National Imaging Facility

National Imaging Facility Quarterly Newsletter Issue Three 2016

Computed Tomography (CT) image of a Seahorse

Anthony Romilio & Vera Weisbecker - School of Biological Sciences, The University of Queensland
Karine Mardon - Centre for Advanced Imaging, The University of Queensland

National Imaging Facility

In This Issue

Director's Message

Since our last newsletter, the NIF team has been busy. As well as continuing to work with our academic and industry users in great research, some of which has been highlighted in this newsletter, we have been developing our plans for the next Roadmap for Research Infrastructure. Led by the Chief Scientist, Dr Alan Finkel, the Roadmap will inform government of the research infrastructure needs for the next decade and beyond. Since starting in 2007, the NIF infrastructure and people have supported world-class research around Australia, but we know there is more we can do. The NIF team is committed to working with you, to understand your research needs, and develop the best approach using a wide range of imaging technologies.

In this issue of the NIF Quarterly you can read about how imaging is able to validate different animal models of disease, from diabetes to trauma. The studies demonstrate the range of imaging technology, and the different size animals that are available. We are confident that somewhere within the NIF family, there is the capability to answer your imaging questions.

NIF also sees education as an important part of its role. From producing 3D images of different species, for use in anatomy or physiology, to talking to school students about the potential career paths in science, our NIF Facility Fellows are excited to help.

And all of our nodes, around Australia, run symposia throughout the year, to understand more of the imaging capability that exists. In this issue we highlight events in Brisbane and Western Sydney, where you will be most welcome, and be given the opportunity to meet with the team to discuss your research questions.

Professor Graham Galloway
Director of Operations

National Imaging Facility

Investigating the Impact of Diabetes Treatment

Industry Collaboration

A reconstruction of Positron Emission Tomography (PET) and Computed Tomography (CT) imaging data of a *db/db* mouse 10 s after administration of [^{18}F]fludeoxyglucose ([^{18}F]FDG) via intravenous injection in the lateral tail vein.

Image courtesy of Dr. Blake J. Cochran, School of Medical Sciences, The University of New South Wales

Type 2 diabetes represents more than 80% of all diabetes cases and is typically caused by the increased resistance to the effects of insulin or the pancreas loss of ability to produce sufficient insulin. The disease is characterized by decreased High Density Lipoproteins (HDL) cholesterol, as well as decreased level of apolipoprotein A-I (apoA-I). Therapeutic interventions that increase plasma HDL levels improve glycaemic control in patients with type 2 diabetes, and treatment with HDL or apoA-I has been shown to increase glucose uptake into skeletal muscle and adipose tissue. Furthermore, treatment with HDL or apoA-I increases insulin secretion and production in isolated pancreatic islets and insulinoma beta cell lines.

In a project by Dr. Blake Cochran, in vivo Positron Emission Tomography (PET) imaging with radiopharmaceutical [^{18}F] FDG was used to investigate the mechanisms associated with the improvements in glucose uptake due to apoA-I treatments in a mouse model of type 2 diabetes. The study demonstrated that a single infusion of apoA-I significantly increases the rate of glucose uptake by skeletal muscle in *db/db* mice. No significant increase in glucose uptake was observed when muscle samples were treated with insulin alone, which is a reflection of the insulin resistant state of *db/db* mice. Treatment of the mice with apoA-I alone significantly increased glucose uptake. When the mice were treated with apoA-I and the skeletal muscle was subsequently treated with insulin, glucose uptake was increased over and above that of apoA-I alone. This is indicative of apoA-I not only increasing the glucose uptake, but also improving insulin sensitivity. The flexibility of PET imaging allows the study to be extended to investigating multiple organs and even longitudinal experiments.

For more information on this work, contact Dr. Blake Cochran (b.cochran@unsw.edu.au).

Collaborators
School of Medical Sciences, Faculty of Medicine, University of New South Wales
Brain and Mind Centre, University of Sydney
ANSTO LifeSciences
Faculty of Health Sciences, and Faculty of Medicine, University of Sydney
Department of Cardiology, Concord Repatriation General Hospital, Sydney

Cochran, B. J., Ryder, W. J., Parmar, A., Tang, S., Reilhac, A., Arthur, A., Charil, A., Hamze, H., Barter, P.J., Kritharides, L., Meikle, S. R., Gregoire, M., Rye, K., (2016). In vivo PET imaging with [18F] FDG to explain improved glucose uptake in an apolipoprotein AI treated mouse model of diabetes. Diabetologia, 1-8.

