

ACRF IMAGE **X** INSTITUTE

AUSTRALIAN
CANCER
RESEARCH
FOUNDATION 



THE UNIVERSITY OF
SYDNEY

ANNUAL REPORT **2021**



Pictured: The Seimens ARTIS Pheno, funded by the ACRF.



THE ACRF IMAGE X INSTITUTE MISSION IS TO CREATE, SHARE AND APPLY SCIENTIFIC KNOWLEDGE TO IMPROVE HUMAN HEALTH.

WITHIN OUR MISSION, WE AIM TO
REVOLUTIONISE MEDICAL IMAGING
PIONEER FUNCTIONALLY TARGETED RADIOTHERAPY
ENABLE GLOBAL ACCESS TO CANCER RADIOTHERAPY

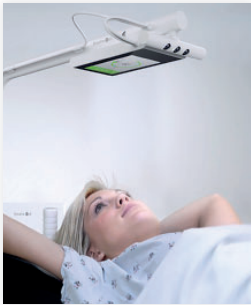


2

New **patent**
applications

24

papers
published



5

Clinical
trials active

8

New **records**
of invention

\$2.5M+

grants awarded in 2021

SNAPSHOT 2021

55

Patients
participated in
clinical trials

52

Conference
presentations and
invited talks given

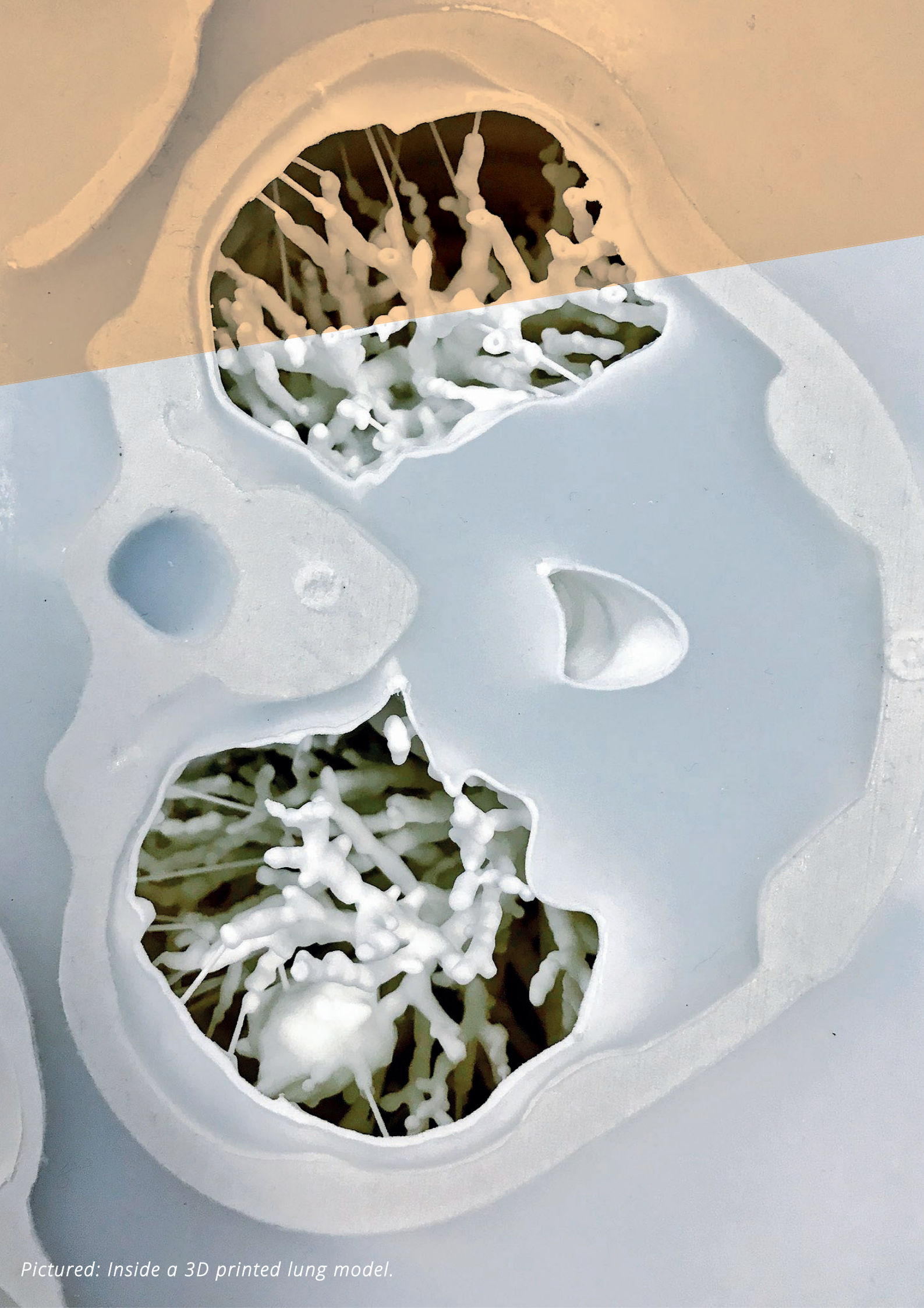
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License
agreements
& assignments signed

6

New **clinical studies**
approved for 2022





Pictured: Inside a 3D printed lung model.

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Director's Message

The resilience of the ACRF Image X Institute was again tested in 2021. Despite the pandemic limiting critical clinical trial activity, laboratory work and in-person engagement, the Image X team produced numerous successful scientific, clinical and translational achievements that will have an impact on the lives of cancer patients in the short, medium and longer term. In the last year of funding of the ACRF, we want to particularly acknowledge the central role they have had in the success of Image X.

The ACRF awarded funding in 2015 to establish the ACRF Image X institute and to support three key pieces of infrastructure; the robotic C-arm imaging system at the Charles Perkins Centre, the MRI-Linac prototype at Ingham Institute of Applied Medical

Research and the Nano-X compact radiotherapy system at the Nelune Comprehensive Cancer Centre. In this final year of the agreement, it is pleasing to see the investment bear such substantial returns. Both prototype radiotherapy systems have been commissioned and have open clinical patient studies. The robotic C-arm is part of the state-of-the-art interventional suite in the Hybrid Theatre.

One of the rewards of developing unique infrastructure is the opportunity for creativity and innovation, particularly for our early career researchers. Dr Tess Reynolds has partnered with Siemens Healthcare to gain exclusive access to the control system of the robotic C-arm imaging system. She developed Adaptive CaRdiac cOne BEAm computed Tomography (ACROBREAT), a new technology that enables imaging and treatment hardware to beat in sync with the patient, delivering clearer, faster, and safer medical images. She was named a top-3 finalist for the 2021

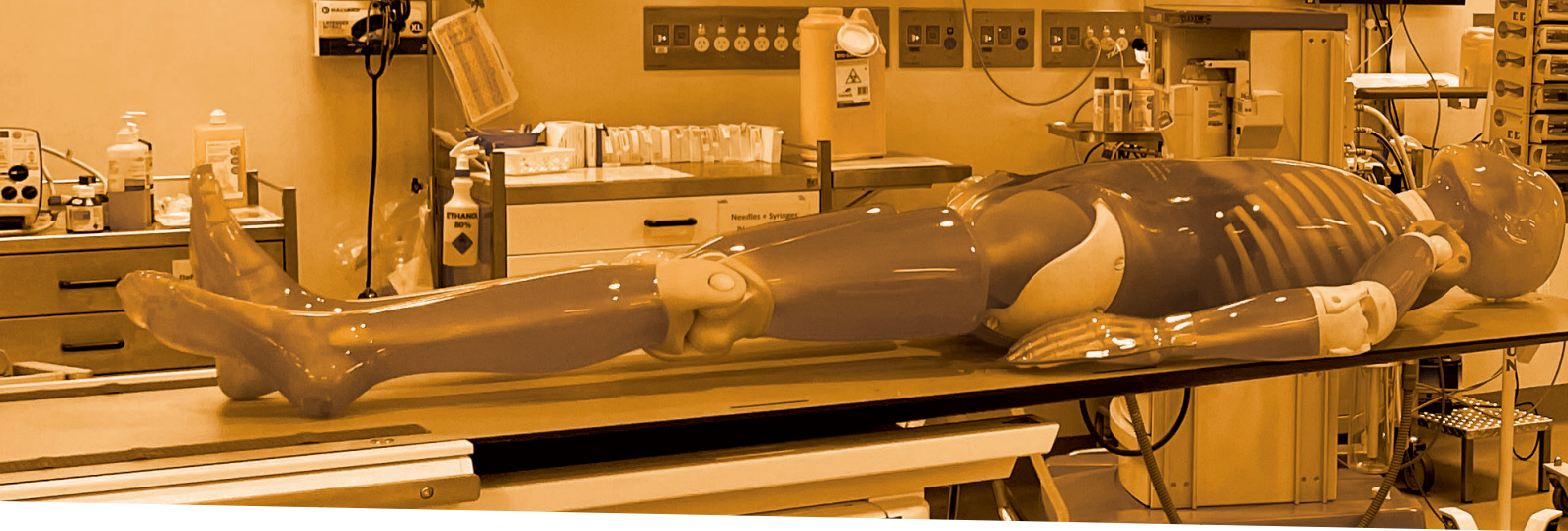
Australian Museum Eureka Prize for Outstanding Early Career Researcher for this work. Her methods to improve spinal surgery received an Early Career Researcher award at the largest international medical physics conference and she will extend this work to derisk surgery for cancer patients with spinal metastases in her Cancer Institute Early Career Fellowship. Outstanding research and access to the MRI-Linac prototype, has also resulted in the previous awards of Early Career Fellowships for Drs Paul Liu, David Waddington and Brendan Whelan.

Other benefits this infrastructure has produced include research grants, industry agreements, intellectual property and publications. It has strengthened the collaborative networks between the University of Sydney, MRI-Linac program consortium and the Nelune Comprehensive Cancer Centre. Finally, the establishment and growth of ACRF Image X Institute has led to increased productivity, funding and institutional support. It has been impressive to see our team navigate the challenges of 2021, maintaining their dedication and productivity, with over fifty people participating in our clinical studies and more records of invention submitted than any previous year.

I would like to thank our supporters including the ACRF and other funders, University of Sydney leadership and professional teams, collaborators, consumers and study participants. I would particularly like to acknowledge Professor Ricky O'Brien, Deputy Director, whose important contributions have underpinned the successes of the institute. We wish him well on establishing his new research group at RMIT and look forward to continuing our collaborations.

A handwritten signature in blue ink, appearing to read 'P. Keall', is positioned above the printed name.

Prof Paul Keall



Research Themes 2021

Our research streams fall under three main themes which make up the major components of radiation therapy: seeing the cancer (Medical Imaging), hitting the cancer with radiation (Cancer Targeting) and developing new systems and applications for radiotherapy delivery (Novel Radiation Therapy Systems and Applications)

MEDICAL IMAGING

● THE PATIENT CONNECTED IMAGING PROGRAM

Using physiological signals to achieve clearer images for more accurate treatment planning.

● CT IMAGING

Improving CT image quality by pausing the process in response to the patient's breathing variations.

● CBCT IMAGING

Improving imaging quality by adapting CBCT image acquisition to account for the

● CARDIAC & RESPIRATORY COMBINED GUIDANCE

Imaging technology that operates in sync with the patient's cardiac and respiratory cycles to give clearer images in less time.

