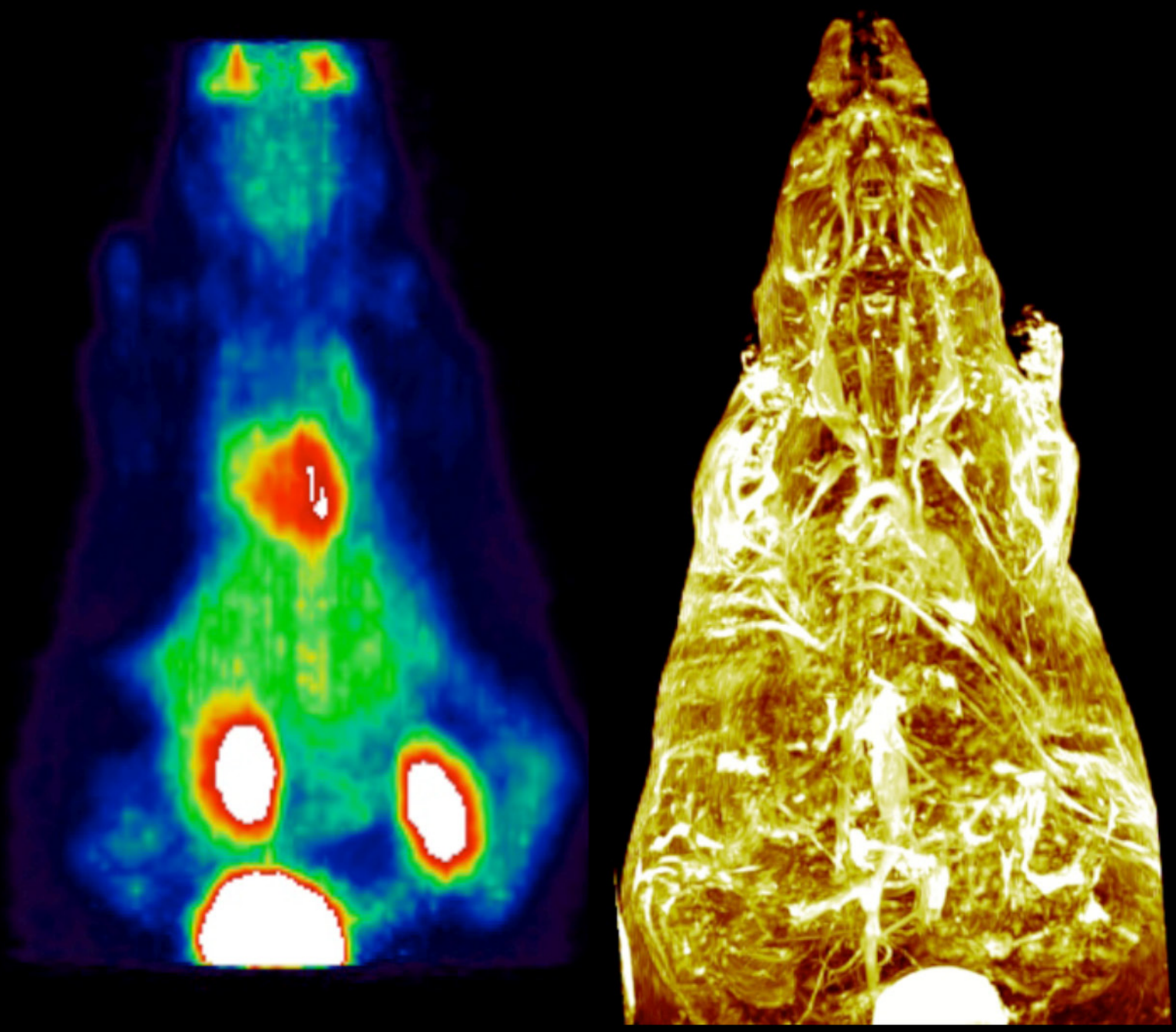
National Imaging Facility

Exploring Inner Space

NIF Quarterly • Q4, 2014

Positron Emission Tomography (PET, left) and 3D Magnetic Resonance Imaging (MRI, right) images acquired simultaneously following the injection of the PET tracer 18F-FDG and MRI gadolinium contrast agent Gadovist from a single syringe.
- Dr Gary Cowin, Centre for Advanced Imaging, NIF - University of Queensland node



Reconstructed image from MicroCT scans of the Guinea Pig Cochlea.
- Dr Daniel Brown, Research Fellow at Sydney Medical School,
Head of the Meniere's Research Laboratory,
Brain & Mind Research Institute, University of Sydney.

Director's Message

"In 2015, National Imaging Facility will demonstrate how we can help you cross those scientific boundaries, as we highlight opportunities to go beyond NIF, and join the much bigger NCRIS family."

What is NCRIS? Those of us within the program have our own ideas, and they are all valid. They are about providing research capability to the Australian research community, but each of us tells the story in a different way. At the recent NCRIS Capabilities Forum, the Capabilities worked with the Research and Higher Education Infrastructure Branch to develop a consistent and concise message.

1) NCRIS delivers world class research facilities so that Australian researchers can solve complex problems both here in Australia and around the globe.

