

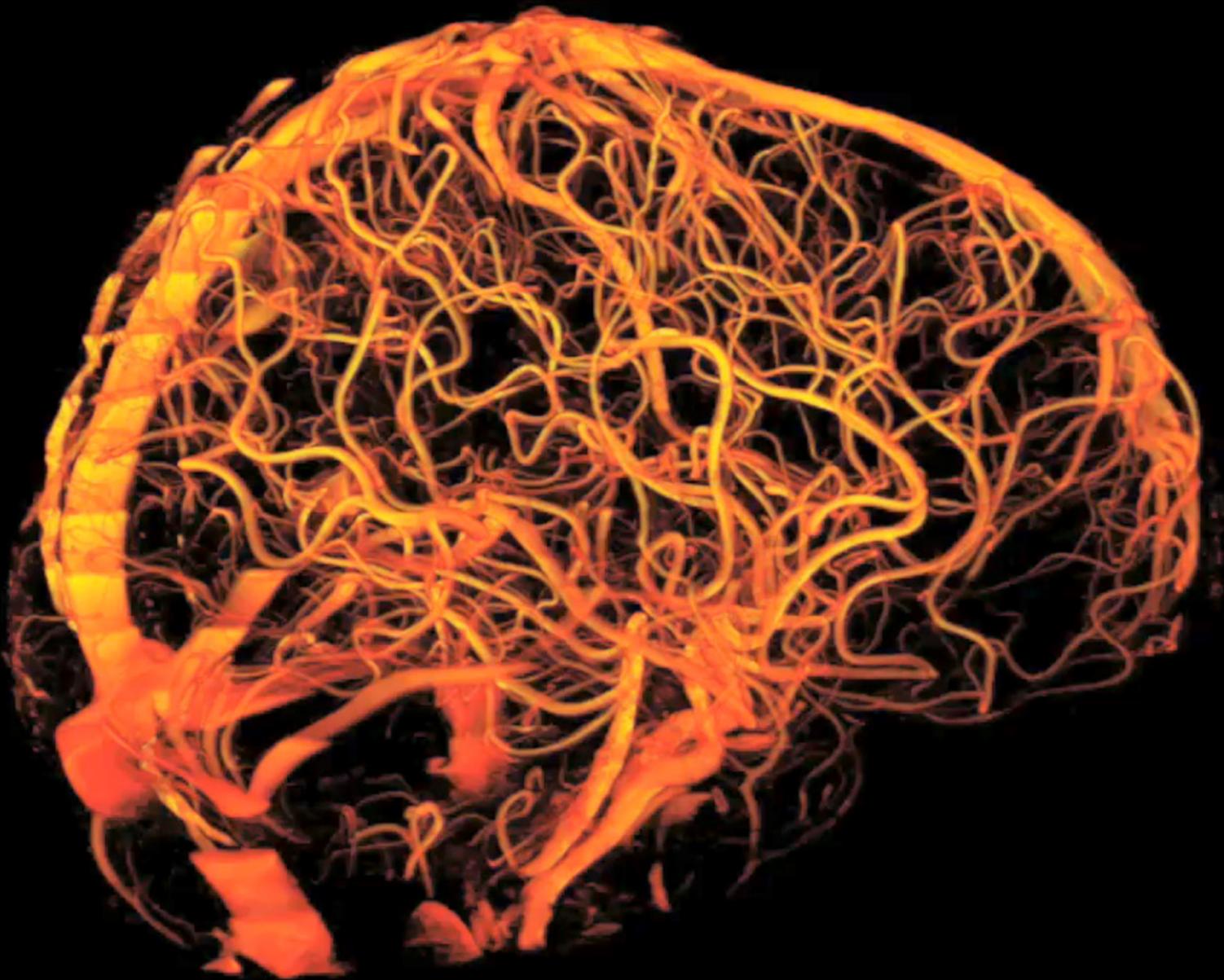


National  
Imaging  
Facility

*Exploring Inner Space*

NIF Quarterly • Q3, 2014

*Time-of-flight angiography of the human brain at 7 Tesla*  
- Dr Zuyao Shan, Centre for Advanced Imaging,  
NIF - University of Queensland node



