



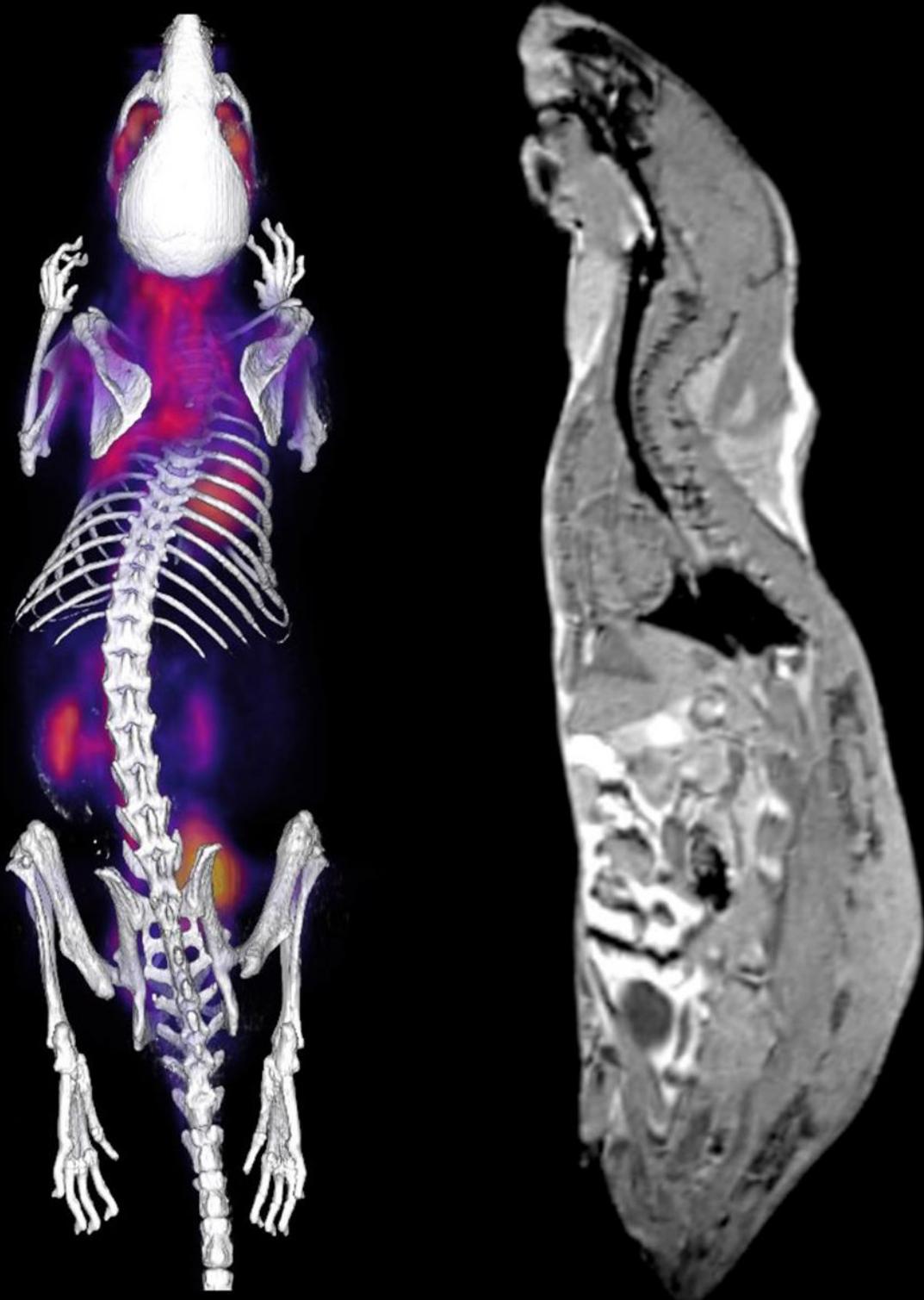
National
Imaging
Facility

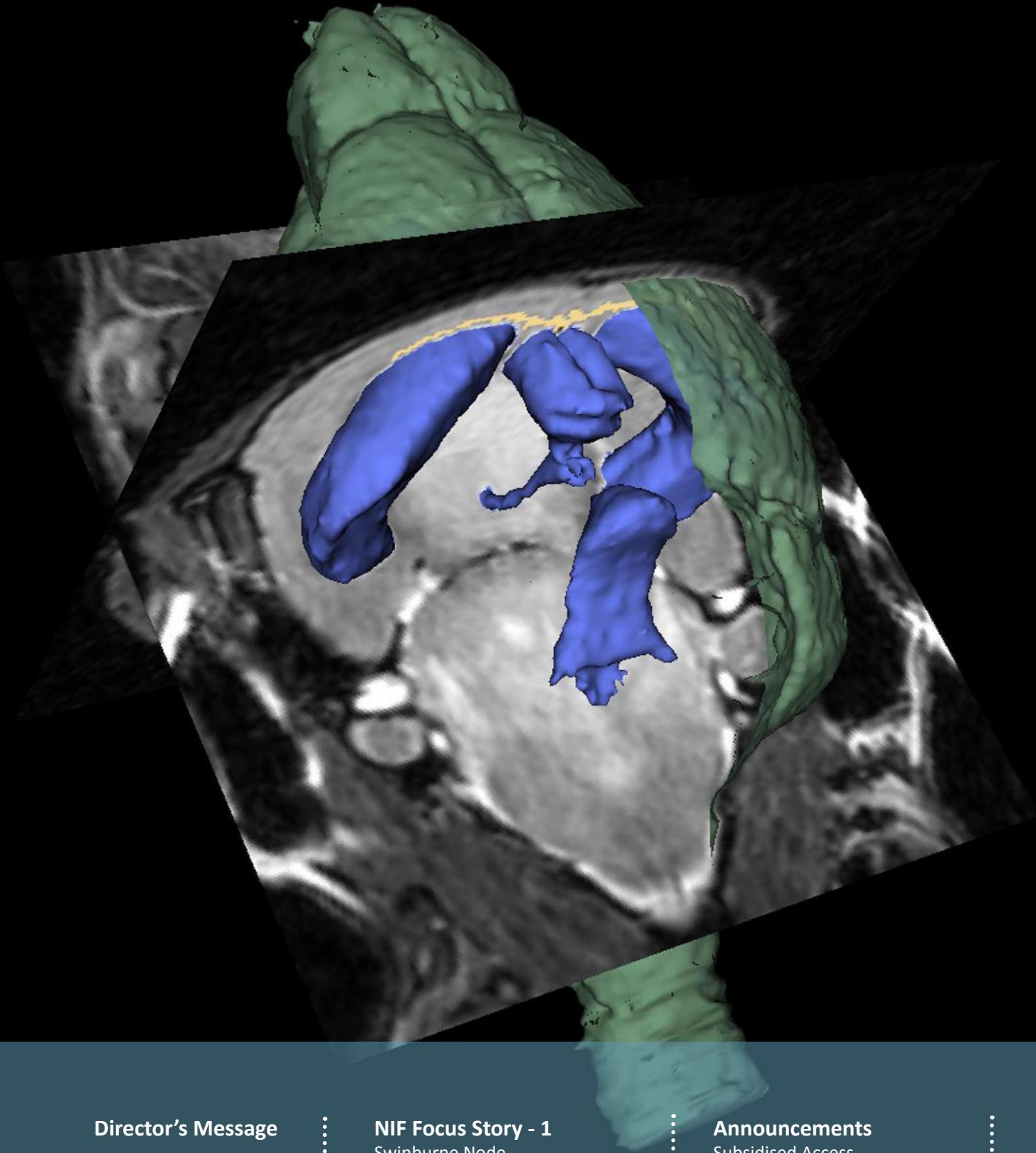
NIF Quarterly • Q2 , 2013

Exploring Inner Space

MRI/PET/CT imaging of brown fat in mice. MRI detects localisation and volume of brown fat, PET measures glucose uptake, or activity, of the brown fat.

Prof. G. Muscat, Dr P Lau (Institute of Molecular Bioscience),
and Dr G. Cowin, Dr K. Mardon (NIF-UQ Node),
University of Queensland.





Director's Message

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Show the world the inner artists in you, NIFers!

Volumetric analysis of brain and ventricle structures in an ASPA knock out mouse model for the investigation of Canavan disease. *Dr Matthias Klugmann, Dr Georg Von Jonquieres, Dr Andre Bonders (UNSW-BRIL Node)*.

“NIF is not only about equipment, it provides the researchers of Australia with access to the necessary expertise.”



DIRECTOR'S MESSAGE

One of the many privileges of my position as Director of Operations is the opportunity to attend the launch of new research capability. Not only do I get to see the great facilities that are being delivered, but I meet with the staff, the supporters and the users, both current and future. So, the highlights for this quarter have been the opening of the Biological Research Imaging Laboratory at the University of New South Wales, and the launch of the new animal facilities at the Large Animal Research and Imaging Facility in Adelaide. These events are featured in this Newsletter.

NIF is not only about equipment, it provides the researchers of Australia with access to the necessary expertise. The Node Directors and the Facility Fellows are there to help you with your research, so in each newsletter we will be highlighting the people behind the equipment. Get to know them, they are keen to get to know you. NIF is also about training. Read about the workshops you have missed, and don't panic, the analysis workshop was popular, I am sure it will be a repeat event. But check out the ones that are coming up, and register early.

