX(E), and FX (C) Pro modules for synthesis of PET radionuclides for clinical and research applications. A radiochemical quality control (QC) laboratory (approx. 500 sq. ft) is adjacent to the cyclotron/radiochemistry laboratory. The QC laboratory has analytical equipment to confirm radiochemical purity, chemical purity, apyrogenicity, sterility and radionuclidic purity of the produced radiopharmaceuticals, including radio-TLC (Carroll and Ramsey Associates), radio-HPLC (Shimadzu), GC-FID (SRI Instruments), GC-mass spectrometry (Shimadzu), pyrogenicity testing (Charles River), and sterility testing. Radiopharmaceuticals that have cleared the QC process are dispensed for human use in an adjacent pharmacy, also residing within a cleanroom environment. The pharmacy employs an automatic dose dispensing unit (NukeMed) to minimize radiation exposure.

Chemistry Laboratory: Chemistry laboratory space (400 sq. ft) for the synthesis of labeling precursors is located in the Thorn research building, which is adjacent and directly connected to the Cyclotron/Radiochemistry laboratory.

Biochemistry/Cell Biology Laboratory: A biochemistry/biological laboratory (400 SF) for performing in vitro binding, tissue culture, and molecular studies is located in the Thorn research building, adjacent to the chemistry laboratory. These laboratories are equipped to perform tissue culture (laminar flow hood, incubators, inverted phase microscope, autoclave, etc.), immunocytochemistry, molecular studies, and for performing tracer studies in small animals (autoradiography). In addition, the laboratory contains basic equipment such as balances, pH meters, refrigerator, freezers, etc. This laboratory includes cold chemistry HPLC (Shimadzu), gamma counter (Beckman), centrifuges (Eppendorf), ultracentrifuge (Beckman), UV/Vis spectrometer (Varian), microscopes, electrophoresis equipment (Biorad), and tissue homogenizers.

Office: The Cyclotron and Radiopharmaceutical Chemistry group has approximately 650 sq. ft of office space in the Thorn building adjacent to the cyclotron facility.

Animal: Complementing the research laboratories in the Thorn research building is a dedicated small animal imaging facility (~500 SF). It houses a micro PET/CT system (GE Vista

animal PET/CT scanner), and optical scanners. This laboratory has dedicated space for animal instrumentation and preparation.
Computer: Within this area are 10 Windows PCs. All the computers and internet connection are managed by a full-time system administrator.

Nuclear Medicine Physics

Office
All physics investigators have office space in the Thorn Research Building at BWH.

Computer
All physics investigators have desktop computers. The nuclear medicine physics group also has 3 SUN workstations, 4 Dell dual-processor systems, and a custom-built Linux cluster with 18 processors for running Monte Carlo simulations, iterative image reconstructions, and radiation dosimetry calculations. In addition, our micro-SPECT facility has a 6-processor SUN workstation currently used mostly for iterative micro-SPECT reconstructions. The physics group also has available a Hermes image-processing computer, a Mirada image-registration workstation, and a system for running Solidworks 3D CAD software for development of new phantoms.

Equipment
A variety of phantoms are available to the nuclear medicine physics group. These include two Data Spectrum torso/heart/lung phantoms, two Data Spectrum SPECT performance phantoms, one General Electric PET well-counter calibration phantom, one General Electric CT image performance phantom, mini- and micro-Derenzo phantoms, a RSD anthropomorphic torso phantom (Radiology Support Devices, Inc., California), a RSD head phantom containing realistic bone anatomy and separately fillable striata and brain background compartments, and a variety of custom-built phantoms designed by our group and fabricated using three-dimensional stereolithography.

Surgical Planning Laboratory (SPL)

With the BWH is the SPL that provides a clinical and research infrastructure for biomedical imaging processing and visualization and analysis.

