The University Of Queensland
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Centre for Advanced Imaging

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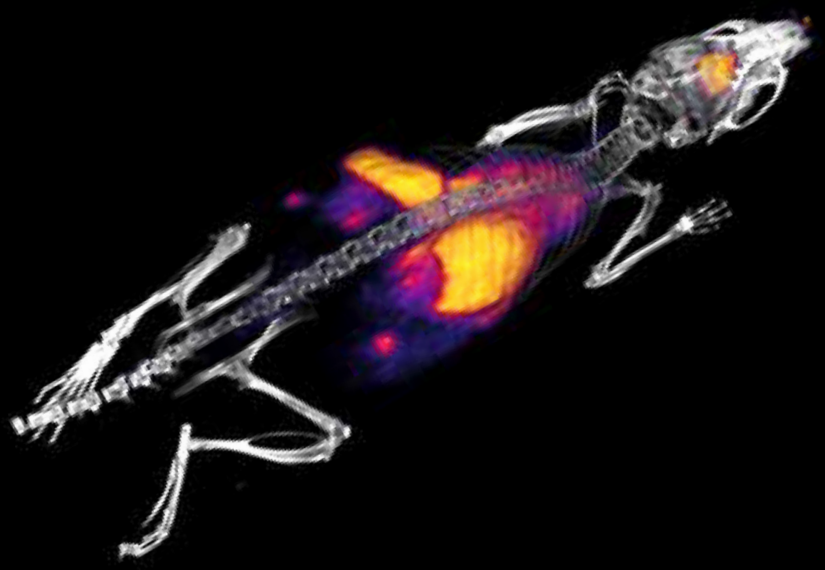
Molecular Imaging



The University of Queensland's Centre for Advanced Imaging (CAI) contains a comprehensive range of molecular imaging technologies. Expertise and facilities are available for Positron Emission Tomography (PET), Computed Tomography (CT), optical imaging, mass spectrometry imaging and Magnetic Resonance Imaging (MRI) applications, as well as the development of radioactive tracers.

Access to the molecular imaging facilities is available on a fee basis. Expert staff at CAI offer the following services:

- Planning for *in vivo* projects
- Animal anaesthesia and other *in vivo* techniques
- Holding rooms for radioactive and non-radioactive animals
- Production, preparation and formulation of radiopharmaceuticals
- Reconstruction and analysis of static or dynamic image data
- Kinetic modelling of dynamic image data
- Biodistribution studies
- Autoradiography

MALDI-TOF Mass Spectrometry Imaging (MSI)

A Bruker Autoflex MALDI-TOF/TOF MSI facility is available for both advanced MSI and protein analysis. MSI enables the spatial distribution of ions to be imaged directly in tissue sections down to a resolution of 50 µm. Example applications include biomarker studies in cancer and drug distribution. Tissue sections analysed by MSI can be subsequently stained and examined by histology. The technology is an ideal platform for mass analysis of biomolecules and characterisation of protein folding and sequencing. A robotic LC-spotter allows full-scale proteomic experimentation.

Capabilities:

- MS analysis of a wide range of molecules by MALDI-MS spot analysis
- Top-down proteomics of purified proteins by MALDI-ISD-MS
- LC-MS analysis of complex samples by LC-MALDI-MS
- Bottom-up proteomics of enzymatically digested protein samples by LC-MALDI-MS/MS
- Spatial distribution of molecules in tissues by imaging mass spectrometry

Image: PET/CT scan of mouse with Glioblastoma injected with Cu-64-labelled mAb

Inveon PET/CT

The Inveon multimodality PET/CT imaging scanner is capable of providing three dimensional CT and PET images of live mouse and rat as well as fixed biological samples and materials.

Capabilities:

- Anatomical CT and functional PET images are automatically co-registered for easy analysis
- An integrated isoflurane anaesthetic gas system and physiologic monitoring system allow for image gating and animal monitoring during scanning
- The Inveon PET component delivers 1.4 mm full width at half maximum (FWHM) spatial resolution at the centre of field of view (FOV) with an axial FOV of 12.7 cm
- The PET scanner uses molecular imaging probes labelled with positron-emitting radionuclides (i.e. 18F, 11C, 64Cu, 89Zr)
- The CT component has a large area 125 mm X-ray camera and incorporates a high resolution, low noise X-ray imaging detector with 3072 x 2048 pixels and can be configured for a FOV as large as 8.4 cm x 5.5 cm
- Delivers high spatial resolution *ex vivo* CT images down to 8 µm for a 20 mm FOV, allowing separate analysis of cortical and trabecular compartments of bone
- Multiple Inveon Research Workplace workstations for multimodality image review, fusion, and analysis
- Workstations support CT, PET and MR data in DICOM and Siemens CT and PET formats
- Quantitative analysis can be performed on static, gated and dynamic data

Higher resolution *ex vivo* and *in vitro* technologies are available at CAI for validation of pre-clinical *in vivo* PET imaging data:

- Biodistribution studies (Perkin Elmer Wizard Gamma well counter)
- *Ex vivo* autoradiography (Leica cryostat and an Amersham Typhoon Biomolecular Imager)

This is a flagship instrument of the National Imaging Facility.