Of course, the thing that excites us all is great science. So we have included some great examples to

whet your appetite. Read them, and see what can be done. Whether it is to understand how we think, using animal models to follow the disease process, or the development of novel radiotracers, NIF is there, advancing the technology. Read about what is being done to image conscious, moving animals (a world first), to see how they think. Then, consider how these tools can enhance your research. Don't worry about not knowing where to start. Contact one of the Facility Fellows, and they will help you find the best tools, the optimal experiment and the correct analysis.

NIF is also about communication. That is why we were at the CRC Conference. We want to share with you the great things that can be done with imaging. If you can't wait for the next newsletter, then follow us on LinkedIn. If you are really "Hip", we are also on Twitter (hashtag on back cover).

Professor Graham Galloway
Director of Operations



UNSW Node: Neuroimaging Analysis Workshop

It has been a very exciting quarter for NIFers at the University of New South Wales Node! On the 4th of April, Prof. Lindy Rae (UNSW Node Director) and her team hosted a "Skeptical Neuroimaging Analysis Workshop" at NeuRA (Neuroscience Research Australia). With the intention to keep keen imaging researchers at the forefront of imaging analysis and statistical methods, the workshop took participants through a journey of major types of imaging, the common problems/pitfalls, potential solutions

and 'software packages' that are out there. A great panel of Australian neuroimaging experts presented at the workshop, including Dr Leigh Johnston (another NIFer at the



Florey Node!), as well as two international speakers from Emory University (Dr DuPois Bowman) and University of California San Francisco (Prof. Roland Henry) at the USA.



Official Launch of 9.4T MRI

On the 21st of May 2013, the 9.4T MRI Facility that is located within the Biological Resources Imaging Laboratory (BRIL) was officially opened by UNSW DVC-R Prof. Les Field. A joint imaging symposium was also held as part of the day to showcase the frontier research that is currently conducted at BRIL, and the capabilities BRIL has to offer. International speaker, Dr Ivan Tkac (University of Minnesota, USA) brought us the benefit of many years of research in MR spectroscopy. BRIL aims to focus on providing researchers with access to state-of-the-art clinically relevant imaging technologies such as MR, CT, PET, ultrasound imaging and x-ray, and also research focused instruments such as optical imaging systems for detection of bioluminescence and fluorescence imaging of live animals and intravital microscopy.

Overall, both events were well received. Congratulations to UNSW Node!

For more info about NeuRA and BRIL, please contact Prof. Lindy Rae (Node Director): www.anif.org.au/contact-information/node-directors.html

NIF News

LARIF Node: Official Facility Opening

Another opening event for NIF! The Large Animal Research & Imaging Facility (LARIF) was officially opened on the 22nd of May, 2013. Located at Gilles Plains, Adelaide, LARIF houses a fully serviced operating theatre complex complete with a 1.5T Siemens Sonata MRI and CT, which is available exclusively for researchers using large animals (sheep and pigs). LARIF has fully compatible surgical suites and supporting services which are linked to a large animal holding facility. This facility encompasses experimental rooms, tissue collection facility plus a cold room, deep litter sheep pens, pig pens to hold 20-30 pigs individually, and rooms to hold sheep in expandable metabolism crates. The facility has a workshop for physicists to design and create new RF coils to optimise MR images. LARIF also houses a DEXA scanner, Image Intensifier equipment, and telemetric physiological monitoring equipment for both large and small animals.

The opening event was a great success! Look forward to more large animal imaging in future!



* See NIF Focus Story for an exemplar project that is supported by LARIF.

L - R: Prof. Graham Galloway (NIF Director), Dr Tim Kuchel (NIF-LARIF Node Director), Prof. Steve Wesselingh (SAHMRI Executive Director), Ms. Leesa Vlahos (SA Parliamentary Secretary for Health and Ageing).

NIF @ CRC Conference

Together with our colleagues from the National Characterisation Council (AMMRF, Australian Synchrotron, and ANSTO), NIF participated in the 2013 CRC Conference, Melbourne, May 2013. By co-hosting an exhibition booth, NIF was well represented with a number of our local NIFers participating at the conference. The event was well received and had attracted a number of potential collaborators.





NIF Focus Story

Swinburne Node:

How hard is our brain working to delay short-term fulfillment? Imaging Technology tells you how.

As human beings we are constantly mentally exercising 'delay fulfilment (for larger reward)' - ie, do not sleep-in and enjoy the warmth of my bed in cold winter morning so I can make it to work on time. The ability to forego short-term rewards in exchange for larger long-term goals is an integral component of mental and physical wellbeing. Studies have shown that this ability of control predicts a number of outcomes in later life, such as academic success, stress management, cognitive control, and reduced levels of drug use. So, exactly which parts of our brain (and how?) play in this ability of self-control?