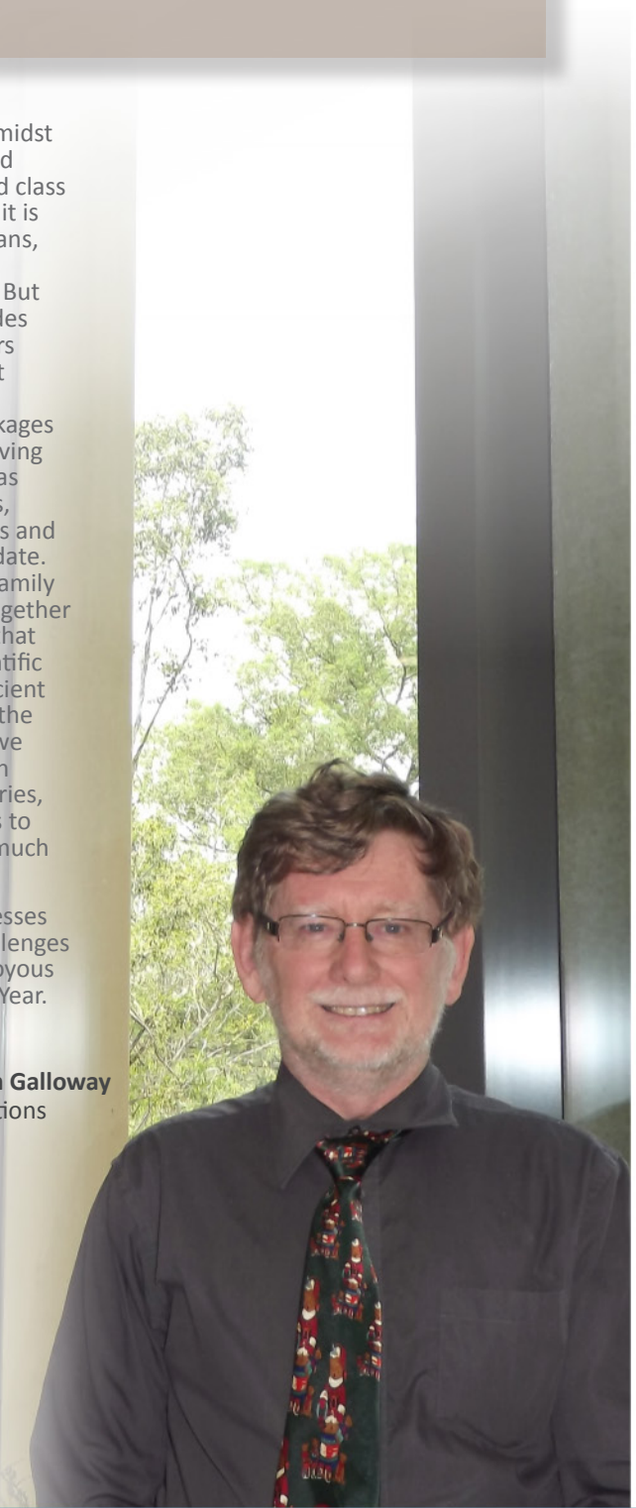
2) NCRIS is the most efficient and strategic way to invest in national scale research infrastructure, driving collaboration to bring economic, environmental, health and social benefits for Australia

What more do I need to say? Except to confirm that NIF is committed to these ideas. Read about NIF in this Newsletter. New infrastructure, ready for you to use. Novel research, to tell you how NIF is contributing to solving these research problems, and give you ideas, about how NIF can help solve your research problems. Outreach, to the research community, and beyond.

The NCRIS Showcase, in the midst of government, demonstrated how NCRIS is delivering world class research capability, and how it is driving collaboration. Politicians, industry and public saw the breadth and depth of NCRIS. But more than that, NCRIS provides opportunities for stakeholders and users to put the different Capabilities into a context of coordinated activity, with linkages between the Capabilities, driving new collaborations. NCRIS was established as 16 Capabilities, providing world class facilities and it has delivered on that mandate. NCRIS has developed into a family of 27 Capabilities, working together to tackle complex problems that cross the boundaries of scientific disciplines, delivering an efficient and strategic investment for the future of Australia. In 2015, we will demonstrate how NIF can help you cross those boundaries, as we highlight opportunities to go beyond NIF, and join the much bigger NCRIS family.

As we look back on the successes of 2014, and ponder the challenges ahead, I wish you all a very joyous Christmas and a Happy New Year.

Professor Graham Galloway
Director of Operations



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NIF News

New machine offers powerhouse to the brain

- Official Launch of 7 Tesla MRI at NIF University of Melbourne Node

Representing the Prime Minister, Senator Scott Ryan, Parliamentary Secretary to the Minister for Education, officially opened the new Siemens ultra-high field 7 Tesla human MRI machine at the University of Melbourne, 14th October 2014.

Co-funded by the Australian Federal Government through National Imaging Facility, the Florey, and the University of Melbourne, the human 7 Tesla MRI is one of the most powerful scanner in the Southern Hemisphere, with the capability of providing heist sensitivity and spatial resolution for human in vivo imaging. Building on University of Melbourne's strong record in imaging technology and engineering, the state-of-the-art scanner is an exciting opportunity for scientists and engineers in Victoria and beyond to play a significant role in the next generation of medical technology.

"The MRI will offer unprecedented clarity of the brain's workings," says Professor Roger Ordidge, the Node Director for NIF-UoM node and Chair of Imaging Science at the University of Melbourne. "The difference between the 7 Tesla and the more common 3 Tesla is extraordinary and demonstrates how quickly technology advances for improved results." says Prof. Ordidge.

As the host for the National Imaging Facility – University of Melbourne node, the Melbourne Brain Centre in Parkville brings together skills of a critical mass of researchers and state-of-the-art research instruments to analyse and understand dementia, stroke, multiple sclerosis, epilepsy, post-traumatic stress and other neurological disorders.

The Siemens human 7T MRI is a flagship instrument of the University of Melbourne Node of the National Imaging Facility (NIF), of which NIF is an Australian government initiative that connects state-of-art imaging capabilities across all mainland states in Australia.