Laboratory: The SPL occupies approximately 2200 sq ft of custom-designed lab space adjacent to the clinical MR space on level L1 of the Ambulatory II Building (AMBII) of Brigham and Women's Hospital The space includes a state-of-the-art-computer room, a high-end network plant with UTP and fiber optic connections to each workspace. The main purpose of this area is to provide an environment for the interaction between computer scientists and medical researchers. The MR Division has a 9,000 square-foot area on level L1 of the Ambulatory II Building to support patient and research activities (including the SPL, detailed above). The imaging systems (one dedicated to research and two to patient activities) are fully supported with inpatient and outpatient facilities. Also housed in this facility are secretarial areas, scheduling rooms, reading rooms, darkrooms, waiting and nursing rooms, a crash area, and a physics and biological support area. Imaging results are interpreted at electronic as well as film reading stations, and the systems are connected to the Ethernet, enabling transfer of images and raw data locally and over computer network systems. In addition, the MR Division also has a specially designed, 3500 sq ft MR Therapy suite on level L2 of the Center for Women and Newborns (at BWH). The procedure room in which the open magnet is physically located measures 25'x25' and meets OSHA standards for an operating room environment. A complete integrated patient monitoring system (ECG, SpO2, CAPNO, Non-invasive BP, Temperature monitor, and Invasive BP) is adjacent to the magnet in the shielded room. The remaining portion of the suite consists of separate decontamination and clean assembly rooms and a 3-bed pre/post procedure area with a nurses' station, where patients recover after a procedure

Office: The hospital has allocated two large and two small rooms in the Thorn Building to the SPL, with a total area of approximately 1100 sq ft. The area was renovated and new furniture was installed to create 14 office seats. In 2004 and again in 2007, BWH provided total of 5000 sq ft office space at 1249 Boylston Street, for 24 researchers and 10 "drop-in" areas. Additionally, a conference/training room for up to 24 persons and a very high resolution projection system powered by Sun V880z visualization server drives a multiple-projector display in the conference/training room.

Computer: A state-of-the-art computer room is located within SPL laboratory in the AMBII space as well at 1249 Boylston Street. SPL provides tiered computing needs for its researchers' demands: a) 80+ desktop workstations running Linux and very powerful processors and memory for individual researchers, b) four monolithic, multi-processor machines specifically targeted at large-scale data applications, each machine has 16 processing cores, 64GB or 128GB of RAM and a top-of-the-line graphics accelerator, c) compute-clusters of 100 cluster cores running Linux for heavy computational tasks such as automated processing of large numbers of subject studies or population. For storage, SPL currently has 34 terabytes of network-accessed storage (NAS) from EMC with performance capabilities to handle larger medical image data sets, anatomical models, and simulations. A Qualstar SAIT tape storage library of 128 TB capacity allows archival data on tape backup. Legato software manages the archival functions. In addition, there are 4 very high-end network switches that provide 10 Gb per second connection between SPL main campus and four "hubs"; there are a number of "edge" connections with smaller network switches fanning out from the hubs at 1 Gb per second connections.

Equipment: The SPL maintains its own IT infrastructure, including its own high-bandwidth fiber optic network. The following describes its most important components:

- Linux compute cluster: The most powerful data processing tool of the SPL is our Dell compute cluster. The cluster's head node is a dual Xeon 3.6GHz system with 4GB of RAM. The system disks are two 146GB SCSI disks configured as a mirrored RAID. The head node also has a 1.6TB RAID 5 array with a hot spare attached. There are also 50 dual Xeon 3.2GHz compute nodes with 4GB of ram each and 36GB SCSI hard drives, 16GB of which is available as /state/partition1 on the compute nodes. The cluster has an Infiniband interconnect.
- Fat Nodes: The SPL has four 16-processor Linux super workstations, three with 64 GB of memory, and one with 128 GB. Each "Fat Node" also features a powerful Nvidia graphics processor. Fat Nodes run exactly the same Fedora Core 7 Linux operating system software as our more numerous SPL graphics workstation described below. This allows researchers to develop experiments on a workstation and, when larger datasets dictate the need for either additional memory or processing power, easily move their experiments to one of the Fat Nodes with absolutely no programming changes required.
- Linux Graphic Workstations: The SPL has replaced its previous Sun Microsystems workstations with Dell workstations running the Fedora Core 7 Linux operating system. The Dell workstations feature either two or four CPU processing "cores", with a memory complement of 2 GB per processing core.
- EMC NAS storage array: With the exception of the compute cluster, the SPL's EMC NAS (Network-attached storage) array holds all research, Web and personal data for the SPL. The current array has a capacity of 19 TB. In 2008, this unit will be replaced with a newer EMC unit having an initial capacity of 34 TB, expandable to 64 TB should requirements dictate such expansion.
- Qualstar SAIT tape library: The SPL uses a Qualstar SAIT tape backup library to insure the contents of both the EMC storage array, andalso to hold system images for the SPL's key servers. The Qualstar was recently increased in capacity from 64 TB to 128 TB in anticipation of the new larger EMC storage array.
- The SPL network: The SPL maintains its won internal network. This network connects the primary SPL machine room facility in room L1-050 of BWH to several other satellite sites, including 1249 Boylston Street, the LMRC, the Thorn Research building, and the Harvard Medical School. Most inter-nodal connections are 10 GB fiber, whereas connections to computers are either 1GB or 100 MB.

More on Slicer Surgical Navigation Software (http://www.slicer.org)

Out of the SPL and its developmental tools emerged Slicer, or 3D Slicer, a free, open source software package for visualization and image analysis that is continually being developed within the SPL community. See Slicer's website at 3D Slicer is natively designed to be available on multiple platforms, including Windows, Linux and Mac Os x.

Slicer's capabilities include: interactive visualization of images, manual editing, fusion and co-registering of data, automatic segmentation, analysis of diffuse tensor imaging data, and visualization of tracking information for image-guided procedures.

In 2010, a new, completely re-architected version of Slicer was developed and released.

Portal pages on this the Slicer website (http://slicer.spl.harvard.edu/) have been designed for end users or developers. Some of the core functionality that enables the applications listed above includes the capability to save and restore scenes using a format called MRML, a plug-in architecture to interface to external programs including ITK, a sophisticated statistical classification environment based on the EM algorithm, capabilities for rigid and non-rigid data fusion and registration, and processing of DTI MRI data.

Slicer executables and source code are available under a BSD-style, free open source licensing agreement under which there are no reciprocity requirements, no restrictions on use, and no guarantees of performance. Slicer leverages a variety of toolkits and software methodologies that have been labeled the NA-MIC kit. Please click here to read more about the NA-MIC kit.

With IRB clinical protocols appropriately created and managed, Slicer has been used in clinical research. In image-guided therapy research, Slicer is frequently used to construct and visualize collections of MRI data that are available pre- and intraoperatively to allow for the acquiring of spatial coordinates for instrument tracking. In fact, Slicer has already played such a pivotal role in image-guided therapy, it could be thought of as growing up alongside that field.

In addition to producing 3D models from conventional MRI images, Slicer has also been used to present information derived from fMRI (using MRI to assess blood flow in the brain related to neural or spinal cord activity), DTI (using MRI to measure the restricted diffusion of water in imaged tissue), and electrocardiography. For example, Slicer's DTI package allows the conversion and analysis of DTI images. The results of such analysis can be integrated with the results from analysis of morphologic MRI, MR angiograms and fMRI.