Putting a new dimension into student learning

Life presents itself in an intriguing array of three-dimensional structures. Through hands-on examination of specimens, students are presented with a highly valuable resource that aids their understanding of the diversity and complexity of taxa. However, the fragility, rarity and cost restricts the number and diversity of physical specimens that educators can provide to their classes. Additionally, student access to these specimens is often restricted to very narrow time periods. As a consequence, students tend to have life forms visualized to them using two-dimensional formats that include photographs and schematics.

However, high fidelity 3D virtual models are often used in medicine and science to reveal 'hidden' properties of organisms to aid diagnose and visualize research data. Using state-of-the-art technologies and computer software, the resulting 3D data are visually highly engaging and intellectually stimulating. These are key qualities that educators are looking for to involve students in subject material, and as such, 3D virtual models of 'real-life' biological structures have an enormous potential for utilization in education.

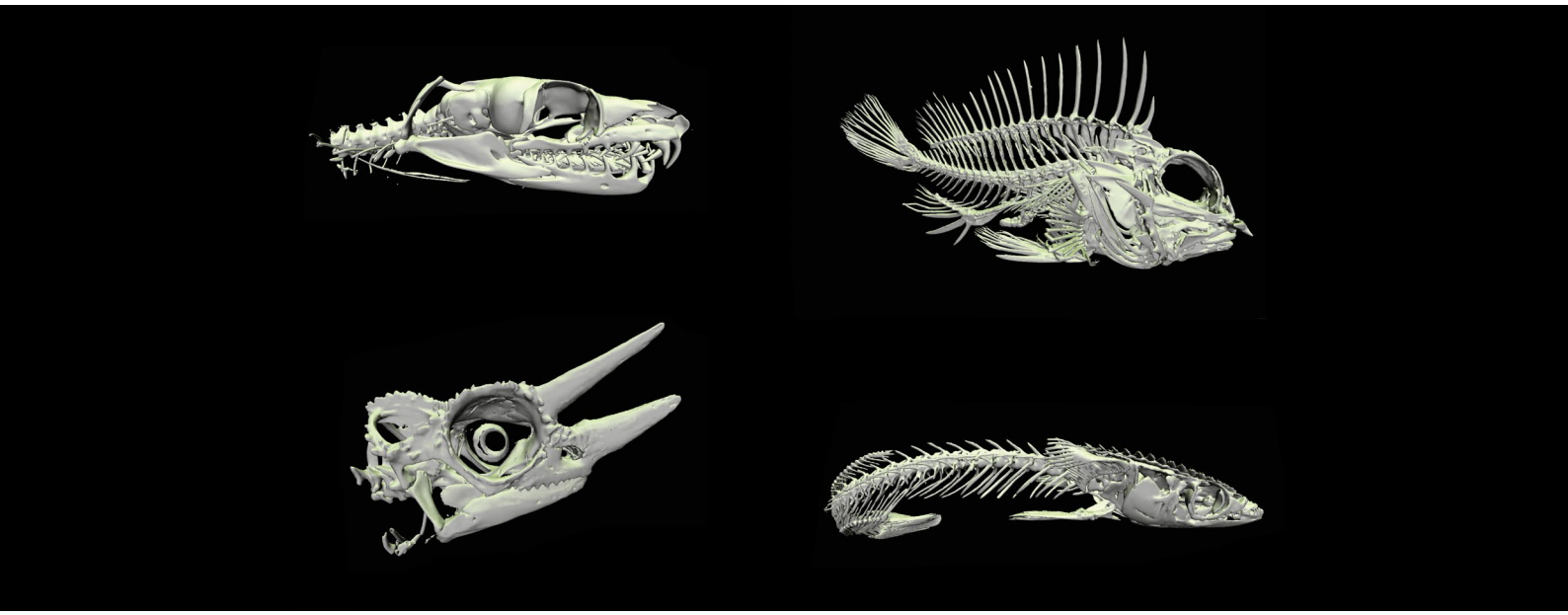
Recently, an initiative lead by Dr Vera Weisbecker, from the School of Biological Sciences, The University of Queensland has lead the incorporation of such models into undergraduate studies. This has been an expansion from her research into aspect of mammalian cranial development where she has used her expertise in the area of microCT to develop a novel online resource for use in her third year course that explores the diversity of extant and extinct vertebrate taxa. To get microCT scans of many of the specimens, she relies on facilities and expertise of National Imaging Facility at the Centre for Advanced Imaging at UQ node. These scans are processed by the author, who was given free-range to populate the online site and design the layout of the library interface. The library has expanded to incorporate models derived from both microCT scans and digital photogrammetry (the latter is the author's specialty) in addition to receiving permission to incorporate models from numerous national and international institutions (e.g., Smithsonian Institute, Idaho Museum of Natural History, University of New England). This translates to an increased benefit for enrolled students that have limitless access to every model, which can be viewed during relevant lectures and practicals, or at any other time for revision and exploration.