Key facts:

- The Siemens 7 Tesla system is 140,000 times stronger than the Earth's magnetic field, enabling extraordinarily detailed images of human anatomy.
- Comparing a 3 Tesla system with a 7 Tesla system is like comparing an everyday sedan to a Formula 1 car.
- The Melbourne Brain Centre Imaging Unit represents a total investment of approximately $20 million and includes a state-of-the-art combined Positron Emission Tomography (PET) / Computer Tomography (CT) scanner. This enables molecular imaging and high quality x-rays to be accompanied in addition to the images acquired by the 7 Tesla scanner.
- The magnet contains kilometres of super-conducting wire that has zero resistance when cooled to -270 ^{O}C.
- The only liquid that can be used for cooling is liquid helium. Helium is the second most common element in the Universe, being a major constituent of the sun and stars. However, it is very rare on Earth since it is so light that it quickly escapes the Earth's gravity and rises into outer space. It has such a low boiling point because the atomic forces between helium atoms are very low.

National Imaging Facility - University of Melbourne Node Director, Professor Roger Ordidge at thenew Siemens Human 7 Tesla MRI scanner.

More Information

For more information about the NIF-UoM node at the Melbourne Brain Centre Imaging Unit, access and collaboration opportunities, please go to http://www.melbournebraincentre.edu.au/; or email NIF-UoM Node Director Prof. Roger Ordidge at roger.ordidge@unimelb.edu.au.

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NIF News

National Collaborative Research Infrastructure Strategy Showcase

On the 30th September 2014, all National Collaborative Research Infrastructure Strategy (NCRIS) research capabilities came together and showcased our current research work and achievements to the public. Hosted by the Department of Education, the showcase was held at the Great Hall, Parliament House, as a collection of exciting interactive displays. The showcase focused on Australia's best research infrastructure and expertise, and how they are supporting researchers in fields such as advanced manufacturing, imaging, translational research, geology, astronomy, and ocean observation.

As part of the NCRIS network, National Imaging Facility was proud to be part of the showcase and was keen to introduce the research outcomes our users had achieved through accessing NIF. Through galleries of scientific images, NIF was able to communicate to the public on the wider applications of imaging technology, and that imaging is very relatable to everyday life.

Big thank you to the organisers of the Showcase, and congratulations to all that had participated on the day – the Showcase had successfully attracted more than 500 public audiences, and the day was a great success!

NCRIS: Introduced in 2006 as an Australian Government initiative, the NCRIS is a network of 27 Australia's cutting edge research infrastructures and capabilities, all with the common goal of providing open access and aptitude to an array of technology, enabling the Australian research community to innovate and achieve world leading research.

For more info and updates on all NCRIS capabilities, please go to: http://education.gov.au/national-collaborative-research-infrastructure-strategy-ncris.

World's First Bruker ClinScan MR/PET

Open for Business!

Available to all Australian researchers, the world's first Bruker ClinScan combined MR/PET is open for business and ready to rock!

As a flagship research infrastructure for the National Imaging Facility, the MR/PET is hosted by the Centre for Advanced Imaging at the NIF University of Queensland node. In close collaborations with scientists from Bruker and University of Tubingen, Facility Fellows at the NIF-UQ node have developed and optimised protocols which are adaptable to the best features of both MR and PET imaging technologies.

This system allows simultaneous acquisition of MRI and PET images of an animal or sample. The technology combines the exquisite structural and functional characterisation of tissue provided by MRI with the extreme sensitivity of PET imaging of metabolism and tracking of uniquely labeled cell types or cell receptors. The MRI system is comprised of a 7 Tesla, 30 cm bore superconducting magnet, with operating software identical to the Siemens clinical MRI platform.

For example of current projects on MR/PET, please refer to Focus Story 1.

Do you have news?!

Published a paper?
New collaborations?
Discovered something?
Any updates from your Node —
we need to know!
Email: communications@anif.org.au

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NIF Focus Story - 1

UQ Node:

Multi-Organ Simultaneous Dynamic Gd-MRI and FDG PET in the Mouse

Targeted or "smart" biological compounds are a rapidly expanding field for the next generation of drugs for disease treatment and enhancing plant and animal production. Traditional methods, such as MRI and PET, measure the uptake of an agent with a single label via a single imaging modality, these results include a combinations of the delivery (flow, perfusion etc) and metabolic activity (binding potential, cellular transport, metabolic kinetics etc). These two components are not easily separated. In contrast, simultaneous imaging, using modality specific compounds with Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI), has the ability to determine metabolic activity, independent of delivery. This is essential for the field of targeted diagnostic and therapeutic agents. For human use, "theranostic" agents, combining therapeutic and diagnostic potential, has a huge potential for personalised medicine and is a rapidly growing industry in Australia and Internationally. The development of protocols to simultaneously performing PET and MRI assessments will give a competitive edge to Australian researchers and industries for development of these compounds and early phase preclinical trial of novel drugs.

Bruker ClinScan MR/PET scanner, Dr Gary Cowin.

Hosted by the Centre for Advanced Imaging at the University of Queensland node, the world's first Bruker ClinScan MR/PET scanner is a flagship technology for the NIF-UQ node. NIF Facility Fellows have collaborated closely with scientists from Bruker and University of Tubingen, Germany, in optimising the best features of both MR and PET imaging technologies.