## Director's Message

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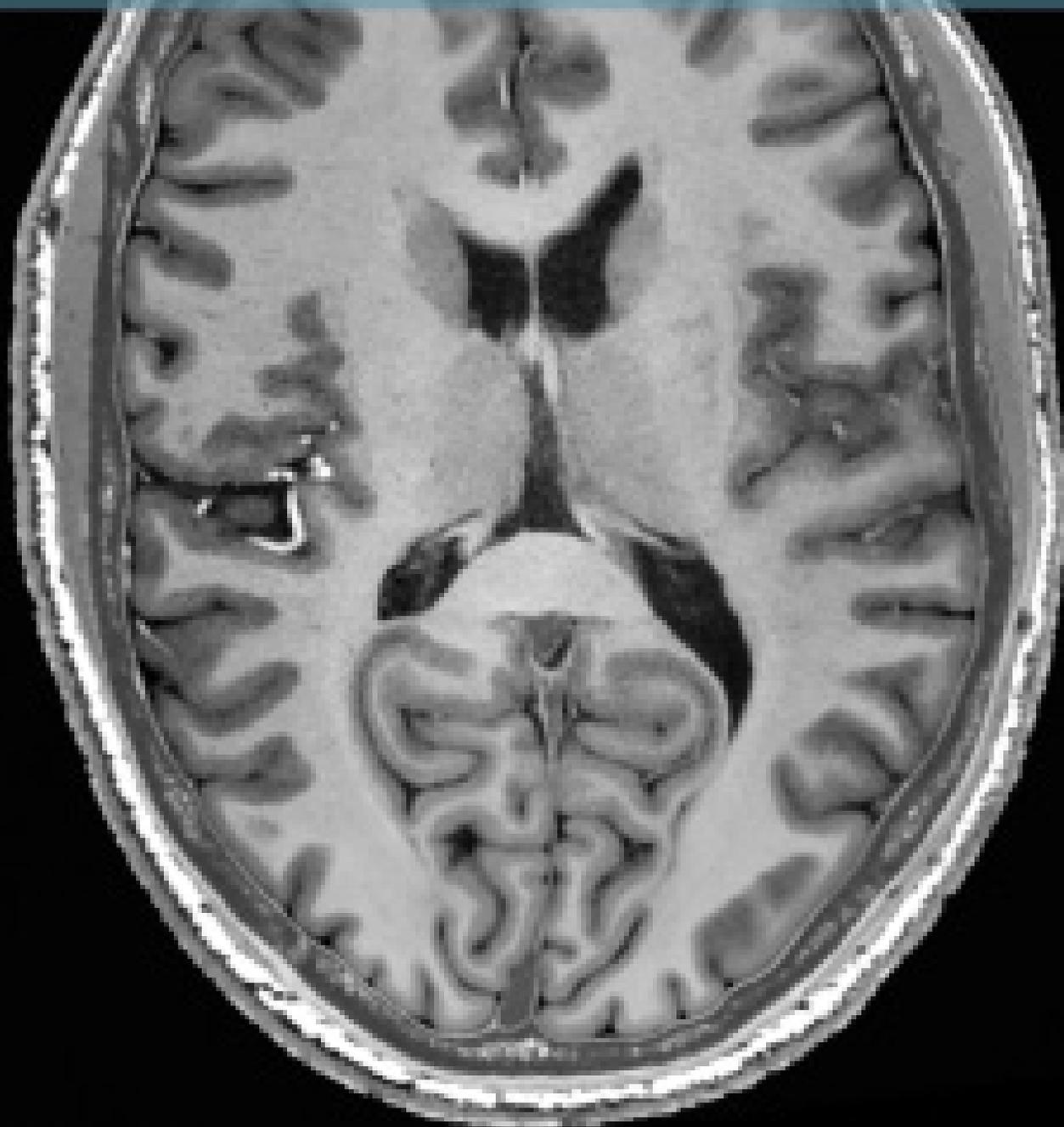
Synthesis of a Multi-Modal Molecular Imaging Probe based on a Hyperbranched Polymer Architecture

### NIF Focus Story - 3

Clarity uses a Cutting-edge Imaging Technique to guide Drug Development

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Pre-clinical Physician Training for a novel leadless Pacemaker



*Highest spatial resolution T1 weighted anatomical image of the human brain at 7 Tesla in vivo with whole brain coverage - more than 20x higher spatial resolution compared to standard 1mm protocols.  
- Dr Andrew Janke, Dr Kieran O'Brien, A/Prof. Markus Barth;  
Centre for Advanced imaging, University of Queensland.*



# DIRECTOR'S MESSAGE

*“National Imaging Facility is innovating to make research relevant to the real world, sharing capability with industry, be it multi-national or Australian start-ups.”*

Earlier this month representatives of National Research Infrastructure met together with the team from Research and Higher Education Infrastructure Branch of the Department of Education, at the NCRIS Capabilities Forum. What did we learn? The government remains committed to research and recognises that research infrastructure is an absolute requirement, if Australia is to be competitive in a global economy. How do we develop and maintain a competitive edge – Innovation!

This message is coming strongly from many directions, notably a recent speech by Australia's Chief Scientist, Prof Ian Chubb – “Science is infrastructure and it is critical to our future. We must align our scientific effort to the national interest; focus on areas of particular importance or need; and do it on a scale that will make a difference to Australia and a changing world.” And the Queensland Science Minister, Hon Ian Walker – “We're investing in science, because it has the potential to improve our quality of life”.

How does NIF contribute? Read the articles in this Quarterly Newsletter, and I am sure that you will agree with me, the NIF team is working hard at making a difference. We are opening new facilities, branching out into new areas of research, and working alongside industry to translate research into that competitive edge.

Our science needs to be transformative. Two of the big areas, currently transforming our view of the world, are personalised medicine and nanomaterials. NIF is innovating through the development of targeted drugs, bringing material scientists and biologists together.

Our science needs to be relevant. NIF is innovating to understand how their human knowledge and experience can inform computer analysis of mammograms, working with expert radiologists.

Our science needs to be “out there”. NIF is innovating to make research relevant to the real world, sharing capability with industry, be it multi-national or Australian start-ups.

Do you have an innovative idea that could use imaging to demonstrate its value? We want to work with you, to help your research make a difference.

**Professor Graham Galloway**  
Director of Operations



# NIF News

## Leading node for NIF - UQ's Centre for Advanced Imaging Officially Opened

Science Minister Ian Walker officially opened the new Centre for Advanced Imaging (CAI) at The University of Queensland's St Lucia campus, 21<sup>st</sup> August 2014.

As the leading node for the National Imaging Facility, the CAI brings together the skills of a critical mass of researchers and state-of-the-art research instruments to improve diagnostics of Alzheimer's disease, Parkinson's disease, multiple sclerosis and epilepsy, as well as joint degeneration and injury.

The University of Queensland Vice-Chancellor and President Professor Peter Høj said the flagship imaging facility was the only one of its type in Australia and one of only a handful of such centres in the world.

"The Centre has also allowed us to attract the world's best and brightest minds and bring together the skills of a critical mass of researchers to tackle problems of global significance," Professor Høj said.

"Scientists in collaboration with partners such as Siemens and Global Medical Solutions can now conceive of and conduct experiments that were previously near impossible to reach.

"This is leading to new insights into some of the key issues facing Twenty-First century healthcare, from earlier diagnosis to a clearer understanding of neurodegenerative diseases."

Since the Centre became operational in August 2013, researchers have gained significant insights into heart disease and liver disease, and CAI researchers have become leaders in brain atlas creation.

Science Minister Ian Walker said investing in research and converting it into innovative solutions was one of the top 10 priorities of The Queensland Plan: a 30-year vision for Queensland.

"We're investing in Queensland science because it has the potential to improve our quality of life," Mr Walker said.

"One example of UQ success is the electromagnetic noise compensation technology, which improves the quality of images, now used in more than 10,000 magnetic resonance imaging (MRI) systems around the world.

"The Queensland Government provided \$4.75 million towards stage one of the Centre for Advanced Imaging, which places us at the forefront of medical imaging in Australia."