● SAVING HEALTHY LUNG TISSUE

Sparing healthy lung tissue from radiation using CT imaging technology that highlights healthy lung tissue

● INTERVENTIONAL IMAGING

Harnessing the full flexibility of robotic imaging systems to increase surgical accuracy and possibilities.



CANCER TARGETING

- **REAL-TIME TUMOUR TRACKING**
Technologies that track moving tumours using a standard linac.
- **BEAM ADAPTATION**
Adapting the treatment beam aperture to target the tumour in real-time
- **SURFACE IMAGING**
Patient guidance and monitoring to improve treatment accuracy and reduce side effects.
- **BIOFEEDBACK**
Monitoring the patient's movement, and using this data to guide the patient's breath and positioning during treatment.
- **REMOVE THE MASK**
Detecting & guiding patient motion, to allow us to "remove the mask" from head & neck cancer radiotherapy.

NOVEL RADIATION THERAPY SYSTEMS AND APPLICATIONS

- **THE AUSTRALIAN MRI-LINAC PROGRAM**
Seeing cancer in real-time during treatment.
- **NANO-X**
Accessible radiation therapy through novel system design & engineering.
- **CARDIAC RADIOABLATION**
Mapping and irradiating small areas of the beating heart, to facilitate cutting edge life-saving procedures.

Pictured: An anatomical phantom receiving a CT scan.

The Patient Connected Imaging Program

Program Overview

The Patient Connected Imaging Program is a suite of projects which use the patient's respiratory or cardiac signals to improve the images we can achieve across different imaging techniques.

By connecting the patient's physiological signals to imaging acquisition, we can ensure clearer images, lower imaging dose and faster acquisition.

Highlights of 2021

CT IMAGING

4DCT acquires multiple CT images over time but currently does not account for changes to a patient's breathing during imaging. This leads to errors in the resulting image. These errors can propagate throughout the radiotherapy treatment process.

Respiratory Adaptive Computer Tomography (REACT) aims to reduce these imaging errors, by accounting for changes to a patient's breathing and gating (halting) the CT beam automatically during the imaging process. In 2021, we received ethics approval to conduct a pilot feasibility study to determine the incidence of imaging artifacts with REACT in comparison to conventional 4DCT.

Natasha Morton demonstrated the benefit of accounting for both respiratory and cardiac motion with a digital phantom study. Elshin Mathias and Natasha Morton extended REACT to reduce artifacts in the helical mode of 4DCT imaging which led to an oral presentation in American Association of Physicists in Medicine 2021 conference.

Researchers

Elshin Mathias

Ricky O'Brien

Joseph Prinable

Tess Reynolds

Students

Natasha Morton

Pictured: Dr Tess Reynolds, Dr Owen Dillon and a former summer student set up for an experiment.



CBCT (Cone-Beam) IMAGING

Adaptive CT for Personalised Thoracic Imaging (ADAPT) connects the x-ray imaging system attached to standard radiotherapy systems to patient respiration, monitored in real time with an external depth-sensing camera. By coordinating the imaging hardware with patient respiration, a smaller number of x-ray images can be taken that still capture the patient anatomy and motion.

In the 30 patient ADAPT clinical trial, we have found that our adaptive acquisition and motion compensated reconstruction

method allow clearer imaging from 65% faster and 85% lower dose scans. *The first-in-human implementation of adaptive 4D cone beam CT for lung cancer radiotherapy: 4DCBCT in less time with less dose* was published in Radiotherapy and Oncology. PhD student Benjamin Lau used the imaging data acquired in the ADAPT trial to compare image reconstruction methods and find the optimal approach for motion-compensated reconstructions in *Reducing 4DCBCT scan time and dose through motion compensated acquisition and reconstruction*.

Researchers

Samuel Blake

Owen Dillon

Michelle Dunbar

Ricky O'Brien

Tess Reynolds

Students

Benjamin Lau

Farhan Ameen

Xiaoyuan Liang

Associated Studies

ADAPT

the ADaptive CT for Personalised Thoracic imaging trial completed recruitment of 30 lung cancer patients for adapting image acquisition to patient respiration.

REACT

Respiratory Adaptive Computer Tomography received ethics approval in a pilot study on 30 cancer patients to gate image acquisition when breathing becomes irregular.

CARDIAC & RESPIRATORY COMBINED GUIDANCE

Adaptive CaRdiac cOne BEAm computed Tomography (ACROBEAT) is a volumetric imaging protocol that connects patients with hardware, allowing the patient's physiological signals to personalise the image acquisition. Potential applications for this technology include pre-treatment patient alignment imaging for cancer radiotherapy and cardiac radioablation, as well as image guidance and surgical verification during cardiology and neurology procedures. In 2021, ACROBEAT was implemented on a clinical robotic imager for the first time, enabling 40% improvement in image quality with a 90% reduction

in imaging dose compared to current imaging techniques. This work was published in *Adaptive CaRdiac cOne BEAm computed Tomography (ACROBEAT): Developing the next generation of cardiac cone beam CT imaging*. Dr Tess Reynolds was invited to host and speak in a Symposium at the 2021 American Association of Physicists in Medicine Annual Meeting, named a 2021 Eureka Prize Finalist in the Outstanding Early Career Researcher category and was the runner up for the NSW Cardiovascular Research Network's HEART Pitch for inventing and leading the development of ACROBEAT from concept to implementation.

Researchers

Michelle Dunbar

Elshin Mathias

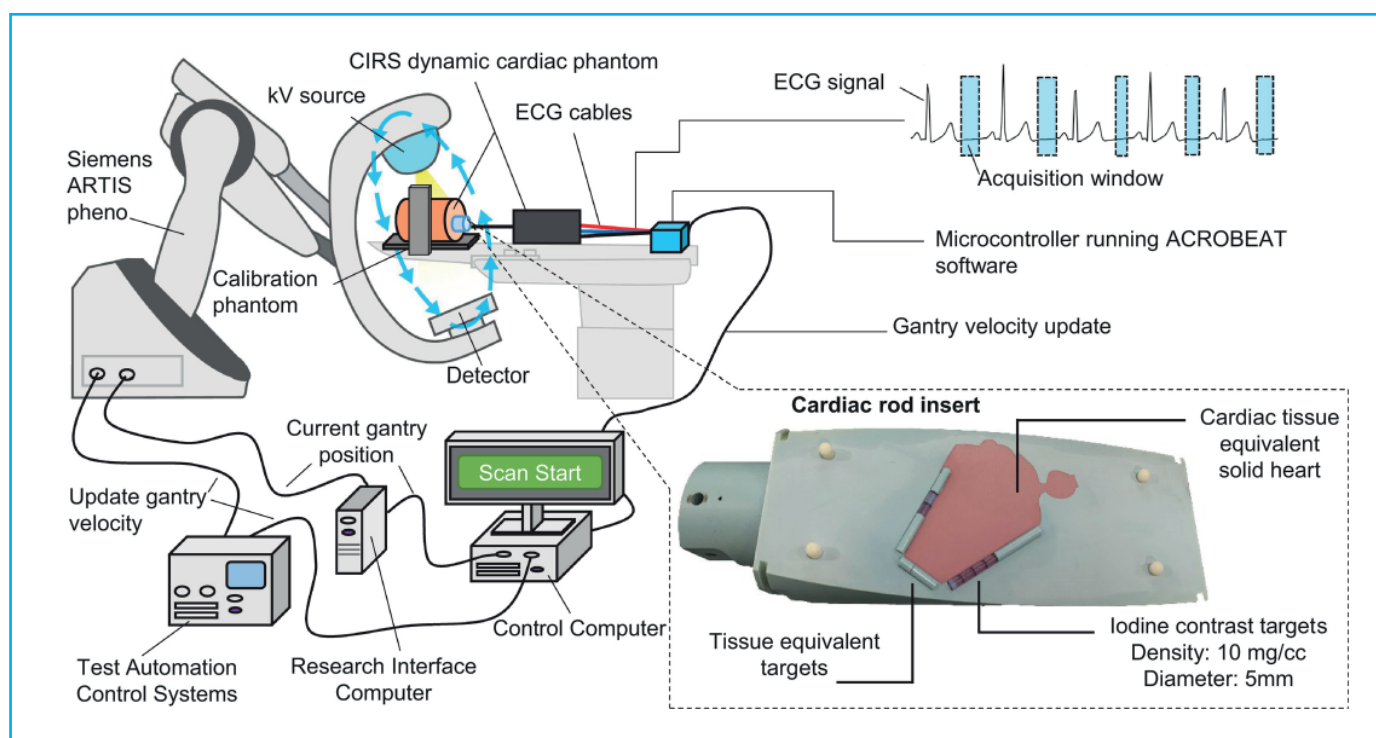
Ricky O'Brien

Joseph Prinable

Tess Reynolds

Students

Irena Janevska-Pejoska



Pictured: Experimental setup for undertaking cardiac imaging with ACROBEAT

Interventional Imaging

Project Overview

Improving intraoperative imaging and developing novel 3D-printed solutions are key pathways towards safer surgical procedures. We use the state-of-the-art Hybrid Theatre to develop new imaging technologies in the interventional suite. A centrepiece

of the theatre is the ACRF-funded Siemens ARTIS pheno robotic C-arm imaging system. Our partnership with Siemens Healthcare provides unique access to its control system to implement new imaging methods. Current research aims to extend

the field-of view for intraoperative imaging and reduce metal artifacts from surgical hardware. In addition, the robotic imager is being investigated as a low-dose and low-cost alternative to CT scanners for producing 3D printed surgical guides.

Highlights of 2021

In partnership with Siemens Healthcare (Germany) and Johns Hopkins University (USA), Dr Tess Reynolds developed a novel imaging technique that extends the intraoperative imaging field-of-view by over 370%, allowing long anatomical sites, such as the spine, to be visualised in a single 3D image intraoperatively for the first time. She received the 2021 Jack Fowler Early Career Investigator Award from the American Association of Physicists in Medicine (AAPM) for this work. The technique was successfully tested for surgical verification during procedures on an ovine cadaver. Metal hardware, commonly used in fixation and fusion procedures, interferes with current imaging techniques. With Johns Hopkins University, we performed the first implementation of imaging techniques optimised to avoid metal hardware on a clinical robotic imager. This work was also recognised by the AAPM, receiving the John R. Cameron Early Career Award.

Partnering with Dr Andrew Kanawati (Westmead Hospital), Dr Reynolds is using the robotic imager as a low-cost and low-dose alternative to CT scanners, to develop 3D-printed surgical guides. Surgical guides reduce the risk of errors during surgical procedures, alleviating the reliance on experience and intraoperative imaging.



Pictured: 3D printed spine parts, and helical screws

Researchers

Owen Dillon

Ricky O'Brien

Tess Reynolds

CT Ventilation Imaging

Project Overview

CT Ventilation is a software technique for spatially mapping the function in patients' lungs. Using CT images from the radiotherapy planning process, 3D maps can be produced identifying which parts of the lung are functioning well or poorly.

Radiotherapy is recommended for 77% of lung cancer patients. However, up to 18% of lung cancer patients experience severe radiation pneumonitis following treatment.

Taking lung function into account during radiotherapy planning

can allow clinicians to spare high functioning lung and reduce radiation side effects for patients.

