The Center for Biomolecular Imaging
Wake Forest School of Medicine

Recognizing that imaging has the capacity to be an important translational tool, Wake Forest School of Medicine (WFSM) developed the Center for Biomolecular Imaging (CBI) as an institutional shared resource that provides an imaging technology infrastructure, as well as expertise in imaging protocol development, image data storage and image analysis to assist individual scientists, program projects, research centers and research institutes. The CBI occupies approximately 14,500 square feet in three locations which house a Siemens 3.0T MR scanner, a Bruker 7T small animal MR scanner, a GE 16-slice PET/CT scanner, a Toshiba 32-row CT scanner, and a Vevo LAZR Photoacoustic Imaging System. The CBI has a dedicated radiotracer lab and metabolite lab and a GE PETtrace 10 cyclotron for radiotracer development. To date, the CBI has established successful imaging cores within the Wake Forest Baptist Medical Center Clinical Research Unit and the Translational Science Institute. In addition, the CBI has the Imaging Informatics infrastructure required to interactively share data and analysis techniques and results with colleagues nationally and internationally.

Resources and Environment

The CBI occupies the ground and first floors (11,000 square feet) of the MRI building, 2,000 square feet in the Nutrition Research Center, and 1,500 in the Richard H. Dean Biomedical Research Building downtown. Several large bench laboratories and multiple small bench laboratories, which are used for the production of radionuclides and radiopharmaceuticals, and an image analysis lab and a cyclotron are included. These laboratories are well-equipped with current technologies. The ground floor and first floor of the MRI building contain an office suite for faculty and staff as well as for bioinformatics that includes a climate-controlled computer room, plus cubicles for programmers and analysts.

Major Resources Available

3.0T MRI Facility

The Center for Biomolecular Imaging's 1,750 square foot MRI research facility is located on the first floor of the MRI Building. It is operated by dedicated MR-registered technologists who have experience in all aspects of MR imaging research, as well as with a wide variety of animal imaging. The facility is equipped with all necessary supplies, including resuscitation equipment. Both human and non-human participants can be scanned during normal business hours. There is a dedicated participant dressing area and waiting area. Scans are performed by MR-registered technologists as well as by Ph.D. and M.D. level faculty. All image data is supplied to investigators in compliance with IRB and HIPAA regulations. Data can be downloaded to dedicated research image workstations for investigator analysis and/or be formatted for transmission to offsite reading centers.

Center for Biomolecular Imaging Members engaged in MRI research and who also serve as consultants to other investigators are Robert Kraft, PhD, Assistant Professor of the Department of Biomedical Engineering, who is a physicist working in the field of fMRI; and Youngkyoo Jung, PhD, who is an Assistant Professor of the Department of Radiology.

3.0T Siemens SKYRA MRI Scanner

- 3T Siemens SKYRA operating at 11.0 VD platform
- Gradient field strength of 45 mT/m, SR 200 T/m/s
- 70 cm open bore design, weight limit 500 lbs
- Capable of Advanced DTI, BOLD, Spectroscopy, ASL, Map-It (cartilage) and Advanced Cardiac Imaging
- Equipped with stimulation equipment for fMRI studies
- Various coils including 32 channel head coil, 20 channel head/neck, 18 channel body, 32 channel spine, 15 channel knee and surface loop coils.
- Contrast Power Injector

PET Research Facility

The GE 16-slice PET/CT Discovery ST 16 Scanner, which has 24 detector rings, provides 47 contiguous image planes over a maximum 70 cm transaxial field of view with CT attenuation correction. Axial spatial resolution of this scanner is 3.27 mm at the center of the gantry. Data acquisition modes include static, dynamic, whole body, and gated. The room is equipped with anesthesia gases and exhaust for scavenging the gases. There is a dedicated viewing area to interpret scans and a data analysis room. In addition, a dedicated research PACS for PET has been created to store PET data in DICOM format (images and raw data).