The 5,500m<sup>2</sup>, \$55 million CAI building was funded by the Federal Education Investment Fund in 2010 and contains over \$50 million of imaging and spectroscopy equipment.

The CAI also hosts the largest node for National Imaging Facility, which is an Australian government initiative that connects state-of-art imaging capabilities across all mainland states in Australia.

For more information about the Centre for Advanced Imaging, please go to [www.cai.uq.edu.au](http://www.cai.uq.edu.au).

- UQ News <http://www.uq.edu.au/news/article/2014/08/uq%E2%80%99s-centre-advanced-imaging-officially-opened>



Centre for Advanced Imaging



From Left to Right: Prof. David Reutens (CAI Director), Prof. Peter Høj (UQ Vice-Chancellor and President), Hon. Ian Walker (Queensland State Minister for Science, Information Technology, Innovation and the Arts), and Mr John Story (UQ Chancellor).



CAI Opening Ceremony

Hon. Ian Walker (Queensland State Minister for Science, Information Technology, Innovation and the Arts)



## NIF News

### UQ & Siemens Collaborate to Advance MRI Technology

A collaboration agreement between The University of Queensland and Siemens Australia will boost research and development in Magnetic Resonance Imaging (MRI), leading to better diagnosis and treatment of degenerative diseases.

The agreement was signed on the 27<sup>th</sup> June 2014 by UQ Vice-Chancellor Prof. Peter Høj and Mr Toby Carrington, Vice President Finance for Siemens Healthcare in Australia and New Zealand.

“This collaboration with Siemens, a globally operating technology company and a world leader in magnetic resonance, is a perfect fit with UQ’s strength in this area, enhancing UQ’s capacity to be a global leader in imaging research.” Professor Høj said.

Professor Høj said the agreement focused specifically on research enabled by the powerful Siemens MAGNETOM 7 Tesla (7T) scanner, the first 7T whole-body MRI scanner in the Southern Hemisphere, which was installed at UQ’s Centre for Advanced Imaging this year. Funded by the Federal Government’s Education investment Fund initiative, the prestige MRI scanner is also a flagship imaging capability for the National Imaging Facility UQ node, which is located at CAI.

Mr Carrington said Siemens Australian and New Zealand was proud to be part of this strong and long-term collaborative partnership centred around high-end research technology.

“What’s really exciting about this collaboration isn’t so much the technology, but the application of this technology by Australian researchers who now have an extraordinary new weapon in their arsenal to better understand and ultimately fight diseases and their progression,” said Mr Carrington.

“One thing we realised very early on is that technology can’t reach its full potential inside a Siemens factory. To really advance human health we need partnerships like this where the best technology is combined with Australia’s brightest research minds. The new collaboration agreement is the foundation of a common goal to exploit the full potential and benefits of whole-body 7Tesla MRI. The research program will help find answers to world’s most challenging healthcare questions. By partnering with the UQ, we help define new standards-of-care in order to advance human health.”

For full article, please go to UQ News <http://www.uq.edu.au/news/article/2014/06/uq-and-siemens-collaboration-advance-mri-technology>.



Mr Toby Carrington (Siemens Healthcare in Aus and NZ) and Prof. Peter Høj (UQ Vice-Chancellor and President).

### WA Premier’s Science Awards 2014



NIF - University of Western Australia Node Director, Winthrop Professor David Sampson, was among 13 finalists who were shortlisted for the Western Australia

2014 Scientist of the Year award. Announced by WA Premier and Science Minister Colin Barnett on the 22<sup>nd</sup> July 2014, the finalists were congratulated and acknowledged for the significant role they play in building WA’s science capacity.

W/Prof. Sampson is also the Director of the Centre for Microscopy, Characterisation & Analysis (CMCA), a core facility of the University of Western Australia, and the Western Australian node of the Australian Microscopy & Microanalysis Research Facility (AMMRF). W/Prof. Sampson leads UWA’s Bioimaging Initiative aimed at increasing the uptake and quality of microscopic imaging and related technologies in medicine and the life sciences. W/Prof. Sampson’s research interests are in biomedical optical engineering, with an emphasis on photonics, imaging and microscopy. He and his team are involved in activities ranging from the invention and investigation of new optical techniques, to the engineering of these techniques into practical instruments, and their application in clinical medicine and biology. For more info about NIF-UWA node and CMCA please go to <http://www.cmca.uwa.edu.au/>.

### NIF Supporting MND #IceBucketChallenge

MND (Motor Neurone Disease), also known as ALS (Amyotrophic Lateral Sclerosis) and Lou Gehrig’s Disease, is a brain-related condition where the steady loss of brain nerve cells (neurons) results in progressive deterioration in controlling muscle movement and function. Affecting ~2,000 Australians, MND is a terminal disease and to date there is no known cure nor effective treatment. NIF is keen to raise awareness about MND and how imaging can help to research and further understand the disease. A number of NIF members have undertaken the #IceBucketChallenge, and here’s proof from NIF Director Prof. Graham Galloway! On 25<sup>th</sup> August 2014, Prof. Galloway took the challenge and doused with icy water - lucky it was sunny that day! For more info about NIF supporting MND and #IceBucketChallenge, check out NIF Twitter @NIFAus!.



NIF Director Prof. Graham, #IceBucketChallenge.

## NIF Focus Story - 1

USyd / ANSTO Node:

### Automatic Breast Density Evaluation and Modeling Visual Search Patterns of Radiologists Reading Mammograms

Breast cancer is the most common cancer worldwide (excluding non-melanoma skin cancer) and one of the leading causes of cancer-related death among women. Increased breast density, as evidenced by the presence of visually bright fibroglandular tissue on mammograms, is a strong risk factor for developing breast cancer. Currently the most common approach among radiologists for breast density assessment is the use of the Breast Imaging Reporting and Data System (BIRADS) which classifies mammograms into four categories: entirely fatty (BIRADS I), scattered fibroglandular densities (BIRADS II), heterogeneously dense (BIRADS III), and extremely dense (BIRADS IV). The main drawback of BIRADS is its subjectiveness. Although recently various quantitative algorithms have been introduced to objectively quantify breast density, none of them has been widely accepted by radiologists.