By providing expertise and access to clinical MRI technology, Prof. Susan Rossell (Director of NIF-Swinburne Node) helped researchers at the University of Melbourne to investigate on the neural basis of our ability to resist immediate reward stimuli. Through carefully designed psychological tests with various amounts of rewards, brain activities of a group of adult test subjects were scanned using MRI facility that is available at the Swinburne Node. Dr O'Connor and his team have found that regions of the brain previously implicated in visual attention (as well as emotion and inhibitory control) were hypoactive when fulfilment was being delayed.

The data derived from this study also shows the amount of attention we allocate to an activity has a prominent role in our ability to apply self-control - in the effect of ignoring or distracting ourselves from the stimuli to further improve our ability to delay fulfilment.

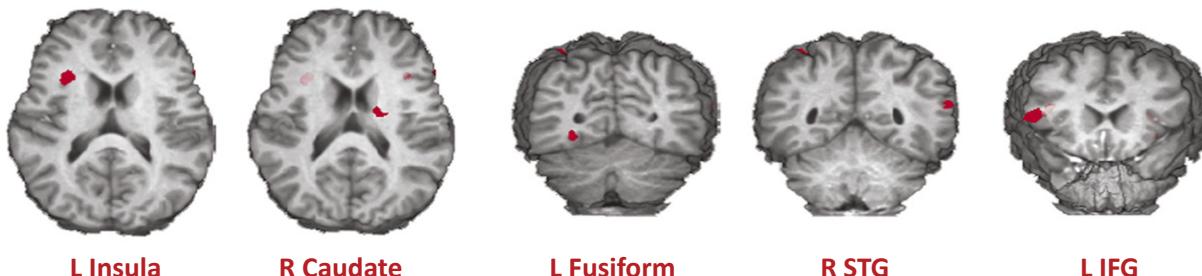


Figure 1: Brain MRI images of regions showing activities differentiating rewards from no-rewards during successful inhibitory controls. **For more info about the project:** O'Connor, D. A., Rossiter, S., Yucel, M., Lubman, D. I., & Hester, R. Successful inhibitory control over an immediate reward is associated with attentional disengagement in visual processing areas. *Neuroimage*, 62(3), 1841-1847.



MEET PROF. SUSAN ROSELL:

As the Director for NIF-Swinburne Node, Prof. Rossell is a Professorial Research Fellow at the Brain and Psychological Sciences, Swinburne University of Technology, and at the Monash Alfred Psychiatry Research Centre. Having held numerous prestige academic positions at the Functional Imaging Lab (UK), Macquarie University, and Mental Health Research Institute of Victoria, Susan focuses her research on understanding the cognitive and neurobiological process involved in psychosis and related disorders. Prof. Rossell was awarded both the International and European Award for Young Investigator into Schizophrenia Research.

In particular, the caudate is a region of the striatum that is associated with impulsivity, reward sensitivity in motivation-influenced cognitive control, and coding for expected reward magnitude. In order to successfully refrain from responding to an immediate rewarding stimulus in exchange for a larger delayed reward, inhibition of the caudate would be necessary.

In future, the research team hopes to investigate whether this effect is observed in groups who are less able to delay fulfilment and what impacts this might have on drug-taking and -seeking behaviours.

For further information about access to the scanner, collaborations, and imaging, please contact Prof. Susan Rossell, at the Swinburne Node, www.anif.org.au/contact-information/node-directors.html



NIF Focus Story

LARIF Node:

Meeehhrino Sheep.... model for Stroke.

As shown in the 2012 statistics provided by National Stroke Foundation, stroke is Australia's second biggest killer after coronary (ischaemic) heart disease, and a leading cause of disability [1]. Stroke is the rapid loss of brain functions due to disturbances in the blood supply to the brain. The middle cerebral artery (MCA) is by far the largest cerebral artery and untreated MCA occlusion (MCAO) stroke will lead to long-term disability in >70% and mortality in 20% of patients [2]. The physiological changes involved in MCAO stroke is very complex, only timely and very rapid recanalisation treatment, achieved within minutes (or at most a few hours) after stroke has occurred but before irreversible brain damage develops, will be effective.

Animal models are essential to study the pathophysiological changes associated with MCAO stroke and to investigate novel therapies. Currently used rodent models have yielded little clinical success. Therefore, as a collaborative project between researchers from the University of Adelaide, South Australia Pathology, Royal Adelaide Hospital and the NIF-LARIF node (Large Animal Research and Imaging Facility), the research team have designed a model study of MCAO stroke in sheep, including both permanent and transient occlusion with reperfusion