The scanner has high-sensitivity, uniform spatial resolution across the whole field of view and includes a laser alignment system for accurate positioning. Advanced detector technology - BGO crystals (6.3 mm transaxial, 6.3 mm axial, 30 mm radial) for high sensitivity and photo-fraction. There are 10,080 individual cut crystals for efficient light detection arranged in 24 rings of 420 crystals each. Large detector ring produces uniform resolution important for whole body imaging, especially for lymph nodes under the arm and where skin lesions can be on distant parts of the body. Thick, long-bore collimators and end-shield caps reduce scatter and random events. Excellent electronics provide high bandwidth, and very high count rate capability with low dead time. Large display panel for easy monitoring with bilaterally placed control panels for easy access. The scanner has fast movement with simultaneous up/in or down/out with convenient foot pedals for up/down and accommodates patients that weigh up to 400 lbs.

Laboratories

Organic chemistry laboratory (860 sq ft): three fume hoods, two rotary evaporators, one Perkin Elmer series 1600 FT-IR for characterization of synthesized compounds, a high range vacuum pump, several (more than five) HPLC systems attached with radioisotope and UV detectors for radiochemical synthesis, Varian GLC (TC and radiation detectors), and TLC scanner.

A second organic chemistry laboratory (478 sq. ft.): three chemical fume hoods, a rotary evaporator, two high vacuum pumps, and routine laboratory instrumentation to perform chemical synthesis.

Metabolite analysis lab: Varian Analytical HPLC (attached with UV and radioisotope detectors) for metabolite analysis, three micro-centrifuges, a rotary evaporator, and a Packard Cobra II auto-gamma counter.

Radiochemistry laboratory (1,350 sq. ft.): Two Capintech Hot Cells, two Comecere hot cells, four mini-cells, and one GE [11C] methyl iodide synthesis box for radiochemistry. In an area remote from the hot cells and shielded fume hood is a laboratory containing three fume hoods, a shielded rotary evaporator, a rotary chromatatron, and a laminar flow hood. Two additional Hot Cells were installed in 2005.

GE PETtrace 10 Cyclotron
The PET Center has an on-site GE PETtrace Radiotracer Production System, which is a compact, automated cyclotron and radiochemistry system designed for the fast, easy, and efficient production of PET radiotracers. The PETtrace System is centered on a compact negative ion cyclotron of proven design. The PETtrace Cyclotron features a vertical mid-plane and can accelerate protons to 16.5 MeV and deuterons to 8.4 MeV of energy. The system can be configured with various targets/process systems for production of common PET radioisotopes. The high performance, flexible design is ideal for applications in a research setting.

The PET isotopes, which can be produced by the PETtrace System, including oxygen-15, nitrogen-13, carbon-11, and fluorine-18, are automatically transferred to the radiochemistry processing systems for efficient conversion into finished radiotracers or precursors for use in preparing other labeled molecules.

While this facility explores a wide array of research questions, it currently empasizes the area of oncology and neurosciences, with a long grant-funded history in these research fields.

7T MRI Facility

The 7T Facility is located on the basement level of the Nutrition Research Building. This facility houses a Bruker Biospin 7T microMRI scanner. John Olson, MS, is the Coordinator of the Small Animal Imaging Facility. MR techniques currently available on this scanner include:

- in vivo mouse, rat, and non-human primate imaging with sub 0.1mm resolution
- magnetically labeled cell tracking
- mouse and rat cardiac and atherosclerosis imaging
- proton spectroscopy
- diffusion tensor imaging.

7T Bruker microMR Scanner

Superconducting Magnet System

- Actively-shielded superconducting wide-bore magnet
- Nitrogen free (no cryogenic maintenance by customer)
- Cryo-refrigerator (Minimal helium consumption, long hold-times, long maintenance intervals)
- Reduced stray field
- Screening against external field perturbations
- Table attached to the magnet front side with integrated rail for animal handling system
- Field strength: 7 T
- Diameter of clear bore: > 300 mm
- Stray-field (5 Gauss): +/- 3 m axial, +/- 2 m radial
- Length: 1.45 m
- Diameter: 1.655 m
- Passive RT shim system
- Vibration damping (absorber)

Gradient system B-GA 20S with RT-shim and related power supplies

- Actively shielded gradients
- Integrated shim set up to 2nd order
- Outer / inner diameter: 301.5 mm / 200.5 mm
- Gradient amplitude: 200 mT/m
- Max. slew rate: 1100 T/m/s

