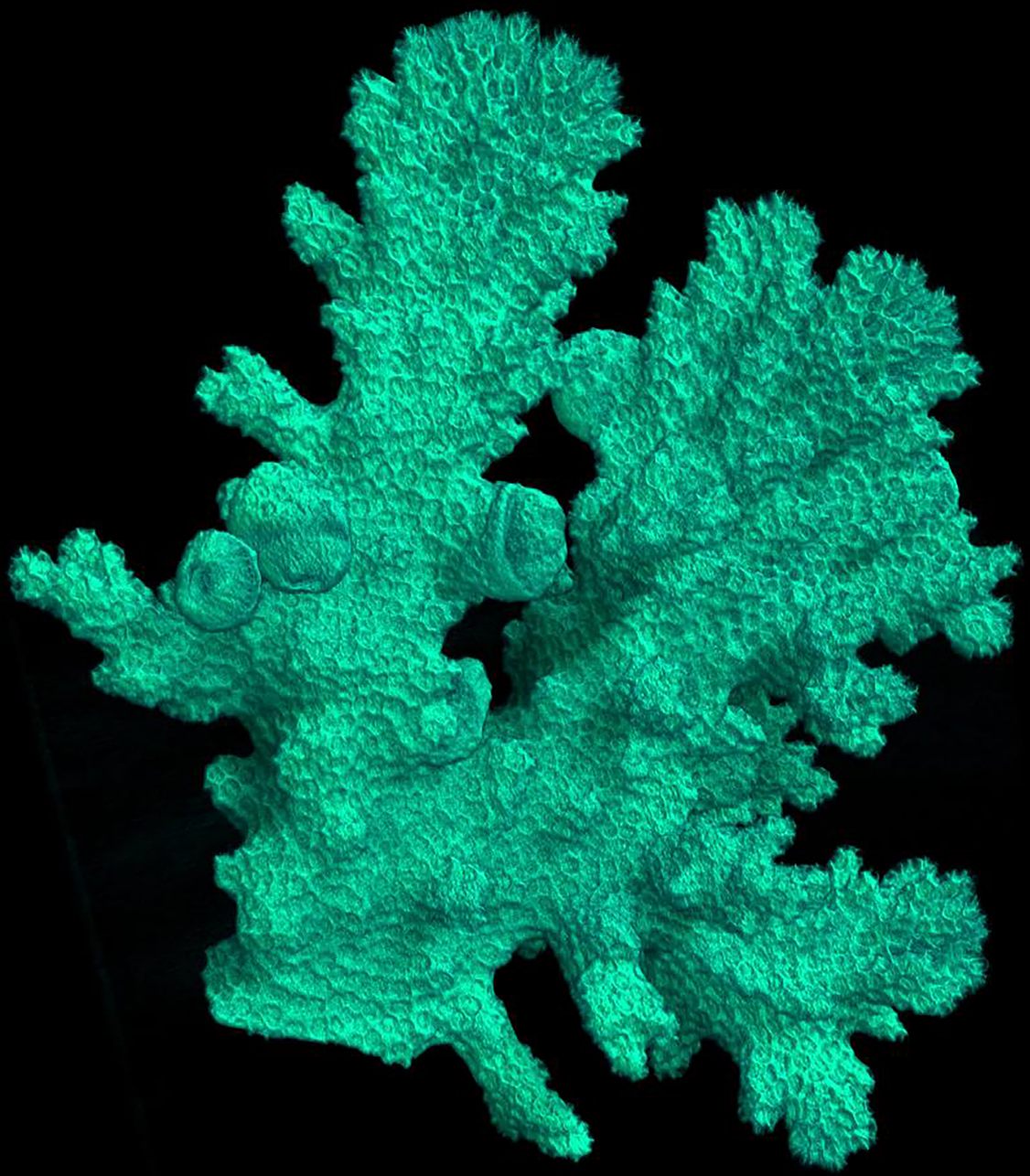
National Imaging Facility

National Imaging Facility Quarterly Newsletter Issue Three 2017



3D volume rendered image developed in Bruker CTVox Software of a coral skeleton from the genus Pocillopora by WA NIF Facility Fellow, Diana Engineer. This CT scan shows the intricate details of the surface of the coral skeleton.

The scan can be used to accurately derive the volume, surface area, and density of the skeleton.This sample is approximately 5 cm in length.