We developed iDensity, an automated algorithm inspired by the human visual system, for classification of mammograms into one of the four BIRADS density categories. Gabor filters in different scales and orientations were used to model the human visual system, and mammograms were filtered using them. A Gaussian filter was also added to the filter bank to aid in the differentiation of homogenous glandular tissue from homogenous fatty tissue. To design the Gabor filter bank, parameters were chosen using physiological evidence and an iterative optimization process was used to select appropriate values of central frequency of the filters.

Six statistical features were extracted from each filtered image. A two-stage classifier was used, where mammograms were separated in two groups, low- or high- density, at the first stage of classification. In the second stage, the low density group was subdivided into BIRADS I or II, and the high density group into BIRADS III or IV. iDensity was cross validated using 320 cases from the Digital Database for Screening Mammography (80 cases per each BIRADS category). For each case only the left medial-lateral oblique view was used. The performance of

the algorithm is shown in Figure 1. As it can be seen, iDensity achieved very good sensitivity and specificity at both levels of classification.

Currently we are working on modeling the visual search pattern of radiologists when reading mammograms, aiming to establish error patterns that may lead to missed cancer. Previous research has shown that most unreported cancers in mammograms do attract visual attention. Hence, determination of visual search and breast background characteristics that may lead to incorrect decisions may aid in the reduction in the number of missed malignancies at screening mammography.

For this purpose, we monitor the radiologists' visual inspection of digital mammograms using an eye-tracking system, as shown in Figure 2. The eye-tracker contains a camera that captures the pupil and first corneal reflections and a magnetic head tracker which keeps track of the radiologists' head movements. It has a spatial coverage of about 50 degrees horizontally and 40 degrees vertically, which allows it to properly monitor two medical grade 5 MP displays placed side-by-side with a spatial resolution of less than 1 degree of visual angle.

Currently we are analyzing eye-position recording data from 8 breast radiologists which read 120 two-view digital mammograms. We model both the peripheral vision and the high-resolution central (a.k.a. "foveal") vision of radiologists. To model foveal vision, we extract a range of texture features from each fixation point. The final goal of this study is to develop a system which analyses the breast tissue and the areas visually inspected by the radiologists and then predict the radiologists' reporting of lesions, whether correct (true cancer detections) or not (misses and false alarms). Figure 3 shows an example of a 2-view mammogram case with an outline of the breast as well as areas fixated by radiologists. In this figure we also highlight areas that attracted attention for prolonged periods of time – 1 second or longer – which are shown as the large circles. These areas mark the locations where radiologists detected a possible perturbation, investigated the location and cognitively decided whether to report the location as containing a cancer or not.

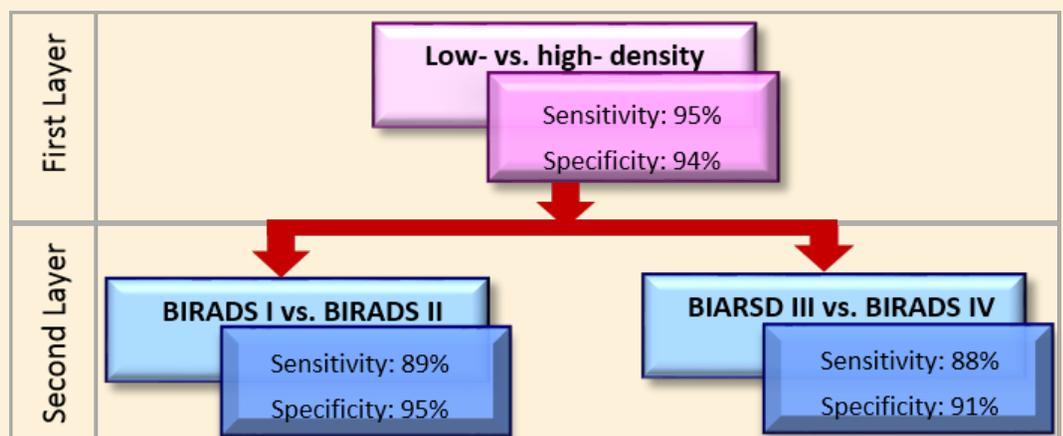


Figure 1: Performance of iDensity.



Exploring Inner Space

A downside to our studies using mammograms is their high computational cost due to large image size. Spatial resolution of digitized mammograms used in our study for automatic breast density evaluation and digital mammograms used for the eye tracking study is less than 70µm×70µm per pixel with 12-bit pixel depth. In addition, we tested a range of values for tuning Gabor filters' wavelength which further introduced a high degree of complexity to the problem. Besides, the process of leave one out cross validation and extracting various texture features for more than 30000 fixation points also added computational burden. BMRI Imaging Compute Platform helped us to carry out such heavy computations. Dr Ryder from NIF assisted us in writing PBS script for running MATLAB on clusters and provided us with informative solutions in different stages of our work whenever we encountered any problem using the clusters. Meanwhile, online wiki BMRI was a great source for finding answers to some of our questions about submitting jobs to the clusters.

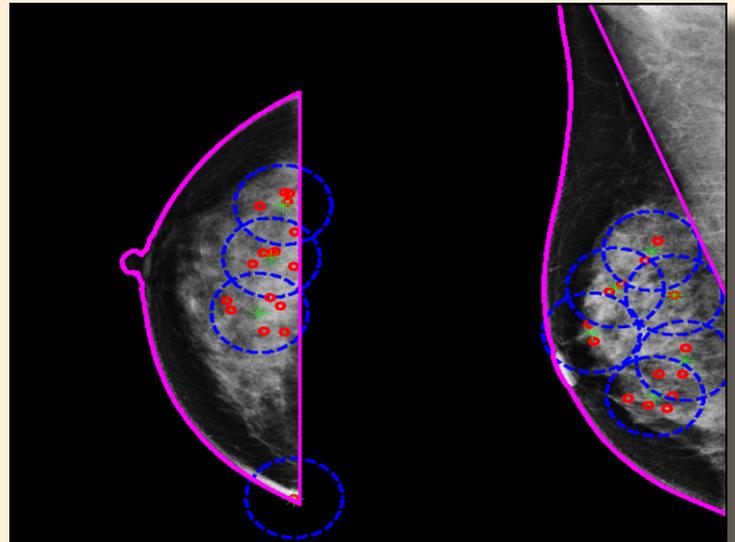


Figure 3: Two view mammogram of a breast; purple boundaries outline the skin line. Red circles are the fixation points, and green asterisks mark the center of clusters of fixations in a 2.5 visual angle neighborhood (corresponding to central vision). These clusters are depicted by dashed circles.