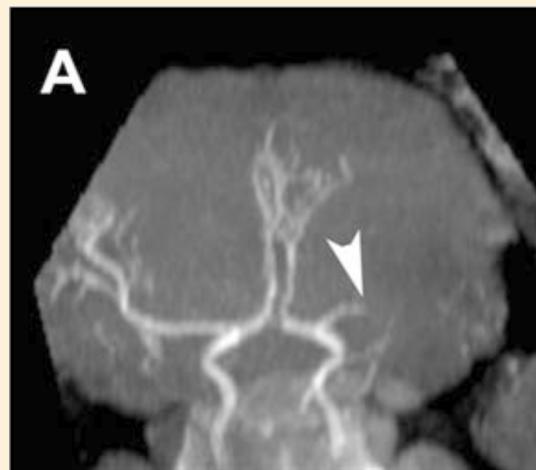
With imaging capabilities and expertise provided by LARIF, 6 adult Merino sheep were imaged using 1.5T Siemens Sonata Magnetic

Resonance Imaging instrument and examined using 3 methodologies:

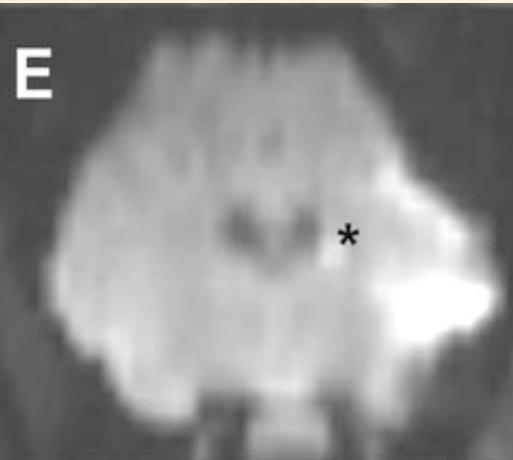
1. Magnetic Resonance Angiography (MRA),
2. Diffusion-weighted imaging (DWI, highly sensitive and specific in early clinical detection of acute ischaemia), and
3. T2 weighted imaging.

The combination of results confirmed that permanent MCAO resulted in complete and sustained occlusion of the proximal MCA, and that 2 hours of temporary MCAO with an aneurysm clip results in restoration of blood flow distal to the occlusion.

PERMANENT (> 4 HOURS) MCAO:



TEMPORARY (< 2 HOURS) MCAO:

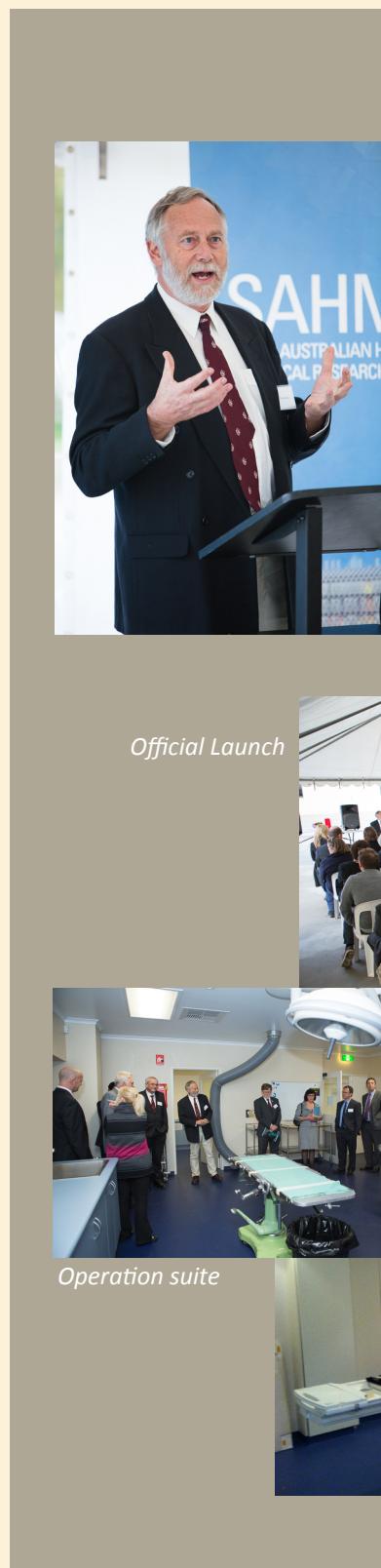
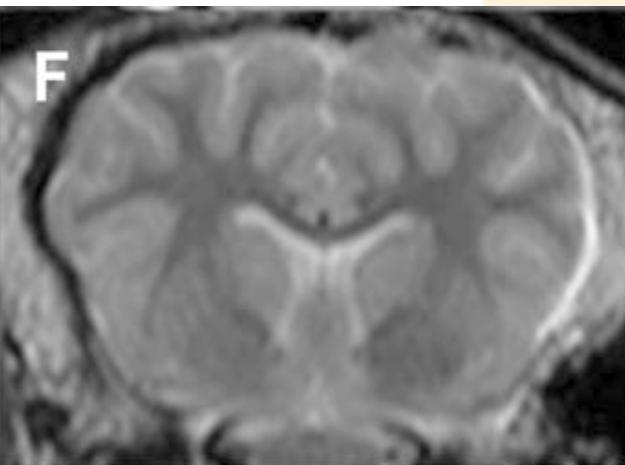
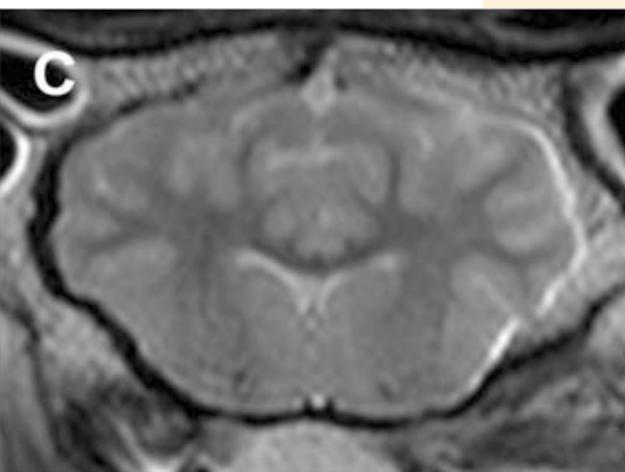