We are working towards a clinical implementation of this technology to gather the evidence needed to support uptake of this technology in hospitals.

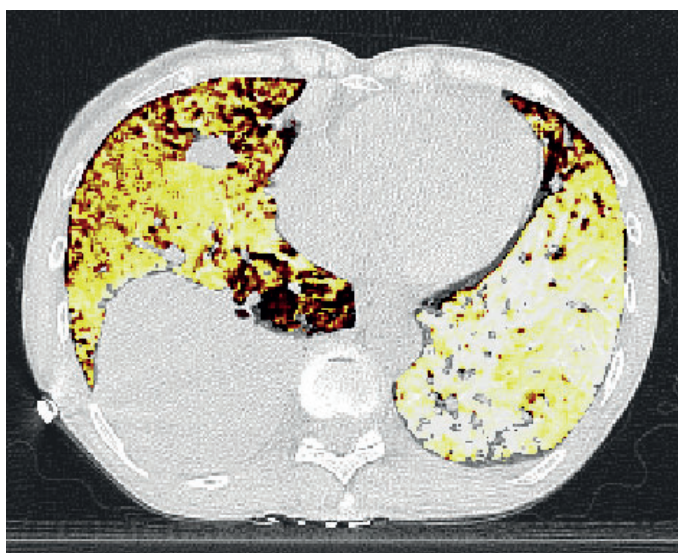
Highlights of 2021

The major achievement for the CT Ventilation team was the award of \$1M funding through the NHMRC Development Grant scheme.

Led by Professor Ricky O'Brien, the grant funds a multi-disciplinary team of Image X researchers, hospital clinicians and an industry partner. Planned work will investigate the clinical application and readiness of the CT Ventilation Imaging technology and extensions outside radiotherapy.

Building on the same industry collaboration, we also celebrate the 2022 award of a REDI fellowship from MTPConnect supporting Dr Hilary Byrne to work closely with our industry partner over the coming year.

James Grover carried out a project in fulfilment of his Master of Medical Physics degree, developing machine learning to directly predict ventilation maps from CT images. This resulted in a publication submitted to the leading journal Medical Physics. James presented his research at the MedPhys21 conference. Dr Byrne also presented at EPSM 2021 on CT ventilation applied to high-quality daily CT images obtained in the recent ADAPT trial. She was invited to speak on CT Ventilation to the imaging registration special interest group.



Pictured: CT Ventilation Imaging shows the healthy tissue (lighter) and the less healthy tissue (darker).

Researchers

Hilary Byrne

Owen Dillon

Paul Keall

Ricky O'Brien

Tess Reynolds

Students

James Grover

Jeremy Lim

Kilovoltage Intrafraction Monitoring

Project Overview

During a radiotherapy treatment or fraction, tumours in the prostate, liver, lung and pancreas can move up to a few centimetres from the planned treatment position. If the precise position of a tumour is not known, the radiation beam may not accurately hit the tumour and may radiate nearby healthy

tissues, potentially impacting treatment outcomes.

Kilovoltage intrafraction monitoring (KIM) is a novel intrafraction real-time tumour tracking modality that can detect the translational and rotational motion of the tumour with sub-millimetre and sub-degree

accuracy and guide the treatment team to correct for significant motion by shifting the radiation beam or the treatment couch. KIM is a software solution and can be easily integrated with any standard linear accelerator, making it accessible to all cancer patients.

Highlights of 2021

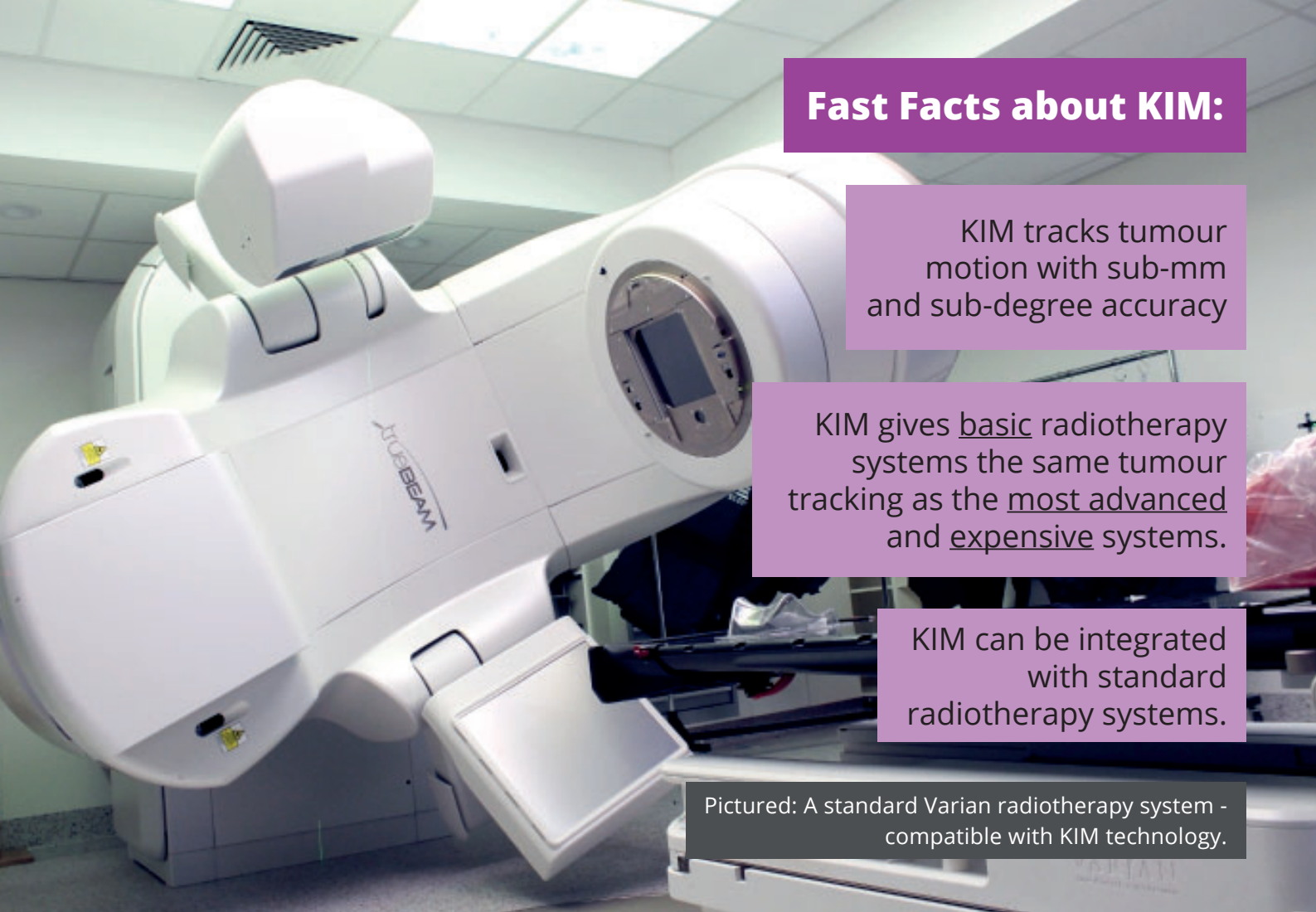
KIM technology has expanded rapidly in the last year. It has been used to treat 15 liver cancer patients and 5 prostate cancer patients in the TROG 17.03 LARK trial and the TROG 18.01 NINJA trial respectively and offline, to assess the feasibility of using KIM for pancreatic cancer patients in the SPAN-C trial.

In the LARK trial, KIM was implemented on systems from the two major radiotherapy system manufacturers, Varian and Elekta. KIM-guidance significantly improved geometric and dosimetric outcomes as compared to standard of care treatment. These preliminary results were presented at EPSM 2021 with Dr Chandrima Sengupta awarded 'Best Radiation Oncology Oral Presentation'. The protocol for the trial was published in the BMC Cancer journal. Our focus has also been on adapting to motion of multiple independent targets and the concept was demonstrated in a simulation study then evaluated in an experimental study published in the Medical Physics and Radiotherapy & Oncology journals with PhD student Emily Hewson as first author.

Supported by a Cancer Australia grant commencing in 2022, we will extend KIM to other tumour sites such as spine, treat multiple targets such as prostate and lymph nodes to fully account for the differential motion of these targets and use smaller markers to reduce risk of marker implantation and toxicity, ultimately moving towards marker-less approaches. The Image X Team thanks A/Prof Jeremy Booth and Dr Maegan Gargett for lending their valuable input and expertise during implementation of KIM in the clinic.



Pictured: Paul, Chandrima, Trang and the Westmead Hospital team oversee the first patient's treatment in the LARK Trial.



Fast Facts about KIM:

KIM tracks tumour motion with sub-mm and sub-degree accuracy

KIM gives basic radiotherapy systems the same tumour tracking as the most advanced and expensive systems.

KIM can be integrated with standard radiotherapy systems.

Pictured: A standard Varian radiotherapy system - compatible with KIM technology.

Associated Studies

LARK

The Liver Ablative Radiotherapy utilising KIM trial aims to quantify the cancer targeting accuracy and dosimetric accuracy achieved during liver SBRT with KIM guidance for 46 liver cancer patients.

NINJA

The Novel Integration of New prostate radiation therapy schedules with adjuvant Androgen deprivation trial is comparing two emerging SBRT regimens for efficacy with technical substudies.

ROCK RT

Radio-opaque contrast agents for liver cancer targeting with KIM during radiation therapy is a non-interventional feasibility study of 50 participants who are receiving or have received RT for liver cancer.

SPAN-C

The Stereotactic Body Radiotherapy for high-risk Pancreatic cancer study collects data from pancreatic cancer patients to retrospectively assess the feasibility of using KIM during treatment

Researchers

Indrajit Ghosh

Xiaoshui Huang

Chandrima Sengupta

Doan Trang Nguyen (Affiliate)

Paul Keall

Lars Mejnertson

Ricky O'Brien

Students

Emily Hewson

Dominique Lee

Amelia Martin

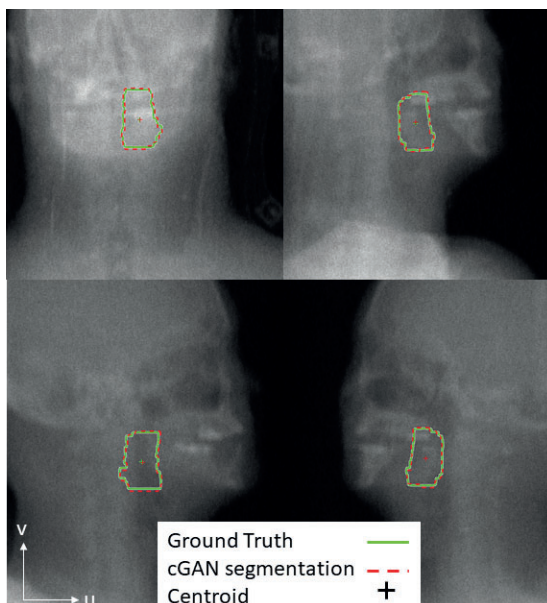
Markerless Tumour Tracking

Project Overview

To track the location of a tumour, a patient may have fiducial markers surgically implanted in and around their tumour. The markers are a surrogate of the tumour position during imaging and treatment. However, this procedure is invasive, expensive,

time consuming, and carries risk. Markerless tracking is a software solution that tracks the target without the need for implanted markers. To achieve this, we're using the imager on a standard radiotherapy unit combined with our advanced algorithms. This

solution eliminates the invasive surgical implantation of markers and allows the tumour to be accurately targeted. The collateral damage to healthy tissue is minimised, thus improving the outcomes for cancer patients.