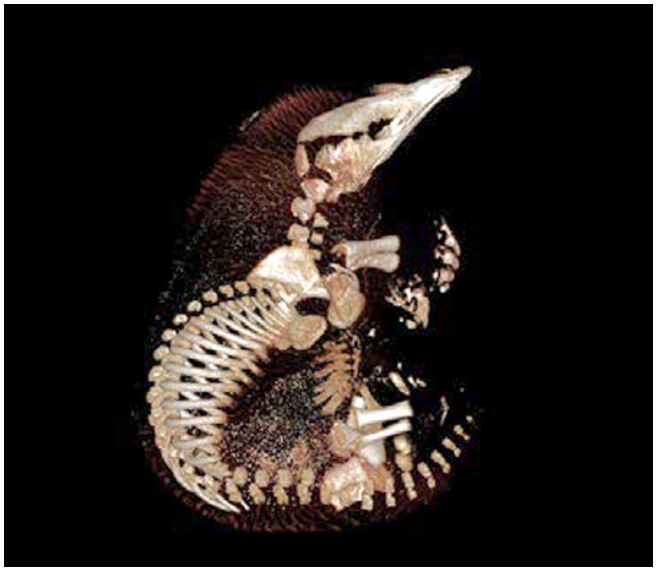
Biograph Horizon PET/CT Large Bore Scanner

Combining X-Ray Computed Tomography (CT) and Positron Emission Tomography (PET) scanners, this instrument enables registration and fusion of physiologic and anatomic information. The CT component is capable of providing three-dimensional computed tomography images. The PET scanner measures the distribution of PET radiopharmaceuticals. CAI has comprehensive cyclotron and radiochemistry facilities for the production of PET radiopharmaceuticals. The Biograph Horizon scanner system is equipped with Siemens multi-modality software, *syngo*. The scanner forms part of an ACRF Facility for human microdosing studies using molecular imaging.

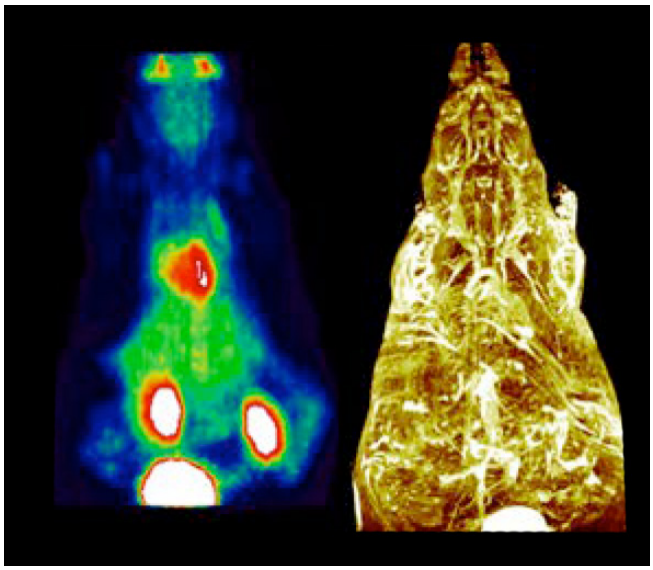
Technical specifications:

- 700 mm CT-16/32 Slice
- PET axial Field of view (FOV) of 164 mm
- Time of Flight (TOF) reconstruction capability
- UltraHD•PET^3 + TrueV (combination of technologies that offers the potential for short scan time and PET scans).
- CT Safire (CT iterative reconstruction for up to 60% lower dose)
- Respiratory gatting option