Figures A/D, B/E, and C/F show MRA, DWI, and T2 weighted imaging of Merino sheep, respectively. Arrowhead on MRA indicates site of arterial occlusion. Asterisk indicates restricted diffusion at caudate head after temporary MCAO. As per permanent MCAO, there was T2 evidence of surgical manipulation but no signal abnormalities and no blood products identified.



Exploring Inner Space

In demonstrating the value of their research model, Dr Wells (lead researcher, University of Adelaide) noted the importance of imaging to the success of the study “without an MRI component, the research would not have been published”. He went on to explain the importance of research dedicated scanners, “Prior to the MRI [instrument] and expertise at LARIF which are specifically dedicated to large animal work, we had to use clinical scanners and we would have been forced to wait several months to conduct the imaging component of research. Worse still, we might have been forced to go overseas or not even include imaging in the study. With the MRI here [at LARIF] we were able to conduct the [imaging] work within a month.”



MEET

DR TIM KUCHEL:

With more than 30 years of experience in veterinary sciences, Dr Kuchel is the Director for NIF-LARIF Node. He is also the Director for Preclinical, Imaging and Research Laboratories (PIRL), which supports the animal-based research work for South Australian Health and Medical Research Institute (SAHMRI).

LARIF NODE:

For more details on this project, please refer to: Wells AJ, Vink R, Blumbergs PC, Brophy BP, Helps SC, et al. (2012) A Surgical Model of Permanent and Transient Middle Cerebral Artery Stroke in the Sheep. PLoS ONE 7(7): e42157. doi:10.1371/journal.pone.0042157
[1] The economic impact of stroke in Australia, National Stroke Foundation 13 March 2013
[2] Cohen J. E., Acute middle cerebral artery occlusion: reappraisal of the role of endovascular revascularisation, Int J Stroke. 2013 Feb;8(2):109-10



Exploring Inner Space

USyd/ANSTO Node:

ANSTO Cyclotron & Radiochemistry

ANSTO has recently welcomed on board Dr Giancarlo Pascali to lead the Camperdown radiochemistry team with his extensive expertise in F-18 and C-11 radiolabelling techniques.

His recent work involving microfluidics and labelled choline analogues exemplifies the breadth and depth of experience he brings to this NIF node. His team at the Camperdown Cyclotron is currently developing the expertise needed for the synthesis of clinically relevant C-11 tracers (such as Raclopride, Choline and PIB) and studying novel radiochemical routes for the introduction of positron emitting nuclides into useful biomolecules.

The arrival of Dr Pascali has also coincided with the finalisation of the synthesis and F-18 radiolabelling of the guanosine analogue FHGB (9-[4-fluoro-3-(hydroxymethyl)butyl]guanine). This probe can be used in conjunction with PET imaging as a non-invasive method to monitor the efficiency of gene delivery using viral vectors into different cells in living systems.

The ¹⁸F-FHGB project was originally proposed to the NIF by Dr Padraig Strappe from Charles Sturt University. Dr Strappe saw a unique opportunity to combine his expertise in PET reporter gene vector technology to form a multidisciplinary team incorporating the radiochemistry and *in vivo* imaging capabilities present at the Camperdown NIF node.



ANSTO Camperdown site Cyclotron

NIF Focus Story

When we add the skills of Prof Bernie Tuch and Dr Vijay Vaithilingam from CSIRO in pancreatic stem cell biology we are well equipped to address the overall aim of assessing novel stem cell treatments for diabetes.