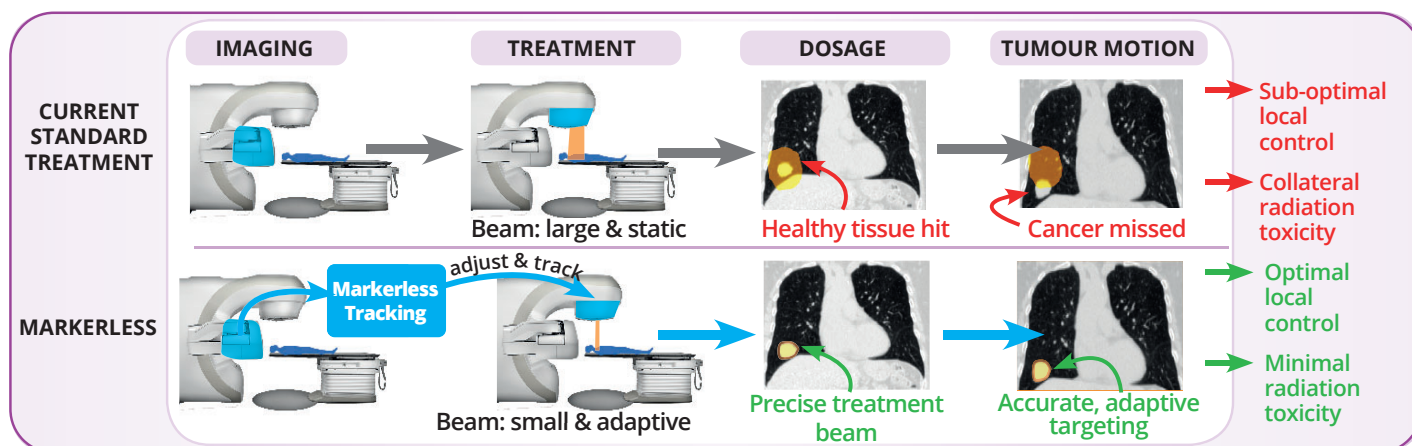
Picture: Multiple X-rays of a person's head, as well as an estimation of the tumour outline (red) compared with the actual tumour outline (green), and the centres of the tumours (+).

Highlights of 2021

Over 2021, our markerless technology has rapidly expanded to track a range of cancer targets. Our focus has been on the development of a novel deep learning approach for the tracking of low contrast cancer targets and surrounding organs at risk. The deep learning approach has been implemented on lung, prostate, pancreatic, and head and neck cancers. Furthermore, the deep learning model can be used for the simultaneous tracking of lung tumours and the lung. Our researchers have presented our new deep learning approach at several conferences. This includes three presentations at the AAPM annual meeting and two presentations at EPSM. PhD student Marco Mueller led an international challenge to benchmark methods for markerless lung target tracking with *The markerless lung target tracking AAPM Grand Challenge (MATCH) results* published in the Medical Physics journal.

In 2022 we plan to expand markerless tracking technology to liver cancer. This will be achieved through the ROCK-RT feasibility study which uses contrast agents for markerless liver tracking.

The MAGIK and VALKIM clinical trials were approved for accrual during 2021. However, they were unable to accrue any patients, due to the ongoing impact of COVID on elective surgeries preventing markers being implanted in eligible patients. In 2022, we hope to see both these trials start to accrue patients.



Pictured: A basic comparison of standard radiotherapy and markerless tumour tracking.

Associated Studies

MAGIK

Using implanted markers to determine the feasibility of Markerless Image Guidance using Intrafraction Kilovoltage X-ray Imaging: A Phase I Interventional Study of Lung Cancer Radiotherapy.

VALKIM

Validation of Markerless Image Guidance using Intrafraction Kilovoltage X-ray Imaging using implanted fiducials: Phase I Interventional Study of Lung Cancer Radiotherapy.

ROCK RT

Radio-opaque contrast agents for liver cancer targeting with KIM during radiation therapy is a non-interventional feasibility study of 50 participants who are receiving or have received RT for liver cancer.

Researchers

Mark Gardner

Jonathan Hindmarsh

Paul Keall

Doan Trang Nguyen (Affiliate)

Students

Ze Yao Li

Marco Mueller

Adam Mylonas

Beam Adaptation

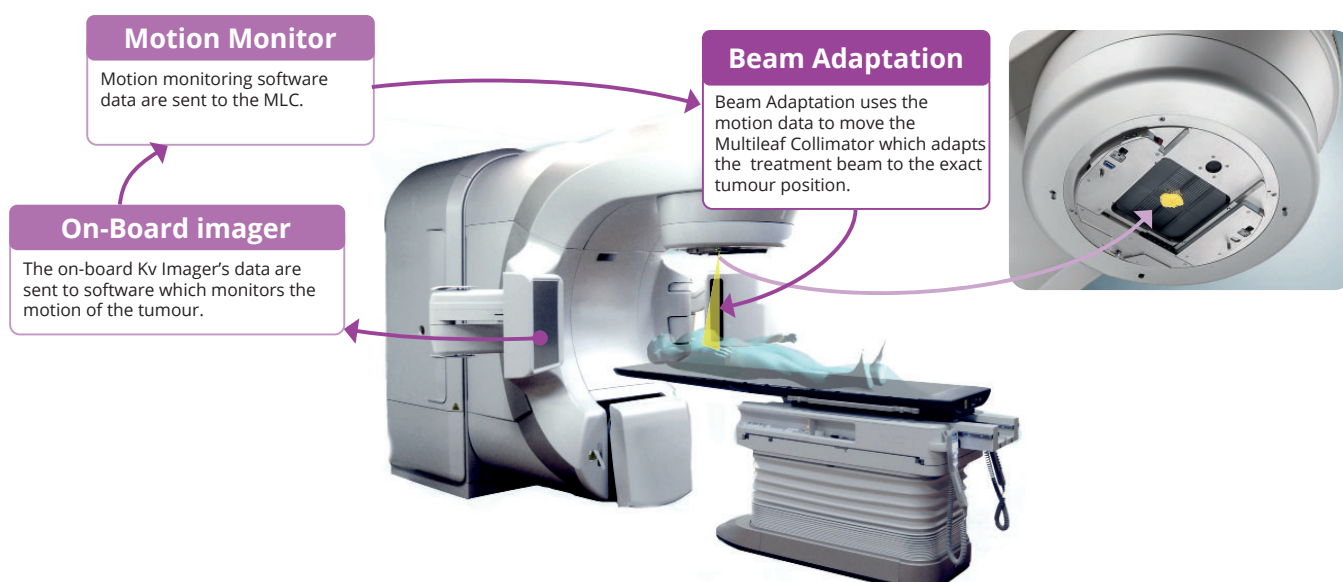
Project Overview

Beam Adaptation is a system that changes the shape and position of the radiation beam in real-time during treatment to follow the movement of the tumour. This adaptation ensures the radiation beam always hits the tumour and while sparing the surrounding healthy tissue. It uses the real-time information

from the radiotherapy system's on-board imaging equipment to adapt the shape and position of the radiation beam.

While some high-end radiotherapy systems are now capable of adapting the beam to the tumour, they are inaccessible to most cancer treatment centres due to their high cost.

Our Beam Adaptation technology is the only solution designed to be compatible for installation on 95% of radiotherapy machines already in use today. This makes it an affordable and achievable way for cancer centres all over the world to offer cutting-edge treatment to cancer patients.



Pictured: How Beam Adaptation Works



Highlights of 2021

Beam Adaptation has seen some exciting improvements in 2021. With the field of adaptive radiotherapy moving toward adapting treatments based on the radiation dose deposited during treatment, our team is pioneering dose-based beam adaptation. A proof of concept was published in 2021, demonstrating the ability to move and shape the beam based on previously delivered dose in real-time. This method forms the basis of the patent application Dose-based optimisation for multi-leaf collimator (MLC) tracking during radiation therapy.

The dose-based optimisation method has been extended to include multiple targets, allowing two treatment sites to be treated simultaneously, accounting for their individual motions. Real-Time Dose-Optimized Multi-Target MLC Tracking for Locally Advanced Prostate Cancer was a conference presentation by PhD student Emily Hewson together with senior author Dr Lars Mejnertsen.

It received a Best in Physics award at the American Association of Physicists in Medicine Annual Meeting, judged in the top 1% , and featured as a conference highlight in Physics World

Furthermore, improvements to the dose-based beam adaptation method are being investigated, such as including not only dose previously delivered, but also looking at dose that has yet to be delivered. The aim is not only to correct the dose delivery with beam adaptation but to reduce radiation dose to healthy tissue while maintaining dose to the target tumour.

Researchers

Emily Hewson

Paul Keall

Lars Mejnertsen

Pictured: Close up of a multi-leaf collimator, the device which shapes the radiation beam.

Surface Imaging and Audiovisual Biofeedback

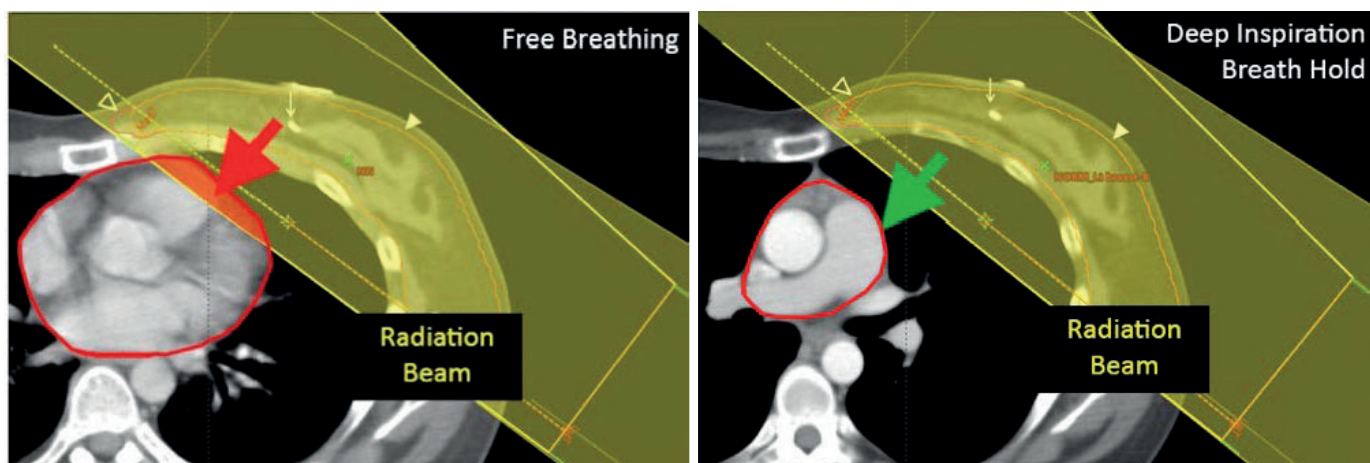
Project Overview

Managing patient motion is one of the main challenges in medical imaging and radiotherapy. Surface imaging uses optical cameras to image the surface of the patient and detect motion. Unlike medical imaging technology, it does not use x-ray radiation, so is virtually risk free

and can serve as a powerful tool for motion management. Surface imaging is used in multiple Image X projects and is an integral part of our work on audiovisual biofeedback (AVB).

