Indiana Institute for Biomedical Imaging Sciences
Resources and Capabilities

New research laboratory space was opened in early 2003 that will support the activities of the Indiana Institute for Biomedical Imaging Sciences (IIBIS). A new research imaging center is located in the Research Institute II (R2) building which is in close proximity to all of the cancer research activities on our campus. The first floor and basement level of the R2 building house comprehensive facilities for human and animal imaging (MRI, PET, and CT) along with ancillary support space including wet laboratories, surgery suites, an image processing laboratory, a machine shop, and an electronics shop. The imaging center is housed within approximately 30,000gsf space. A second new building, the Biomedical Research and Training Center (BRTC), houses our tracer and contrast agent development program. This space can accommodate 2 medical cyclotrons (1 is currently located in the facility) and has extensive synthetic chemistry space, radiochemistry space, molecular biology laboratories, cell culture labs, and ancillary support labs for shared instrumentation and device construction. The total space in the BRTC for this program is approximately 15,000 gsf. The two buildings are linked by a pneumatic tube system that permits the rapid transfer of short-lived PET radiopharmaceuticals from the chemistry laboratories to the PET imaging systems.

Biomedical Imaging Systems

Multiple biomedical imaging systems are available to investigators at IU to investigators from other institutions and industry through the IIBIS. The imaging systems are categorized below as base and alternative systems.

Small Animal Imaging Systems

EVS-R9 microCT. The EVS-R9 microCT scanner (Enhanced Vision Systems Corp, London, Ontario N6G 4X8) operates at 50 kVp and 1 mA maximum tube current. It is capable of 50 micron or 100 micron voxel resolution with 2x2 or 4x4 binning in the detector panel. The radiation dose associated with various imaging parameters (exposure time and angular samplings) is measured to obtain a guideline on imaging protocol designing. For each radiation dose level, image noise is also measured by the standard deviation of CT number in the water region. The noise to dose relationship is established for various detector-binning modes.

IndyPET II. The IndyPET-II scanner has been developed at Indiana University by Dr. Hutchins as a high resolution, high sensitivity research PET scanner for use in small animal imaging studies. The system consists of four, approximately planar detector banks mounted on a rotating gantry. The detectors cover a transaxial FOV of 23cm and an axial FOV of 15 cm. This configuration reduces parallax distortions and produces a relatively uniform resolution throughout the FOV. The two pairs of opposing detectors banks are offset to give increased sampling density and increased spatial resolution. The average (radial and transverse) FWHM resolution is 2.5mm at the center of the FOV and increases to less than 3.5mm at the edge of the FOV. The NEMA-2001 sensitivity is 9030 cps/MBq at the center of the scanner and 4250 cps/MBq at a radius of 10cm. The NEMA-1994 sensitivity is 23.0 cps/MBq/ml.

IndyPET III. The IndyPET III scanner was developed at Indiana University by Dr. Hutchins The system was designed to achieve 1 uL volumetric spatial resolution suitable for whole body mouse imaging. The scanner uses 8 planar detector banks consisting of 48/spl times/108 array of 20 mm long LSO crystals

with an array pitch of 0.87 mm coupled to two Hamamatsu H8500 large area, 64-anode photomultiplier tubes. The detector modules are mounted on a rotatable gantry offset from the center of rotation to allow increased sampling density. Transaxial resolution is 1.1 mm FWHM with an axial resolution of 1.5 mm FWHM. Sensitivity has been measured to be 4.0% of all decays. The scanner design allows for the addition of 14 additional detector banks for improved resolution and sensitivity.

Varian 9.4T MRI Horizontal Bore. The Varian 9.4 T / 31 cm actively shielded horizontal bore MR system is suitable for in vivo imaging and sprectroscopy investigations of small animals ranging from mice to rabbits. The system is equipped with two sets of actively shielded gradient sets: 1) a 21 cm inner diameter gradient set capable of generating 20 G/cm, and 2) a 12 cm inner diameter gradient set capable of generating 40 G/cm. The state-of-the-art Varian Unity Inova console on the system is capable of performing multinuclear investigations and has waveform generators on all RF and gradient channels, which allow arbitrary pulse shaping and easy implementation of sophisticated imaging and spectroscopy pulse sequences. A number of single-tuned quadrature and dual-tuned linear imaging coils, slotted tube resonators and surface coils are available for multinuclear MR studies. MR methods, which are used for a variety of applications, include echo-planar imaging, diffusion weighted imaging, back-plane reconstruction, single voxel localized spectroscopy, chemical-shift imaging, gradient-enhanced spectral editing, multiple-quantum techniques and other specialty pulse sequences.