This work is supported by funding from the Australian Government under the Diagnostic Imaging Quality Program.

Further information about this work can be obtained by contacting Ziba Gandomkar at [ziba.gandomkar@sydney.edu.au](mailto:ziba.gandomkar@sydney.edu.au) or Associate Professor Claudia Mello-Thoms, at [claudia.mello-thoms@sydney.edu.au](mailto:claudia.mello-thoms@sydney.edu.au).

For further information on accessing the imaging facilities, current research projects and collaborative opportunities available at the NIF-University of Sydney node, please contact USyd Node Facility Fellow at [will.ryder@sydney.edu.au](mailto:will.ryder@sydney.edu.au); <http://www.anif.org.au/aboutnif/nodes/USYD-Node.html>.



Figure 2: Eye-tracking system showing radiologist reading a 2-view digital mammogram.

IMAGING AT NIF - USYD / ANSTO NODE:

Funded by the Australian federal initiative National Collaborative Research Infrastructure Strategy (NCRIS), the University of Sydney/ANSTO node is a shared facility that provides the research community with access to cyclotron based radioisotopes (<sup>18</sup>F and <sup>11</sup>C) and radiochemistry/pre-clinical imaging technologies on a collaborative basis. The NCRIS-funded research cyclotron and associated radiochemistry hotcells are housed in the ANSTO Camperdown facility adjacent to the University of Sydney Brain and Mind Research Institute (BMRI) and supported by the expertise of ANSTO cyclotron engineers and radiochemists. The pre-clinical imaging platform is located in the purpose built laboratories of the BMRI and jointly operated by ANSTO and BMRI teams with long standing expertise in molecular imaging. Dr Will Ryder is the research Facility Fellow based at the NIF USyd/ANSTO node, supporting the research user community through assistance with project design, project management, staff/student training and, where appropriate, data analysis.



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



## NIF Focus Story - 2

### UQ Node:

## Synthesis of a Multi-Modal Molecular Imaging Probe based on a Hyperbranched Polymer Architecture

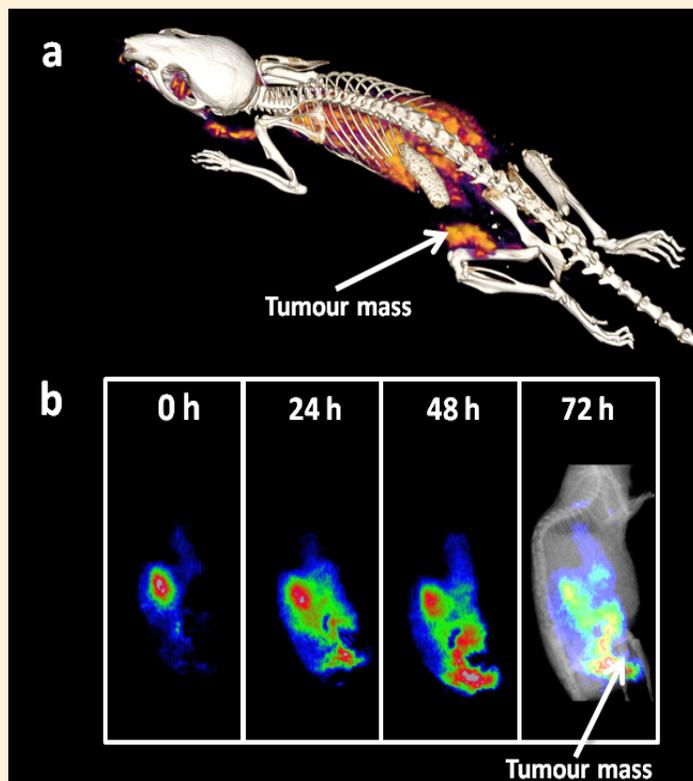
Molecular imaging is a widely utilised tool in modern medicine. It allows for the monitoring of biological processes *in vivo*, without the use of invasive techniques (such as biopsies) therefore minimising impact on the patients. The ultimate goal in the development of new molecular imaging agents is a single construct, which can diagnose a disease or identify diseased tissue, offer a prognosis and ultimately monitor disease progression during treatment.

Polymeric molecular imaging agents have received increased attention in recent years due to the inherent advantages of using macromolecules *in vivo*. The multivalent nature of polymeric materials allows for attachment of multiple imaging agents. In the case of cancer imaging, the enhanced permeation and retention (EPR) effect exhibited by nanomaterials (including polymers) can also be exploited to greatly enhance the signal-to-noise ratio of tumour tissue to background. Finally, certain polymers can impart stealth properties, avoiding or minimising recognition by the innate immune system. Polyethylene glycol (PEG) is one of the most widely studied of these materials.

One of the major limitations of molecular imaging is that there is no single imaging modality that possesses high sensitivity, high resolution and the capability for high throughput processing of subjects. Researchers from the Centre for Advanced Imaging and the Australian Institute for Bioengineering and Nanotechnology are looking to overcome this issue, by developing multimodal polymeric devices which combine the advantages of numerous imaging modalities into a single construct.

They have achieved this goal by incorporating complementary imaging probes onto a novel PEG based polymeric platform. Specifically they have utilised the complementary imaging modalities of optical imaging and positron emission tomography (PET). *In vivo* optical imaging is a commonly used pre-clinical technique due to its relatively low cost and capacity for high throughput scanning. On the other hand, PET imaging is highly sensitive, has no limitation on tissue penetration depth, and suffers from minimal background interference.