National Imaging Facility

In this issue

Director's Message

"We would love to talk to you about your research and develop innovative ways of answering your research question"

This edition of the NIF newsletter really has an ecological feel to it. With the front cover boasting a 3D rendered image of a coral skeleton extracted from the coast of Western Australia to the 3D printing conducted at the Monash node of NIF where scientists are piecing together the evolution of a now extinct Australian animal that once adapted to their changing and harsh environment. Have a further look at how microCT imaging is used to better understand the dynamic environment on our coral reefs and how this international collaboration is helping us to understand the biology of the reef, giving us new insights into the environmental impact of factors like acidification.

These new applications for image technology are just part of what NIF, as part of Australia's National Research Infrastructure, can offer you. Whether your research is in following disease progression, as in our article on brain morphology in HIV patients, or developing new biomarkers for cardiovascular disease, our NIF Facility Fellows would love to talk to you about your research and develop innovative ways of answering your research question.

NIF is also committed to education, whether it's using imaging to develop new tools for teaching surgeons, or participating in educational symposia; NIF has the expertise. If you would like to keep abreast of what is happening in imaging research, why not follow us on Twitter? Coming up soon we will be attending eResearch 2017 in Brisbane, and Ausbiotech 2017 in Adelaide. We look forward to sharing our activities with you and the exciting research that is being facilitated by our team.

Professor Graham Galloway
Director of Operations

National Imaging Facility

Construction a
of Coral Reefs in

International Collaboration

Coral reefs are built from the calcium carbonate ($CaCO_3$) skeletons of corals and other calcifiers over thousands of years. Yet, for most contemporary coral reefs, rates of $CaCO_3$ production only slightly exceed those of erosion and dissolution. As the oceans absorb anthropogenic CO_2, seawater pH declines and conditions tip less in favour of calcification and more in favour of dissolution, posing a major threat to the persistence of intact coral reef ecosystems. However, little is known about the primary controls on erosion and dissolution of coral skeletons in the natural environment. For example, natural daily variability in seawater pH may influence rates of coral skeleton dissolution, thereby modulating the sensitivity of some coral reefs to ocean acidification.

Dr. Thomas DeCarlo, of the Oceans Institute and School of Earth Sciences at the University of Western Australia, is part of a team using computed tomography (CT) to quantify rates of coral skeleton erosion and dissolution. The team is deploying experimental blocks of skeleton in coral reefs along the coast of Western Australia. CT scans of the skeletons before and after deployment will be compared to determine the rates of $CaCO_3$ loss and to identify the primary environmental drivers.

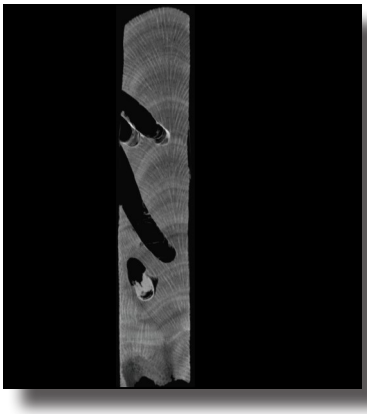
The research project involves collaboration between California State University at Northridge, the Australian Research Council's Centre of Excellence for Coral Reef Studies, the UWA Oceans Institute, and the National Imaging Facility, where the coral skeletons are being analysed with the SkyScan 1176 micro CT scanner.

Above: Micro CT offers the unique ability to visualise the interior architecture of the coral skeletons. This image shows a slice of a Pocillopora colony, revealing the complex growth patterns of the coral. The sample is approximately 2 cm in length.

ND DESTRUCTION
N A CHANGING OCEAN

Pieces of coral skeleton are collected from the field, cleaned of any burrowing organisms or detritus, and thoroughly dried. The skeletons are then CT scanned at 35 micron resolution with voltage of 90 kV and a 0.1 mm thick Cu filter. After scanning, the skeletons are deployed back in the field by fastening them with wire to the reef structure. Following a 6 to 12 month deployment, the skeletons will be collected and CT scanned again. A software program designed for these analyses will automatically align the pre- and post-deployment scans and compute the amount of $CaCO_3$ eroded or dissolved.