Berthold LB981 NightOwl The NightOWL system consists of a Peltier cooled CCD camera (578 x 385 pixels) housed within a 102x60x40 cm light tight enclosure for imaging luciferase and GFP expression in small animals. The system is interfaced to a Pentium 200 MHz for data acquisition and analysis.

Interventional Radiology Research Laboratory. This laboratory is focused on research in atherosclerosis, restenosis, and directed drug delivery for the treatment of the cancer and vascular disease. The laboratory includes an animal operating room for microsurgeries as well as intraabdominal and intrathoracic surgeries, two Toshiba X-ray machines with fluoroscopic and DSA imaging capabilities, and associated ancillary equipment for subject monitoring and support.

Human Imaging Systems

Siemens MAGNETOM Trio 3T Unlimited MRI. The Trio 3T MRI, located in the R2 building, is a 3 tesla whole body imaging system operating with Syngo software. The system is equipped with a 200 T/m/s gradient system and 8 RF-channels. The flexible RF system has the capability of performing multinuclear and spectroscopy studies.

GE Signa Advantage 1.5T MRI. A dedicated research MRI system is located in the high technology imaging center of University Hospital. This system is a 1.5 tesla General Electric Signa Advantage system operating under software version 9.0. The system currently has the capability to perform hydrogen magnetic resonance spectroscopy and functional brain imaging studies using Echospeed. Two additional 1.5T General Electric MRI systems (1 each in University and Riley hospitals) have echo-planar imaging capabilities and are available on a limited basis for research studies.

Siemens ECAT HR+ PET. The Siemens ECAT HR+ PET scanner is located in the R2 building. The whole body imaging system has an axial field-of-view of 15 cm, is equipped with BGO detector technology and has retractable septa for 3-D volumetric imaging. Both conventional filtered backprojection and OSEM reconstruction algorithms are available and used routinely.

Siemens Biograph PET/CT. The Biograph PET/CT scanner is located in the Clinical building located in the IUPUI campus and is scheduled to be relocated to the R2 building. This system is a whole-body static imaging system equipped with BGO detector technology and capable of 3-D volumetric imaging. The axial field-of-view is 15 cm. Both conventional filtered backprojection and OSEM reconstruction algorithms are available and used routinely.

Alternative Animal Imaging Systems

Optosonics Thermoacoustic Tomography System. This new imaging modality, conceived and developed at Optosonics, Inc (Indianapolis, IN) in collaboration with the Indiana-CEBI, produces images of tissue RF absorption contrast by detecting sonic waves produced by thermal expansion of tissue. A small animal system has been constructed using a tunable laser enabling optical absorption spectroscopy and imaging. The current system has a spatial resolution of 200 microns and can image using optical wavelengths in 532-1064nm wavelength range using an Optotek, Inc laser.

Radionuclide Production Systems

RDS-Eclipse Cyclotron: Housed within the BRTC building is a Siemens RDS-Eclipse cyclotron. This system consists of an 11 MeV proton cyclotron, target systems for the production of 11C, ^{18}F, ^{13}N and ^{15}O used in the synthesis of PET tracers.

IIBIS Imaging Services Core

The IIBIS provides a range of services that include education of cancer center investigators on the capabilities and application of imaging technologies, consultation to assist with imaging study design, production of PET tracers, performance of imaging studies, resources for image processing and data analysis, and quality control for all chemistry and imaging systems housed within the R2 and BRTC facilities. A brief description of the core services follows:

PET Tracer Production: PET Carbon-11, Nitrogen-13, Oxygen-15 and Fluorine-18 tracers are produced for PET imaging studies. Numerous tracers are in various stages of development for support of cancer, cardiovascular and neuroscience research.

