UW Small Animal Imaging

MISSION

The mission of the UW Small Animal Imaging Facility is to provide innovative, state-of-the-art, affordable, noninvasive, high-resolution, in-vivo and ex-vivo imaging support to UW Carbone Cancer Center members, UW researchers, and industries that use small animal models in their research.

Consultation

The facility director and manager provide consultation to investigators to determine which imaging methodologies are most suited to meet their research objectives. The following are parameters that can be tailored to answer your specific questions: animal diet and temperature, anesthesia, imaging modality, contrast agent, imaging time points, scan duration, gating, temporal and spatial resolution, static or dynamic framing, and image reconstruction.

The director and manager can provide guidance to your overall study design, for example, whether to include control groups or to determine the number of subjects for statistical significance. Lastly, we can train you to accurately and efficiently analyze your data using our free-of-charge post-processing computers.

We provide three powerful PCs equipped with up to 64GB of RAM, dual 3.1 GHz processors, NVIDIA Quadro 4000 graphics cards, on a 64-bit Windows 7 OS to facilitate 2-D and 3-D image viewing, manipulation, and quantitative analysis of large files. The workstations are furnished with several imaging software packages including Siemens Inveon Research Workplace, Image J, GIMP, Amira, VivoQuant, and IVIS’s Living Image. We can easily convert imaging data to a universal DICOM format if you choose to perform analysis on your own workstation.

Anatomic microCT scanning

In December 2005, we acquired the microCATII from Siemens. This scanner has a large field-of-view for scanning large rodents (i.e. rats up to 300 grams), and a variable source for high-resolution scanning (~20 microns). This scanner was funded entirely by an NCRR shared instrumentation grant awarded to Dr. Weichert.

In late December 2006, we received the first Inveon microCT scanner from Siemens. This CT can achieve 50 micron spatial resolution, but it is primarily used to acquire anatomical images for functional PET scanning.

Functional microPET and hybrid microPET/CT scanning

In late December 2006, we received the first ever Inveon hybrid microPET/CT scanner from Siemens. Coupled with our own proprietary cell-selective imaging contrast agents, this scanner affords our investigators unique disease detection and evaluation which can only be provided at the UW. This scanner provides unsurpassed PET sensitivity (>10%), 1.2mm resolution, and a large axial field of view (13 cm). The anatomical CT and the functional PET images are automatically co-registered for easy analysis. An integrated isoflurane anesthetic gas system and physiologic monitoring system allow for image gating and animal monitoring during scanning.
Optical scanning
The IVIS Spectrum (Perkin Elmer) is capable of both bioluminescence and fluorescence scanning. We routinely use this system for non-invasive longitudinal monitoring of cancer progression, metastatic cell trafficking and gene expression and delivery in living animals. This system is also used to assess hypoxia, enzyme activity, angiogenesis, apoptosis, arthritis, neurological and infectious diseases, among many other applications. An optimized set of high efficiency filters and spectral un-mixing algorithms affords non-invasive imaging of bioluminescent and fluorescent reporters across the visible light spectrum up to the near-infrared wavelength. It also offers single-view 3D tomography for both fluorescent and bioluminescent reporters that can be analyzed in an anatomical context using a digital mouse atlas. The Spectrum can excite from the bottom (trans-illumination) for deep tissue or from the top (epi-illumination) to illuminate in-vivo fluorescent probes. 3D diffuse fluorescence tomography can be performed to determine source localization and concentration using the combination of structured light and trans-illumination fluorescent images. The instrument is equipped with ten 30nm bandwidth excitation filters and eighteen 20nm bandwidth emission filters that significantly reduce auto-fluorescence by the spectral scanning of filters and the use of spectral un-mixing algorithms. In addition, the spectral un-mixing tools allow the researcher to separate signals from multiple fluorescent reporters within the same animal.

Intraoperative real-time NIR scanning
The SAIF is one of the first facilities in the US to obtain the Fluobeam™ (Fluoptics) hand-held imaging system which detects in-vivo near-infrared fluorescence in 2D. This system has a laser excitation dialed in at 780nm and a long pass emission filter at >820nm, and a crown of LEDs allowing one to work under white light in open space with a direct access to the animal. Focused on cancer surgery improvement, this technology will afford oncology surgeons a radically new efficiency in tumor resection. The success of this concept will largely depend on the ability of the optical agent to selectively localize in the tumor prior to surgery. Several UW investigators are currently developing tumor-specific NIR optical probes for intravenous administration that may potentially afford real-time intraoperative tumor margin illumination. Intraoperative margin illumination could have a significant impact in glioma resection and determining lymph node involvement during breast cancer resection, for example. This newly introduced unit is designed to be used in a surgical suite and therefore offers rapid clinical translation potential.