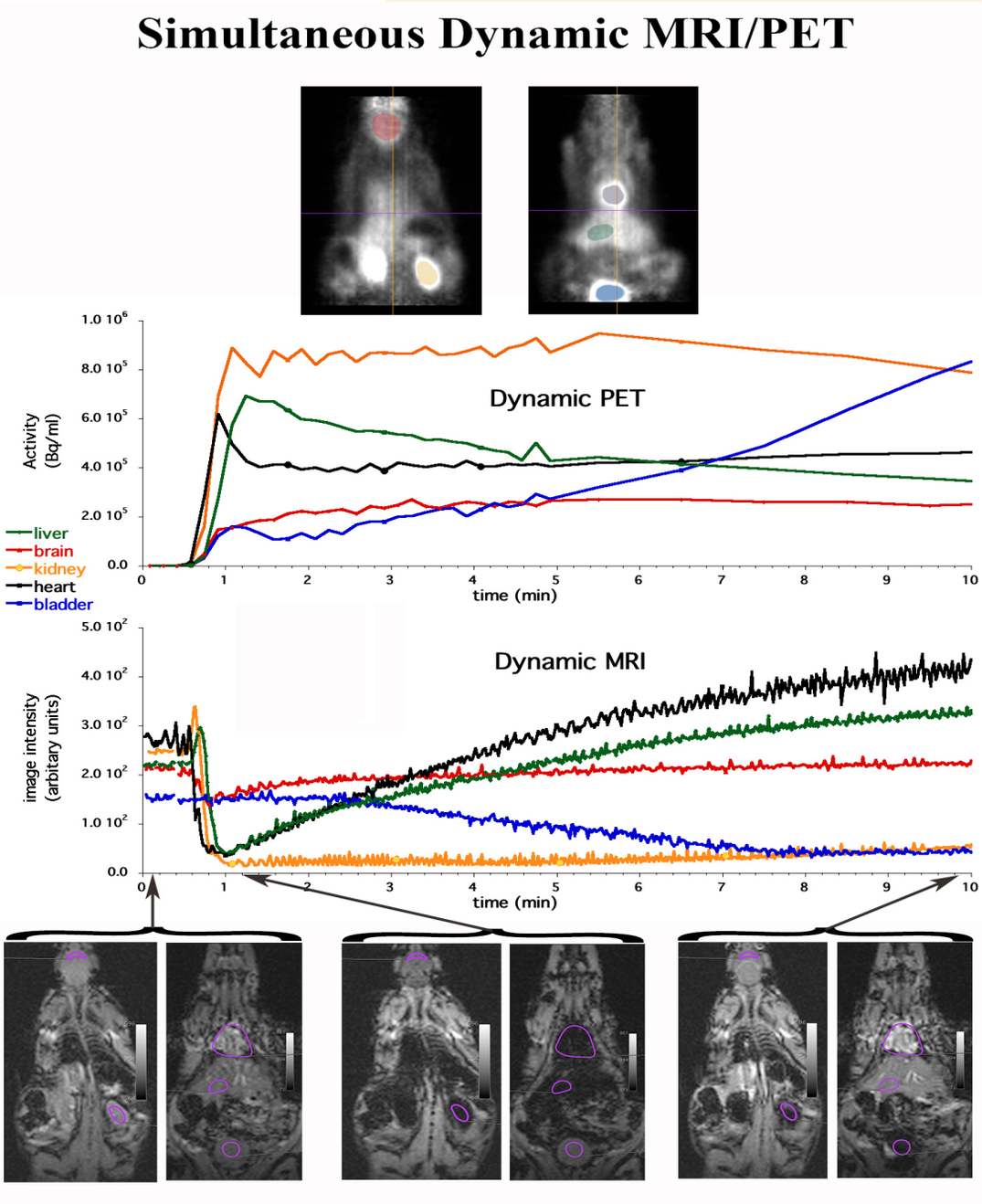
Development of the tools for simultaneous dynamic assessment of PET and MRI contrast agents commenced with the two most commonly used contrast agents for PET and MRI, F18-fluorodeoxyglucose (FDG) and complexes of Gadolinium (Gd), respectively. FDG, an analogue of glucose, is the most commonly available PET agent, used primarily for oncology, as a marker for increased tissue metabolism. FDG is transported into cells via normal glucose transporters, where it is trapped since it cannot be metabolised along the entire length of the glycolytic pathway. Therefore, increase in signal intensity of FDG results from a combination of tracer within the vascular bed and glucose transported into the cells. MRI Gd contrast agents are used for MR angiography and to measure tissue perfusion, and vascular integrity. The Gd agents are designed to remain in the vascular system and not cross into cells. The real-time measurement of the delivery of the Gd contrasts agents is called Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI). Simultaneous dynamic measurement of the uptake of gadolinium (Gd) MRI perfusion agents and the glucose PET analogue 18F fluorodeoxyglucose (18-FDG) enables independent assessment of tissue delivery and cellular transport of FDG.

An anaesthesised mouse was placed in a combined MRI/PET system, comprising a 300mm bore 7T ClinScan, running Siemens VB17, and removable PET insert containing 3 rings of 16 detector blocks with 15x15 LSO crystals (1.6x1.6x10mm) per block1, at the centre of the magnet bore operating under Siemens Inveon Acquisition Workplace (IAW) (Bruker, Germany). An 86 mm ID rat body MRI rf coil centred inside the PET ring was used to acquire whole mouse images simultaneously with the PET acquisition. Following MR localiser images, two coronal gradient echo image slices were positioned to include the brain and kidney in one slice and the heart, liver and bladder in a second slice with the following parameters: temporal resolution of 1.3 sec, TR=20 msec, TE=3.5msec, FOV =80x45 mm, 25° pulse angle, resolution 0.625x0.625x1.4mm with 512 measures acquired over 10 min. A 30 min dynamic PET acquisition was started simultaneously with the dynamic

MR. Following baseline scanning of ~30 sec, a single injection containing Gadolinium (Gadovist, 52 µl) and 18-FDG (5.8MBq) was administered in a total volume of 104 µl via a cannula inserted into the tail vein. PET images were reconstructed with OSEM2D in IAW. The reconstruction time frames were 10 sec during the first 5 min, and 60 sec thereafter.