The AVB project uses information provided by our surface imaging

system to image a patient's chest and abdomen and track a patient's breathing. The breathing signal is then used to provide audio and visual real-time feedback to the patient to help them breathe in a reproducible pattern during their treatment.



Pictured: A comparison of treatment without, and with breathhold guided by AVB. You can see in the picture on the right, the heart doesn't come in to contact with the radiation beam (yellow) - AVB is being used to guide the patient's breath-hold.

Associated Studies

AVIATOR

a multiinstitutional study uses audiovisual biofeedback to assist regular breathing for lung cancer radiotherapy patients.

BRAVEHeart

a trial to improve reproducibility of deep inspiration breath holds for breast cancer patients reached full accrual in 2021.



Pictured: Breathe Well, the device used in BRAVEHeart Trial

Highlights of 2021

There are two current clinical trials of our AVB technology. The AVIATOR trial is a multi-institutional trial to evaluate the impact of our AVB technology on the breathing regularity of a free-breathing patient. Patient recruitment at Westmead hospital started in February 2021 and more than half the targeted number of patients was accrued despite lengthy delays caused by COVID-19. Furthermore, we have met our accrual target at the Canberra Hospital in Q4 2021.

The second study is the BRAVEHeart clinical trial which aims to improve the reproducibility of deep inspiration breath holds in breast cancer radiotherapy treatment. BRAVEHeart restarted recruitment after an interim analysis in March

2021 and completed treatment of the last patient in September with 32 patients recruited in that period. Preliminary results were presented at the Sydney Cancer Conference in September and at the Engineering and Physical Sciences in Medicine conference in November. A manuscript of the protocol has been submitted and the final results will be published in 2022.

Researchers

Youssef Ben Bouchta
Hilary Byrne
Mark Garner
Paul Keall
Kuldeep Makhija

Surface Imaging and Remove the Mask

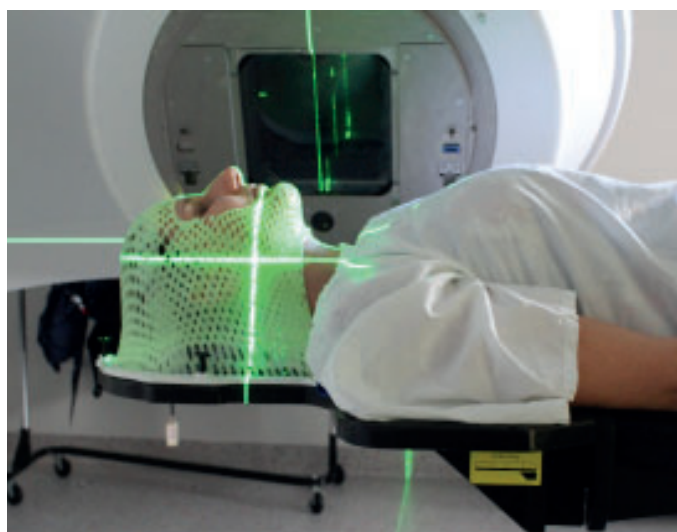
Project Overview

Immobilisation masks are used during head and neck cancer (HNC) radiotherapy to ensure an accurate treatment, by holding the patient's head and shoulders still.

Up to 50% of HNC patients fear being enclosed and trapped by the mask, experiencing anxiety and distress. Some patients need to undergo counselling or sedation to help them cope with the immobilisation, and this anxiety can affect the treatment quality leading to decreased survival rates among HNC patients.

We are working to “remove the mask” from HNC radiotherapy treatment, by monitoring patient motion during treatment using a combination of surface monitoring and internal motion monitoring technologies. By monitoring patient motion, we can focus the treatment radiation on the tumour and avoid the nearby vital organs.

The aim of “Remove the Mask” is to provide safe and effective radiotherapy, reduce patient anxiety and improve patient experience.

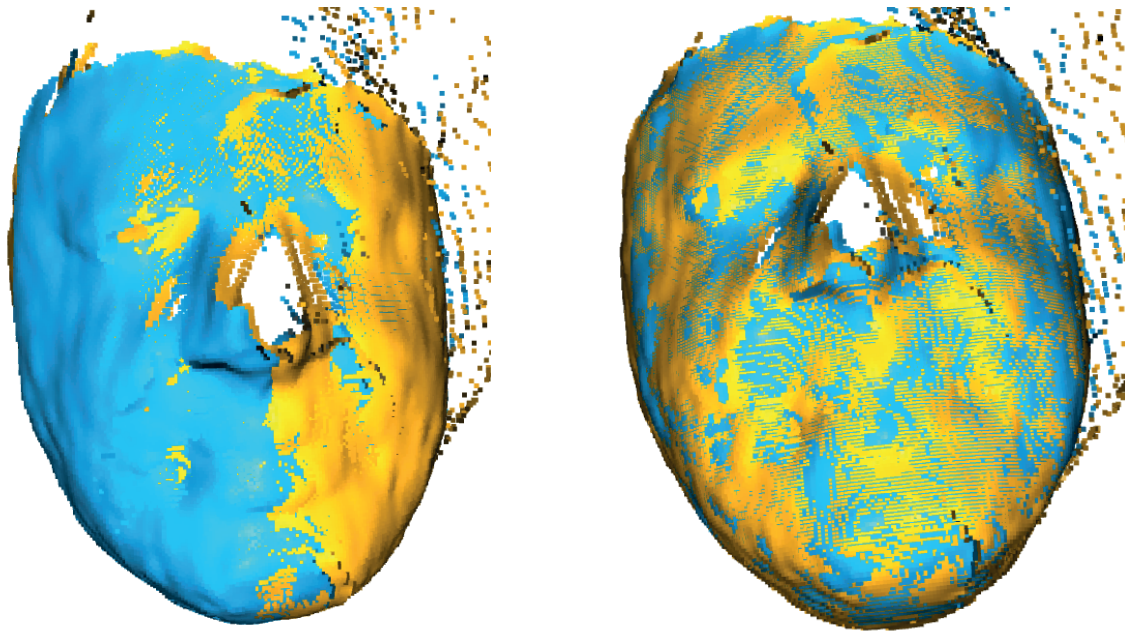


Pictured: A researcher experiences the immobilisation mask.



Pictured: Images from the Remove the Mask surface imaging system.

This is an example of minute facial motion that can be imaged by the Remove the Mask system.



Pictured: A reconstruction of a model of a human the blue image shows the planned position and yellow the actual position. In the image on the right, the two image are overlapping, showing that we can accurately reposition the phantom with the Remove the Mask surface imaging system.

Highlights of 2021

Safe and accurate treatment involves monitoring both surface motion and internal organ motion. Dr Youssef Ben Bouchta leads the development of the surface monitoring technology, engineering software to accurately track a person's face as they move. He has tested the technology using a robotic arm and a realistic looking face mask. He also wrote an approved clinical study protocol to test the method on people and to gather data on how much people are expected to move without the mask. This volunteer study is commencing in March 2022.

Dr Mark Gardner has been developing methods to monitor the internal organ motion during treatment. Using previously collected patient data he has developed a method for identifying the tumour location in x-ray images acquired during treatment. He demonstrated this method on artificial images of HNC patients. Dr Gardner wrote an approved clinical study protocol to acquire images of patients during radiotherapy. As part of the study, he will demonstrate that tracking of the internal tumour motion using the acquired images is possible during radiotherapy.

Associated Studies

CHIRP

The Collection of Protocol Images During Radiotherapy received ethics approval in 2021 and will acquire images for tracking of HNC tumours during radiotherapy

VISION

The Visual Investigation with Surface Imaging for Oncological Needs study received ethics approval in 2021 and will test methods for surface motion monitoring in volunteers.

Researchers

Youssef Ben Bouchta

Mark Gardner

Paul Keall

Kuldeep Makhija

Students

Chen Cheng

The Australian MRI Linac Program

Program Overview

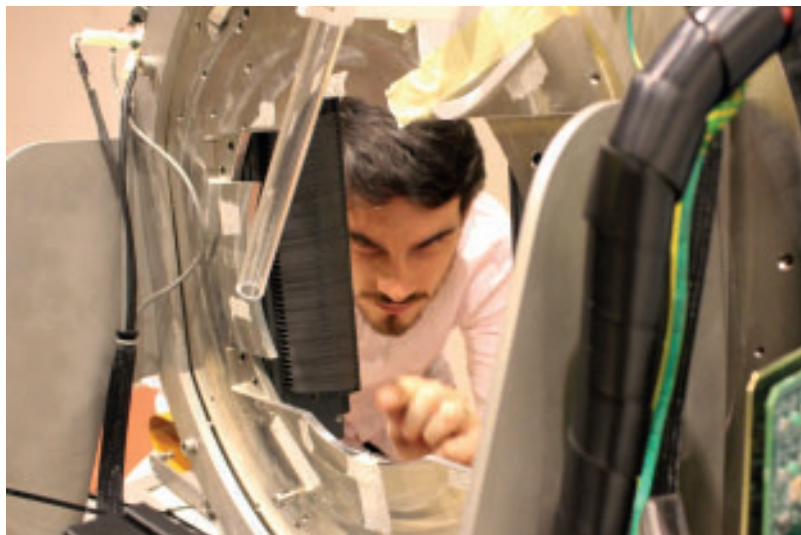
Magnetic Resonance Imaging (MRI) devices produce high resolution images providing detailed anatomical and functional information. Linear accelerators (Linacs) accelerate charged particles to create x-rays and deliver therapeutic radiotherapy. Combining an MRI device with a Linac

creates a device with the goal to deliver precise cancer targeting with radiation, avoiding surrounding healthy tissue, and to differentially target tumour regions with higher radiation dose, providing new options to treat the most aggressive and resistant regions of the tumour. The Australian MRI-Linac program

is a \$30M multi-institutional collaboration that spans building a prototype MRI-Linac system, one of four unique designs globally, to developing software and functional techniques that can also be deployed on commercial MRI-Linac systems.

Highlights of 2021

It was a big year for the Australian MRI-Linac program despite COVID restrictions limiting experimental work and delaying commencement of clinical studies. Cancer Institute NSW Early Career Fellow Dr David Waddington led the world's first deployment of neural networks to an MRI-Linac, using artificial intelligence to more accurately track tumours in work that won the International Society of Magnetic Resonance in Medicine ANZ ECR Prize. Artificial intelligence has transformed medical imaging and its application to MRI Linacs will improve the accuracy of radiation delivery on MRI-Linacs. Meanwhile, Dr Caterina Brighi had great success using functional techniques to more precisely image brain tumours with quantitative techniques, now accepted for publication. Quantitative imaging techniques could allow adaptation of treatments during a course of radiation therapy, enabling breakthroughs for cancers with poor prognosis, such as brain cancer. MRI-Linacs are particularly well suited to quantitative imaging as functional imaging can be performed with the MRI alongside the radiation treatment.



Pictured: Dr David Waddington inspects equipment at the MRI Linac.



Associated Studies

MANTRA

Mri-linAc Treatments for RAdiotherapy Patients is a pilot study on the use of the Australian MRI-Linac to treat cancer radiotherapy patients, the first clinical trial of an inline MRI-Linac.