Surgical Navigation and Robotics Laboratory

Laboratory: The Surgical Navigation and Robotics Laboratory is a 330-sq-ft laboratory within the Surgical Planning Laboratory, Department of Radiology, on the L1 floor of the Brigham and Women's Hospital (BWH). This main laboratory is located immediately adjacent to the surgical suites at BWH. Just down the hall from the laboratory lies the Department of Radiology's main imaging center, which includes scanners for magnetic resonance imaging (MRI), computed tomography (CT), nuclear medicine, and other imaging technologies, all connected via high-speed networking to the laboratory through SPL's networking facility and the hospital's information system. The main laboratory is subdivided into a computer laboratory (200 sq ft) and device room (130 sq ft). The computer laboratory is equipped with two graphics workstations dedicated for device and navigation research, and five graphics workstations for medical image processing research. The device room is equipped with two workbenches and storage shelves. In addition to this main laboratory in the BWH, the PI is also assigned a 400-sq-ft laboratory in the satellite office complex of the Department of Radiology at 1249 Boylston Street, Boston, MA, approximately a mile from a the main hospital. This second laboratory has 14 office cubicles and is primarily used for development and testing of software that doesn't involve immediate clinical applications.

Office: The PI's 70-sq-ft office is adjacent to the laboratory in the main laboratory. It is equipped with desk, credenza, desk and task chairs, and three 4-drawer filing cabinets. SPL provides network infrastructure with four CAT5e ports and four optical ports, each of which provides 1Gbit/sec network capacity. The students and technicians have office cubicles in the second laboratory at 1249 Boylston Street. The cubicles are also equipped with 1GBbit/sec network connectivity.

Computer: The PI's office contains two computers (1) Apple PowerMAC, two 2.66GHz Dual-Core Intel Xeon with 32-inch LCD monitor and (2) Apple PowerBook G4 with a 15-inch monitor. The office has a laser printer (Dell 1710) and Fujitsu Scan Snap scanner. The laboratory has three sets of computers with distinguishably different configurations. The first set consists of four Dell graphics workstations uniquely configured to fit the needs of the device-dependent including navigation software development using tracking devices. The second set consists of fifteen graphics workstations provided and maintained by the Surgical Planning Laboratory. All workstations are connected directly to the SPL's computing infrastructure via dedicated network links, but have minimal room for project-specific configuration. The third set of computers consists of three laptop computers (Dell, Inspiron 1510, Linux and Windows) for off-site experiments.

Equipment/Other:
<u>Shared facility:</u>
Surgical Planning Laboratory (See above)
The SPL provides the PI computing infrastructure for his laboratory, namely Network Attached Storage (EMS Clarion, 19TB) with daily automatic backup capability, high-speed network switcher (Alcatel 7020/Omnicore 5052 enterprise-class routing switch), 10Gbit/sec network backbone, and 1Gbit/sec laboratory wide network. SPL also provides SNR laboratory web hosting (www.snrlab.org), mail hosting (@bwh.harvard.edu) and user account management.

Harvard Animal Facility

The Center for Animal Resources and Comparative Medicine (ARCM) at Harvard Medical School provides animal housing, preparation, and surgical operation rooms.

Partners BioMedical Engineering Model Shop
Partners Healthcare System, the parent entity of Brigham and Women's Hospital Machine has machine and electronic shop called Partners Biomedical Engineering. The shop is located on the main campus of Brigham and Women's Hospital in the basement of the Peter Bent Brigham building, Room 011. The shop offers custom designs and tooling to meet the needs of researchers and clinicians within Partners Healthcare.

221 Longwood Advanced Imaging Center (See above under MR Facilities)

CT/Tumor Ablation Program Facilities

Laboratory and Clinical: The Tumor Ablation Program (TAP) provides tumor ablation therapy to approximately 90 patients per year. Ablation procedures take place in the interventional CT procedure room (L1 ASB2 Room 124), using the L1 level MRI scanners and the PET/CT scanner in Nuclear Medicine. The latter two sites are resources that are shared.

Office: Office space exists for principals involved in the ablation.

Computer: Standard hospital personal computers are available for TAP.

