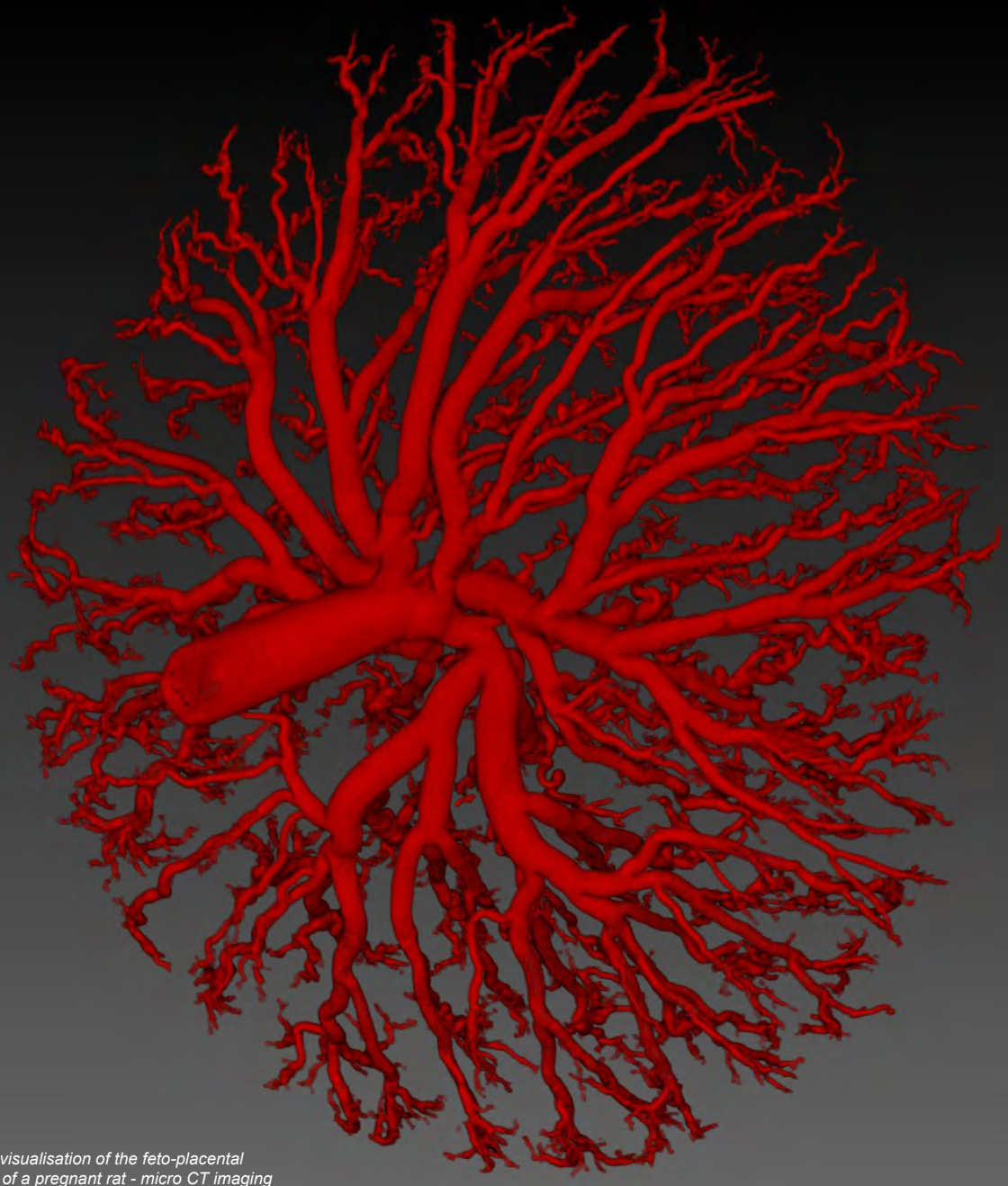
National Imaging Facility

National Imaging Facility Quarterly Newsletter Issue Two 2016



Three-dimensional visualisation of the feto-placental arterial vasculature of a pregnant rat - micro CT imaging

