University of Pittsburgh PET Facility

The PET Facility at the University of Pittsburgh has been operational since 1992, and is administered as a research division of the Department of Radiology under the direction of N. Scott Mason, Ph.D. The PET Facility is housed in over 12,000 square feet of the ninth floor of the B-wing in Presbyterian-University Hospital, University of Pittsburgh Medical Center (UPMC) Health System. The entire floor space of the ninth floor, B-wing is dedicated to the PET Facility. This space includes two 500 sq. ft. patient scanning rooms, two scanner control rooms, and inpatient and outpatient preparation rooms. The space also includes a 300 sq. ft. small animal surgery/radiometabolite analysis laboratory. The Radiochemistry Laboratory is included within the PET Facility and is divided into a cold chemistry laboratory of 1000 sq. ft., a hot radiochemistry laboratory of 1000 sq. ft., and a 1200 sq. ft. cyclotron room housing a self-shielded Siemens Eclipse HP medical cyclotron and ancillary supporting electronics and equipment. Research investigators and PET Facility staff utilize a 450 sq. ft. data and image processing laboratory. Offices for the PET Facility director, physicists, chemists, computer programmers, research faculty, residents and post-doctoral fellows, and nuclear medicine technologists are contained within the facility. In addition, there is a small 200 sq. ft. electrical and machine shop. Presently, the PET Facility comprises a dedicated full-time research staff of approximately 30 FTE, including eight full-time Radiology faculty members, four chemistry staff, four data analysts, two systems administrators, three nuclear medicine technologists, and administrative staff. Located on the University of Pittsburgh Main Campus, the PET Facility benefits from its central location to the major clinical and research activities of the institution. The PET Facility maintains an array of dedicated research scanners and equipment.

Radiochemistry: The PET Radiochemistry Laboratory produces radionuclides for PET imaging using a dedicated Siemens Eclipse HP medical cyclotron. The Eclipse HP is a negative-ion cyclotron capable of producing a beam of 11 MeV protons, which is designed for the production of positron-emitting radionuclides such as carbon-11 (as $[^{11}C]CO_2$), fluorine-18 (as $[^{18}F]$fluoride and $[^{18}F]$fluorine), nitrogen-13 (as $[^{13}N]$ammonia), and oxygen-15 (as $[^{15}O]$oxygen). The Eclipse HP deep-valley magnet design provides improved beam transmission, reduced levels of internal activation, and higher production yields. A key advantage of the Eclipse HP configuration is the use of a 4-position target carousel as well as the inclusion of a second extraction port equipped with a second 4-position target carousel, which increases the maximum number of mounted targets to a total of eight. The PET Facility's Eclipse HP configuration presently includes seven targets: two $[^{18}F]$fluoride targets, two $[^{11}C]CO_2$ targets, one $[^{13}N]NH_3$ target, and one $[^{15}O]$oxygen target. Two of the eight target positions are free for future expansion in accordance with need. Increased yields from the $[^{18}F]$fluoride and $[^{11}C]CO_2$ targets (as well as the ability to irradiate two $[^{11}C]CO_2$ targets simultaneously) allows for shorter irradiation cycles and quicker turnaround in production capabilities, which in concert with new automated radiosynthesis equipment has significantly increased the radiopharmaceutical production capacity of PET Facility both in volume and scope. Equipment for the remote synthesis of carbon-11 and fluorine-18 labeled radiopharmaceuticals includes a G.E. Healthcare TRACERLab™ FX MeI gas-phase $[^{11}C]$methyl-iodide system, two TRACERLab™ FX M carbon-11 incorporation platforms, and a ORA NEPTIS PERFORM fluorine-18 incorporation platform. The radiochemistry laboratory is equipped with three full-size Capintec-brand hot cells (each fitted remote manipulators) for operator-assisted radiopharmaceutical productions. In addition, there are two large stacked Capintec mini-cells and four smaller Capintec mini-caves for routine automated productions, three radioisotope fume hoods, five organic synthesis fume hoods, three laminar flow hoods, fifteen radio-HPLC systems (including gradient pumps, variable wavelength UV detectors, four photodiode array detectors, a refractive index detector, approximately 20 radioactivity detectors), and miscellaneous analytical equipment including a radio-TLC scanner, radio-GC, two gamma well counters (Packard Cobra model 5003), and a GE Typhoon FLA-7000 phosphor imager. Additional analytical equipment and services (e.g., 300 and 500 MHz NMR's, high and low-resolution mass spectrometers, and glass, electrical, and machine shops) are available to PET Facility chemists in the University of Pittsburgh Chemistry Department on an hourly recharge basis.