AMPI

The Australian MRI-Linac Patient Imaging trial will test the feasibility of treating different types of cancers on an inline MRI-Linac.

Researchers

Caterina Brighi

James Grover

Paul Keall

Paul Liu

Shanshan Shan

David Waddington

Brendan Whelan

Students

Kevin Jang

Sony Jufri

Athena Kam

Pictured: A volunteer from the MRI Linac team is set up for a scan.

Nano-X Compact Radiotherapy System

Program Overview

Nano-X is a new class of radiotherapy system that will deliver significant cost reductions, by introducing state-of-the-art clinical radiotherapy precision with a machine that has a significantly smaller footprint, much reduced shielding requirements and lower staff-to-patient ratios. We do this with fixed treatment and imaging

beams, and a custom-made patient rotation system.

The Nano-X system solves the complex problem of how to target a tumour with precision and accuracy even as the patient's anatomy changes during treatment. Our system is built with real-time imaging guidance and adaptation at the

heart of the treatment process; and complex processing tasks have been moved from hardware to software, enabling radical changes to machine design. Together, these innovations will ensure better treatment outcomes and increased safety and reliability.

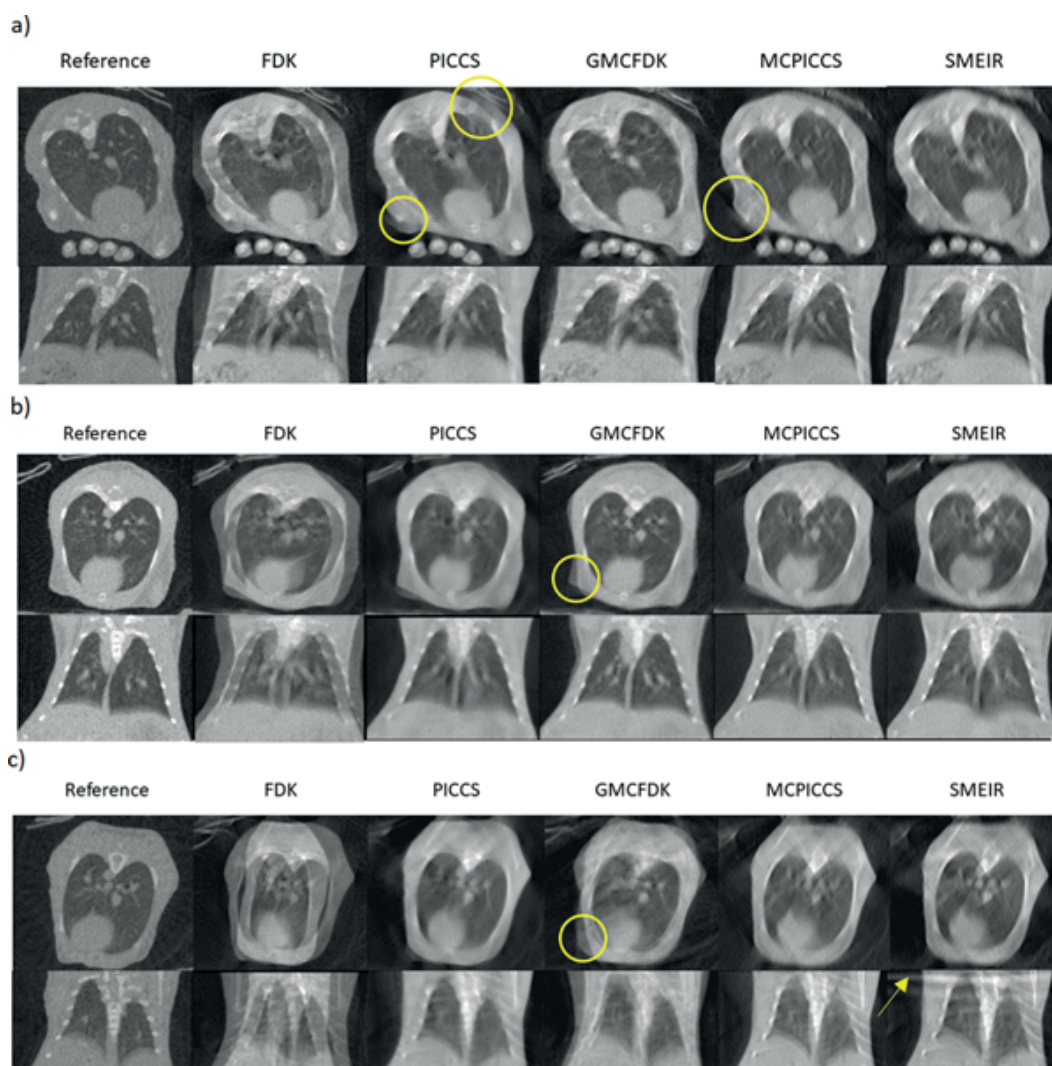
Highlights of 2021

Despite the COVID pandemic, the Nano-X project reached recruitment of over 40 patients to the patient experience study in 2021. This study examines cancer patients' experience of the rotation system measuring possible responses including anxiety and claustrophobia. We also received ethics approval for a second study which will collect imaging data from the patients as they are rotated. As anatomy changes with the gravitational forces experienced during rotation, it is important to develop image processing methods to enable image-guided radiotherapy for a system using patient rotation.



Pictured: Professor Ricky O'Brien shows a student the patient rotation system.

Pre-treatment and real-time image guidance for a fixed-beam radiotherapy system developed and experimentally verified these methods using an imaging phantom. As phantoms do not experience organ deformation



Pictured: Images of rabbit 1 (a), rabbit 2 (b) and rabbit 3 (c) lungs from axial (top) and coronal (bottom) views, using different image reconstruction methods.

during rotation, the next step was a preclinical study with rabbits which was published in *The adaptation and investigation of cone-beam CT reconstruction algorithms for horizontal rotation fixed-gantry scans of rabbits*. Both publications in the Physics in Medicine & Biology journal lay the groundwork for the patient imaging study which will commence recruitment in 2022.

Associated Studies

NanoX PE (Patient Experience)

A 100 participant study that assesses patient experience of rotation.

NanoX IG (Image Guidance)

A 20 participant study that collects images of patients as they rotate for developing image-guided radiotherapy on the Nano-X system.

Researchers

Mir Massoud Aghili Yajadda
Emily Debrot
Mark Gardner
Paul Keall
Paul Liu

Cardiac Radioablation

Project Overview

Cardiac radioablation is a revolutionary non-invasive method of producing ablative scarring to block aberrant electrical signals responsible for causing Atrial Fibrillation (AF) and Ventricular Tachycardia (VT), affecting over 33.5 million patients globally. The potential of radioablation has been demonstrated through recent clinical trials. However,

radioablation remains a high-risk procedure, with some patients experiencing serious adverse events.

To ensure cardiac radioablation treatment efficacy and safety, it is vital that radiation is carefully delivered to the cardiac target that is moving with both cardiac contraction and respiration but steered away from the healthy

organs and cardiac substructures that are often in very close proximity. We are addressing the motion management problem for cardiac radioablation by inventing imaging technologies for the entire treatment pathway from (1) CT simulation, to (2) pre-treatment patient-connected imaging, and (3) during treatment delivery.

Highlights of 2021

2021 was a productive year for the newly formed Image X cardiac radioablation team, with papers, a student graduated, a patent filed and media interest in our work. *Adaptive CaRdiac cOne BEAm computed Tomography (ACROBEAT): developing the next generation of cardiac cone beam CT imaging*, published in Medical Physics, experimentally demonstrates that using the patient's physiological signals to optimally control imaging produces 40% better image quality with 90% less dose. This work led to first author Dr Tess Reynolds being a finalist for the Outstanding ECR Eureka prize.

PhD students Nicholas Hindley and Suzanne Lydiard led work on x-ray-based, *Proof-of-concept for x-ray based real-time image guidance during cardiac radioablation*, and MRI-based, *MRI-guided cardiac-*

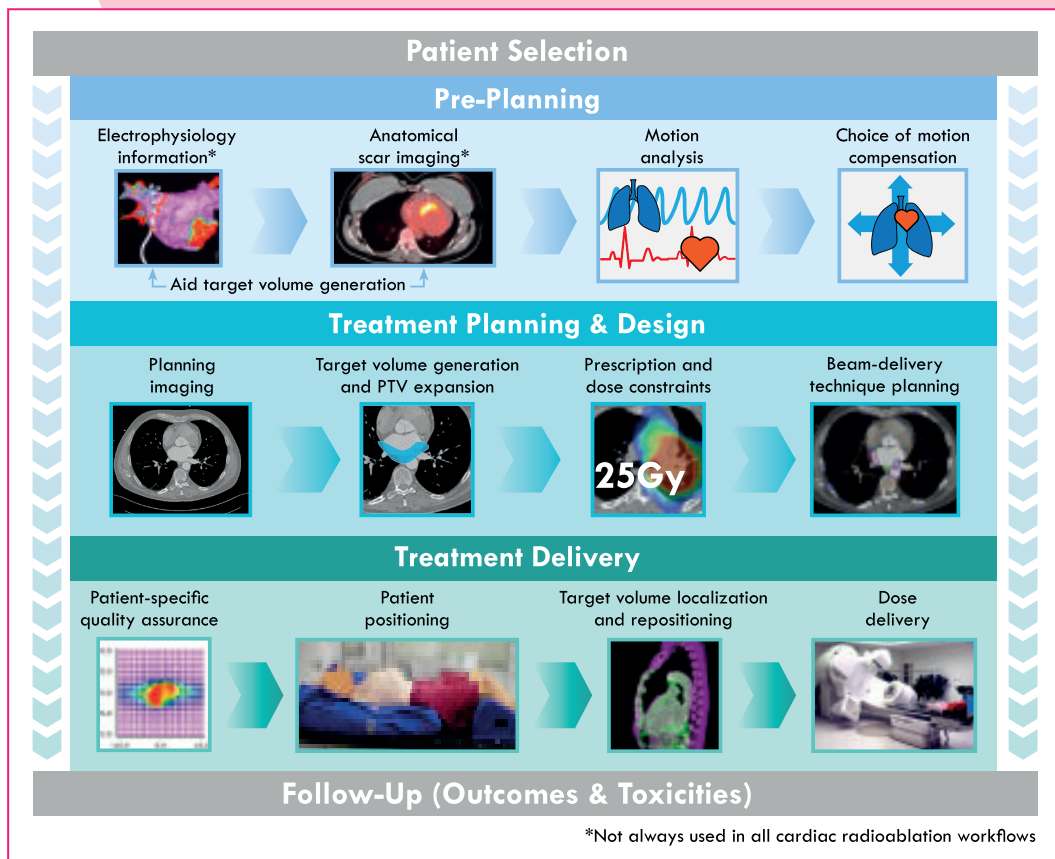
induced target tracking for atrial fibrillation cardiac radioablation, imaging modalities for understanding cardiac target motion and tracking cardiac targets during treatment delivery. Nicholas's paper forms the basis for the patent application on the System and method for cardiac structure tracking and was highlighted in PhysicsWorld. Suzanne Lydiard was awarded her PhD and her thesis included *A review of cardiac radioablation (CR) for arrhythmias: procedures, technology and future opportunities* published in the International Journal of Radiation Oncology, Biology, Physics journal, along with four other first-author papers.