Caitlin Wyrwoll, Tim Crough – School of Anatomy, Physiology and Human Biology, The University of Western Australia
Andrew Mehnert, Jeremy Shaw, Diana Engineer – Centre for Microscopy, Characterisation and Analysis, The University of Western Australia

In This Issue

Director's Message

Professor Graham Galloway
Director of Operations

Innovation, Science and Research continues to be on many people's lips, but having listened to some of the aftermath of the recent elections in Australia, many in the community don't understand what it means, nor what relevance it has for them, but they are not to blame. Some politicians have recognised this, maybe out of self-preservation, but accept that there needs to be better communication. This is not just up to the politicians or the bureaucrats. As scientists, it is in our and the nation's interest that we share how research contributes to a better life and a healthier economy.

This issue of the NIF Quarterly specifically highlights the interaction between our university based research capability and the end-user, be that in the development of new varieties of grapes, more tolerant of weather extremes (Western Sydney University), supporting clinicians in diagnosis and treatment of patients with psychiatric diseases (Swinburne), or assessing more accurate and less invasive diagnosis of prostate (University of New South Wales), NIF is playing a role. And what is more important than ensuring every baby is born with the best possible chance. So at the University of Western Australia, new methods are being developed to image the ability of the placenta to properly nourish the developing foetus.

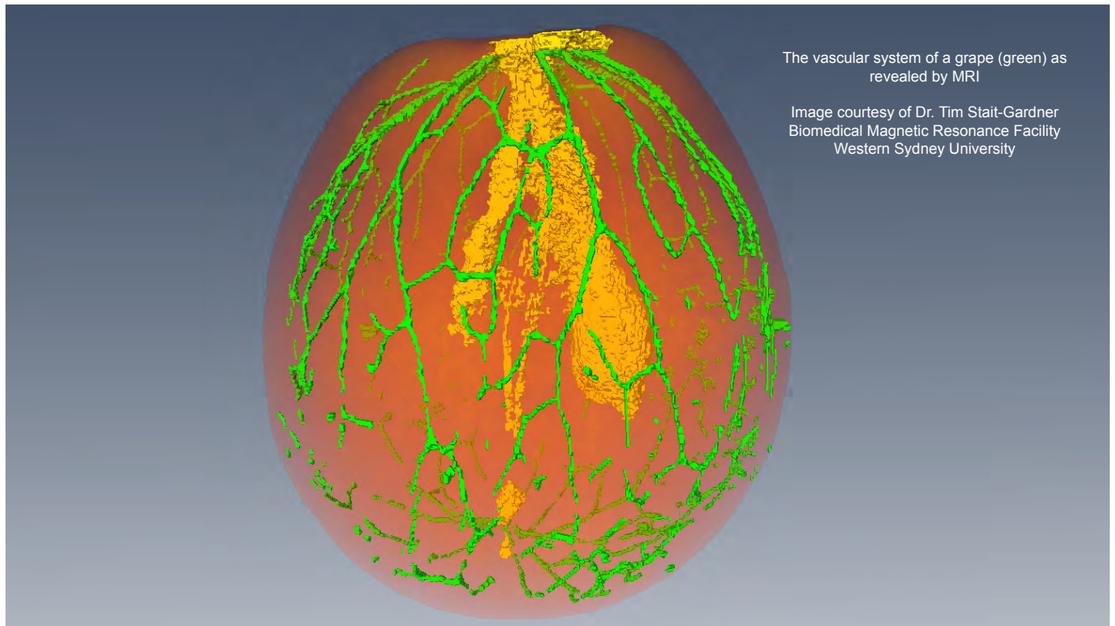
NIF works because of teamwork, which requires opportunities for communication. The launch of the MR-PET highlighted the collaboration between Monash, CSIRO and Siemens Healthcare. Internationally, NIF, along with AMMRF, has joined GlobalBioImaging, launched in June, with a vision to share expertise, experience and data. And within the NIF family, we are working to support each other, through our annual workshop, and reach out through Research Imaging symposia. This year we went to Adelaide. Read about it on page 11.