- Linearity 130 / 100 mm DSV: < ± 3%, < ± 2%
- Water cooled

Gradient system BGA12-S with RT-shim and related power supplies

- Actively shielded gradients
- Integrated shim set 1st & 2nd order
- Outer/inner diameter 206mm / 116 mm
- Gradient amplitude 660 mT/m
- Max slew rate: 4570 T/m/s
- Linearity/DSV (+/- %/mm) 3/130
- Water cooled

Gradient system BGA6-S

- Actively shielded gradients
- Integrated shim set; up to 2nd order
- Outer / inner diameter: 113mm / 60mm
- Gradient amplitude: 1000 mT/m
- Max. slew rate: 11250 T/m/s
- Linearity/DSV (+/- %/mm) 5/35
- Water cooled

User Interface: Linux Workstation

- ParaVision4.0
- Topspin1.5
- Jive6.0

RF Coils

- Volume coils
    - Litzcage RF Volume coils
        - 25 mm (mice), 38 mm (rat brains), 50 mm (rat brains)
    - Bruker 72 mm volume coil (rats up to 600 grams)
    - Bruker 150 mm volume coil (non-human primate brains)
- Surface coils
    - 25 mm (Tx/Rx), 35 mm (Rx only);

Anesthesia/Monitoring

- Surgivet anesthesia machine - Isoflurane and oxygen
- SA Instruments animal monitoring
    - ECG monitoring, respiratory monitoring, temperature monitoring
    - Animal warmer – temperature maintained with thermostatically controlled warm air

Micro-Ultrasound and Photoacoustic Imaging Suite

The Micro-Ultrasound and Photoacoustic Imaging Suite is located on the 6th floor of the Hanes Building.

Vevo® LAZR Photoacoustic Imaging System

Photoacoustics imaging technology integrates the sensitivity of light-based imaging with the resolution of high-frequency sound waves to provide never-before-seen insights into living tissue cellular environment and flow of blood. It produces the non-invasive functional, anatomic and visual information needed to assess potential treatments for the major diseases that affect people around the world.

Photoacoustics Features:

- Inherent co-registration of photoacoustic signal to 2-D/3-D anatomical target
- Sensitive, specific molecular data for tumor microenvironment studies

- Real-time, *in vivo* imaging of deep tissue
- Resolution down to 45 µm allows detailed anatomical analysis
- 3-D imaging with respiration gating
- Longitudinal tumor imaging for therapeutic/drug studies
- *In vivo* nanoparticle imaging

Applications include:

- Quantification of oxygen saturation and hemoglobin content
- Microvascular hemodynamics in real-time
- Molecular and cellular imaging
- 3-D volumetric acquisition
- Vevo Multiplexer tool to detect signal from multiple sources and co-register to anatomy
- Longitudinal monitoring for therapeutic interventions in the same animal over time
- High sensitivity, high specificity, real-time 3-D imaging
- Spectro functionality for characterization of photoacoustic signal throughout the 680 – 970 nm range
- 3-D Thresholding for optimized signal intensity during data analysis
- Vevo Color for differentiating various anatomical targets

Richard H. Dean Biomedical Research Building

The downtown CT facility is located in the Vivarium of the Richard H. Dean Biomedical Research Building. It houses a Toshiba 32-slice Aquilion CT Scanner that is dedicated to animal imaging. It has a gantry speed of 0.5 seconds and is equipped with cardiac gaiting. All image data is networked to the TeraRecon system for investigators.

32-slice Toshiba Aquilion CT Scanner (www.toshiba.com)

- 0.5mm resolution
- 32 slices per rotation X .5mm Scanning in high resolution
- 7.5 mHu Tube
- 500 mA Capability
- VoiceLink System
- SureFlouro System
- Scan FOV: 18, 24, 32, 40, 50
- Helical scanning
- Rotation speed: .5, .6, .75, 1.0, 1.5
- PF / HP
  - .656 / 21
  - .844 / 27
- 1.406 / 45
- Bore size = 720 mm (500mm maximum FOV)
  Table weight limit = 450 lb.
- Can cardiac gate
- Have power injector for bolus contrast injection

Imaging Informatics

Josh Tan, MS, CBI's Medical Imaging Engineer/Analyst Programmer oversees all phases of database design, development, and management for the Center. He is also responsible for administration of the TeraRecon servers and workstations, as well as training of investigators, faculty, and study coordinators in best methods of data collection and image analysis using TeraRecon and data storage. He collaborates with investigators to determine image analysis requirements to achieve study/grant objectives. CBI is endeavoring to increase research in the area of image analysis as well as create new imaging technologies and applications. This will have direct benefit to the investigators who use CBI.