Equipment: TAP uses a Siemens Somatom CT scanner (located on hospital level L1 in ASB2 Room 124). The scanner is fully used for interventions by TAP and the BWH Cross-Sectional Interventional Service; an ultrasound scanner (adjacent to CT room L1, ASB2 Room 124) for interventions by TAP and the BWH cross-sectional interventional service; a shared GE 1.5T MRI scanner; a shared Siemens 3T scanner; and a shared GE PET/CT scanner. In the "Pike" area, there also exists a Toshiba 64 Slice CT.

Conjugate and Medicinal Chemistry Laboratory

The Conjugate and Medicinal Chemistry Laboratory is located at the main building, the Thorn building, within the BWH. The laboratory is designated to provide technical support in design, synthesis, and chemical/biological characterization of molecular imaging agents, theranostic compounds or so-called therapy-enabling diagnostic agents for investigators from the BWH Radiology Department and other local hospitals and researchers at the Harvard Medical School. Research projects from the lab include the development of target-specific and nanoparticle-based multi-functional molecular imaging agents for Alzheimer's disease and other neurological disorders, brain tumor, tumors, and fibrosis; and in vivo animal imaging platforms for pre-clinical characterization of lead theranostic compounds. These include: design, synthesis, and chemical/biological characterization of molecular imaging agents and/or theranostic compounds, using conjugate and medicinal chemistry techniques. In particular, by employing both MRI and optical imaging technologies, we are trying to determine lesion-specific biomarkers for Alzheimer's disease, cancer, and fibrosis.

Laboratory: The Conjugate and Medicinal Laboratory has a total shared laboratory space of more than 1,500 sq. ft. at the Thorn Building of Brigham and Women's Hospital. The wet laboratory has equipment and instruments for cell culture, synthetic organic chemistry, small animal handling, cellular and animal imaging, and rodent surgery facility, etc. The director has access to the animal housing facility managed by the veterinarian services. Three full-time postdoctoral fellows and one technician support the lab director. In addition, the lab has approximately 1,000 sq. ft office and dry lab space within the newly established Center for Advanced Medical Imaging (CAMI) of BWH Radiology Department, located at the Crosstown Building (801 Massachusetts Avenue). The lab has a high-end data storage server (9TB). Two full-time postdoctoral fellows are working on several integrated informatics and computing projects (medical imaging informatics, bioinformatics, and cheminformatics).

Office: The laboratory director has an office space of more than 150 sq. ft. at the BWH.

Computer: The laboratory has 7 Windows PCs available for computing, processing and archiving data. A high-end data storage server (9TB) connected to image archive system at LMRC is available for us to back up and archive data. All the computers are connected via an Internet II high-speed network. All the computers and the internet connection are managed by a full-time system administrator.

Equipment: The laboratory has the following major equipment: AMAXA Nucleofector II (AAD-1001S), Molecular Devices Microplate Reader (SpectraMax M5**/**M5**e**) for various biochemical assays and high throughput screening (HTS) of lead compounds, Bio-Rad VersaDoc™ Digital Imaging System (MP4000) for various digital gel documentation, Olympus Trinocular Zoom Stereo Microscope with Boom Stand and Altra 20 Digital Camera (Model SZ61TR) for small animal surgery. In addition, we have access to the following facilities and instruments: μ-SPECT, μ-PET/CT, and General Electric PET-Trace dual particle accelerator (cyclotron) facilities, an IVIS 100 bioluminescence imaging station from Caliper Life Science Corp., and a NightOwl LB981 fluorescence imaging station from Berthold Technologies, Inc. Both machines can image small animals and well plates with high sensitivity and provide quantification results. The fluorescence imaging station, with proper configuration of filters, can capture signals at the wavelength range from green to near-infrared. In addition, our lab has access to the following equipment: Cryostat machine and microtome equipment, BioRad Mini-gel electrophoresis tanks and transfer apparatuses, three Beckman L-8 ultracentrifuges with multiple rotors (VTi70, SW28, SW40, etc.), four Sorvall RC5C centrifuges, LKB 1209 rack beta liquid scintillation counter, LKB gamma counter, Isco peristaltic pumps, fraction collector and UA-5 absorbance/fluorescence detector, Affymatrix GeneChip Arrayer for the whole genome analysis, Millipore 501 HPLC system, Beckman DU65 spectrophotometer, BRL4000 power supplies, balances, rockers, water baths, microfuges and vortices, and a Nikon Eclipse TE-300 inverted fluorescence microscope supported by a Macintosh G3 imaging system, and a behavioral testing apparatus. A rodent stereotactic brace as well as an anesthetic machine are available as a shared resource. Further, we have access to facilities outside BWH Radiology Department: (1) inductively coupled plasma-optical emission spectrometer (ICP-OES, SPECTRO CIROS VISION) at MIT Nuclear Reactor Lab for elemental analyses in the parts per trillion range; (2) laser capture microdissection (LCM) equipment at MGH/Harvard Center for NeuroDiscovery; (3) high-energy X-ray fluorescence microscopy (μ-XRM) at Argonne National Lab; (4) High Throughput Drug Screening Facility at the Harvard Medical School.