Simultaneous dynamic uptake was measured in the brain, heart, liver, kidney and bladder for 18-FDG PET and Gd-MRI (Figure 1). Delivery and uptake of FDG was monitored as the increase in PET activity in the organs. Vascular delivery of high concentrations of Gd is characterised by a decrease in MRI signal intensity. Low concentrations of Gd enhance MRI signal intensity as exemplified by initial enhancement in the liver and late myocardial enhancement.

The developed methods for simultaneous FDG-PET and DCE-MRI assessment, will enable differentiation of the relative contribution of changes in cellular transport of glucose and/or delivery of FDG when altered FDG signal is measured. These methods will then be able to be applied to novel biologically active agents.



For more information about the project, access to the MR/PET, and collaboration opportunities, please contact NIF-UQ node Facility Fellow Dr Gary Cowin gary.cowin@cai.uq.edu.au.

Research team

Dr Gary Cowin, Dr Karine Mardon, Prof. Ian Brereton, and Prof. Graham Galloway

Centre for Advanced Imaging, University of Queensland.

Reference

1. Wehrl et.al Nature Medicine, 19(9), 1184-1190, 2013.

Figure 1: Simultaneously acquired dynamic MRI and PET data following the injection of Gadolinium MRI contrast agent and the PET tracer 18F-FDG. Top two PET images illustrate positions of the regions of interest used to measure the dynamic uptake of the FDG shown in the top plot. Bottom three pairs of images are representative pairs of images acquired before (left pair), just after (middle pair) and 10 min post gadolinium injection with regions of interest used to generate the dynamic MRI data (bottom plot).

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NIF Focus Story - 2

UQ Node:

Monotreme middle ear evolution and development using 3D reconstructions

Few people would expect that the most of our middle ear actually used to be a lower jaw. Nevertheless, it is well documented that the postdentary jaw bones of early mammalian ancestors gradually diminished in size and ultimately detached to form the tympanic ring, hammer, and anvil of the mammalian middle ear. It is all the more exciting that this detachment process is partially re-enacted during mammalian development, allowing us insights into how the bizarre transition to the middle ear happened. However, developmental data are patchy and data on monotremes (echidna and platypus) are nearly entirely missing. This is a major gap in our knowledge because monotremes are the earliest-diverging mammals and are well known to display developmental traits that the other mammals have lost. In addition, it is uncertain whether monotremes and the remaining mammals have detached their middle ear independently, which would mean that the ancestor of living mammals still had the middle ear attached to the lower jaw.

In collaboration with Dr Karine Mardon at the NIF-UQ node (Centre for Advanced Imaging, University of Queensland), Dr Vera Weisbecker and her team have used CT (computerised tomography) imaging technology to non-destructively evaluate rare and valuable museum specimens of monotremes. CT imaging enabled tracking of monotreme middle ear and skull development for the first time in the short-beaked echidna (Figure 1A, C), and the platypus (Figure 1B, D), using the 3D software package Mimics®. We are struck by how different the two species are in their middle ear development, and other structures as the dentary (Figure 1), and how different the bones look, compared to other mammals. Surprisingly for us, the lower jaw and the middle ear bones of the echidna flip from a vertical position to a horizontal one during development, which suggests an unexpectedly strong link between the two at least in monotremes and thus possibly in all mammals. In most other aspects, monotreme middle ear bones develop similarly to those of the other mammals we have looked at. Therefore, the evidence for and against independent middle ear origin in monotremes and other mammals is fairly even so far. Further morphometric studies on the specimens are currently underway to provide a better quantitative characterization of the developmental processes in monotremes vs. marsupials.

Research team:

Dr Vera Weisbecker, and Héctor E. Ramírez-Chaves, School of Biological Sciences, University of Queensland.

A/Prof. Stephen Wroe, Division of Zoology, School of Environmental and Rural Sciences, University of New England.

This project is supported by a Hermon Slade Foundation Grant and an ARC Discovery grant. For more info regarding the project, please visit: http://weisbeckerlab.com.au/.