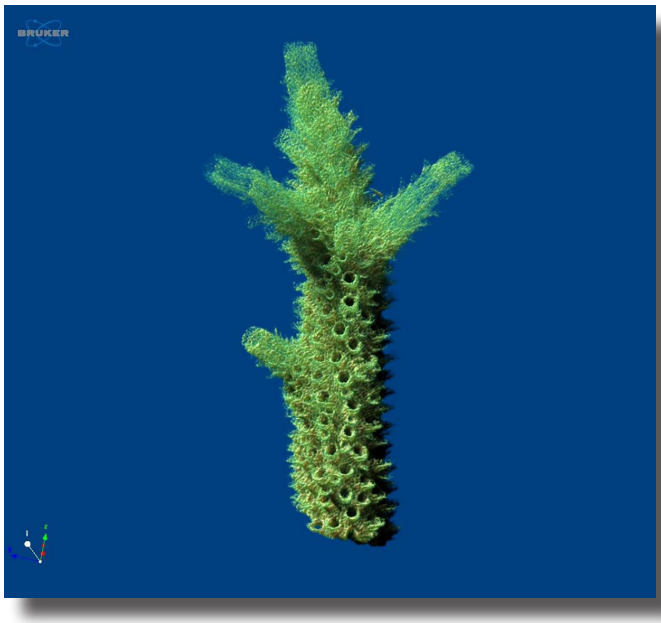
The team has successfully CT-scanned and deployed skeletons at two coral reef sites in the Kimberley region of northwest Australia. These samples will be collected later in the year for post-deployment analysis. Similar deployments are planned for other coral reefs along the coast. Similar sampling schemes are being utilised by various scientists and governmental organisations around the world, but few studies have investigated the erosion and dissolution dynamics on Australian coral reefs. This effort will provide key baseline data for Western Australia and will contribute to a growing global database. Further, the team is laying the foundation for the NIF to serve as an Australian hub for CT scanning coral skeletons to better understand their sensitivity to ocean acidification.



Left: CT scans can be used to visualise coral growth and erosion. This scan shows a core of Porites skeleton, with the alternating light and dark bands indicating annual growth increments. The black boreholes in the skeleton were excavated by bioeroding molluscs. This sample is approximately 15 cm tall.

> "... skeletons are being analysed with the SkyScan 1176 micro CT scanner".

Below: 3D volume rendered image developed in Bruker CTVox Software of a coral skeleton from the genus Acropora by WA NIF Facility Fellow, Diana Engineer. This specimen was collected from Rottnest Island offshore of Perth, and the CT scan allows researchers to track changes in the skeletal morphology of corals living along the Western Australian coast.



For more information on this work, contact Dr Thomas DeCarlo (thomas.decarlo@uwa.edu.au).

> "...the team is laying the foundation for the National Imaging Facility to serve as an Australian hub for CT scanning coral skeletons..."

Collaborators
California State University Northridge
School of Earth Sciences, the University of Western Australia
Oceans Institute, the University of Western Australia
Centre for Microscopy, Characterisation and Analysis, the University of Western Australia

National Imaging Facility

3D Printing brings th

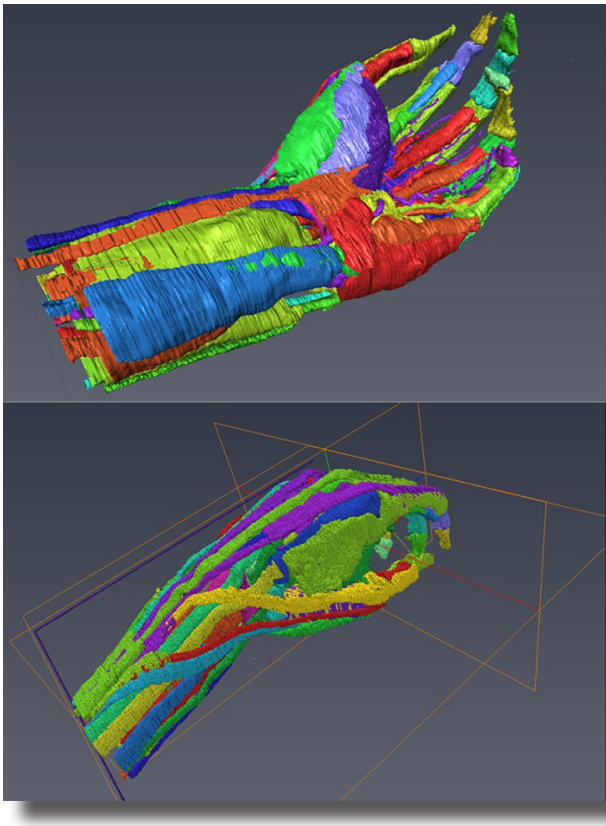
RESEARCH PROJECT

What do long extinct pig-footed bandicoots, anatomical education and 3D printing have in common?