By employing pre-clinical PET/CT imaging technology available at the NIF-UQ node, they have been able to image their polymers, which have been labelled with copper-64, and injected into a mouse model for melanoma. PET/CT provides for very sensitive detection of the polymers in a live mouse, allowing for multiple imaging time points to be completed, on the one subject over time. The researchers were able to use this technique to



**Figure 1:** Mouse with a subcutaneous melanoma tumour, injected with a polymeric multimodal molecular imaging agent. a) PET/CT image 24 hours post injection, showing significant uptake in the tumour. b) 72 hour time course performed with optical imaging, showing maximum uptake in the tumour is achieved after 48 hours.

demonstrate that their polymeric materials accumulate in the tumour tissue (Figure 1). They have also combined PET/CT with *in vivo* optical imaging, demonstrating the capability of these materials for multimodal molecular imaging. Using this modality they have been able to rapidly screen new generations of nanomaterials and to also image over longer time periods than what is capable with PET/CT. Both of these results make these materials promising candidates for imaging agents for cancer, able to detect and visualise diseased tissues. This could aid greatly in the treatment and surgical resection of tumours in patients.

Beyond showing uptake into tumours, the researchers have also been able to use PET/CT to measure the biodistribution and clearance of these materials, to begin to understand some of the complex pharmacokinetic properties often observed for nanomaterials (Figure 2). They produced two different sized polymer systems; a small polymer (~5 nm) which should undergo clearance through the kidneys and a larger polymer (~11 nm), which should be too large to be filtered by the kidneys. The researchers injected these materials, labelled with copper-64, into two healthy mice, and followed the biodistribution in each mouse over time. What they were able to show is that the smaller material shows a larger and much more rapid clearance from the body, over the course of the experiment, in comparison to the larger material (Figure 3). The larger material is retained

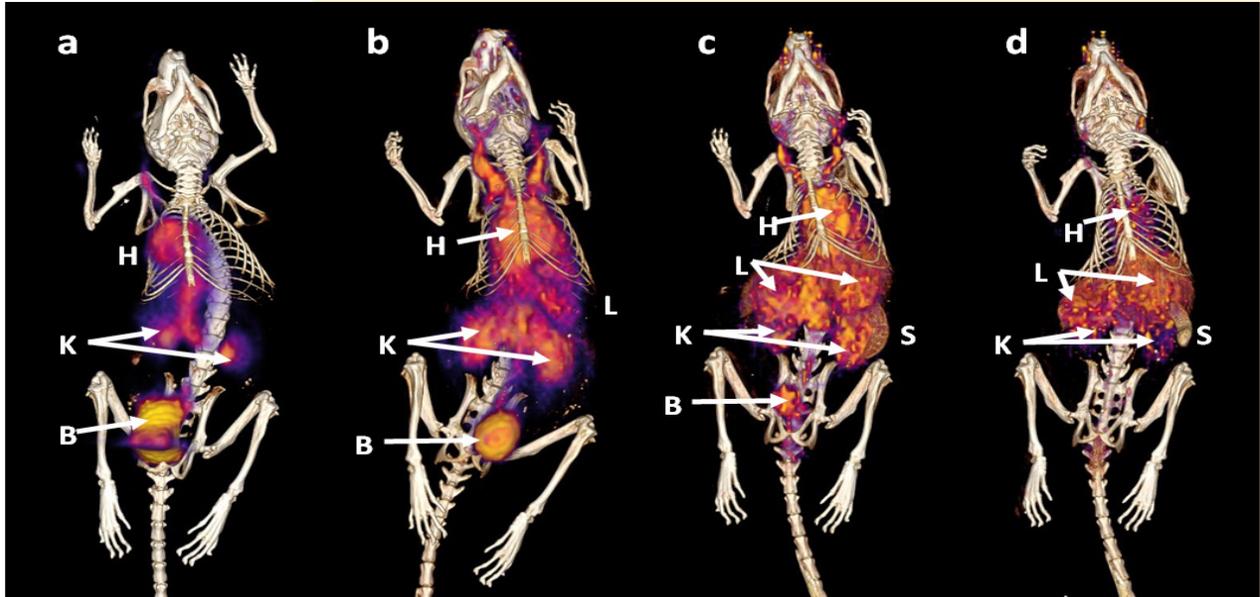


Figure 2: Healthy mouse injected with <sup>64</sup>Cu-labelled polymer. PET/CT images at a) 1 hr b) 5 hrs c) 21 hrs and d) 45 hrs. (H: heart, K: kidney, L: liver, B: bladder, S: spleen)

within the mouse, circulating for much longer and eventually being cleared through the liver and gut. By simply changing the size of these nanomaterials, it is possible to drastically change their biological behaviour.

This is an important result, as different diseases and therapies will require the nanomaterials to behave differently in the body. It is important to be able to understand the fundamental relationships between the physicochemical properties of the materials and their biological behaviour. The researchers are currently looking at more complex material properties, and by continuing to use the imaging

techniques available at NIF, they hope to better measure how these properties affect uptake into different organs and tissues and even measure the distribution across specific tissue type, such as a tumour. This information will prove critical in providing for more rapid and efficient development of the next generation of nanomedicines, based on polymeric materials.

For more details about the project please contact Dr Kristofer Thurecht at [k.thurecht@uq.edu.au](mailto:k.thurecht@uq.edu.au) or Mr Nathan Boase at [nathan.boase@uqconnect.edu.au](mailto:nathan.boase@uqconnect.edu.au).

For more details about the PET/CT imaging component and access to imaging facilities at NIF-UQ node, please contact Dr Karine Mardon at [k.mardon@uq.edu.au](mailto:k.mardon@uq.edu.au), or <http://www.anif.org.au/aboutnif/nodes/UQ-Node.html>.

Reference

Boase, Nathan R. B., Blakey, Idriss, Rolfe, Barbara E., Mardon, Karine and Thurecht, Kristofer J. (2014) Synthesis of a multimodal molecular imaging probe based on a hyperbranched polymer architecture. *Polymer Chemistry*, 5 15: 4450-4458.