"As scientists, it is in our and the nation's interest that we share how research contributes to a better life and a healthier economy"

So back to where I started, after you have read this newsletter, you can share it with your friends, and start a conversation about the relevance of research to a better Australia.

Imaging to Rescue National Wine & Grape Industry

Industry Project



The vascular system of a grape (green) as revealed by MRI

Image courtesy of Dr. Tim Stait-Gardner
Biomedical Magnetic Resonance Facility
Western Sydney University

Berry split is a condition in which the grape epidermis splits. This often occurs during periods of high rainfall and is a significant cause of grape crop loss. In cool damp conditions there is increased uptake of water via osmosis and decreased water loss from transpiration. This net uptake of water increases turgor pressure within the berry and can eventually lead to the mechanical failure of the epidermis. The resultant wounds in the berry epidermis will encourage berry desiccation and greatly increase the probability of microbial infection, leading to reduced crop yields and berry quality.

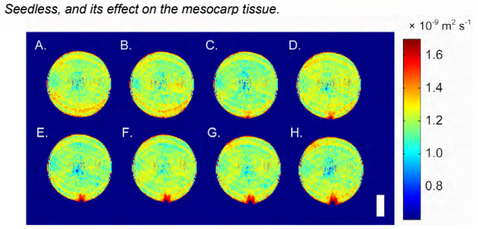
In order to examine and characterise the immediate effect of fruit split on grape tissue structure, National Wine & Grape Industry Centre, NSW Department of Primary Industries, and the Western Sydney University node have been collaborating on an ongoing project, which investigates the physical changes within the grape berry both before and after splitting using diffusion Magnetic Resonance Imaging (MRI). Thirty-six ripe table grape berries of the Thompson Seedless variety were studied: 12 were assigned to a control group, 12 were wrapped in damp tissue and the remainder were wholly immersed in water. Five axial images (including diffusion tensor images) spaced evenly apart along the length of each berry were acquired simultaneously every hour to create a time-course study of each grape.
For each grape that split within the MRI during the study, it was observed that there was an immediate change in the diffusion coefficient in the region of the wound.

This region increased in volume over the course of the subsequent scans and correlated with regions of non-vital cells (as determined by fluorescence microscopy). It was determined from the study that grape berries left exposed to standing water after splitting exhibit greater cell death within the vicinity of the split. Therefore, the surface of split berries should be kept dry if possible to reduce further damage[1,2].

For more information on this project, contact Dr. Timothy Stait-Gardner (T.Stait-Gardner@westernsydney.edu.au).

Collaborators
Nanoscale Organisation and Dynamics Group, Western Sydney University
School of Medicine, Western Sydney University
National Wine & Grape Industry Centre, Charles Sturt University
NSW Department of Primary Industries

The development of a single split in the epidermis of a ripe table grape, Thompson Seedless, and its effect on the mesocarp tissue.



1. Dean, R. J., Bobek, G., Stait-Gardner, T., Clarke, S. J., Rogiers, S. Y., & Price, W. S. (2015). Time-course study of grape berry split using diffusion magnetic resonance imaging. Australian Journal of Grape and Wine Research.
2. Dean R.J., Stait-Gardner, T., Clarke, S.J., Rogiers, S.Y., Bobek, G. and Price, W.S. (2014) Use of diffusion magnetic resonance imaging to correlate the developmental changes in grape berry tissue structure with water diffusion patterns. Plant methods 10(1):35

Functional Connectivity of the Brain in Anorexia Nervosa

Industry Collaboration

Anorexia Nervosa (AN) is a serious psychiatric condition characterised by significantly low body weight and a fear of weight gain. A disturbance in the experience of one's own body weight or shape is a core feature of the illness, which has a mortality rate among the highest of any mental illness. Thus, it is critical to gain a better understanding of the neurobiological basis of the illness which currently remains unclear.