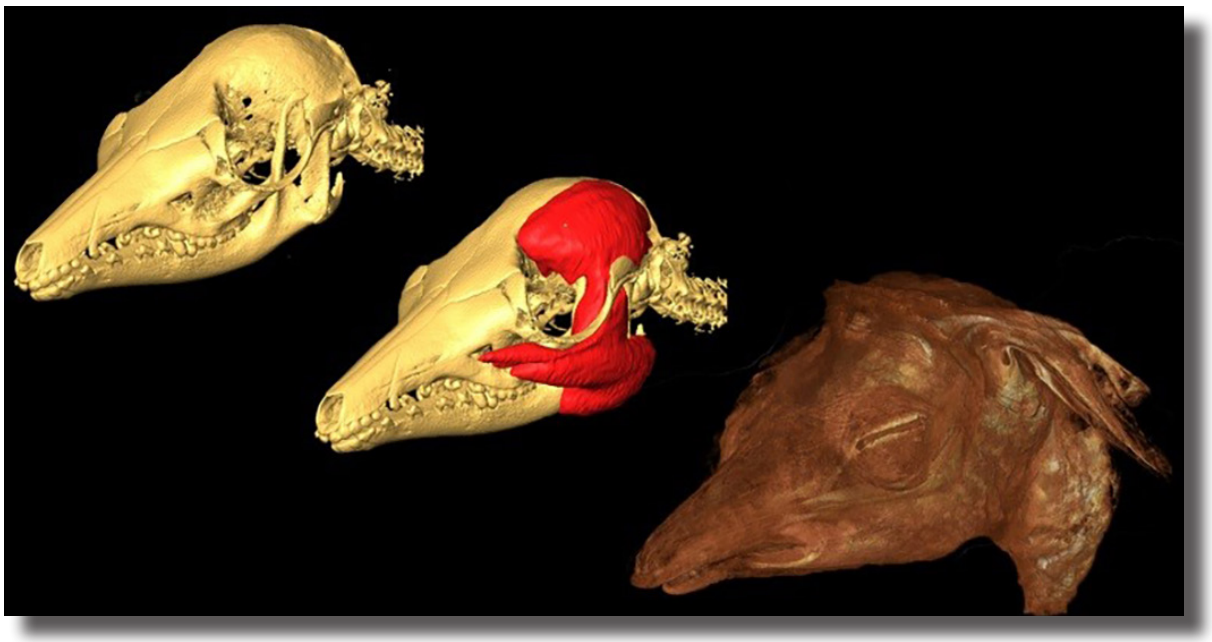
The team at the Centre for Human Anatomy Education (CHAE) at the Monash Department of Anatomy and Developmental Biology are using imaging data generated by Monash's National Imaging Facility node fellows and the radiography team at Monash Biomedical Imaging. Their work developing highly detailed tissue models of human anatomy and long extinct Australian fauna is bringing the dead back to life.

Surgical training using simulators is now becoming more commonplace. In one project run out of the CHAE, PhD student Dr Raf Ratinam, an aspiring surgical trainee, has been using high resolution CT and MRI data of cadaver hands, and biomechanical data available on the different tissues of the hand to maximise anatomical and biomechanical accuracy in the development of a hand surgery simulator. The team at CHAE, supported by the NIF fellows use the small bore Inveon CT and extended structural scans on the Skyra 3T MRI to generate high resolution images of preserved human tissue specimens. The CT and MR images are then reconstructed and "stitched" together to generate the tissue maps, further segmentation, 3D rendering and highlighting allow students to visualise the tissue morphology during surgical training and anatomy classes.

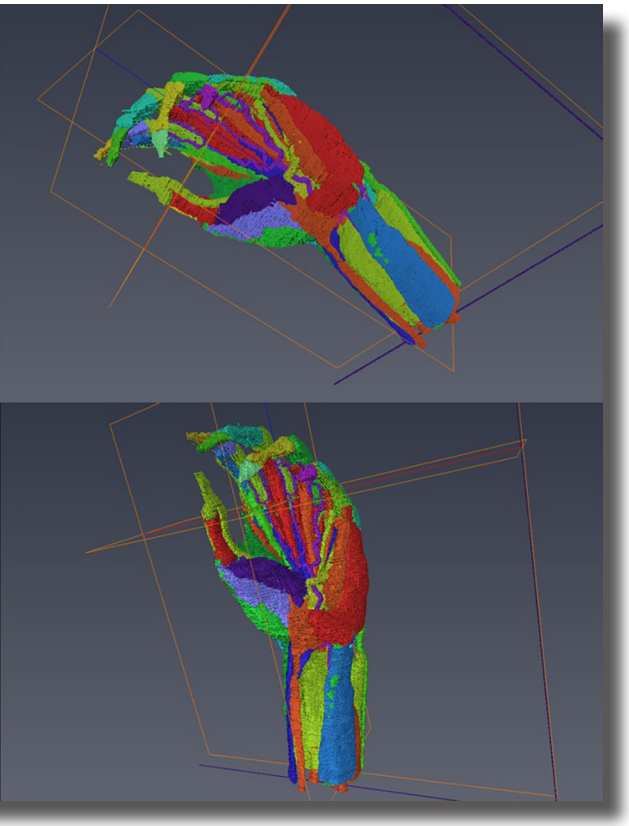
The datasets are then 3D printed using multiple materials to mimic human tissue densities and generate highly realistic physical models of hand anatomy for surgical practice and training. The CHAE team also use the techniques with patient clinical CT scans to 3D print fractured bones to produce 3D models that allow surgeons to better locate fastening points for structural support and the relative location of small bone fragments, improving patient outcomes. I wonder if patients could keep it as a souvenir of their bone fracture or break, it would make an interesting trophy in the pool room!