The PET Facility radiochemistry laboratory routinely performs high-specific activity carbon-11 radiosynthetic work utilizing [^{11}C]methyl iodide, [^{11}C]methyl triflate and [^{11}C]carbon dioxide. We also routinely utilize nucleophilic [^{18}F]fluoride methodologies for radiochemistry projects. In addition, we have a dedicated radioiodination hood suitable for [^{125}I] and [^{123}I] work and shielded space for [^{99m}Tc], [^{68}Ga] and [^{64}Cu] radiochemistry projects. The facility has four high sensitivity radio-HPLC analytical HPLC systems dedicated to radiometabolite analysis work. In addition, we are able to perform radiometabolite analyses utilizing a variety of other methods including, solid-phase extraction techniques, aqueous/organic extraction methods, and thin-layer chromatography techniques.

An array of > 30 different investigational radiopharmaceuticals are approved for human use at the University of Pittsburgh PET Facility:

Agent (target):

[^{15}O]H_2O	(perfusion)
[^{15}O]O_2	(oxygen metabolism)
[^{13}N]Ammonia	(Myocardial blood flow)
[^{18}F]FMISO	(hypoxia)
[^{11}C]3-O-methylglucose	(glucose transport)
[^{11}C]PMP	(acetylcholinesterase substrate)
[^{18}F]FLT	(thymidine kinase substrate)
[^{18}F]ML10	(apoptosis)
[^{11}C]flumazenil	(central benzodiazepine receptor)
[^{11}C]PK-11195	(TSPO, aka peripheral benzodiazepine receptor)
[^{11}C]PBR-28	(TSPO, aka peripheral benzodiazepine receptor)
[^{11}C]DASB	(serotonin transporter)
[*carbonyl*-^{11}C]WAY100635	(serotonin 5-HT1A receptor)
[^{11}C]CUMI-101	(serotonin 5-HT1A receptor agonist)
[^{18}F]altanserin	(serotonin 5-HT2A receptor)
[^{11}C]DTBZ	(VMAT2 vesicular monoamine transporter)
[^{18}F]FDOPA	(AADC substrate)
[^{11}C]CFT	(dopamine transporter)
[^{11}C]FLB457	(dopamine D2/D3 receptor)
[^{11}C]raclopride	(dopamine D2/D3 receptor)
[^{11}C]fallypride	(dopamine D2/D3 receptor)
[^{11}C]NPA	(dopamine D2 receptor agonist)
[^{11}C]ABP 688	(metabotropic glutamate receptor subtype 5)
[^{11}C]NOP-1A	(nociceptin/orphanin FQ peptide receptor)
[^{11}C]PIB	(beta-amyloid)
[^{18}F]flutemetamol	(beta-amyloid)
[^{18}F]AV1451	(tau)
[^{18}F]MK 6240	(tau)
[^{18}F]BCPP-EF	(mitochondrial complex-1)
[^{11}C]UCB-J	(SV2A)
[^{11}C]IMA107	(PDE10A)
[^{68}Ga]PRGD2	(integrin $\alpha V\beta 3$)
[^{64}Cu]LLP2A	(Very Late Antigen-4, VLA-4)

In addition, the PET Facility has synthesized over 300 radiolabeled compounds for non-clinical imaging studies in animals.