TeraRecon Systems (www.terarecon.com)

- 3 TeraRecon AquariusNET servers
  - Distributed 2-D/3-D/4-D real-time rendering and visualization on any windows PC via local network
  - Total of 6TB of storage space for Medical Imaging in RAID5+1 configuration directly connected to servers
  - Concurrently render ~13,800 images in real-time
  - Render images from any modality in 3-D from a stack of 2-D DICOM images
  - Virtual Endoscopy
  - MPR, MIP, 3-D, 4-D
  - Image fusion
  - JPEG and AVI output

- 3 TeraRecon Aquarius Workstations
  - Advanced 2-D/3-D/4-D real-time rendering and visualization imaging workstation
  - 500GB of direct attached storage space for storage of medical images
  - Each workstation can concurrently render 3,400 images in real-time
  - Render images from any modality in 3-D from a stack of 2-D DICOM images
  - Volumetric, area, and distance measurement capabilities
  - Advanced segmentation and analysis modules
  - Virtual Endoscopy
  - MPR, MIP, 3-D, 4-D
  - Image fusion
  - JPEG and AVI output

OsiriX (www.osirix-viewer.com)

- 2-D/3-D/4-D advanced imaging software for Macintosh
- Volumetric, area, and distance measurement capabilities
- Advanced segmentation and analysis modules
- Open source software
- Quick Time Virtual Reality movies
  - Interactive movies for medical imaging
  - Embeddable movies into PowerPoint presentations
  - Embeddable movies into web pages

Mimics (www.materialise.com/mimics)

- Advanced 2-D/3-D modeling software for PC
- Volumetric, area, and distance measurement capabilities
- Advanced segmentation and analysis modules
- Generates 3-D AutoCAD files for printing on 3-D printer

Amira (www.amiravis.com)

- Advanced 2-D/3-D modeling software for PC
- Volumetric, area, and distance measurement capabilities
- Advanced segmentation and analysis modules
- Generates 3-D AutoCAD files for printing on 3-D printer

ImageJ (http://rsb.info.nih.gov/ij/)

- Advanced imaging software
- Open source software
- Based on Java for various platforms of operating systems
- Advanced segmentation and analysis capabilities

LCModel 6.1 (http://s-provencher.com/pages/lcmodel.shtml)

- Automatic quantification of in vivo proton MR spectra
- Fully developed over 15 years with spectra analyzed from a wide variety of scanners and field strengths at more than 400 sites

GE Advantage Workstations (www.gehealthcare.com/usen/aw/index.html)

- Advanced 2-D/3-D/4-D real-time rendering and visualization imaging workstation
- Render images from any modality in 3-D from a stack of 2-D DICOM images
- Volumetric, area, and distance measurement capabilities
- Advanced segmentation and analysis modules
- MPR, MIP, 3-D, 4-D

MIPAV (http://mipav.cit.nih.gov)

- Advanced imaging software
- Advanced segmentation and analysis capabilities

DICOM Server

- Digital Imaging and Communications in Medicine
- Network storage of medical images from all modalities in DICOM format
- Imaging workstation and imaging modalities can send images in DICOM format for storage and retrieval from the DICOM server
- Image database for organization of medical images
- DCM4CHEE (www.dcm4che.org)
- PHP (www.php.net)
- MYSQL (www.mysql.com)
- Apache (www.apache.org)

Apple Workstations (www.apple.com)

- Blue-ray DVD backup
- Exabyte 320GB tape archive
- Audio/Video editing and encoding workstations
- Training videos and images generated on these workstations
- Website development
- Database development
- 3-D/4-D medical animation and illustration

Zcorp 3-D Printer (www.zcorp.com)

- Imports 3-D model created in Mimics
- Prints a model, layer-by-layer
- 3-D prints can be passed around for hands-on discussion.