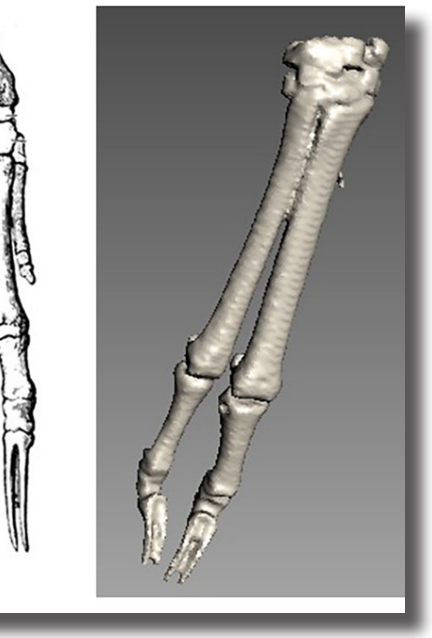
Above: Development of a hand surgery simulator usin Ratinam who is supervised by Prof Paul McM



HE DEAD BACK TO 'LIFE'



g co-registered CT and MRI data. Prepared by Dr Raf enamin, Dr Quentin Fogg and Dr John Crock.



Not only content with helping the medical community and medical students become better surgeons, the CHAE team are also using the same methodologies to digitally resurrect some of Australia's extinct marsupial fauna. Australia's museums are invaluable repositories of biological data, including exotic marsupial species that went extinct over the past two hundred years. The imaging expertise of the NIF supported fellows and high resolution medical imaging equipment at MBI are being used to generate anatomical and biological data from these rare, irreplaceable species; like the recently extinct pig-footed bandicoot which had unusual adaptations to live in the Central Australian desert.

This fascinating work has shed light onto the unique musculoskeletal structures that allowed the bandicoot (*Chaeropus ecaudatus*) to thrive in a hot dry climate before introduced predators and competitor species drove them to extinction. Tooth and jaw morphology is being used to understand how they ate, and the species unique front leg musculoskeletal system is providing insights into how the bandicoot ran. The findings from the 3D models are currently being used to piece together the evolution of morphological differences amongst Australian marsupials and to teach anatomy students how these unique creatures moved. Sadly, any sightings of these amazing bandicoots running about the semi-arid Australian landscape will be restricted to a screen.

Above: Taxidermied 'Chaeropus ecaudatus' or the Pig-footed Bandicoot (National Museum of Victoria state collection).

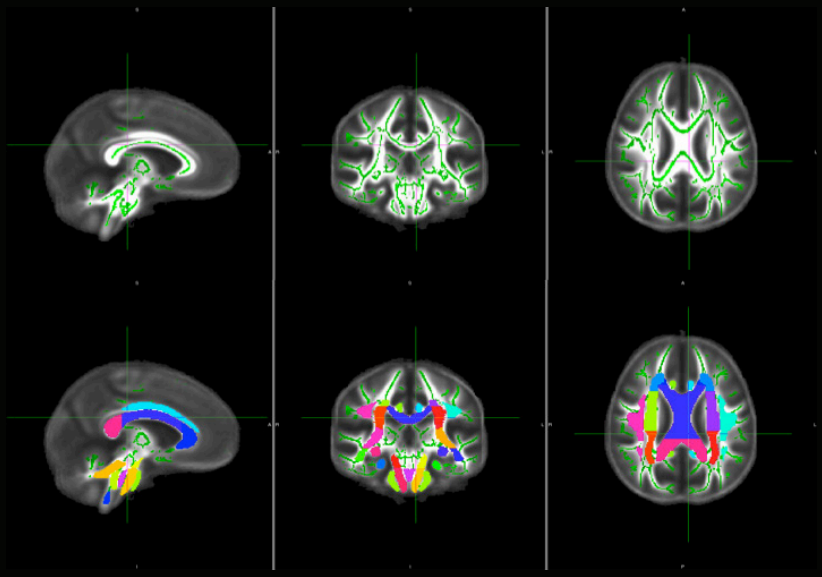
Far left & left: A virtual dissection of the extinct pig-footed bandicoot's (Chaeropus ecaudatus) chewing muscles guided by co-registered CT and MRI data (far left) from Monash Biomedical Imaging, and comparison of the unique front limb skeleton of the pig-footed and regular bandicoots (left). This work was in part created during an Honours project by Alexander McDonald, supervised by Dr Justin Adams.