Instrumentation: The PET Facility operates three dedicated human research scanners: a Siemens ECAT Exact HR+, a Siemens mMR (combined PET and 3T MR) scanner, and a Siemens Biograph mCT Flow™ TrueV PET/CT scanner. Non-human primate PET image data collected will be acquired on a Siemens Biograph mCT Flow™ TrueV PET/CT scanner (Siemens Medical Solutions USA, Malvern, PA) installed in the University of Pittsburgh PET Facility in 1Q 2015. The installed Biograph mCT configuration has a 78 cm patient bore and is comprised of a 64-slice helical CT scanner (SOMATOM definition AS 64) and four rings of lutetium oxyorthosilicate (LSO) Hi-REZ PET detector blocks (48

blocks/ring, 4.0 x 4.0 x 20 mm crystal size; 13 x 13 crystals per block). This PET detector configuration acquires 109 transverse image planes (2.027 mm) over a 22.1 cm axial field-of-view with a maximum intrinsic spatial resolution (NEMA NU-2, 2007) of 4.1 mm FWHM (transverse) x 4.7 mm FWHM (axial) (Jakoby et al., 2011). The PET subsystem supports incorporation of time-of-flight (TOF) measurement into the reconstruction to yield improvements in randoms corrections and overall image signal-to-noise. The CT subsystem can be operated in diagnostic mode, either alone or in concert with the PET data acquisition, and is equipped with CARE dose reduction technology, gating capabilities, and supports continuous bed motion acquisition. A low-dose mode is supported whereby a non-diagnostic CT scan is acquired to provide scatter and attenuation correction of PET emission data. The effective dose from the low-dose CT scan of the head is < 16 mrem, which is comparable to the dose a subject receives from transmission imaging with $^{68}Ga/^{68}Ge$ rod sources. PET emission data can be reconstructed using analytic and/or iterative reconstruction algorithms on grid sizes ranging from 128 x 128 up to 400 x 400 voxels.

Computing: The PET Facility operates an extensive state-of-the-art data processing network that supports 57 active PET imaging research protocols, many of which are dynamic quantitative imaging protocols. The central servers are a Sun SPARC Enterprise T5220, Dell PowerEdge R710 linux server with 96GB RAM and a SUN Fire X4450 linux server with approximately 36TB of external RAID5 storage housed in five raid disk arrays, including both magneto-optical and DVD-R/W library systems for data archiving and retrieval. Data analysis is performed on a distributed network of over 25 Sun UNIX workstations, consisting of one Mercury RM206 Server, one Sun Sparc T5221 server, one Sun Fire V440 server, three SunBlade 2000, one Sunblade 1000, three Ultra-Sparc 60, two Ultra-Sparc 80, six Sunblade 1500, three SunBlade 150, and 4 Sun Ray. The PET Facility also maintains a network of over 50 Macintosh and Windows computers, including a Mac OS file-server, tape backup system, two color laser printers. All computers are directly linked to the internet through a local twisted pair ethernet network. Systems are interfaced to a high-speed (1GB/sec) local area network for data transfer to workstations and for analysis and linkage to the MR center. The computational power for the research network is supplied by multiple server resources. These resources include an eight node linux CPU cluster providing 16 Intel Xeon E5-2667 2.90GHz Six-Core Processors, 2 TB DDR3-1600 Reg ECC Memory and operating on 6Gb/s Interface Solid State Drives. Another resource is a linux GPU cluster with four Nvidia M2090 GPUs, two Intel Xeon E5-2667 2.90GHz Six-Core Processors, 256GB DDR3-1600 Reg ECC Memory and operating on 6Gb/s Interface Solid State Drives. The MRRC also utilizes a Linux cluster with four 2.0GHz dual-core Opterons. The Linux servers provide over 200TB of online data storage.

Data Analysis: Standard image analysis software has been implemented for region-of-interest definition, statistical parametric mapping (SPM) analysis, and within- and cross-modality image co-registration. The PET Facility data analysis group consists of 4 full-time data analysts, an informatics specialist, and a computer systems administrator. PET data analysis support includes image registration, image segmentation/parcellation, manual and automated region-of-interest definition, parametric image generation, partial volume correction, statistical analyses, input function determination, and the implementation and validation of pharmacokinetic methods for radiotracers under study. Data analysis software tools are available that include: PMOD (9 licenses), SPM2 through SPM12, AFNI, FSL, DTI Studio, Freesurfer, and many others. The processed data and analysis results are stored in custom-configured relational databases. The informatics specialist focuses data tracking, database development, archiving of analysis results, and data quality control reviews, consistent with policies concerning the protection of patient information.