Despite its recent generation, the 3D virtual library has received positive feedback from students and academics alike. The resource material continues to expand the number and diversity of specimens within the library, as well as new formats to present the information for student interaction (e.g., 3D pdf practical manuals). Perhaps not surprising, additional UQ courses have begun to incorporate visualizations from the site.

For more information, contact Dr Anthony Romilio (a.romilio@uq.edu.au) and visit https://fieldsites.earth.uq.edu.au/ and for details about the microCT and PET-CT facilities at UQ node of National Imaging Facility contact Dr. Karine Mardon (k.mardon@uq.edu.au).

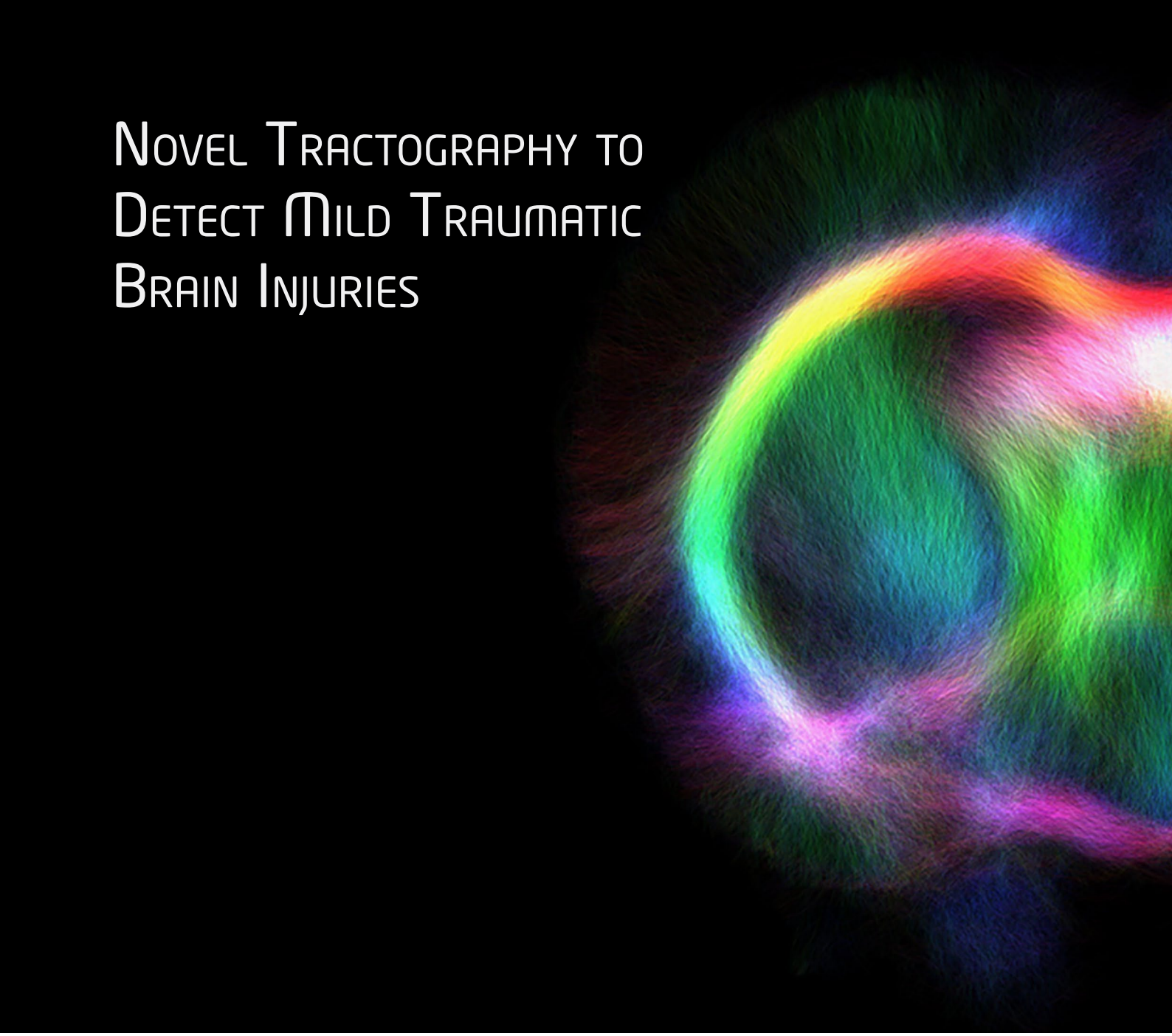
In addition to developing teaching material for several UQ courses, Anthony is currently compiling a 3D digital database of Western Australia's dinosaur coast, a stretch of 80km coastline where countless fossil footprints occur.