<u>Collaborators</u>
Michael de Veer, Tara Sepehrizadeh and Gang Zheng in collaboration with Justin Adams, Raf Ratinam and Paul McMenamin, Monash University

National Imaging Facility

White matter measures in HIV patients

INTERNATIONAL COLLABORATION



1. Cysique, L. A., J. R. Soares, G. Geng, M. Scarpetta, K. Moffat, M. Green, B. J. Brew, R. G. Henry and C. Rae (2017). "White matter measures are near normal in controlled HIV infection except in those with cognitive impairment and longer HIV duration." Journal of NeuroVirology: 1-9.

In Australia, human immunodeficiency virus (HIV) affects over 25,000 people. While advances in combination antiretroviral treatment (cART) have meant many HIV+ individuals can expect to live almost as long as HIV-uninfected individuals, up to 30% show cognitive symptoms of mostly mild degree. These have been termed HIV associated neurocognitive disorders (HAND).

Treatment for HIV has suppressed HIV replication, but it does not totally eradicate HIV from cells in the body and the brain. These remnant HIV "reservoirs" are associated with chronic immune activation, which in turn has been associated with HAND. The prevalence of HAND has remained constant, despite new treatments because HIV+ people are aging; because of residual HIV replication in the central nervous system where antiretroviral penetration is suboptimal; irreversible injury prior to treatment; and possible antiretroviral toxicities.

MR diffusion imaging has been a useful technique for characterising white matter injury in HIV+ individuals with severe HAND and untreated HIV+ people. But its effectiveness at teasing out white matter degradation and pathology in treated HIV+ individuals with viral suppression is unclear with wide variability in acquired measurements.

The large variability is postulated to be due to different acquisition parameters across studies which can be sensitive to pathological changes and the variation in HIV+ participants which can result from different antiretroviral status, different level of suppression, the nature of the HIV disease and the age of the patients.

A recent study[1] led by NeuRA researcher Lucette Cysique (UNSW NIF Node) aimed to investigate these variabilities through MR diffusion imaging. White matter abnormalities in stable and suppressed HIV+ men were compared with HIV- controls while carefully taking into account demographic and disease factors.

White matter diffusion tensor imaging measures of fractional anisotropy (FA) and mean diffusivity (MD) in 11 fronto-striatal and fronto-parietal regions were compared between the two groups using a Philips 3T Achieva TX MRI system. Images were acquired using a single-shot EPI sequence (b=1000 s/mm2) in 32-diffusion gradient directions.

The hypothesis that there would be significant differences in the diffusion measures between HIV+ and controls was proven incorrect with no significant differences seen in the 11 regions of interest in FA and MD.

However, within HIV+ group differences in the DTI measures were found as a function of HAND severity and longer HIV duration. Also, antiretroviral treatment that better penetrates the central nervous system, and improved immune function were all associated with increased FA and decreased MD.

The study has shown that MR diffusion imaging may be capable of detecting improvement in white matter integrity in HIV+ individuals after immune suppression and of quantifying a treatment effect but longitudinal data is required. Further, high angular resolution diffusion-weighted imaging (HARDI) would be an important future study to explore white matter characterisation during treatment in greater detail