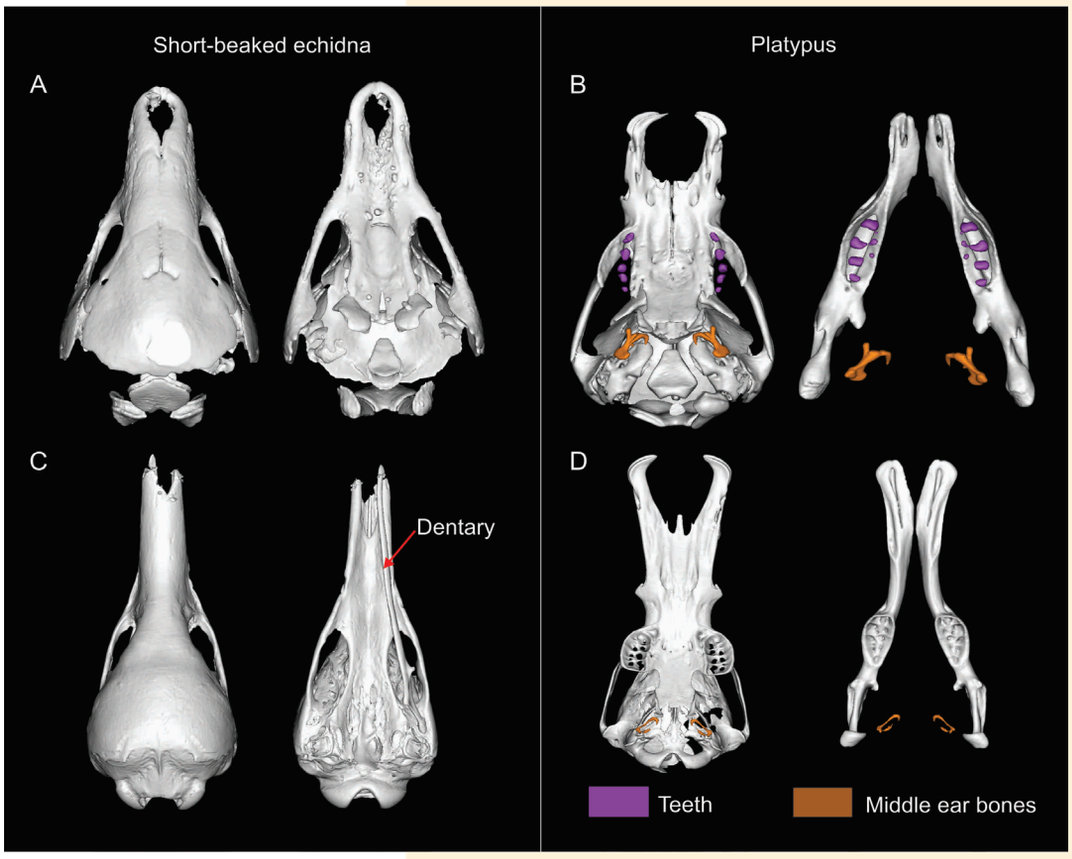

Figure 1. A. Cranium of a juvenile short-beaked echidna (dorsal and ventral view). **B.** Cranium and dentary of a juvenile platypus (ventral and dorsal view), showing the position of the middle ear bones (malleus and ectotympanic). **C.** Cranium of an adult short-beaked echidna (dorsal and ventral view), showing different degree of development and ossification of skull bones in comparison with a juvenile, and the position of the dentary. **D.** Cranium and dentary of an adult platypus (ventral and dorsal view). In juvenile platypus, it is possible to observe upper and lower teeth that are lost during development (absent in adults). These reconstructions allow us to describe how the growing trajectories of all the skull bones occur.

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NIF Focus Story - 3

UWS Node:

Characterisation Study of Preeclampsia using MRI

Preeclampsia is a significant and common complication of pregnancy, with characteristic symptoms of hypertension (high blood pressure) and proteinuria (an excess of blood plasma protein in the urine). Altered placental perfusion as a result of placental abnormalities is implicated in the development of this syndrome that affects 5% of women and which is a leading cause of morbidity and mortality in both mothers and infants. This study utilises magnetic resonance imaging (MRI) for visualisation of placental anatomy and for the analysis of changes in tissue morphology in experimental mouse models of preeclampsia and is part of a larger collaboration on preeclampsia between the University of Western Sydney NIF Node and the University Of Western Sydney School of Medicine led by Mrs Gabriele Bobek (PhD student) and Prof. Annemarie Hennessy.

High resolution gradient echo MR images (voxel size, 50 x 50 x 50 µm) were taken of isolated fixed placentas in order to create a placental atlas to identify features of the placenta and to assess structural changes between experimental model animals. The figure below is of a representative slice from a gradient echo scan of a placenta (left: without segmentation, right: segmented into regions of the placenta). The labyrinth, junctional zone, decidua, spiral arteries, central canal and umbilical vein artery can be clearly differentiated.

Using the 3D visualisation and segmentation software (Amira™) it was possible to reconstruct 3D models of the placenta. This is still a work in progress as multiple placentas from a number of different mouse models of preeclampsia are being scanned and segmented. Some example 3D images constructed from data from the present study are displayed in the figure below.

The segmented data from multiple placentas of control and experimental preeclampsia models were subjected to volumetric analysis. Preliminary data suggests there may be measurable changes in the junctional zone of experimental model animals, but this remains to be validated with increased numbers. This innovative technique has the potential to visualise and quantify placental structural change in experimental models of perturbed pregnancies.

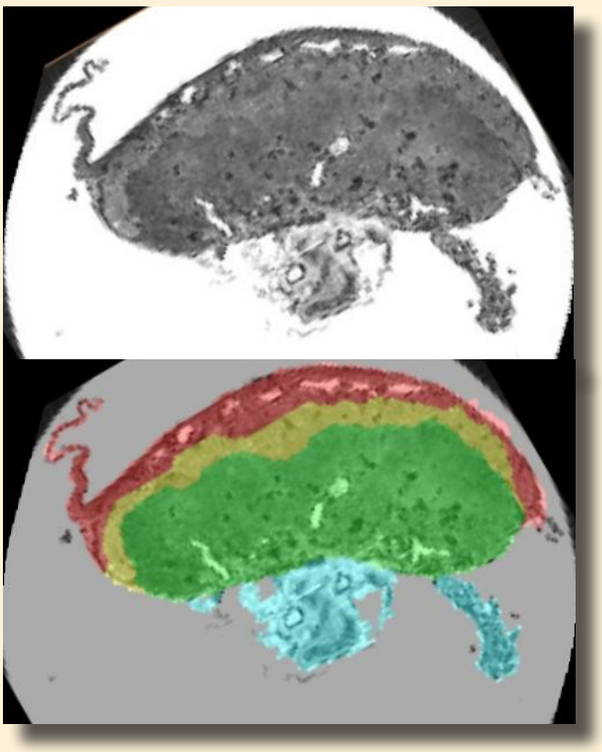


Figure 1: A slice from the gradient echo image is shown on the left. On the right is the same slice segmented into labelled regions; deciduas (red), junctional zone (yellow), labyrinth (green) and amniotic membrane (blue).

For more details about the project, and imaging at NIF-UWS node, please contact Dr Tim Stait-Gardner at T.Stait-Gardner@uws.edu.au.

Or please visit NIF website: http://www.anif.org.au/aboutnif/nodes/UWS-Node.html;

UWS - Nanoscale Organisation and Dynamics Group: http://www.uws.edu.au/nanoscale.