Collaborators
School of Biological Sciences, The University of Queensland
Centre for Advanced Imaging, The University of Queensland



Interactive 3D library permits comparative observation. Top-left: Emerald Tree Boa (Corallus caninus), Top-right: Scorpionfish (Scorpaenidae), Bottom-left: Jackson's chameleon (Chameleo jacksoni), Bottom-right: Remona (Echeneidae).

Novel Tractography to Detect Mild Traumatic Brain Injuries



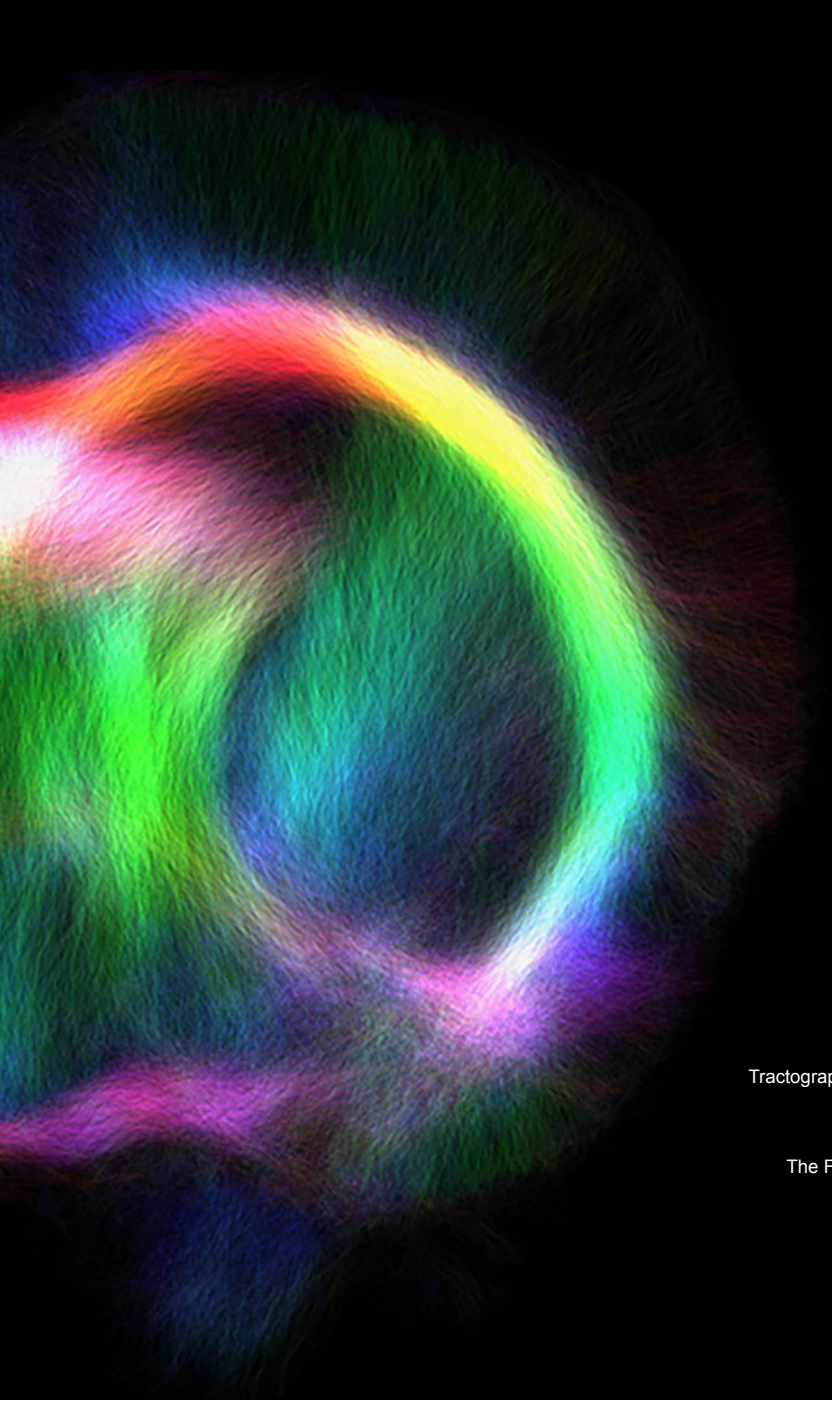
A mild traumatic brain injury (mTBI), often referred to as a concussion, rarely has lasting effects and is often presumed to cause only transient disturbances to brain function. However, repeated mTBIs, particularly those occurring in the sports and military settings, have been associated with cumulative and chronic neurological impairments, and the development of neurodegenerative diseases such as chronic traumatic encephalopathy (CTE).