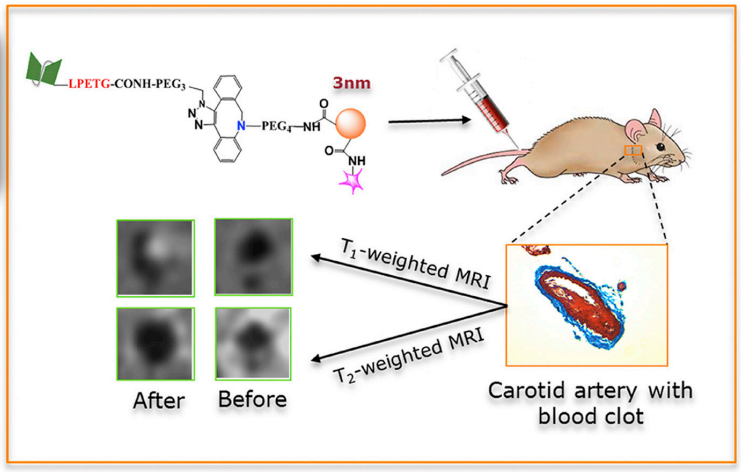
Collaborators
Neuroscience Research Australia, Sydney, NSW, Australia
Faculty of Medicine, UNSW, Sydney, NSW Australia
Peter Duncan Neuroscience Research Unit, St. Vincent's Applied Medical Research Centre, Sydney, NSW, Australia
Department of Neurology, St. Vincent's Hospital, Sydney, NSW, Australia
Department of Immunology, St. Vincent's Hospital, Sydney, NSW, Australia
School of Medicine, Department of Neurology, University of California San Francisco, California, USA

Molecular imaging of activated platelets via antibody-targeted ultra-small dual -contrast iron oxide nanoparticles

Despite significant advances in diagnostic and therapeutic technologies, cardiovascular disease (CVD) remains the global leading cause of death, accounting for 17.3 million deaths per year, and is expected to grow to more than 23.6 million by 2030. This represents 30% of all global deaths and 80% of this occurs in low- and middle-income countries. CVD claims more lives than all forms of cancers combined. Of all CVDs, stroke and coronary artery disease account for more than 70% of all deaths.

The most common form of CVD and also the leading cause of sudden death is atherosclerosis, a chronic progressive inflammatory disease of the arterial vessels. The process of atherosclerosis involves a complex interplay between various cells, particular leukocytes and platelets. Unstable, vulnerable atherosclerotic plaques can rupture and cause thrombosis, resulting in myocardial infarction (MI) and stroke. Recent studies have confirmed that (micro)thrombi containing activated platelets exist long before the presentation of sudden coronary death, indicating that vessel occlusion is often preceded by a variable period of localised coagulation and inflammation. Currently, the prevention of MI and stroke is limited due to the lack of sensitive imaging methods. Those available usually involve invasive procedures such as coronary angiograms, which are potentially associated with complications, including death caused by MI or bleeding. Hence, there is a great need for new diagnostic strategies to determine whether the individual patient is at risk of MI or stroke, which then would allow for effective and early preventative treatment and improved clinical outcome.

Right: Targeted ultra-small dual-contrast iron oxide nanoparticles helped to detect mouse carotid artery blood clot by enhancing signal in T1-weighted MRI and decreasing signal in T2-weighted MRI.



Molecular imaging, the non-invasive visualisation of fundamental (disease) biomarkers in living organisms, holds the key to transform the diagnosis of CVD, profoundly impacting future clinical CVD care. Non-invasive detection of thrombosis employs various contrast agents that are equipped with moieties targeting the biological features associated with thrombosis formation such as fibrin, factor XIII, and activated platelets. For molecular imaging of thrombosis, platelets are an ideal choice for targeting since they are the major component of thrombi.

Magnetic resonance imaging (MRI) is a powerful and indispensable tool in medical research, clinical diagnosis, and patient care, due to its high spatial resolution and non-limited penetration depth. The simultaneous use of positive and negative MRI imaging that employs the same contrast agents will significantly improve detection accuracy. Here we report the development of functional multimodal iron oxide nanoparticles for targeted MRI of atherothrombosis using a combination of chemical and biological conjugation techniques. Monodisperse, water-soluble and biocompatible ultra-small magnetic dual contrast iron oxide nanoparticles (DCIONs) were generated using a high-temperature co-precipitation route and appeared to be efficient positive and negative dual contrast agents for magnetic resonance imaging.

For more information on this study,
please contact the primary author Dr Hang Ta (h.ta@uq.edu.au),
or Dr Gary Cowin (gary.cowin@cai.uq.edu.au).

Collaborators
Australian Institute for Bioengineering and Nanotechnology, The University of Queensland, Brisbane, Australia
ARC Centre of Excellence in Convergent Bio-Nano Science and Technology, Australia
Centre for Molecular Imaging and Nuclear Medicine, School for Radiological and Interdisciplinary Sciences (RAD-X), Soochow University, Collaborative Innovation Centre of Radiation Medicine of Jiangsu Higher Education Institutions, Suzhou 215123, China
Atherothrombosis and Vascular Laboratory, Baker IDI Heart and Diabetes Institute, Melbourne, Australia
Australian Centre for Blood Diseases, Monash University, Melbourne, Australia
Centre for Advanced Imaging, The University of Queensland, Brisbane, Australia
Department of Medicine, Monash University, Melbourne, Australia

In conclusion, the presented data demonstrates a successful and unique approach for MR molecular imaging of thrombosis via a dual mode strategy employing positive and negative contrast iron oxide nanoparticles.