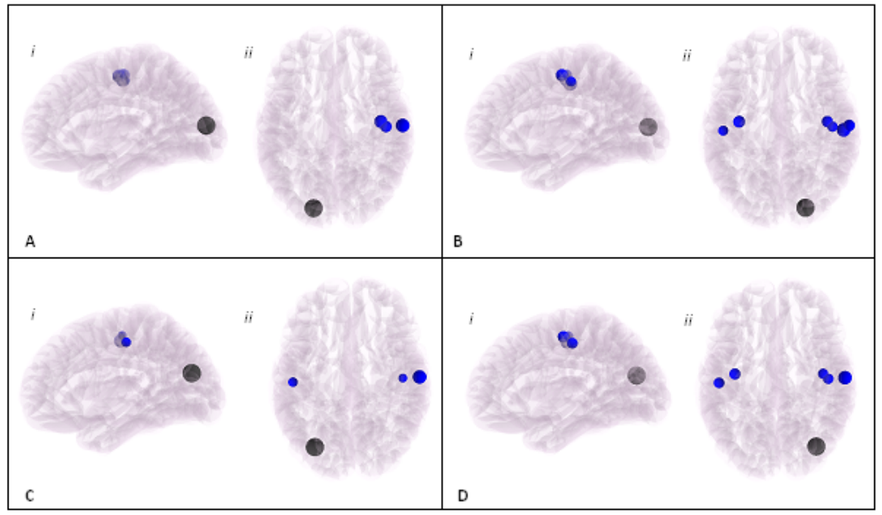
The potential neurobiological underpinnings of AN have typically been investigated with the use of functional Magnetic Resonance Imaging (fMRI), in which brain states evoked during an experimental and a control condition are compared, with the aim of elucidating task-specific activations. Recently, however, researchers have begun to investigate synchronous brain activity at rest to examine 'functional connectivity' between brain regions. The term 'functional connectivity' is used to signify the correlation of activity time courses between brain regions. The examination of functional connectivity at rest provides information about neuronal communication in the brain, and how integration of information may relate to behaviour.

A study completed by the collaborators from University of Melbourne, Swinburne University of Technology node, Austin & St. Vincent's hospitals, and Monash University & the Alfred hospital examined functional connectivity between sensorimotor and visual brain regions in AN. 26 females with AN and 27 healthy controls participated in this study and underwent a resting state functional magnetic resonance imaging scan at the neuroimaging facility at Swinburne University of Technology node.
AN patients showed reduced functional connectivity between visual regions and sensorimotor regions, relative to healthy controls. These findings suggest that reduced functional connectivity between somatosensory and early visual regions may be related to visuospatial processing deficits in AN, and their misperception of body size.

Gaining a better understanding of how deficits in visuospatial processing and reduced functional connectivity within these networks relate to AN may facilitate the development of more effective treatments in the future, specifically designed to improve these disturbances in the illness.

For more information on this study, contact Andrea Phillipou (ap@unimelb.edu.au).