There is evidence that these long-term adverse effects of repeated mTBIs are in part due to the recurring insults occurring before the brain has recovered from the initial mTBI and is in a period of increased cerebral vulnerability (ICV). There is increasing evidence that mTBI triggers complex biological changes including inflammatory, metabolic, neuronal, vascular and axonal abnormalities. It is believed that such changes are responsible for ICV and therefore, the identification of reliable markers that indicate when the brain is no longer in a state of ICV might allow them to be used to guide medical decisions.

The current clinical management of mTBI is largely guided by the presence or absence of neuropsychological symptoms, and typically evaluated by subjective and/or self-reported methods. Symptoms may include physical, cognitive, co-ordination, emotional, and sleep abnormalities. The onset of symptoms, although typically rapid, can take minutes or hours to occur, and symptoms are usually mild, or may even go unrecognized.

Recovery is determined to have occurred after all post-injury symptoms have resolved, at which point patients are commonly cleared to return to pre-injury activity. However, there is now evidence that the resolution of symptoms might not accurately indicate that the brain has recovered from the neuropathophysiological changes induced by mTBI. Therefore, research is required to guide and facilitate more informed medical decisions pertaining to return to pre-injury activity. In particular, it is critical that objective markers sensitive to the brain's changes and recovery after an mTBI are identified.

Magnetic Resonance Imaging (MRI) and blood proteomics might provide objective measures of pathophysiological



Tractography template image of sham rats at 30 days post-injury

Image courtesy of Mr. David Wright,
The University of Melbourne
The Florey Institute of Neuroscience and Mental Health

changes in mTBI, and indicate when the brain is no longer in a state of ICV. In a collaborative study, the use of MRI, blood proteomics, and behavioral methods as markers to detect changes and estimate recovery after experimental mTBI in rat models was investigated. Rats were given a sham or mild fluid percussion injury (mFPI), and behavioral testing, MRI, and blood collections were conducted up to 30 days post-injury.

There were cognitive impairments for three days post-mFPI, before normalizing by day 5 post-injury. In contrast, advanced MRI (i.e., tractography) and blood proteomics (i.e., vascular endothelial growth factor) detected a number of abnormalities, some of which were still present 30 days post-mFPI.

These findings suggest that MRI and blood proteomics are sensitive measures of the molecular and subtle structural changes following mTBI. Of particular significance, this study identified novel tractography measures that are able to detect mTBI and may be more sensitive than traditional diffusion-tensor measures. Furthermore, the blood and MRI findings may have important implications in understanding ICV and are translatable to the clinical setting.

For more information on this project, contact Mr. David Wright (wrightd@unimelb.edu.au).

Collaborators
Anatomy and Neuroscience, The University of Melbourne
The Florey Institute of Neuroscience and Mental Health
Department of Medicine, The Royal Melbourne Hospital
Department of Anatomy, Physiology, and Genetics, Uniformed Services University of the Health Sciences, USA
Department of Electrical and Electronic Engineering, The University of Melbourne
Centre for Stroke and Brain Injury, The University of Newcastle
School of Health Sciences, The University of Newcastle

Wright, D. K. et al. Behavioral, blood, and magnetic resonance imaging biomarkers of experimental mild traumatic brain injury. Sci. Rep. 6, 28713; doi: 10.1038/srep28713 (2016).