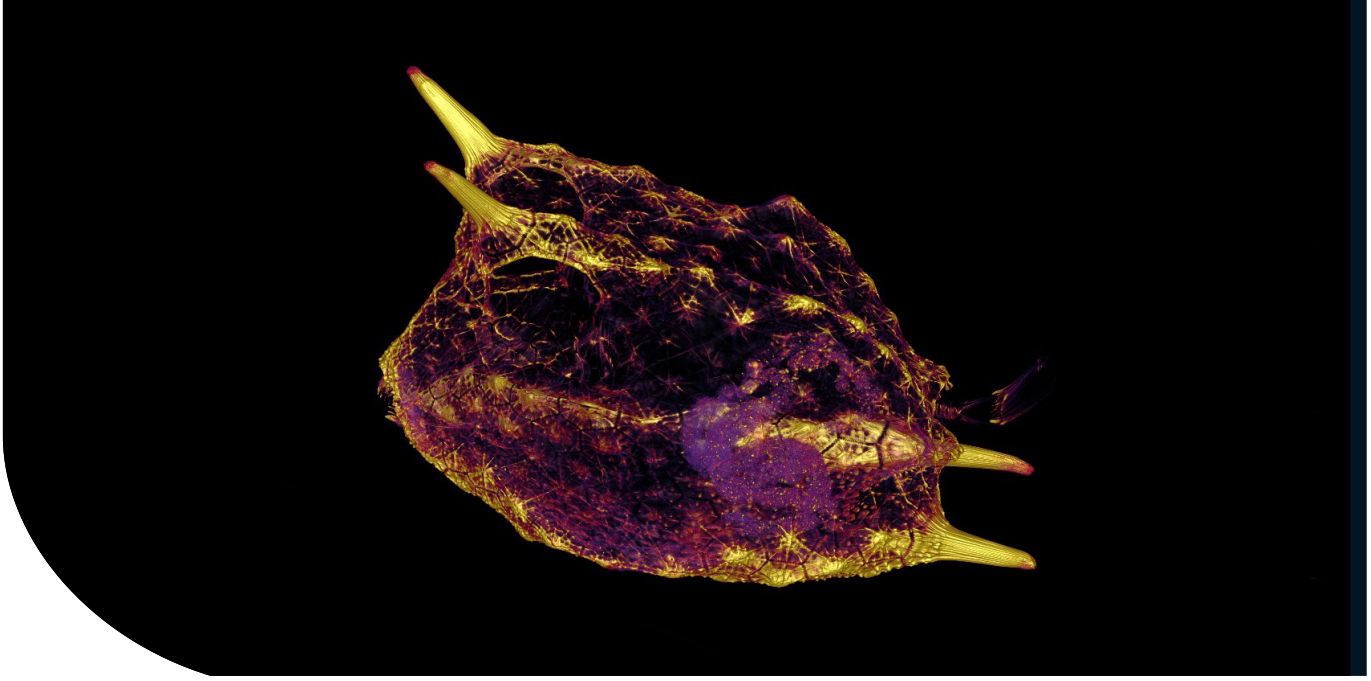
"The Clinscan PET/MR system is the first of its kind worldwide. Combining high field MRI, for high definition anatomical and functional imaging, with a PET insert that provides dynamic metabolic information – this powerful technology is invaluable for studies of cancer and neurodegenerative disease"



CT scan of echidna (53 µm)



Simultaneous PET (left) and 3D-MRI following injection of [^{18}F]-FDG and Gadolinium contrast agent (Gadovist) from a single syringe



CT scan of a longhorn cow fish using the Inveon PET/CT molecular imaging scanner for the purposes of studying anatomical structures and evolution. PET/CT technology combines positron emission tomography (PET) and computed tomography (CT) technologies to produce 3D images. Imaged by Dr Karine Mardon.

Clinscan PET/MR

The Clinscan PET/MR allows simultaneous MRI and PET image acquisition and enables the most direct translation of research outcomes from animals to humans. This system is the first of its kind worldwide combining a high field MRI scanner, for high definition anatomical and functional MRI, with a PET insert that provides dynamic metabolic information. This is a powerful emerging multimodal imaging technology for studies of cancer and neurodegenerative disease.

Capabilities:

- Provides simultaneous acquisition of MRI and PET images of an animal or sample
- 7 Tesla, 30 cm bore superconducting magnet, with operating software identical to the Siemens clinical MRI platform (Syngo)
- Mouse and rat head and body coils for live animal and sample imaging
- 150 mm large sample RF coil
- PET insert has a FOV with a diameter of 5 cm and length of 6 cm
- PET image acquisition is performed with the Siemens Inveon Acquisition Workplace (IAW) software

This is a flagship instrument of the National Imaging Facility.

Optoacoustic Imaging

Multispectral Optoacoustic Imaging – iThera MSOT inVision 256-TF system

The inVision 256-TF MSOT system offers unique imaging capabilities, combining tomographic acoustic imaging with optical sensitivity. The exquisite spectral resolution offered by this instrument provides a powerful methodology for elucidating the presence of both endogenous and exogenous probes.