Industry Engagement

Imagine 2017 - Innovation and Translation in Imaging Symposium

News

Returning to TRI for the second year with 200 people across two days and 7 international speakers, Imagine is an international conference featuring the world's leading imaging specialists sharing their latest developments in imaging, radiology and MRI technology and process.

Hosted by the Translational Research Institute (TRI) in Brisbane, Tuesday 5 September featured a full day of presentations by international researchers and leaders from multinational organisations, followed by two workshop sessions on Wednesday 6 September that examined specific challenges in the innovation and translational process.

The first day commenced with Major General Paul David McLachlan who introduced the first session's topic of "Neuro-deregulation in front line defenders – diagnosis and treatment", and ended off with session 4 on "MR Guided Radiotherapy". Day two covered "Innovation and Commercialisation" with the first session kick started by Queensland's inaugural Chief Entrepreneur, Mark Sowerby, and ended off with the second round table discussion of the day where the session speakers conversed on questions posed by the audience.

For more information on what other interesting topics were discussed and the full list of speakers, please visit TRI's website at https://www.tri.edu.au/news/imagine-2017-wrap.

Top right (from left to right): Graham Galloway (NIF), Stephen Rose (CSIRO), Ashley Gillmann (CSIRO and School of Medicine, University of Queensland). Bottom right (from left to right): Dr Walter Busuttil, Dr Robert Krieg, Major General Paul David McLachlan, Dr John Irvine, Prof Carolyn Mountford, Dr Helen Cartledge, Dr David Crompton.

Core Facilities Showcase - July 2017

Above: Ms Loren and Mr Raj at the LARIF booth.

The South Australian Health and Medical Research Institute (SAHMRI), the Robinson Research Institute, and the University of Adelaide co-hosted their first Core Facilities Showcase on 17 July 2017 in Adelaide at the SAHMRI auditorium. The event attracted over 100 visitors as the objective of the showcase was to offer a better understanding of the biomedical research facilities available to researchers.

Mr. Raj Perumal (Radiographer/ NIF Fellow) and Ms Loren Matthews (Surgical Suite Manager) were in attendance to promote LARIF as the South Australian node of NIF, in particular to advertise LARIF as a dedicated large animal facility for preclinical research and to explain how LARIF can better facilitate and optimise research projects. They also made known their other services available to researchers i.e. surgical suites, veterinary services, and animal holding facilities. The NIF booth was well visited by attendees, some of whom indicated interest in using NIF services in the near future.

Imagine Symposium @ Brisbane
Core Facilities Showcase @ Adelaide
Annual Animal Imaging Workshop @ Brisbane

Annual Animal Imaging Worskhop - September 2017

The Annual Animal Imaging Workshop, which took place on 28 September 2017, is an activity of the Convergent Bio-Nano Science & Technology (CBNS) Education Committee, organised by UQ node representative Zach Houston.

The CBNS is funded by the Australian Research Council through the Centre's of Excellence program and is a collaboration between five Australian universities (Monash University and the Universities of Melbourne, Queensland, New South Wales and South Australia) where the majority of the Centre's research is undertaken.

The imaging workshop comprised of two streams, the first being an introduction to animal imaging with talks by the experts in PET-CT, MRI, optical, and MSOT imaging, as well as information about animal models, ethics, and other experimental considerations. In the afternoon of this introductory session, live animal demonstrations using major modalities were done.

The second stream covered advanced imaging and analysis commencing with the animal imaging experiment in the morning using PET-CT, MRI, optical, and MSOT imaging, followed by a data analysis workshop in the afternoon.

Thanks to UQ's Centre for Advanced Imaging for running the workshop and providing the experts and expertise.

Above: Dr Gary Cowin (NIF Facility Fellow) presented a lecture on Magnetic Resonance Imaging and Dr Karine Mardon (NIF Facility Fellow & Facility Manager PET-CT) presented a lecture on Positron Emission Tomography.

Left: Dr Karine Mardon delivering her introductory stream presentation.

For further information regarding this newsletter, please contact Candace Purdon (admin@anif.org.au).

National Imaging Facility

NCRIS
National Research Infrastructure for Australia
An Australian Government Initiative

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

Follow us on