Researchers

Paul Keall
Ricky O'Brien
Tess Reynolds

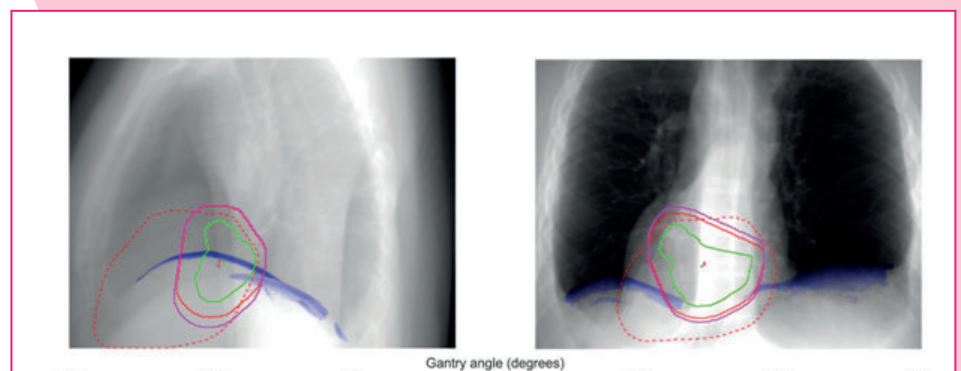
Students

Nicholas Hindley
Irena Janevska-Pejoska
Suzanne Lydiard
Natasha Morton



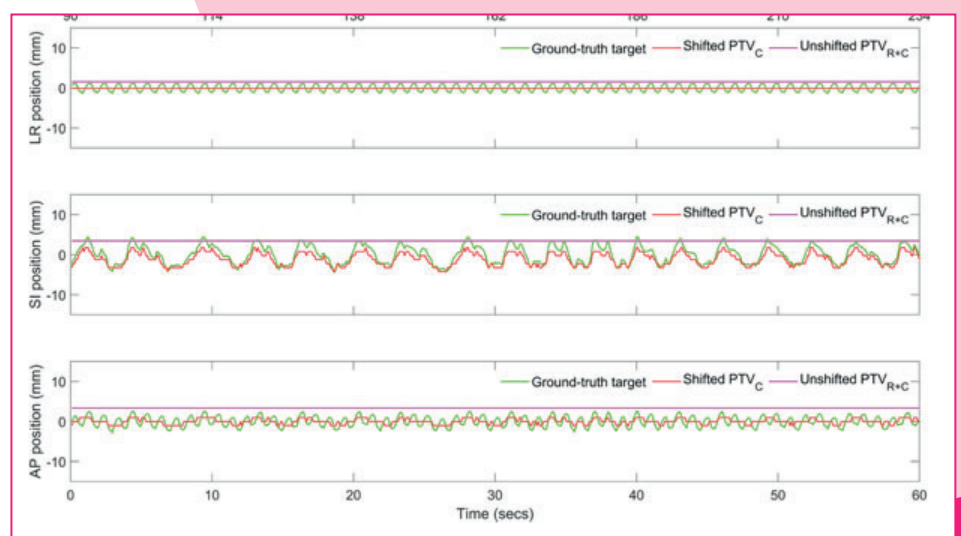
Pictured: This figure from Suzanne's paper outlines the detailed treatment process for Cardiac Radioablation.

Pictured: The areas of interest are being identified (coloured outlines) and tracked by Nicholas's' system.



Pictured: Tracking performance for the first minute of the image-guidance simulation - the coloured lines represent the position of the heart over the course of a minute.

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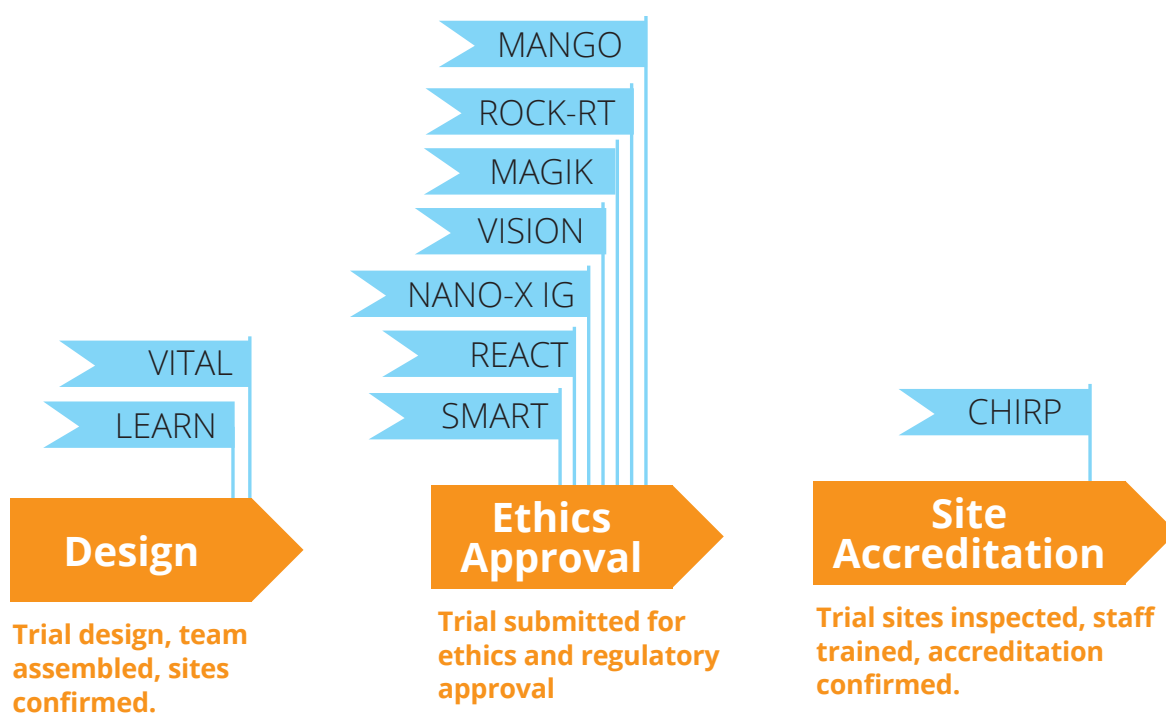
Clinical Studies

Improved health outcomes are at the heart of what we do, and clinical trials help us get there. They are an important step in bringing our work closer to the patients we aim to help.

In 2021 we had 5 clinical trials open and actively recruiting participants. One of these, BRAVEHeart reached full accrual in the middle of the Sydney COVID lockdown in August 2021. This was a great achievement by everyone involved. In total, we recruited 55 participants to our trials in 2021.

In addition to the actively recruiting trials, we had a further 10 studies in various stages of development. These cover the whole trial development process from concept design right through to ethics submission and site start up activities. Six of these studies received ethics approval in 2021 and are expected to open to accrual later in 2022 once hospital COVID restrictions have eased.

STUDY STATUS IN 2021





6

New studies approved

5

Trials open and recruiting patients

55

Patients recruited

NANO-X PE

AVIATOR

LARK

Open - recruiting patients

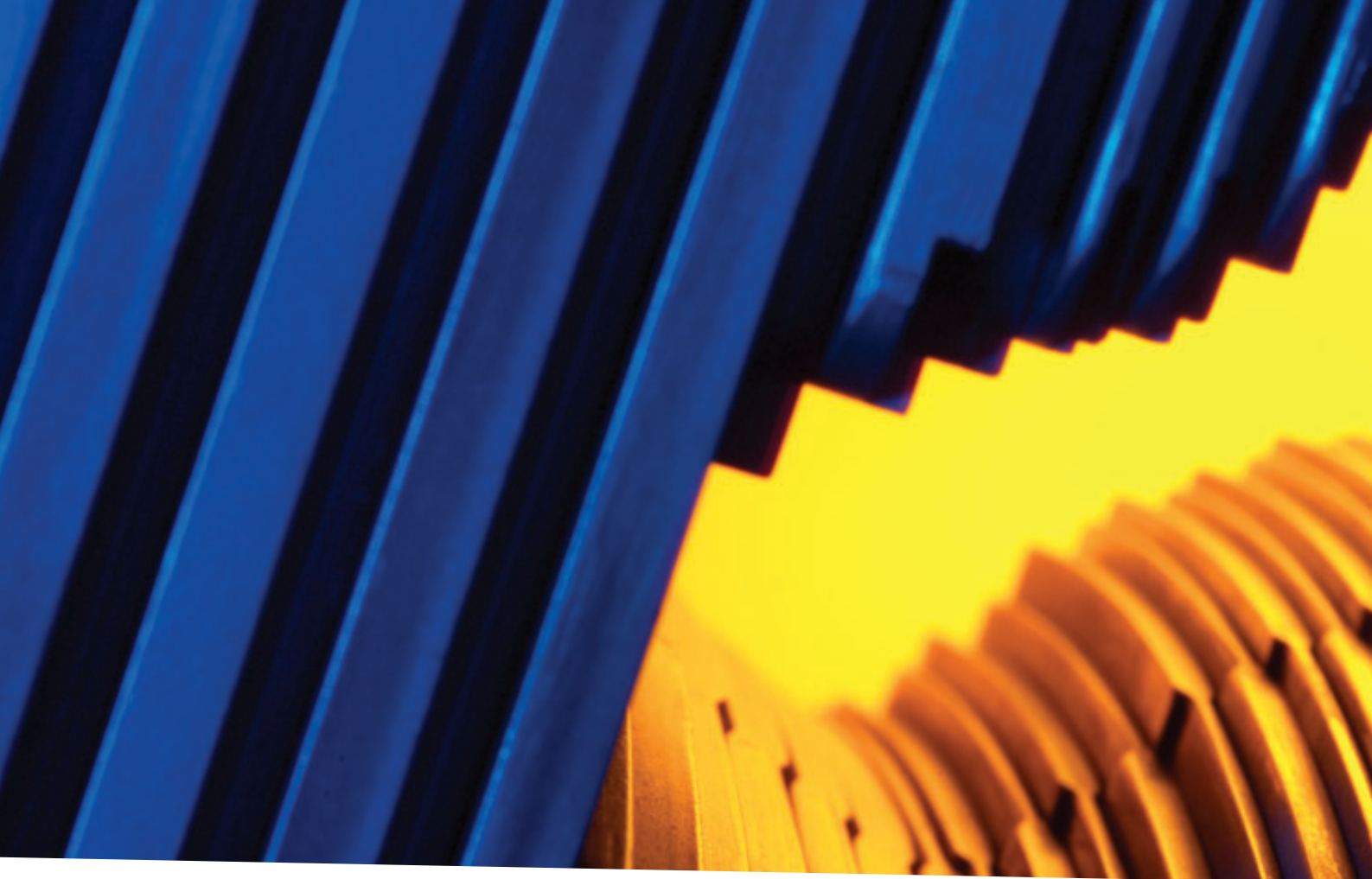
Hospital sites recruit patients to the study.

ADAPT

BRAVEHEART

Analysis & Publication

Results are analysed and submitted for publication in journals.



Translation and Commercialisation

Intellectual Property

To ensure that our technologies are developed for the benefit of the University and community, we work with the Commercialisation team of the Research Portfolio, to protect and commercialise intellectual property.