Capabilities:

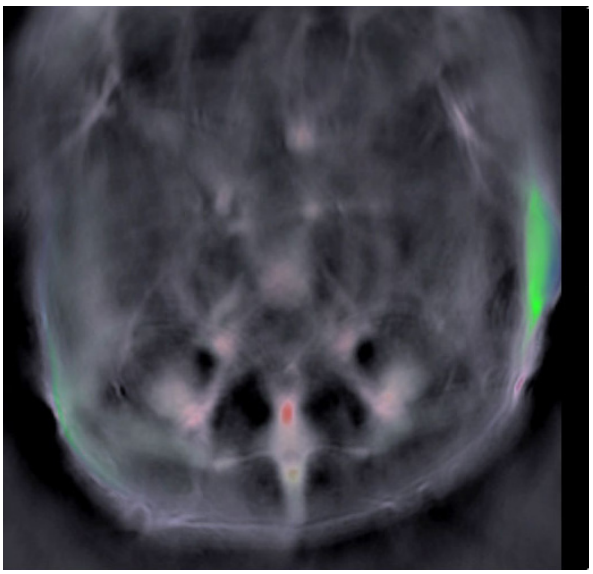
- Single wavelength optoacoustic imaging at 10 Hz
- Real-time spectral component visualisation
- Penetration depth of up to 2–4 cm facilitating enhanced whole animal imaging
- Cross-sectional in-plane resolution of 150 µm
- Tomographic ultrasound detector array with 256 elements
- Rapid processing of temporal and spectral elements in imaging experiments

IVIS Lumina X5 Imaging system

The IVIS® Lumina™ X5 high-throughput 2D optical imaging system combines high-sensitivity bioluminescence and fluorescence with highresolution x-ray. This instrument is the workhorse for those undertaking preclinical assessment of novel therapeutics or imaging agents, with high-throughput enabled by the rapid screening of up to five mice simultaneously.

Capabilities:

- High-throughput optical and x-ray
- High resolution, low dose X-ray with optical overlay
- Supports mouse or rat imaging (20 x 20cm FOV)
- Compute Pure Spectrum (CPS) spectral unmixing
- Full fluorescence tenability through the NIR spectrum (up to 900 nm)
- Rapid data acquisition, analysis with streamlined workflows



Optoacoustic image of gold nanoparticles surface coated with a polymer (highlighted green), imaged by the CAI Thurecht Group.

Radiochemistry Facility

Equipped with 14 hot-cells (nine for research and five for GMP manufacture), automated synthesisers, and radio-analytical equipment, the Radiochemistry Facility supports research, development and GMP manufacture of novel and established radiopharmaceuticals. Further capabilities include radiolabelling and automation optimisation to support commercial development.

The Radiochemistry Facility has separate laboratories for quality control, research, development and GMP activities. The GMP laboratory is a clean-room that can meet EN/ISO 14644-1 standards and manufacture license requirements of the Therapeutic Goods Administration.

A wide range of radioisotopes are handles within the Radiochemistry Facility including carbon-11, fluorine-18, copper-64, gallium-68, zirconium-89, technetium-99m and lutetium-177.

Applications of these radioisotopes include:

- Development of novel PET and SPECT diagnostics for application in neurology and oncology:
  - Labelling small molecules – fluorine-18 and carbon-11
  - Labelling peptides – fluorine-18, gallium-68, copper-64, technetium-99
  - Large molecules (antibodies, particles) – zirconium-89, iodine-124
- Utilisation of labelling to facilitate therapeutic drug development:
  - fluorine-18 and carbon-11 for small molecules
  - zirconium-89, iodine-124 for large molecules
- Development of novel radiotherapeutics lutetium-177 and copper-67 labelled biomolecules

"CAI's Cyclone 18 Twin cyclotron is equipped with a solid target beamline for making isotopes such as copper-64, iodine-124, fluorine-18 and carbon-11"

National Imaging Facility

Cyclone 18 Twin Cyclotron

Radioisotopes are produced in-house using the Centre's cyclotron, an IBA Cyclone 18 Twin dual ion source cyclotron, which accelerates negatively charged hydrogen ions to a fixed energy forming 18 MeV protons.

A feature of the cyclotron is the capability of irradiating solution, gas and solid targets, which allows for preparing a greater range of radioisotopes. The facility is able to manufacture short-lived radioisotopes such as [^{11}C]carbon (half-life = 20 minutes) for immediate use within the Centre's Radiochemistry Facility, eliminating excessive radioactive decay through transport.

The cyclotron is currently equipped with targets to produce the following radioisotopes:

- [^{18}F]Fluorine – as aqueous fluoride
- [^{11}C]Carbon – as carbon dioxide gas
- [^{124}I]Iodine – on solid matrix

The cyclotron's solid target station may also be used to produce other radioisotopes such as [^{64}Cu]copper and for research involving proton irradiation of various materials.

The Cyclone 18 Twin cyclotron

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Enquiries
W: cai.centre.uq.edu.au
T: +61 7 3365 4100
E: molecular_imag@cai.uq.edu.au
radiochemistry@cai.uq.edu.au

Centre for Advanced Imaging
The University of Queensland
Brisbane Qld 4072 Australia

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@UQ_CAI