MIRC Software and Hardware (www.rsna.org/mirc)

- Medical Imaging Resource Center
- WFBMC helped to develop
- Open source
- Software for secure image transmission using the Internet
- Coordinating and reading centers use MIRC to automate the sending and receiving of DICOM images from various hospitals and cities around the world
- Functionality to automatically de-identify medical images

Animal Resources Program

The ARP provides for the procurement, husbandry, and health care of animals used in research and teaching. Scientific and technical support are also provided by the ARP for Wake Forest University (WFU) programs using animals in teaching and research. WFU is committed to providing a high-quality program of animal care and use in compliance with state and federal laws. The ARP operates in accordance with the standards and policies of the US Department of Agriculture's Animal Welfare Information Center (AWIC) and the Department of Health and Human Services' Office of Laboratory Animal Welfare (OLAW). This program has been accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC), since 1966.

Wake Forest University maintains centrally-managed animal facilities and support space consisting of a total of 216,584 square feet. The facilities of Wake Forest University are located at four sites: the Bowman Gray Campus, the Downtown Campus, the Reynolda Campus, and the Friedberg Campus.

Bowman Gray Campus

ARP space, located in four buildings, at the Medical Center (Bowman Gray Campus) totals 53,843 sq. ft. The primary animal facilities are located on the 7th floor of the Hanes Building. Facilities are also located on the 5th and 6th floors of the Nutrition Research Center (NRC) Building (adjacent to the Hanes Building), the G and E floors of the Gray Building (located 100 yards from the Hanes animal facility), and the MRI Building (located approximately 500 yards from the Hanes animal facility).

The Hanes Building animal facilities consist of 15,209 sq. ft. of space. Located here are 5,106 sq. ft. of animal housing space, including 12 multipurpose animal rooms of standard design, and 38 6'x6' cubicles available for the independent housing of small groups of animals and projects. Support and service facilities (totaling 10,103 sq. ft.) include offices, men's and women's dressing shower rooms, personnel break areas, food storage, bedding and supply storage, receiving, waste holding, cage washing, clean cage holding, pharmacy, and procedure rooms. In addition to these multipurpose facilities, a postoperative recovery room and a biohazard (Biosafety Level 2) containment facility are available. Outside the animal facility, on the 8th floor of the Hanes Building, additional space (2,187 sq. ft.) has been acquired for storage of clean caging, supplies, and long-term record storage.

The NRC Building has animal facilities located on the 5th and 6th floors, totaling 24, 149 sq. ft. of space. The 5th floor NRC animal facility consists of 9,887 sq. ft. of animal housing (3,630 sq. ft.) and support space (6,257 sq. ft.). Support and service facilities include cage washing, minor procedure room, and nonhuman primate behavioral testing laboratories. The 6th floor NRC animal facility consists of 14,262 sq. ft. of animal housing (4,039 sq. ft.) and support space (10,223sq. ft.). Approximately 7,420 sq. ft. of space is used to support barrier-maintained, specific pathogen-free rodents and includes 13 holding rooms, five procedure rooms, a mock laboratory and training room, a cage-wash facility equipped with a

tunnel washer and autoclave, and three individual storage rooms/areas for cages, food, and bedding. The remaining 6,842 sq. ft. include six conventional housing rooms, surgery, radiology and necropsy facilities, men's and women's locker rooms, and a break room. There is also a 77 sq. ft. holding area, located on the E floor of this building, for animals from the time of receipt until housed in the facility on the Bowman Gray or Downtown Campus. Located nearby on this floor, is additional space to house the ARP core administrative offices and service area, totaling 1,249 sq. ft.

A total of 10,843 sq. ft. of animal housing (5,781 sq. ft.) and support space (5,062 sq. ft.) are located on the basement and ground floors of the Gray Building. Support and service facilities include food and supply storage, cage washing, nonhuman primate behavioral testing laboratories, restrooms, locker room, and surgery and necropsy facilities.

A 129 sq. ft. animal holding area is located on the first floor of the MRI Building at the Bowman Gray Campus. This area consists of an anteroom (58 sq. ft.) and a housing room (71 sq. ft.) and is used to house animals prior to and following conduction of PET and MRI studies.