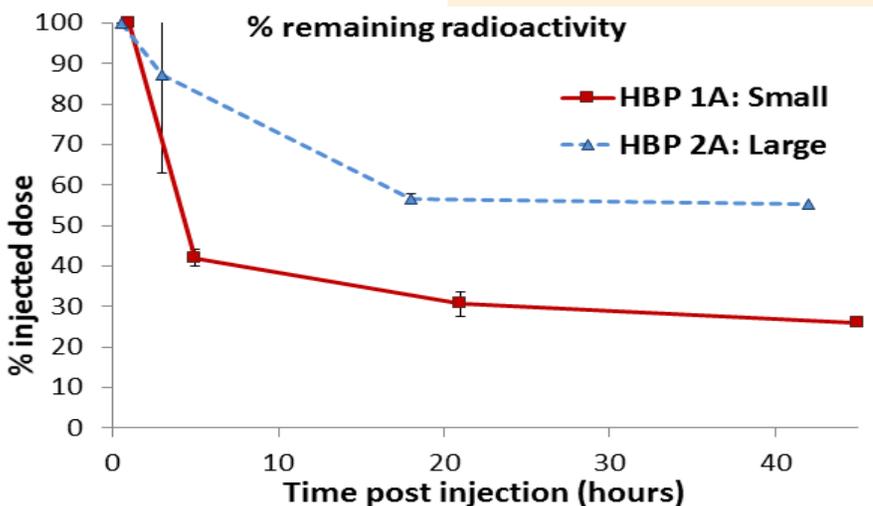
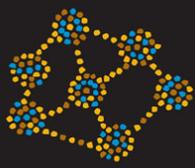


Figure 3: Comparison of the total remaining radioactivity in mice, of a small polymer and a large polymer, labelled with copper-64, over time.



## NIF Focus Story - 3

### Industry Engagement:

## Clarity uses a Cutting-edge Imaging Technique to guide Drug Development

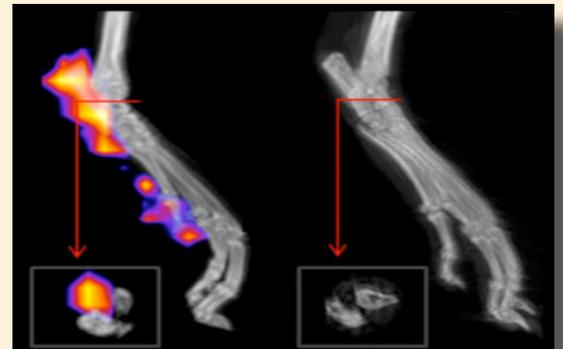
**Clarity Pharmaceuticals** was founded in 2010 with the goal of providing PET imaging services to biopharmaceutical companies that lack the expertise, infrastructure or time to carry out these studies on their own. By collaborating with National Imaging Facility nodes and using technology licensed from the Australian Nuclear Science and Technology Organisation (ANSTO) and the University of Melbourne, the private company offers a full range of preclinical and clinical imaging services in the areas of oncology, inflammation and cardiovascular disease.

“Imaging of new drugs is becoming increasingly important in drug development as regulatory bodies require an increasing amount of data on drug localisation, accumulation and clearance,” said Matt Harris, Clarity’s co-founder and managing director. “We believe that the imaging data we provide can supplement traditional studies and add significant value to any preclinical drug development program.”

**Imaging informs decisions** - Clarity specialises in biopharmaceutical drugs such as antibodies, antibody fragments, scaffolds and peptides, and optimises radiolabeling for each product. The Company ensures that radiolabeling does not alter the biological molecule’s activity, adjusts the amount of radioisotope depending on the signal strength needed and selects from an array of PET radioisotopes and proprietary chelators based on the time course of drug activity. The range of radioisotopes allows PET imaging to visualise a biological molecule in action from ten minutes to a full week after it enters the body (Figure 1).

The Company uses an outsourced business model and therefore has a dependence upon its service providers. Clarity utilises the expertise at the Centre for Advanced Imaging (UQ), the Peter MacCallum Cancer Centre (PeterMac), the University of Melbourne, the Baker IDI Heart and Diabetes Institute, Sir Charles Gardiner Hospital and international groups in Singapore and the USA. Within the Company there is experimental design, radiochemistry and project management expertise. The Company is trying to maximise its probability of success through leveraging the expertise of each group, and takes a collaborative and communicative approach to each project and commercial relationship. The benefit to the academic groups are that these are industry relevant projects, that there are often publication rights worked into the projects and the possibility of larger follow-on contracts if the initial projects are successful.

Clarity is about to embark on its first human clinical trial at the PeterMac with Prof. Rod Hicks which will be closely followed by two more trials. Taking advantage of Australia’s favourable regulatory environment, the Company will be offering Phase 0 first-in-human PET imaging studies that provide



**Figure 1:** Rheumatoid arthritis targeting. using PET/CT, views of a mouse model’s foot and ankle confirm the targeting of a promising biopharmaceutical to arthritis (L) compared to a control (R).

information about the targeting, accumulation, and clearance of a biological molecule. Phase 0 (microdosing) studies are designed to determine a drug candidate’s mechanism of action, confirm that the biological molecule targets the disease site or compare drug candidates. A phase 0 trial can also determine whether a radiolabeled version of a therapeutic product would be useful for selecting the most responsive patients and monitoring patients’ responses to treatment during clinical development.

**Companion diagnostic** - Clarity’s technology for attaching a radioisotope to peptides and antibodies also has important implications for diagnostics. Currently, diagnostic imaging of these longer-lived products is limited because of the short half-life of commonly used PET isotopes. To overcome this obstacle, Clarity uses longer lived isotopes such as copper-64 and zirconium-89, whose longer half-life makes them ideal for diagnostic PET imaging of biological molecules.

This approach can also be used to monitor the spread of disease, make personalised dosing estimates, monitor responses to treatment and determine whether a patient is disease free after treatment.