Collaborators
Department of Optometry & Vision Sciences and Department of Psychiatry, The University of Melbourne
Department of Mental Health, The Austin Hospital
Department of Psychiatry, St Vincent's Hospital
Faculty of Health Sciences, Australian Catholic University
Brain and Psychological Sciences Research Centre, Swinburne University of Technology
Monash Alfred Psychiatry Research Centre, Monash University and The Alfred Hospital



*Reduced functional connectivity in AN compared to healthy controls within the sensorimotor and visual network for seeds at the left secondary visual cortex **(A)**, right secondary visual cortex **(B)**, left associative visual cortex **(C)**, and right associative visual cortex **(D)**. Black dots represent seeds and blue dots represent areas of reduced connectivity in sensorimotor regions, with the size of the dots representing the strength of the correlation. The images are displayed in neurological format in sagittal **(i)** and transverse **(ii)** planes.*

Phillipou, A., Abel, L. A., Castle, D. J., Hughes, M. E., Nibbs, R. G., Gurvich, C., & Rossell, S. L. (2016). Resting state functional connectivity in anorexia nervosa. Psychiatry Research: Neuroimaging, 251, 45-52.

Visualisation and Characterisation of Feto-placental Vasculature

Proper vascular development of the human placenta is crucial for meeting the metabolic needs of the developing fetus during pregnancy. Maternal environmental stressors such as malnutrition disrupt the elaboration of the feto-placental vasculature that in turn impacts on placental function and results in reduced fetal growth. The ramifications of this are not only on short-term fetal health but also long-term health outcomes. Indeed, distortion in placental shape and size strongly associate with later adult health outcomes such as cardiovascular disease, obesity and cancer.

Dr Caitlin Wyrwoll of the School of Anatomy, Physiology and Human Biology, at The University of Western Australia is leading a multidisciplinary team that is investigating, in rodent models, how common environmental stressors in pregnancy alter feto-placental vascular morphology and placental function. Ultimately the team will seek to identify potential therapeutic targets to enhance placental vascular development and then apply this to experimental models to assess the outcomes on fetal development and adult health.

The research project involves collaboration with the Western Australian nodes[1] of the National Imaging Facility and the Australian Microscopy and Microanalysis Research Facility to image, visualise and characterise the geometry of the arterial and venous feto-placental vascular trees using high-resolution X-ray microscopy (ZEISS Xradia 520 Versa). Dexamethasone administration during rodent pregnancy is used as a model to simulate excess placental and fetal glucocorticoid exposure (a known effect of prolonged stress). Control and treated rats are anaesthetised at day 22 of gestation and their uteri collected. The feto-placental units are dissected and fetal anaesthesia induced. The individual feto-placental vascular trees are cleared of blood and perfused with Microfil®, a radio opaque polymer casting compound. Each cast is stabilised in PBS in a plastic vial and imaged using a wide field-of-view of ~13.4 mm, a voltage of 50kV, more than 3000 projections through 360 degrees, and an exposure time of 7s. The ZEISS XMReconstructor software is used to reconstruct an image volume (standard parallel beam backprojection algorithm) with voxels of size ~7.0 µm.

The team have completed a preliminary study involving control and dexamethasone-treated rats and both the venous and arterial feto-placental vasculature trees. A visual comparison of treatment to control indicates that for both types of vascular tree, there is reduced branching in the fine vessels and reduced vessel density. A quantitative comparison indicates reduced total vessel length and total vessel volume.

A methodology is currently being developed for a more comprehensive and automatic quantitative assessment of vasculature morphology and geometry. This includes automatic segmentation, filtering, centre-line extraction and characterisation of the vessel tree in terms of its branching characteristics such as its branching hierarchy and angles, vessel diameters and the tortuosities of vessel segments. Furthermore, these vascular tree images are being used in a world-first study to model placental blood flow using computational fluid dynamics.

For more information on this work, contact Dr. Caitlin Wyrwoll (caitlin.wyrwoll@uwa.edu.au).