¹⁸FHGB can be used as a probe to image the expression of the commonly used PET reporter gene Herpes simplex virus 1 thymidine kinase (HSV-1-tk) *in vivo*. Dr Strappe has developed a suite of vectors, containing the HSV-1-tk gene under the control of cell specific promoters packaged within a lentiviral vector which enables the efficient transduction of a range of cell types including adult stem cells and the pancreatic Min6 cell line.



Dr Giancarlo Pascali

Our initial *in vitro* evaluation of ¹⁸FHGB uptake in 293T cells transfected with the PET reporter gene successfully showed high specific accumulation of radioactivity and prompted further modifications to the vector creating specific expression only in pancreatic insulin secreting cells (Min6).

The next goal of the project is to implant in mice, encapsulated Pancreatic Progenitor (PP) cells specifically engineered to contain an insulin promoter linked with HSV-1-tk PET reporter gene, allowing ¹⁸FHGB to be probe when these progenitor cells have successfully differentiated *in vivo* into insulin secreting cells. The Siemens Inveon small animal PET imaging systems at the Brain and Mind Research Institute coupled with the high specific activity ¹⁸FHGB required for molecular imaging that the radiochemistry team has achieved, will be used to non-invasively image transfected cells *in vivo*.

Dr Pascali remarked that this is one of the first collaborations strongly founded on the radiochemistry potencies at the Camperdown Cyclotron site, as part of NIF. These capabilities perfectly match with the state of art imaging equipment available at the neighbouring BMRI facility, therefore paving the way to answering scientific relevant questions, such as the assessment of stem cell treatments related to this project.

For further info about the cyclotron, the project, and potential collaborations, please contact Dr Giancarlo Pascali (radiolabelling capabilities) and Dr Marie Gregoire for imaging enquiries: <http://www.ansto.gov.au/ResearchHub/Facilities-andInstruments/ResearchCyclotron/index.htm>



Exploring Inner Space

Brain & Mind Research Institute

The ANSTO/BMRI (University of Sydney) NIF node has recently made important progress in the development of the hardware and software technologies for awake animal imaging using positron emission tomography (PET). Last year they were able to demonstrate, for the first time, the feasibility of reconstructing motion-compensated brain images of a freely moving rat in a PET scanner, figure 1. This work was presented at the 2012 World Molecular Imaging Congress in Dublin and the 2013 BrainPET conference in Shanghai.

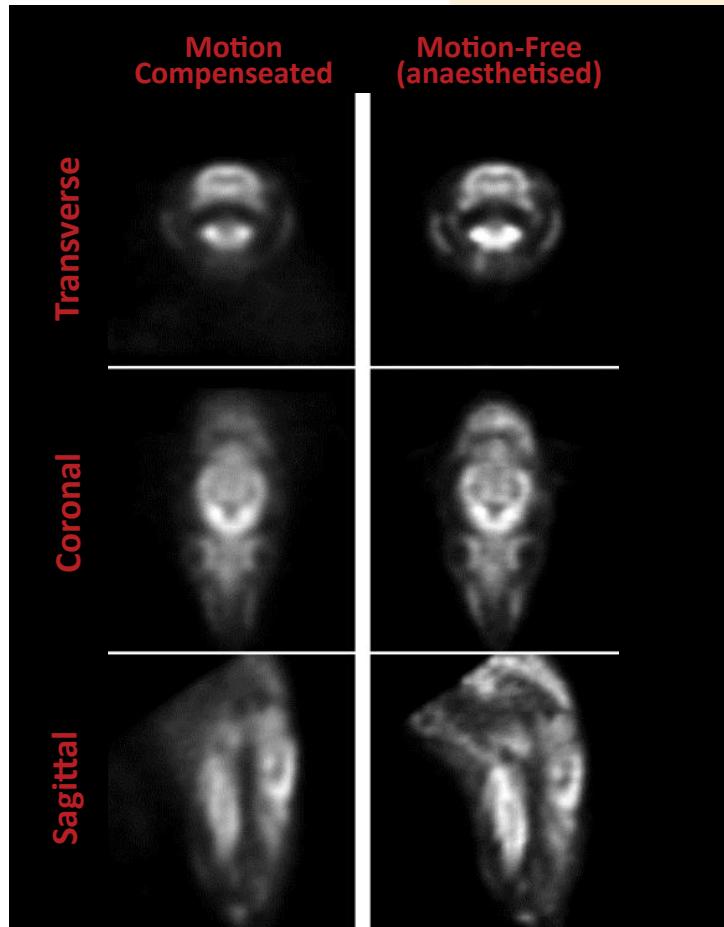


Figure 1: Comparison of the motion-compensated PET reconstruction from a scan of an awake, freely moving rat with the motion-free scan (performed on the anaesthetised animal).