High resolution MRI scanning
Installation of an Agilent 4.7T small animal scanner was completed in April of 2007. The horizontal bore imaging/spectroscopy system gives us the capability to scan rodents up to 600 grams with an in-plane resolution of 50 microns. The system is also equipped with a rodent isoflurane gas anesthesia system and physiologic monitoring system for image gating. We can scan broadband nuclei including 1H, 31P, 19F and 13C. T1 and T2 anatomical scans are possible as well as the creation of T1, T2 and T2* maps. The system is also capable of functional MRI (EPI), diffusion and diffusion tensor imaging, localized spectroscopy (STEAM and PRESS), chemical-shift imaging, and perfusion imaging with Gd-based contrast agents. These specifications allow investigators to visualize and quantify a variety of moieties and processes including metabolites (NMR spectroscopy), anatomical structures, tumor morphology, blood flow/vessels, fiber pathways, drug effects, brain activity, and heart motion. In early 2008, we became one of only 5 institutions in the US to receive a commercial dynamic nuclear polarization system from GE. This system allows rapid in-vivo investigation of biochemical events enhanced with carbon-13 labeled substrates at enhanced sensitivity levels.
Micro-imaging suite
We have enjoyed tremendous institutional support for our first class 2000 square foot facility that was specifically designed for small animal and molecular imaging in the WIMR (Wisconsin Institutes for Medical Research) 1 tower, a 9-story research building attached to the hospital, and adjacent to the School of Pharmacy and the Waisman Research Institute. This new facility houses the Siemens microCATII, Siemens Inveon Hybrid microPET/CT, Perkin Elmer IVIS, Fluoptics Fluobeam, and Agilent 4.7T MRI and associated hyperpolarization apparatus. We have a designated area for image analysis with our high end workstations. We boast our own animal holding room which has strictly regulated temperature, humidity, pressure, and light cycles, and which contains passively ventilated rodent housing racks for holding radioactive animals and those involved in long-term tumor monitoring studies. The new WIMR complex is strategically located adjacent to the new animal vivarium where non-radioactive animals involved in imaging studies are housed. This preclinical and molecular imaging suite is designed with translational research in mind as supported by our lab neighboring the clinical research GE Discovery VCT and GE Discovery 710 PET/CT scanners. Also next to the small animal imaging suite are the cyclotron, radiochemistry, and radiopharmacy facilities which provide expertise on PET agent synthesis in a collaborative and fee-for-service basis. The small animal imaging director and manager can coordinate radionuclide and radiotracer synthesis with the Cyclotron Group led by Drs. Jerry Nickles and Todd Barnhart in the Medical Physics Department. Alternatively, agents may be acquired from commercial sources such as PETNET or IBA Molecular.

Animal housing
In order to ensure and preserve the pathological integrity of the Laboratory Animal Resources (LAR) facilities, investigators are required to transfer their animals to our general microimaging protocol (M02169) by completing the animal transfer form. Only after approval from LAR can animals be transported to our facility in WIMR B1334C. Radioactive animals will remain in our holding facility until the animals are euthanized and the experiment is completed. Under no circumstances are radioactive animals allowed to leave our facility for placement back into their original housing facility. Radioactive materials can only leave the imaging facility if approved by radiation safety. In approved cases, non-radioactive animals can be rehoused in a WIMR vivarium quarantine room.

The SAIF animal housing facility has a passively ventilated rodent cage system in order to ensure healthy maintenance of the animals. Our facility is on an automatic 12hr dark/light cycle, and the temperature, pressure, and humidity are strictly regulated. Animal heath, bedding, food, and water are monitored twice per day and maintained as necessary by the SAIF and LAR staff. Animals are permitted to be housed in our facility for long periods of time for longitudinal studies. No additional housing costs are applied if the animals are part of an imaging experiment. If the animals are not part of an imaging experiment but are housed in the SAIF facility (ie. biodistribution study with radioactive agents), a housing fee will be applied.

Contrast agent development
Our investigators are well-versed in the development of cell-selective contrast imaging agents useful for CT, MRI, optical/NIR, and nuclear medicine. Two agents developed in our labs, Fenestra™ VC and LC, are now commercially available to the research community from Medilumine (Montreal, QC, Canada). Imaging examples and results from our lab can be viewed on the Small Animal Imaging Facility Image and Video Gallery.
**Oversight committee**

The policies of the facility are established and governed by an oversight advisory board committee comprised of imaging scientists, physicists, cancer biologists, and veterinarians. This committee meets every 6 months. At least one member of the committee will always be a current member of the Medical School animal care committee. Administrative support is provided by UWCCC management and personnel.

The small animal imaging facility oversight committee consists of the following people:

- Frank Korosec - Chief of the Imaging Sciences Section of the Department of Radiology, Director of Research Resources, & Director of Clinical MRI Physics
- Jamey Weichert - Associate Professor of Radiology, Medical Physics and Pharmaceutics
- Weibo Cai - Associate Professor & Director of the UW Molecular Imaging and Nanotechnology Lab
- Glenn Kwon – Professor, School of Pharmacy
- Amy Moser - Associate Professor of Human Oncology and Director of the UW Medical School Animal Care Committee
- Rich Halberg – Assistant Professor of Gastroenterology & Hepatology
- Brigitte Raabe – DVM, DACLAM
- Justin Jeffery – Small Animal Imaging Facility manager

**UWCCC Small Animal Imaging Facility Scanners**

- Siemens Inveon microPET/CT
- Siemens MicroCATII
- Agilent 4.7T MRI
- Perkin Elmer IVIS
- Fluoptics Fluobeam (NIR)
MRI: 4.7T Agilent and GE Hyperpolarizer system
Animal Prep: Cell culture, radioactive animal holding (rats and mice), gamma counter, tissue distribution.
Analysis: Three Siemens IRW imaging analysis work stations.
MicroPET/CT: Siemens Inveon Hybrid microPET/CT and Siemens microCATII
Optical: Perkin Elmer IVIS and Fluoptic Fluobeam (NIR)
Hot Lab: Radioactive doses stored, drawn, and assayed in this shielded room.
WIMR Vivarium: Houses rodents (B-level) and non-human primates (Level 1).