Collaborators
School of Anatomy, Physiology and Human Biology, The University of Western Australia
School of Mechanical and Chemical Engineering, The University of Western Australia
Centre for Microscopy, Characterisation and Analysis, The University of Western Australia

1. Located at the Centre for Microscopy, Characterisation and Analysis at The University of Western Australia.

Rendering of a portion of the vascular tree, coloured according to vessel thickness

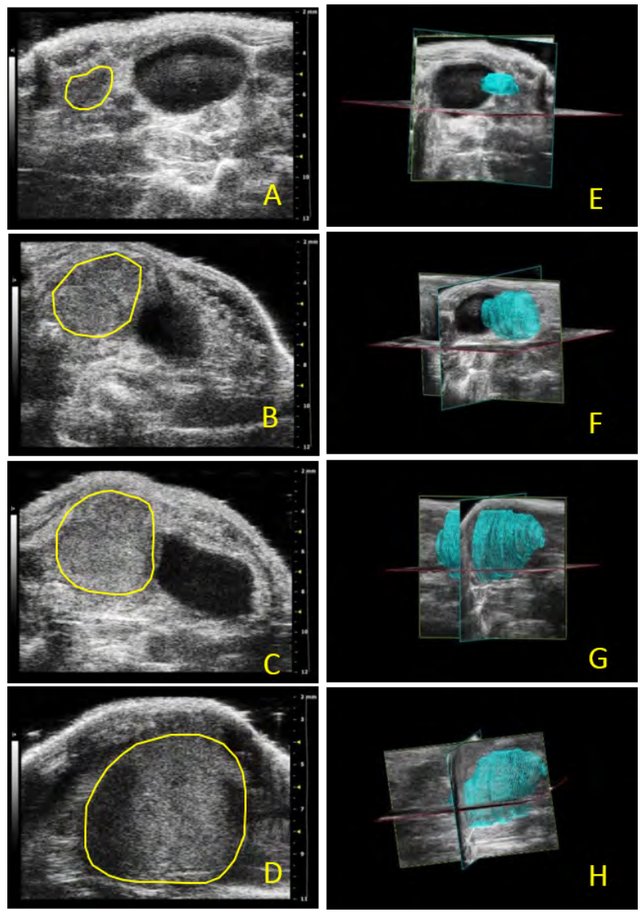
Image courtesy of Dr. Andrew Mehnert
Centre for Microscopy, Characterisation and Analysis,
The University of Western Australia

Monitoring Prostate Tumor Growth Using 3D Ultrasound

Prostate cancer is the most commonly diagnosed cancer, which occurs when abnormal cells develop in the prostate. These abnormal cells can continue to multiply in an uncontrolled way and sometimes spread outside the prostate into nearby or distant parts of the body. Prostate cancer is generally a slow growing disease and the majority of men with low grade prostate cancer live for many years without symptoms and without it spreading and becoming life-threatening. However, high grade disease spreads quickly and can be lethal.

Monitoring prostate tumor growth is one of the most important factors in determining treatment options. Therefore, Biological Resource Imaging Laboratory at the University of New South Wales node, in collaboration with St. George hospital, have investigated the usage of a 3D ultrasound system equipped with photoacoustic (PA) imaging in monitoring longitudinal prostate tumor growth in an orthotopic mouse model. These technologies can continuously monitor *in vivo* tumor development, providing data that traditionally used to be unavailable premortem, such as tumor volume and growth curves.

Ideally, a small-animal cancer imaging technology should be sensitive to tumors; produce high-quality images; acquire images rapidly; and employ equipment that is inexpensive to purchase, feasible to operate, and easy to maintain. Furthermore, when frequent longitudinal studies are required, the imaging examination should be harmless and noninvasive so that as many imaging sessions can be done as necessary without imposing risk. Ultrasound imaging provides an attractive combination of the above-mentioned characteristics.