MEET

DR WILL RYDER:

Based at the BMRI, Dr Will Ryder is the Facility Fellow for NIF USyd/ANSTO Node. Having obtained his PhD in Medical Physics from the Institute of Cancer Research, University of London and trained as a Clinical Medical Physicist in the UK, Dr Ryder has over 13 years of expertise in nuclear medicine imaging. With an impressive professional profile in both industry and academia, Will's research interests focus on the image reconstruction, quantitation and radionuclide dosimetry.

For info and access to NIF facilities at BMRI, please contact Dr Will Ryder at: will.ryder@sydney.edu.au



Prof. Steve Meikle and Dr Will Ryder,
University of Sydney

Pilot experiments were performed to study ^{18}F -FDG uptake in the awake rat brain during reward-based learning. Using a Pavlovian learning paradigm the rats were conditioned to associate a specific auditory stimulus with reception of a food reward. This stimulus was sounded periodically during the radiotracer uptake phase, as the animal was being imaged. The preliminary results indicate that regional differences in brain circuits involved in learning and cognition are able to be detected using PET in this type of experimental paradigm. Further studies are planned for later this year, including studies using ^{11}C -Raclopride to focus specifically on the dopaminergic system.

The significance of these developments lies in the fact that experiments now become possible whereby functional brain PET information is acquired simultaneously with behavioural data. Previously it has not been possible to study correlations between these complementary data sets in animals. We look forward to an exciting future of new experiments for basic neuroscience research with this important technology.



Announcements

Subsidised Access

By providing access and expertise to cutting edge imaging capabilities, the NIF Subsidised Access funding scheme aims to assist the Australian research community in achieving critical data to solve significant scientific problems. Since establishment, NIF has awarded \$130,000+ subsidy to 50+ successful applicants for their innovative ideas. The scheme has not only provided seed funding for outstanding research, but has also established growth in research collaborations between our users and NIF, whereby some have lead to further success in competitive research grants. In the most recent round, NIF has awarded subsidy to seven projects:

- **Dr Kimberly Christie (University of Melbourne)** - *Neuroimaging and pathological biomarkers of mild traumatic brain injury.*
- **Dr Mark Walterfang (Royal Melbourne Hospital)** - *Investigation of the effect of NPC 1-haploinsufficiency on brain white matter.*
- **Dr May Lim (University of New South Wales)** - *Silica encapsulated perfluorodecaline for dual mode biomedical imaging*
- **Dr George Srzednicki (University of New South Wales)** - *Starch gelatinisation in rice kernel during drying in a fluidised bed.*
- **Dr Sarah Thompson (Royal Adelaide Hospital)** - *Sentinel lymph node biopsy in oesophageal adenocarcinoma; improving accuracy & optimising treatment.*
- **Mr Ra'ed Moufqq Al Mashashqbah (Charles Sturt University)** - *The effect of ambient environment temperature on cardiac metabolism and sympathetic innervation using 18F FDG.*
- **Dr Andre Kyme (University of Sydney)** - *Development of a MR/PET normal rat brain template for image quantification in awake animal studies.*

NIF is actively seeking external funding so that we can continue to support the research community with imaging subsidy. Follow NIF on LinkedIn and Twitter (@NIFAus) for the next round of Subsidised Access details.

Do you have news?!

Published a paper? Formed new collaborations? Discovered something?

Any updates from your Node — we need to know!

Email: communications@anif.org.au

Or: a.chen1@uq.edu.au

Upcoming Events

- **Workshop on Preclinical Molecular Imaging - are we solving the right problems and what answers can this technology provide?** 26 Aug 2013. Sydney.

Join NIF's NSW Nodes for a day of presentation and discussion focusing on their molecular imaging capabilities and how these imaging modalities can support your research. The workshop will be Free of charge. Follow NIF (@NIFAus) on Twitter and/or LinkedIn for details.



- **The Sixth Annual World Molecular Imaging Congress;** 18–21 Sept 2013, USA.

www.wmicmeeting.org/



- **The Australian and New Zealand Society for Magnetic Resonance 2013 / Asia-Pacific NMR;** 27–31 Oct 2013. Brisbane. www.apnmr2013.org/



Show the world the inner artists in you, NIFers!



Submit your proudest imaging art piece to **2013 Siemens Preclinical Solutions Image of the Year Competition** - just to bring out the fun in imaging science (*not mentioning the shiny trophy!*)! Winners will be announced at the 2013 World Molecular Imaging Congress. Categories include:

- Inveon Image of the Year*
- Multimodality Image of the Year*
- Translational Image of the Year*
- Best Presented Image of the Year*

Competition closes: 26 July 2013

Competition details: www.healthcare.siemens.co.uk/molecular-imaging/forms/preclinical-foy-2013#



A gradient echo image of a table grape.
Image courtesy of Dr Tim Stait-Gardner,
UWS Node.

NIF Nodes:

University of Queensland

University of Western Australia

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

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