PET Research & Routine Production Radiotracers

1. Heart acetylcholinesterase imaging agents (dog and rat heart imaging):
Cardiac acetylcholinesterase imaging agents [^{11}C]edrophonium, [^{11}C]pyridostigmine

2. Choline kinase imaging agent (tumor mice):
[^{11}C]Choline

3. MMP (Matrix metalloproteinase) imaging agents (tumor mice):
[C-11]Me-CGS 27023A and its analogs
[C-11]Me-halo-CGS 27023A analogs
[C-11]Biphenylsulfonamide analogs

4. Alkylguanine-DNA alkyltransferase (AGT) imaging agents (tumor mice):
Radiolabeled O^6-benzylguanine analogs

5. Herpes simplex virus thymidine kinase (HSV-TK) reporter probes (tumor mice):
[^{18}F]FHBG and other fluorine-18 labeled penciclovir and ganciclovir analogs

6. **Brain dopamine and serotonin transporters ligands (human, pig and rat brain imaging):**
   [^{11}C]β-CFT, [^{11}C]β-CIT, [^{11}C]β-CNT for the study of Parkinson's Disease.
7. **Muscarinic Receptor Ligands (dog heart imaging):**
   [C-11]Methyl-QNB, [C-11]Methyl-TRB
8. **Peripheral Benzodiazepine Receptor Ligand (tumor mice and rat):**
   [^{11}C]DAA1106
9. **D2/D3 receptor ligand (human and rat brain imaging):**
   [^{11}C]Raclopride
10. **β-Amyloid Plaques Ligand for Alzheimer's Disease (human brain imaging):**
    [^{11}C]PIB
11. **Vesicular monoamine transporter ligand (rat brain imaging):**
    [^{11}C]DTBZ
12. **Sympathetic Nervous System (human and dog heart imaging) :**
    [^{11}C]HED
13. **High-affinity choline uptake (HACU) ligands (rats and mice, tumor and heart imaging):**
    [^{11}C]HC-15 and [^{11}C]HC-3
14. **SK_{Ca} channels ligand (rat heart imaging):**
    [^{11}C]NML
15. **Vagal Nervous System (dog heart imaging):**
    [^{11}C]Neostigmine
16. **Luciferase reporter probes (tumor mice):**
    [C-11]D-luciferin methyl ester and [C-11]D-luciferin methyl ether
17. **Blood Flow (human and dog):**
    [O-15]Water, [N-13] Ammonia
18. **Glucose Metabolism (human and animal):**
    [F-18]FDG
19. **Blood Volume (tumor mice):**
    [C-11]CO
20. **Free Fatty Oxidation Rates (human and animal):**
    [C-11]Acetate

Performance of Imaging Studies: The imaging center provides experienced and trained technologist for the acquisition and basic image processing required for all studies. Investigators, or their staff, work closely with the imaging center technologists in the performance of specific studies. The imaging center staff administer anesthesia to the animals, administer PET tracers or contrast agents, and operate the imaging systems. The only exception to this model is for bioluminescence/biofluorescence imaging where investigators can operate the system without support once trained. The imaging center staff is also responsible for all necessary image reconstruction or processing needed for the study. An emphasis for all imaging studies is placed on the collection of data that permits quantitative or semi-quantitative analysis of results.

Image Processing and Data Analysis: The imaging center maintains numerous servers and software packages for the analysis of imaging data. A large base of in-house developed imaging processing software (based upon IDL and/or MATLAB) is maintained by the faculty and staff in the imaging center.

This software enables the generation of multimodality fusion images, navigation throughout image volumes in standard and non-standard image planes, definition of region-of-interests, application of semi-quantitative data analysis methods (SUVs), application of quantitative data analysis methods (compartmental models), and 3-D visualization tools (projections, maximum intensity projections) for subjective evaluation of image data. Tools for the registration of multimodality images have been developed and validated in our laboratory and are utilized routinely so that fused data sets can be easily generated. Access to all software and servers is made available to interested cancer center investigators using X-window emulators and VPN clients. A limited number of image processing workstations are also available in the imaging processing laboratory housed in the imaging center.