National Imaging Facility

Research Project

Stem Cells to Cure Disc Degeneration

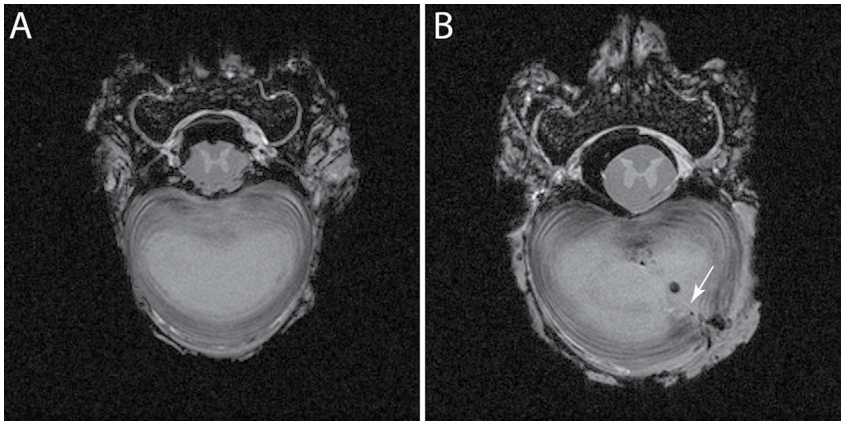
3T MRI of sheep spine prior to stem cell therapy

Lumbar microdiscectomy is a surgical procedure performed for treatment of leg pain due to nerve compression from intervertebal disc degeneration and protrusion. Current surgical treatment involves removal of the offending portion of disc compressing the nerve but fails to address underlying disc degeneration. Progression of the underlying disc degeneration leads to worsening symptoms and in many patients further surgical procedures such as additional microdiscectomy or expensive lumbar fusion surgery. Progress in the fields of tissue engineering and stem cell research have allowed researchers to develop new experimental therapies to enable tissue repair and regeneration. Mesenchymal Precursor Cells (MPCs) (a type of adult stem cell found in many tissues throughout the body) have been shown to hold great promise for disc replacement and regeneration treatments.

A/Prof. Tony Goldschlager from the Department of Neurosurgery, Prof. Graham Jenkin, Prof. Peter Ghosh, Dr. David Oehme and Dr. Chris Daly from The Ritchie Centre (Hudson Institute of Medical Research), Dr. Anne Gibbon and Graham Shillito from Monash Animal Research Platform, are using sheep, a well-established model of disc disease, to develop a novel treatment that will promote the regeneration of degenerate intervertebral discs damaged. Pilot studies completed previously by this group demonstrated that implantation of MPCs with Pentosan Polysulfate (PPS), a medication used for the treatment of arthritis in veterinary practice, produce intervertebral disc regeneration in the sheep. This pioneering work has led to international clinical trials investigating MPCs for the treatment of back pain and disc degeneration.

This research team have previously utilized the Siemens Skyra 3 Tesla and the Agilent 9.4 Tesla magnetic resonance imaging (MRI) scanners at the Monash Biomedical Imaging (MBI) Node of National Imaging Facility located at Clayton to investigate the regenerative potential of MPCs and PPS. Ongoing research is focussed on developing and refining a novel therapy for disc degeneration and investigating the mechanisms by which these amazing cells produce tissue regneration.

For more details about this and related projects please contact Dr. Chris Daly (christopher.daly@monash.edu) and for details about the facilities and access to the MBI Node of National Imaging Facility contact Dr. Charles Hardy (charles.hardy@monash.edu).



9.4T MRI of experimentally injured sheep intervertebral disc prior to stem cell therapy. (A) control disc, (B) injured disc (white arrow)

Collaborators
Hudson Institute of Medical Research
Department of Neurosurgery, Monash Health
Monash Biomedical Imaging, Monash University

Upcoming Events

- 3rd Annual Symposium at The University of Queensland Node

- 7th Biennial Symposium at The Western Sydney University Node

The 3rd annual CAI (Centre for Advanced Imaging) symposium, which will be co-hosted with Singapore Bioimaging Consortium (SBIC), is going to be held on the 19th and 20th of October 2016 in The University of Queensland, Building 21. The symposium will bring together researchers in imaging and spectroscopy providing a vibrant platform for discussions. Sessions will include presentations from both early career and established academics from CAI, SBIC and the broader Australian imaging community, including two plenary speakers:

- Prof. Malini Olivo - Singapore Bioimaging Consortium
- A/Prof. Nat Lenzo - University of Western Australia and Theranostics Australia

The session themes are: Advanced Imaging of Structure, Function and Disease; Advanced Imaging, Diagnostic and Spectroscopic Technologies; Advanced Molecular Characterisation and Design; and Translational Imaging.