Longitudinal 2D and 3D ultrasound images of prostate tumors with gross pathology and histopathology. ***(A-D)****: Transverse prostate tumor (outlined by yellow line) obtained from the same mouse on 4 different time points (Week 0-4).* ***(E-H)****: 3D reconstructed prostate tumor (outlined by blue wire) acquired from the same mouse on 4 different time points (Week 0-4).*

In this work, 2D and 3D ultrasound imaging to monitor the tumor growth in an orthotopic tumor model was used and the acquired data to the true tumor volume compared. Results indicated that ultrasound imaging, whether in 2D or 3D mode, is able to clearly detect prostate cancer in the orthotopic mouse model. The current findings also showed a good correlation and agreement of tumor volumes measured by 3D ultrasound imaging and gross pathology. In addition, the study demonstrated that repeated imaging sessions had been well tolerated by the mice, suggesting that 3D ultrasound imaging is an ideal technique to monitor longitudinal tumor growth. The challenges of ultrasound imaging however include smaller penetration depth, inability to image air-filled organs, vulnerability of ultrasound of easily being scattered, and operator-subjective image variability. Also, it does not produce whole-body cross-sectional images as computed tomography and magnetic resonance imaging (MRI) do. Investigations on comparison of ultrasound and MRI in monitoring tumor growth, as well as on using MRI to monitor longitudinal tumor growth are ongoing.

For more information, contact Dr. Tzong-Tyng Hung (t.hung@unsw.edu.au).

Collaborators
Cancer Care Centre, St George Hospital
St George and Sutherland Clinical School, the University of New South Wales
Department of Surgery, St George Hospital
Biological Resource Imaging Laboratory, the University of New South Wales

Ni, J., Cozzi, P., Hung, T. T., Hao, J., Graham, P., & Li, Y. (2016). Monitoring Prostate Tumor Growth in an Orthotopic Mouse Model Using Three-Dimensional Ultrasound Imaging Technique. Translational oncology, 9(1), 41-45.

New Imaging System Launched at Monash Biomedical Imaging

A revolutionary imaging scanner that will help develop new therapies and medical devices to improve healthcare outcomes was officially launched at Monash Biomedical Imaging on 5 May.

As Australia's only research-dedicated scanner of its kind, it offers new insights into the brain and body through simultaneous images produced by magnetic resonance (MR) and positron emission tomography (PET). Exquisite simultaneous *in vivo* whole body MR and PET imaging can now be achieved in humans and large animal models, producing co-registered images for advanced visualisation. The highly sensitive PET produces images of specific molecular processes, while the MRI provides high resolution structural and functional images of the brain and other soft tissues such as breast, prostate and heart. The technology enables assessment and tracking *in vivo* of new biomaterials, cell therapies and medical devices, as well as biomedical research in neuroscience, cardiology and oncology.

The MR-PET scanner will initially focus on medical device development, as well as studies in mental health, ageing, and understanding brain structure, function and metabolism.

At the launch, Professor Ian Smith, Vice-Provost (Research and Research Infrastructure) said the MR-PET scanner was a key part of a new Monash-CSIRO partnership, the Biomedical Materials Translational Facility (BMTF). The aim of BMTF is to foster rapid progress in materials and biomedical sciences and assist in commercialising the next generation of medical devices, diagnostics and cell therapies. This initiative is supported by the Science and Industry Endowment Fund.

"Two of Australia's research powerhouses, Monash and CSIRO, can use this research tool to strengthen our global competitiveness in biomedical sciences," Professor Smith said.

Professor Gary Egan, Director of Monash Biomedical Imaging, said the MR-PET's true capabilities were still being uncovered. "By collaborating with other institutions and industry, we hope to develop novel non-invasive MR-PET imaging techniques to accelerate our biomedical research," Professor Egan said. "Having such a powerful scanner located alongside the Australian Synchrotron will also attract world-leading researchers to the Clayton precinct, and offer unmatched training opportunities for graduate students and post-doctoral researchers," he added.

The MR-PET scanner at MBI was established with support from the Science and Industry Endowment Fund and Siemens Healthcare.