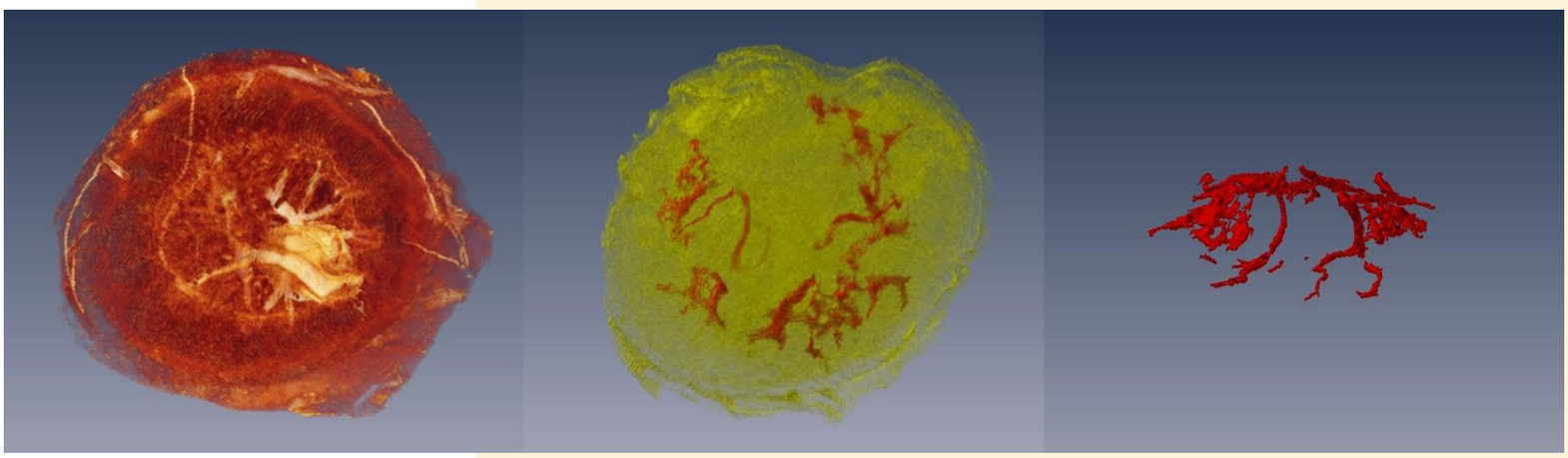


Figure 2: (left) Fetal surface view of the placenta. (middle) Maternal surface view of placenta with overlay showing maternal vasculature. (right) Side view showing maternal vasculature alone.

NIF Focus Story - 4

Industry:

Contrast free MR angiography

Angiography is a common medical imaging technique that is used to visualise organs and blood vessels of the body. In order to obtain best images, Gadolinium-based contrast agent is the most commonly used chemical to enhance the visualisation of the vessels. However, there has been recent evidence linking gadolinium with the serious systemic fibrosing disease Nephrogenic Systemic Fibrosis (NSF)[1]. NSF is a serious condition that involves the fibrosis of skin, joints, eyes and internal organs, of which most of NSF suffering patients will develop severe kidney failure[2].

Currently, there is no known cure for Nephrogenic Systemic Fibrosis. Consequently, there has been a recent trend to develop alternative imaging agents for angiography methods.

Siemens A.G is a worldwide market leader in the production of Magnetic Resonance Imaging scanners for diagnostic imaging. Developers at Siemens Healthcare USA have been working on a new contrast free method for Magnetic Resonance based Angiography for 1.5Tesla MR scanners, the most common clinical field strength. The larger signal available at higher field strengths (>3 Tesla) should allow smaller arteries to be visualised, but the current Radio frequency pulses used in the technique resulted in incomplete suppression of the venous system (Figure 1.)

The Siemens Healthcare USA developers contacted Siemens Ltd Australia, who through their collaboration with National Imaging Facility (NIF) and Centre of Advanced Imaging (CAI, University of Queensland), had access to expertise on radio frequency pulse optimisation. The resultant optimised RF pulses resulted in complete venous suppression, see Figure 2.

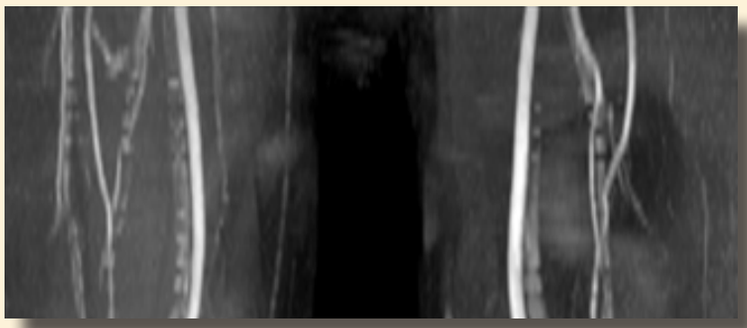


Figure 1. Angiography image with incomplete venous suppression.

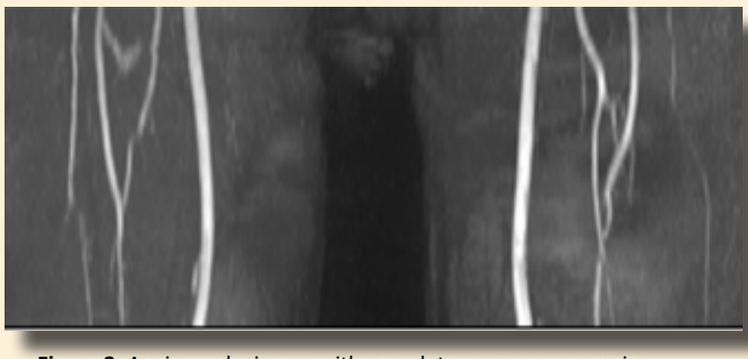


Figure 2. Angiography image with complete venous suppression.