Pathology Laboratory (Assisting Radiology Department)

Laboratory/Office: Extensive pathology resources exist within the BWH, Harvard Medical School, and the Dana-Farber Cancer Institute. The BWH/Dana-Farber Harvard Cancer Care (DFHCC) Specialized Histopathology Core (Thorn 604, 603b and 533, BWH) occupies 1,025 sq. ft. of laboratory and 270 sq. ft. of office space. In addition to routine histopathology carefully correlated with imaging data, there are advanced tissue based systems such as laser capture microdissection, immunohistochemistry (IHC) or in-situ hybridization (ISH) on standard sections, automated image analyzers (AQUA and Ariol Systems). Other resources exist to compare the detection of Quantum Dot-based FISH and IHC using a Spectral Imaging system to conventional methods for simultaneous co-localization of multiple in situ signals in human specimens and to bring the best methods to bear on correlation studies with multimodal imaging data. The Department of Pathology also contains several 12-headed microscopes that are used for regular group review of large project group pathology related results. Among the pathological laboratories of the BWH are the:

Cytogenetics Laboratory: To further improve development and assessment of emerging molecular cytogenetics technologies for translational research and the subsequent introduction of new diagnostic tests, several research laboratories exist at the BWH's Translational Molecular Pathology Units, located in the Thorn Building and 221 Longwood. There, researchers have access to M-FISH, Rx-FISH, Bioview, Array-CGH and fiber-FISH technologies representing state-of-the-art approaches to cytogenetic research.

Note: Importantly, the Pathology Research Support Core (PRSC) will, whenever possible, build upon but not duplicate, the infrastructure and technical expertise of already existing DF/HCC and NIH funded Cores. In particular, the PRSC will utilize the BWH/DFHCC Specialized Histopathology Core that is located within the BWH department of Pathology to prevent duplicating the efforts of existing publicly-funded Cores. Since 2004, the Specialized Histopathology Core has provided a comprehensive set of tissue-based tests and diagnostic services priced at cost for DF/HCC investigators. The available equipment and techniques are listed in Tables 1 and 2. For the performance of more technically-advanced methodological applications and/or for the development of novel cellular assays, the Pathology Core discussed in this proposal has the opportunity to draw upon the infrastructure and expertise of the CMOP. The PRSC will be highly focused on providing specialized tumor analysis services best delivered by efficient tissue utilization, high-throughput service, and the expert tissue analysis by pathologists with extensive human as well as mouse research.

Computer: The labs contain multiple network computers and database software systems for protected sharing of data and results amongst project members and the Core. Of particular importance to the U54 is access to the TMAJ software application for web-based sharing of pathology data from a server system and real-time data serving to multi-institutional sites within the proposed NTR of the U54. As a further resource for collaborative networking, the BWH Department of Pathology has an Aperio Scanscope XT slide scanning system (Aperio Tech. Inc., Vista, CA) to allow users at multiple sites to easily access full resolution scans of pathology data.