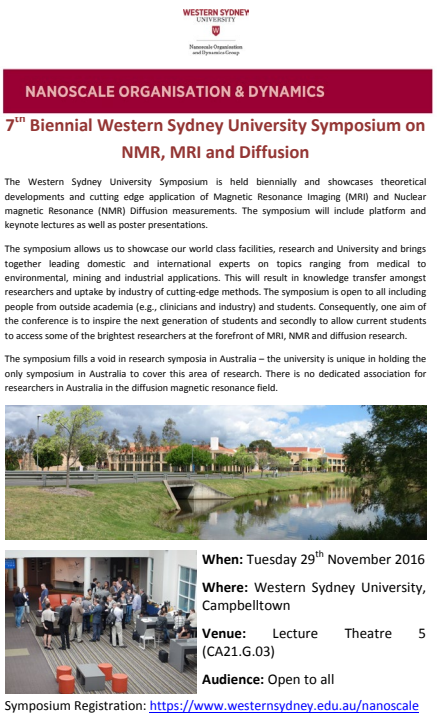
For more information and registration visit symposium wesbsite.

The Western Sydney University's 7th biennial Symposium, which will be held on 29th of November 2016, showcases theoretical developments and cutting edge application of Magnetic Resonance Imaging (MRI) and Nuclear magnetic Resonance (NMR) Diffusion measurements. The symposium will include platform and keynote lectures as well as poster presentations. Invited speakers include:

- Prof. Peter Basser - Senior Investigator in the Tissue Biophysics and Biomimetics department of the Natural Institute of Health
- Prof. Gareth Morris FRS - Professor of Physical Chemistry, in the School of Chemistry at the University of Manchester (skype presentation)
- Professor Masaya Ishikawa – Professor Applied Biological Science, Tokyo University of Science.
- Dr Petrik Galvosas - Senior Research Fellow in the School of Chemical and Physical Sciences (Victoria University of Wellington) and is an Associate Investigator with the MacDiarmid Institute for Advanced Materials and Nanotechnology.

The symposium brings together leading domestic and international experts on topics ranging from medical to environmental, mining and industrial applications. This will result in knowledge transfer amongst researchers and uptake by industry of cutting-edge methods. The symposium is open to all including people from outside academia (e.g., clinicians and industry) and students. Consequently, one aim of the conference is to inspire the next generation of students and secondly to allow current students to access some of the brightest researchers at the forefront of MRI, NMR and diffusion research.

For more information and registration visit symposium wesbsite.



WESTERN SYDNEY UNIVERSITY

NANOSCALE ORGANISATION & DYNAMICS

7TH Biennial Western Sydney University Symposium on NMR, MRI and Diffusion

The Western Sydney University Symposium is held biennially and showcases theoretical developments and cutting edge application of Magnetic Resonance Imaging (MRI) and Nuclear magnetic Resonance (NMR) Diffusion measurements. The symposium will include platform and keynote lectures as well as poster presentations.

The symposium allows us to showcase our world class facilities, research and University and brings together leading domestic and international experts on topics ranging from medical to environmental, mining and industrial applications. This will result in knowledge transfer amongst researchers and uptake by industry of cutting-edge methods. The symposium is open to all including people from outside academia (e.g., clinicians and industry) and students. Consequently, one aim of the conference is to inspire the next generation of students and secondly to allow current students to access some of the brightest researchers at the forefront of MRI, NMR and diffusion research.

The symposium fills a void in research symposia in Australia – the university is unique in holding the only symposium in Australia to cover this area of research. There is no dedicated association for researchers in Australia in the diffusion magnetic resonance field.

When: Tuesday 29th November 2016

Where: Western Sydney University, Campbelltown

Venue: Lecture Theatre 5 (CA21.G.03)

Audience: Open to all

Symposium Registration: https://www.westernsydney.edu.au/nanoscale

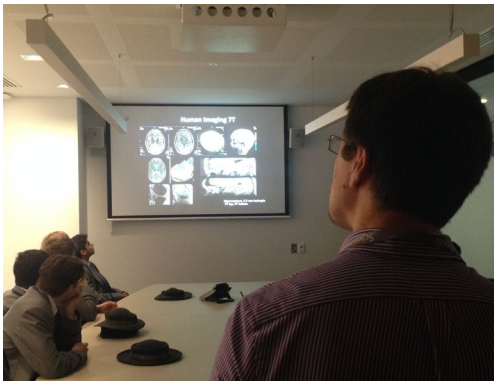
'Scientists in Schools'

As part of the national program 'Scientists in Schools', which is managed by CSIRO, The University of Queensland node at the Centre for Advanced Imaging (CAI) hosted a group of year 12 students in July 2016 to tour the facilities and capabilities of the centre.