The optimised RF pulses were implemented in a Siemens distributed Works in Progress package for clinical validation at Siemen's worldwide clinical partners. Successful application of this new technique will lead to it being released as a commercial product in Siemens' high field clinical scanners. Such a technique will:

i) allow the longitudinal scanning of monitoring of patients with severe renal function who are most at risk of developing Nephrogenic Systemic Fibrosis;

ii) reduce imaging costs; and,

iii) improved patient comfort.

"The collaboration with expert partners like the researchers at NIF and CAI, enables Siemens to continuously improve their products maintaining their competitive edge."

Dr Kieran O'Brien
Scientist MR, Siemens Ltd. Australia & New Zealand;
Adjunct Research Fellow, Centre of Advanced Imaging, University of Queensland.

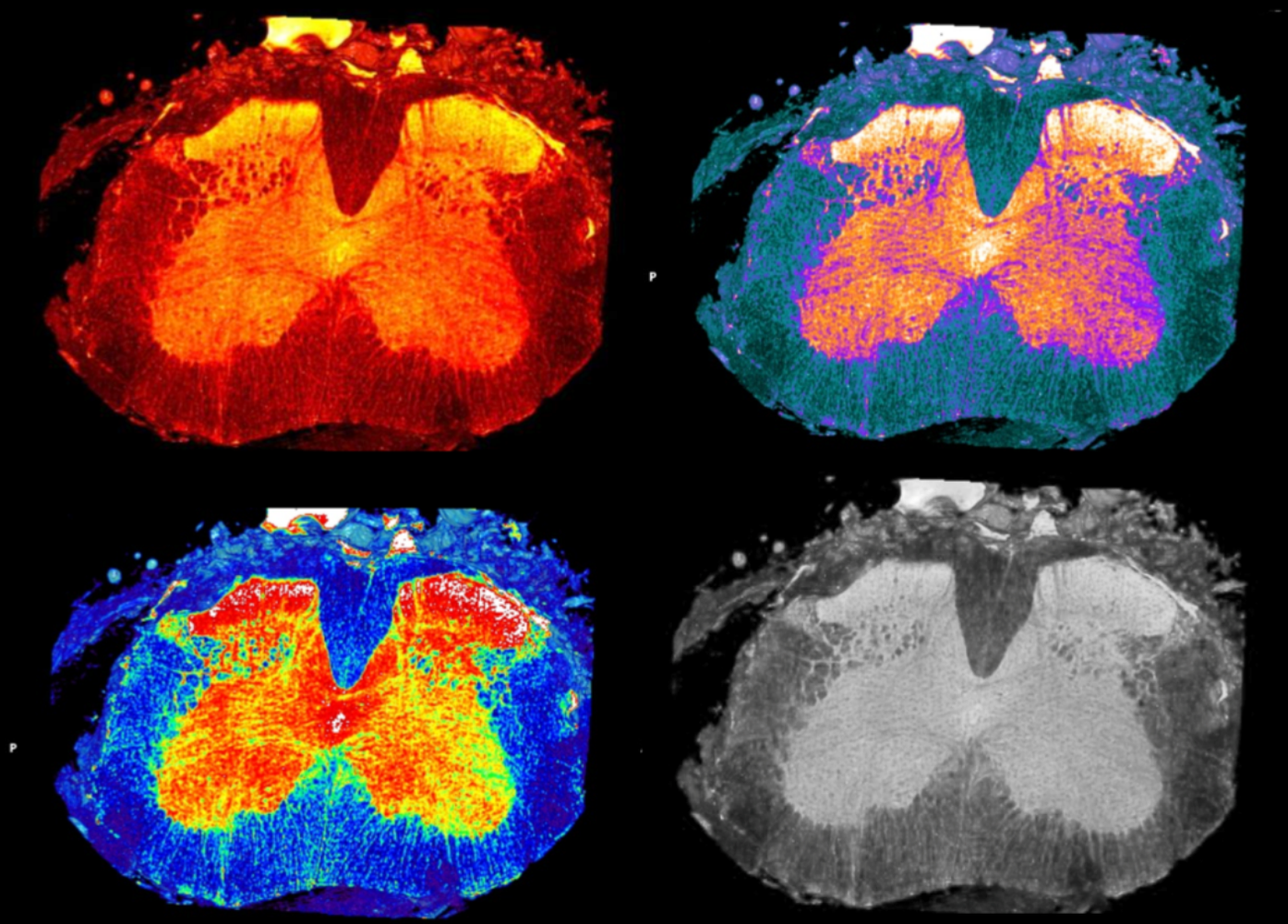
Reference:

1. Thomsen HS. (2009) Nephrogenic systemic fibrosis: history and epidemiology, Radiologic Clinics of North America. 47(5):827-31.

2. Bernstein EJ. (2012) Nephrogenic systemic fibrosis: A systemic fibrosing disease resulting from gadolinium exposure, Best Practice & Research Clinical Rheumatology. 26(4):489-503.

For more information regarding the project, and/or accessing the NIF-UQ node, please go to: http://www.anif.org.au/aboutnif/nodes/UQ-Node.html

MRI of intervertebral disc – functional study on annulus fibrosus for MND/ALS
- Images courtesy of NIF Nodes at
University of Queensland and
University of Western Australia



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University of New South Wales

University of Sydney / ANSTO

University of Western Sydney

University of Melbourne

Monash University

Florey Institute of Neuroscience and Mental Health

Swinburne University of Technology

Large Animal Research & Imaging Facility

Editorial Enquiries:

Dr Annie Chen

Scientific & Engagement Manager

a.chen1@uq.edu.au

www.anif.org.au