Equipment: A list of major equipment is shown in Table 1.

TABLE 1. SPECIALIZED HISTOPATHOLOGY CORE: EQUIPMENT

1 automated tissue processor
1 embedding station
3 microtomes
1 H+E autostainer
1 automated coverslipper
3 automated immunostainers
1 cryostat
1 automated ISH workstation
1 laser capture microdissection system
1 6-headed teaching microscope
1 fluorescence microscope
1 cassette labeler
1 necropsy hood
1 automated peripheral blood analyzer
1 automated nucleic acid isolator (including paraffin embedded tissue)
1 image analysis system (AQUA)

TABLE 2. SPECIALIZED HISTOPATHOLOGY CORE: TECHNIQUES

Conventional Histology

Tissue processing, embedding, sectioning, and staining of paraffin embedded or frozen tissue

Immunohistochemistry

Routine and novel markers

In Situ Hybridization

Fluorescent (FISH), Chromogenic (CISH), or radioactive RNA ISH detection

Laser Capture Microdissection

Automated Quantitative Image Analysis (AQUA)

Nucleic Acid Isolation

Fresh, frozen, or paraffin-embedded tissue

Building for Transformative Medicine (BTM)

The Brigham Building for Transformative Medicine (BTM) was completed and opened in October 2016. There are two areas for imaging in the building, human clinical and research imaging on the L2 level and pre-clinical imaging and vivarium on the 11th floor.

There are five whole body Siemens MRI systems on the L2 level of the building for mixed clinical and research usage:

1. A 1.5T Aera - wide–bore (70cm) MRI
2. A 3.0T Skyra - wide–bore (70cm) MRI
3. A 3.0T Prisma MRI with high performance gradients.
4. A 3.0T Prisma MRI with high performance gradients.
5. A 7.0T Terra MRI.

Specifications for the Prisma scanners include:

• Magnet homogeneity at 40 cm DSV – 0.2 ppm
• Imaging FoV – 50x50x50 cm
• Zero helium boil-off technology
• 80 mT/m @ 200 T/m/s, gradient amplitude simultaneously
• High Power Shim
• TimTX TrueShape
• Tim 4G + Dot
• 64 receive channels
• High-power image reconstructor
• 60 cm bore diameter
• Slew rate = 200 T/m/s

7T MRI at the Building for Transformative Medicine. The BTM L2 floor includes an ultrahigh-field 7 Tesla, actively shielded, 70cm whole-body Siemens Terra MRI with 70 mT/m (200 T/m/s max slew rate) gradient set (SD72d) and 32 RF receiver channels. With its high-performance gradient set, the system can provide better than 100 µm resolution and ultra-fast EPI readouts for reduced image distortion. The system includes a Nova head coil for neuro imaging (32-channel receive - single channel transmit), a transmit-receive knee coil and a loop coil. The knee coil includes one transmit and 28 receive elements. The loop coil has one transmit and one receive elements. Additionally, the system includes 8 independent transmit channels capable of simultaneous parallel excitation with different RF pulse shapes for B1 shimming and/or parallel transmit methods such as transmit SENSE. The 7T scanner environment includes a visual display system and a button box for acquiring subject responses in the scanner. A MedRad power injector is installed in the Bay for the injection of gadolinium contrast agents.

There is also a Siemens CT scanner on the L2 level.

The pre-clinical imaging crescent on the 11th floor has the following equipment:

• MicroPET/CT -

- 3T MRI - Bruker Biospec 3T
- MicroCT - Bruker SkyScan 1176
- Optical imaging - Bruker In-Vivo Extreme II

In addition, there is a full BL2 facility for housing mice and rats for longitudinal studies.