Beyond diagnostics, Clarity’s technology can generate targeted therapeutics by delivering high-energy radioisotopes to disease sites for localised radiotherapy. To develop its therapeutic drug pipeline, Clarity is sourcing and developing biological molecules such as peptides and antibodies. Currently, Clarity is seeking partnerships and licensing opportunities with Universities, Research Institutes and biopharmaceutical companies that have promising drug candidates in the areas of oncology, inflammation, cardiovascular disease and paediatrics. Clarity is fast working towards being Australia’s pre-eminent radiopharmaceutical development company that is able to bridge the gap between academic research, clinical translation and industry.

*Article sourced in part from Nature Biotechnology, Biopharm Dealmakers Sept 2014.*

### CONTACT DETAILS

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# NIF Focus Story - 4

## LARIF Node:

### Pre-clinical Physician Training for a Novel Leadless Pacemaker

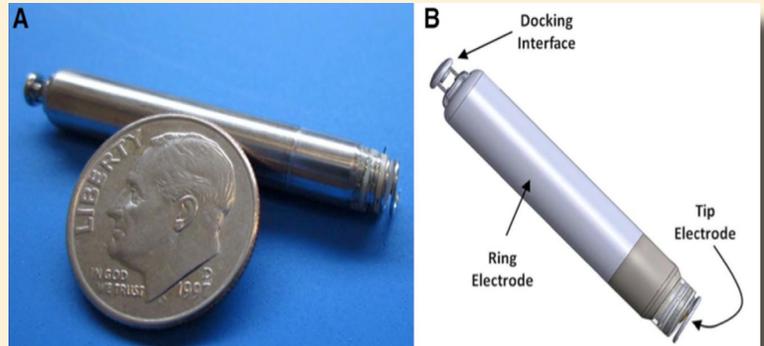
Cardiac pacemaker technology has improved significantly over the last few decades. More recent advance is the development of a leadless pacemaker, Nanostim, manufactured by St. Jude Medical (Figure 1 – Reddy VY *et al*, Circulation 2014).

The novel leadless pacemaker system (Figure 2 – right) has been developed to eliminate the need for pacing leads, pacemaker pockets and connectors required by conventional pacemakers (Figure 2 – left), thereby eliminating the associated complications such as lead failure and device pocket infection. This technology has potential to improve patient comfort and quality of life.

This device has been implanted overseas with good initial results. Currently, a large multi-national trial program (LEADLESS II; U.S., Canada, Australia, and Europe) is underway to further evaluate the performance of this novel product, of which several Australian centres are involved. Given that the technology is novel, training of implanting physician is crucial and this is best done in a pre-clinical setting such as the Large Animal Research and Imaging Facility (LARIF).

#### Pre-clinical Training:

Initial training of 3 physician investigators from 2 different states (including Professor Sanders and Dr Lau from South Australia) was successfully conducted at the LARIF facility based at Gilles Plains, Adelaide, South Australia on the 6th August 2014. In an anesthetised adult sheep, investigators were able to access the right ventricle apex via the right



**Figure 1.** Leadless pacemaker - Nanostim. <http://www.sjm.com/leadlesspacing/intl/options/leadless-pacing>

femoral vein using the Phillips flat- detector C-arm fluoroscopy. The investigators were able to familiarise the procedures for delivering, fixing, maneuvering and retrieving the leadless pacemaker device in the sheep heart.

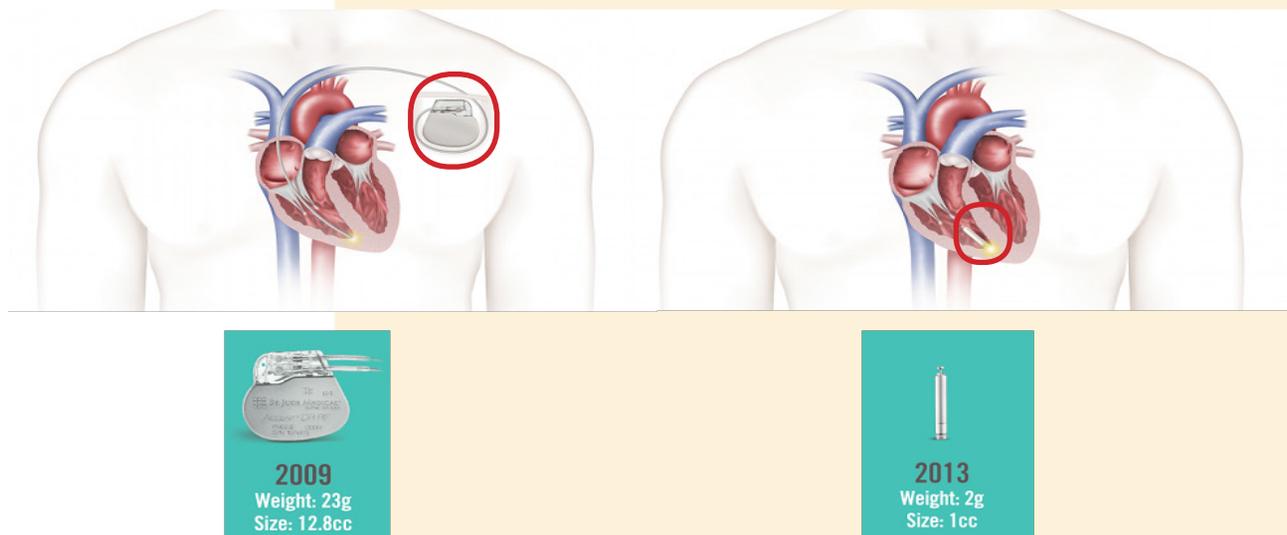
This training was followed by the first successful cases of leadless pacemaker implants in Australia in 2 patients on the following day by Professor Sanders and Dr Lau at The Royal Adelaide Hospital.

[https://www.youtube.com/watch?v=nklybkr4x1k&index=1&list=UUhAumjy26uts\\_hvywCSdgvQ](https://www.youtube.com/watch?v=nklybkr4x1k&index=1&list=UUhAumjy26uts_hvywCSdgvQ)

#### Research Team:

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



**Figure 2.** Schematic comparing traditional pacemaker and Nanostim. Using the novel Nanostim device, all leads and battery are internal to the device. The device is inserted and attached to the right ventricle of the heart.



[www.anif.org.au](http://www.anif.org.au)

**NIF Nodes:**

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