> *"By collaborating with other institutions and industry, we hope to develop novel noninvasive MR-PET imaging techniques to accelerate biomedical research"*
>
> *Professor Gary Egan*
> *Director of Monash Biomedical Imaging*

L-R*: Dr Robert Krieg, Vice-President Product Definition and Innovation, Siemens Germany, Dr Keith McLean, Director CSIRO Manufacturing, Professor Lyn Beazley, Chairperson, Advisory Board, ARC Centre of Excellence for Integrative Brain Function, Professor Ian Smith, Vice-Provost (Research and Research Infrastructure), Monash University, and Professor Gary Egan, Director, Monash Biomedical Imaging.*

Global BioImaging Project
Exchange of Experience

June this year, the representatives of the imaging facilities from around the globe met at the first **Exchange of Experience** Workshop at the European Molecular Biology Laboratory (EMBL) in Heidelberg Germany, as part of the Global BioImaging Project.

More than 70 participants exchanged best practice in benchmarking performance of imaging technology platforms, analysis and management of image data, and training for imaging facility staff. During the workshop, the participants, who represented imaging facility infrastructures from Argentina, Australia, Japan, India, South Africa, USA and Europe, started building the global network for international cooperation in exchange of expertise, reciprocal use of infrastructure services, and strengthening of the international collaboration of imaging infrastructures.

In this workshop, Dr. Miles Apperley, ANSTO, gave the opening keynote, *The global research infrastructures from an Australian perspective*, and Prof. David Sampson, Director of the joint NIF/AMMRF node, represented Australia on the GBI Management Board. NIF Director, Prof. Graham Galloway spoke about data management, and recognising our leadership in this field.

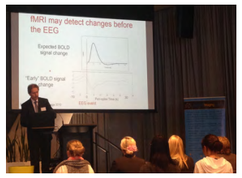
NIF Informatics Fellow, Dr. Andrew Janke, has joined the team for data management, while Prof. Joe Shapter, Flinders node of AMMRF, is in the team developing virtual platforms for training.

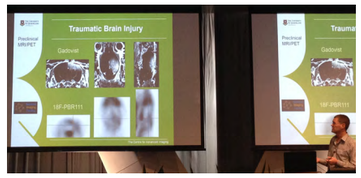
Funded by the European Commission's Horizon 2020 Programme, Global BioImaging project is an initiative from Euro-BioImaging that aims to achieve multi-lateral international cooperation between Euro-BioImaging and its infrastructure counterparts in six countries (Argentina, Australia, India, Japan, South Africa, and the USA) in the field of life sciences - including biological sciences, marine biology, biodiversity, medical sciences and agricultural sciences. It facilitates access to a global network of imaging platforms; enables exchange of experience in technology development; and explores standardisation of access protocols, data formats and processing protocols. Such standardisation, together with the sharing of data, will facilitate transglobal collaborative discovery projects with translation to multi-centre clinical trials. The Global BioImaging project officially started in Dec. 2015.

NIF Networking
Fellows Workshop
Research Imaging Snapshot

Every year, the NIF scientific fellows from all the nodes across the country come together to connect and engage with peers, showcase their research work, and share expertise. This annual networking event provides a great platform to identify and maximize potential opportunities for inter-node collaborations and encourages continuous communication among the fellows throughout the year.

This year, the NIF family met in April in Adelaide, where the Large Animal Research and Imaging Facility (LARIF) is located, and participated in a focused workshop and a few very constructive group discussions. The workshop was then followed by a research imaging snapshot, hosted by South Australian Health & Medical Research Institute (SAHMRI), in which most of NIF fellows presented and shared their expertise in various imaging techniques such as MEG, ultrahigh-field MRI, PET, micro-CT, optical imaging, and fMRI among others. This exercise not only gave the attending researchers and students an insight into the many imaging opportunities at the National Imaging Facility, but also strengthened the ties between different nodes. Both events were very well attended and marked very successful, productive, and exciting days for NIF family.





For further information regarding the newsletter, please contact Saba Salehi (communications@anif.org.au)

T. +61 7 3346 9360
E. admin@anif.org.au
W. www.anif.org.au

Follow us on