The 'Scientists in Schools' program is supported by the Australian Government Department of Education and Training through the Maths and Science participation program and aims at providing opportunities for primary and secondary school students to gain real-world experiences, understand the importance of Science, Technology, Engineering, and Maths (STEM) education, and get motivated and inspired by the exciting careers in STEM.

The CAI visit included a presentation by NIF Informatics fellow, Dr. Andrew Janke, on radiation in biomedical imaging followed by a tour of some of the main capabilities at CAI such as the research Cyclotron along with hands-on experience using the Robotic Arms which is used to handle radioactive materials. They also visited the NIF flagship instruments:

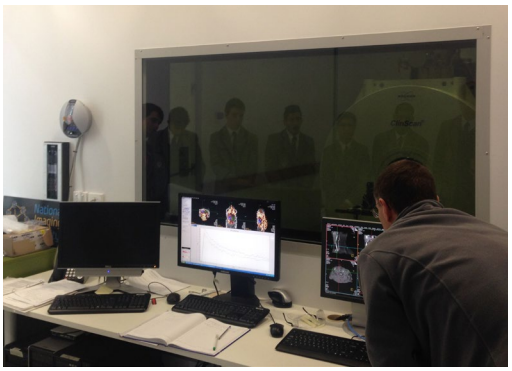
- PET-CT imaging scanner - capable of providing three dimensional CT and PET images of live mouse and rat as well as fixed biological samples and materials.
- MR-PET scanner - which combines a high field MRI scanner, for high definition anatomical and functional MRI, with a PET insert that provides dynamic metabolic information.
- 7T whole body MRI scanner - which includes a high-performance gradient with multi-receive and multi-transmit radiofrequency capabilities to enable increased sensitivity and resolution.



Dr. Andrew Janke presenting the capabilities at CAI

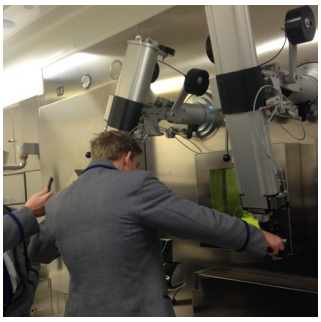
The visit helped students learn about multidisciplinary research and its role and impact in public's every day life and familiarised them with the possible careers in science.

Dr. Karine Mardon, NIF Facility Fellow, explaining the concepts of PET-CT imaging and applications



Dr. Gary Cowin, NIF Facility Fellow, demonstrating how the MR-PET scanner works, its capabilities, advantages of simultaneous MRI and PET image acquisition, and applications

Prof. Ian Brereton, NIF Director at CAI, presenting the importance of increased sensitivity and resolution achieved through Ultra-high field MRI



Students enjoying hands-on experience with the robotic arms

Premier's Science Awards

Professor David Sampson, Director of the University of Western Australia (UWA) node of National Imaging Facility, located at the Centre for Microscopy, Characterisation and Analysis was among the finalists in this year's Premier's Science Awards. He was announced one of four finalists in the Scientist of the Year category. The awards, a State Government initiative, were established in 2002 to honour the outstanding achievements of WA's science and innovation community.

Professor Sampson is a world leader in multiple facets of imaging science and engineering, with over twenty-five years research experience in the fields of optics, photonics, and microscopy, and applications in communications, sensors, and biomedicine. He is internationally recognised for his research in new biomedical imaging technology and its translation, including the multi-award winning Microscope-in-a-Needle and the micro-imaging of stiffness, now being commercialized.

The first application is the assessment of tumour margin status in breast cancer during surgery and his group has demonstrated feasibility on freshly excised human tissue specimens. Used during surgery, this micro-imaging solution has the potential to assess an area of tissue for malignancy on the spot and, thus, ensure more successful removal of breast cancer than is currently achieved.

Beyond his research, as director of the Centre for Microscopy, Characterisation & Analysis, he has built an imaging infrastructure for researchers in WA that attracts the world's best, including the International Atomic Energy Agency, in establishing the world's first university laboratory in its Network of Analytical Laboratories.

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