Downtown Campus

Animal facilities, totaling 41,468 sq. ft., are located in three buildings at the Downtown Campus in downtown Winston-Salem two miles from the Bowman Gray Campus. The primary animal facilities are located on the basement floor of the A1 Building (also referred to as the Dean Building). Facilities are also located on the ground and 2nd floor of the Piedmont Triad Community Research Center (PTCRC) Building (adjacent to the A1 Building), and the 1st floor of the A1a Building (located approximately 4 blocks from the A1 Building).

The A1 Building contains laboratories and offices occupied by the Wake Forest Institute for Regenerative Medicine (WFIRM) and the Department of Pathology, Section on Lipid Sciences. All animals used by investigators in this building are located in the basement of the A1 building, in a centralized, ARP-managed animal facility. The animal facility totals 24,055 sq. ft. (8,279 sq. ft. of animal housing and 15,776 sq. ft. of support). The facility consists of a general housing area with 17 animal rooms, and a rodent barrier facility with 5 animal housing rooms, one of which is made up of 5 isolation cubicles. There is a surgery suite with two operating rooms, two animal preparation rooms, one surgeon's preparation room, and one instrument preparation room. The diagnostic imaging facility contains digital radiography, CT and microCT scanners. The facility has necropsy and tissue preparation rooms, and a morgue cooler for carcass storage. The facility also includes a cage wash area with a tunnel washer, a rack washer, and an autoclave. There are 7 procedure rooms located within the animal facility, 3 within the rodent barrier facility, and 4 within the general animal facility. Finally, office and storage space are on the basement floor as well.

The Piedmont Triad Community Research Center (PTRC) Building contains laboratories and offices occupied by the Department of Physiology and Pharmacology. All animals used by investigators in the PTCRC Building are either housed within the PTCRC's central animal facility or in satellite housing areas within the building. Central (ARP-managed) animal facilities in the building total 7,953 sq. ft. (3,216 sq. ft. of animal housing, 4,737 sq. ft. of support) located on the ground and second floors, described below. Investigator-maintained (satellite) animal housing facilities are found on the same floors and are described in Appendix IV.

The PTCRC central animal facility consists of 8 animal housing rooms, one of which is made up of 6 isolation cubicles. There also is a surgery suite with two operating rooms, a radiology room, a recovery room, and separate preparation areas. In addition, the facility has necropsy and tissue preparation rooms, and a morgue cooler for carcass storage. The facility also includes a cage wash area with both a tunnel

and a rack washer. Offices and storage areas also are located nearby. Rodent housing/procedure space on the 2nd floor of the building (2,554 sq. ft. of the total space) is used by the ARP to accommodate the Department of Physiology and Pharmacology's expanding research programs.

The A1a Building contains offices and laboratories occupied by the Wake Forest University Transgenic Core. All animals used by investigators in the A1a Building are housed within the centralized, ARP-managed animal facility on the first floor. The animal facility consists of 9,460 sq. ft (2,222 sq. ft. of animal housing, 7,238 sq. ft. of support. The animal facility consists of six animal housing rooms, one of which is quarantine housing for rodents to be rederived, while the other five are for the rodent barrier facility. There are two cage wash areas, one for quarantine housing consisting of a rack washer and an autoclave, and one for the rodent barrier facility consisting of a rack washer, tunnel washer, and an autoclave. Finally, there are 5 procedure rooms, one of which is for the quarantine facility.

Reynolda Campus

Animals used by investigators located on the Reynolda Campus are housed in a 1,680 sq. ft. animal facility located in Winston Hall. The facility consists of approximately 1,240 sq. ft. of housing space, much of which is managed by investigators (satellite facilities). An additional 440 sq. ft. of support space includes restrooms, a cage-wash area, and storage areas for food, bedding and supplies. Birds are housed outdoors in 256 cubic foot metal pens located approximately 50 feet from the Winston Hall facility. All of these pens are kept in a secure area surrounded by cyclone fencing. The Reynolda Campus is located 4 miles north of the Bowman Gray Campus.

Friedberg Campus

The Friedberg Campus is a 200-acre developed site located 10 miles south of the Bowman Gray Campus. It serves as home to the Wake Forest University Primate Center and the specialized research programs of the Department of Pathology/Section on Comparative Medicine. Animal housing and support space, totaling 119,593 sq. ft., includes 15 housing units for nonhuman primates, 6 fly pens for pigeons, facilities for housing rodents, three buildings for housing livestock, a cage-washing facility, offices, and other support areas.