In a busy year for records of inventions, patent applications and licence agreements, we are fortunate to have the support of Sebastien Ybert from the Research Portfolio, for IP, commercialisation and engagement activities.

One patent application was Dose-based optimization for multi-leaf collimator (MLC) tracking during radiation therapy led by Dr Lars Mejnertsen.

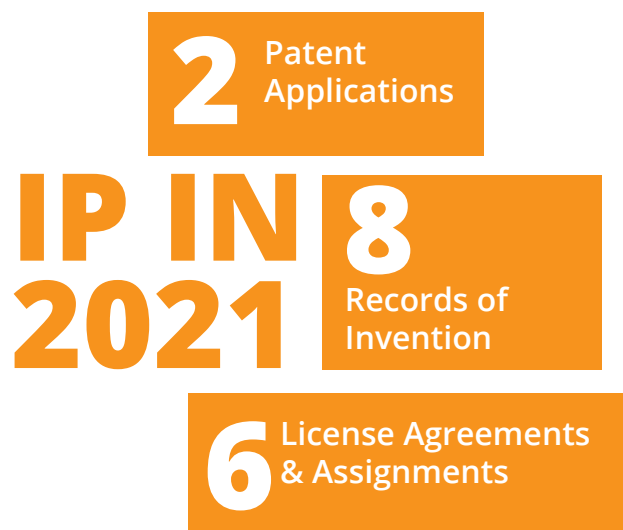
This method overcomes some of the remaining challenges with MLC tracking or adapting the shape of the radiation beam to follow tumour movement. The invention transitions from addressing the geometric alignment between the beam and the target to addressing the dose received in real-time by the cancer target and surrounding tissues. As dose is directly correlated with patient outcomes, the invention is more clinically relevant than our previous method. It has been licensed to a growing radiation oncology company.

In another research theme, CT Ventilation Imaging IP was licensed to a commercial company.



Partnerships

Forming partnerships with industry is key to widespread adoption of our innovations. In 2021, we formed a new partnership with 4DMedical, an Australian medical technology company aiming to change the outcome for patients with lung disease by revolutionising respiratory imaging and ventilation analysis. Professor Ricky O'Brien led a successful application to the NHMRC Development Scheme to work with 4DMedical to commercialise our CT Ventilation Imaging method. The \$1M grant will kickstart further engagement with 4DMedical in 2022, including clinical trials and researcher internships.



Pictured: A close-up of a Multi-leaf collimator (MLC)

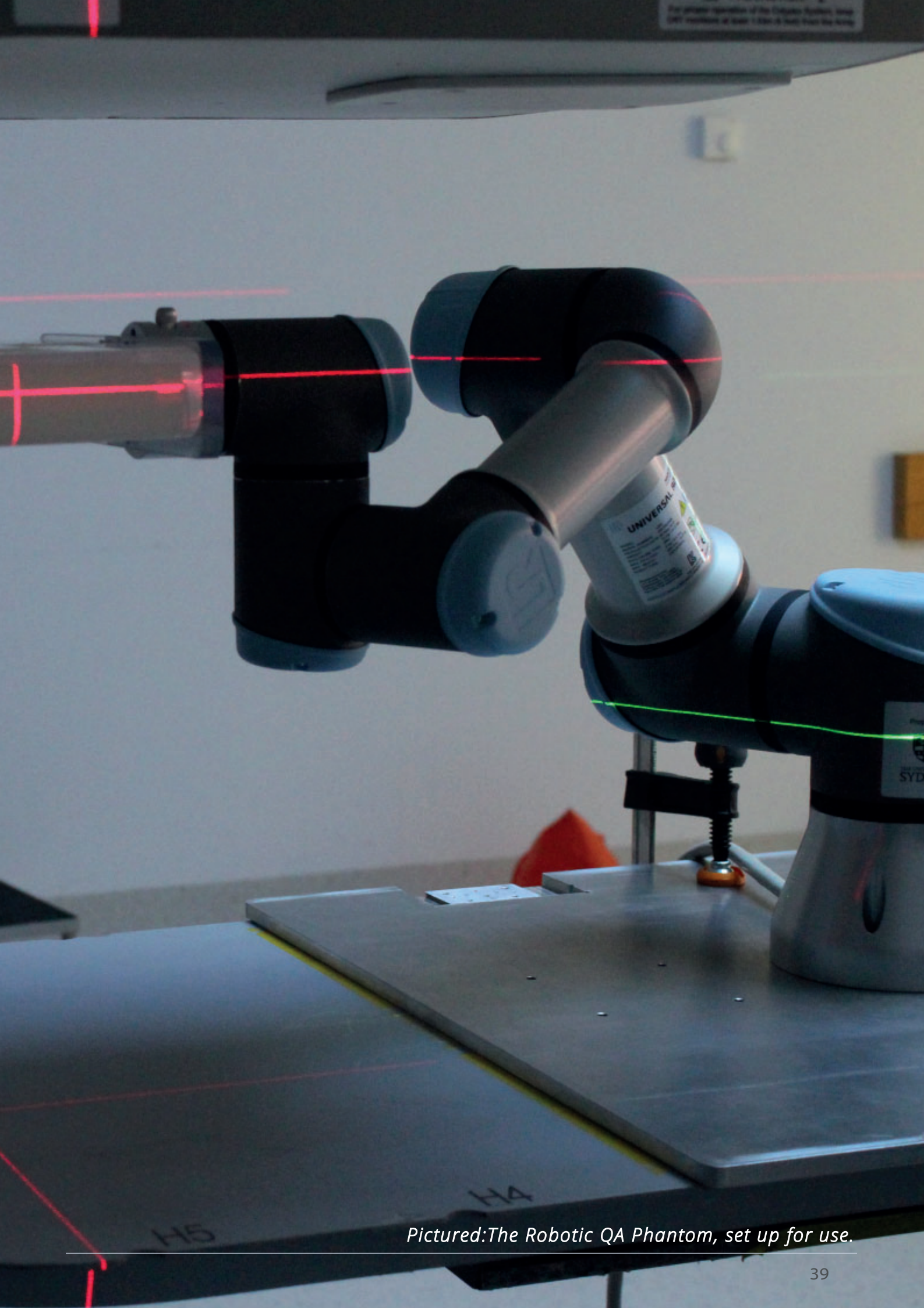


Open Source Tools

We create some devices specifically to test our scientific hypotheses, or address the performance and quality assurance of our cancer imaging and targeting methods.

To support the scientific community, we can maximise the utility and impact of these devices by making the technology open-source and available to other researchers. These open source tools can help teams avoid the additional months and years of development time that we have already invested, letting these teams spend more time on their forward-looking scientific questions than reinventing our tools.

Our first open-source project is the novel robotic phantom quality assurance device that accurately mimics tumour motion in 6 degrees of freedom, ensuring safe implementation of image-guided radiotherapy technologies in the clinic. The robotic QA phantom has been used to ensure clinical studies of image-guided technologies can be performed safely and reproducibly at different sites. We made the software as well as specifications for equipment needed, and full documentation open-source to enable wider use. We have several new open-source projects that we hope to complete in 2022.



Pictured: The Robotic QA Phantom, set up for use.

Awards

Professor Ricky O'Brien

Professor O'Brien was awarded the Outstanding **Cancer Research Fellow Award In the 2021 NSW Premier's Awards for Outstanding Cancer Research**. The award was given for his achievements during his Cancer Institute NSW Career Development Fellowship.



Most people with cancer have several scans over the course of their diagnosis and treatment. Accurate imaging helps to precisely pinpoint the part/s of the body that will receive cancer treatment (for example, targeted radiation therapy). The disadvantages of imaging for the patient is that they can be lengthy and include additional radiation dose. Although some people find the scans nerve-racking, time consuming and tiring, they play important roles in diagnosing many types of cancer and helping clinicians to plan treatment.

Professor O'Brien's fellowship is directly benefiting people with cancer, by delivering shorter scan times and better image quality. Together these can contribute to more accurate results and faster treatments. Changes to scans, such as lower pre-treatment imaging doses, also have the potential to make scans safer for patients. These improvements were demonstrated in the NHMRC-funded ADaptive CT Acquisition for Personalised Thoracic imaging (ADAPT) trial.

Dr Tess Reynolds

Dr Reynolds was a top-3 finalist for the **2021 Australian Museum Eureka Prize for Outstanding Early Career Researcher**. She was nominated by the University of Sydney for developing ACROBEAT (Adaptive CaRdiac cOne BEAm computed Tomography). ACROBEAT is a new technology that enables imaging and treatment hardware to beat in sync with the patient, delivering clearer, faster, and safer medical images.

Dr Reynolds has developed an innovative and award-winning research program using the ACRF-funded robotic clinical C-arm. She has partnered with Siemens Healthcare, the manufacturer of the ARTIS pheno, to gain unique access to the control system of the robotic C-arm imaging system, to implement her imaging technology.

Dr Reynolds formed a collaboration with John Hopkins University to extend the field of view and enable accurate assessment of pedicle screw placement in the spine. Her abstract, Imaging from the Cervical to the Lumbar Spine with a Continuous Multi-Turn Reverse Helical 3D Cone-Beam CT Scan, was awarded the **Jack Fowler Early-Career Investigator Competition** at the American Association of Physics in Medicine Annual Meeting. She will extend this work to derisk surgery for cancer patients with spinal metastases in her Cancer Institute Early Career Fellowship commencing in 2022.

Presentation awards for Dr Reynolds include *De-risking posterior pedicle screw fixation procedures through 3D-printing and novel intraoperative imaging techniques at the 7th CPC EMCR Symposium (Bronze in the Postdoctoral Awards)* and *Move to the ACROBEAT: safer, smarter, and clearer cardiac imaging at the HEART pitch hosted by NSW Cardiovascular Research Network (Silver award)*.



Awards cont'd

PhD student **Emily Hewson** together with senior author **Dr Lars Mejnertsen** received a **Best in Physics** award at the American Association of Physicists in Medicine Annual Meeting for the abstract titled *Real-Time Dose-Optimized Multi-Target MLC Tracking for Locally Advanced Prostate Cancer*. This work combines our target-beam adaptation methods integrating the clinically important metric of radiation dose, with the multi-target tracking technology that Emily developed. This abstract was judged in the **top 1%** of all those submitted and was featured as a conference highlight in science news website Physics World.

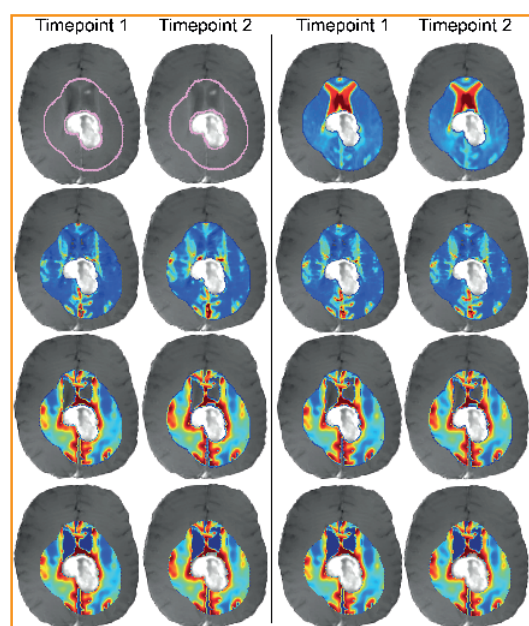
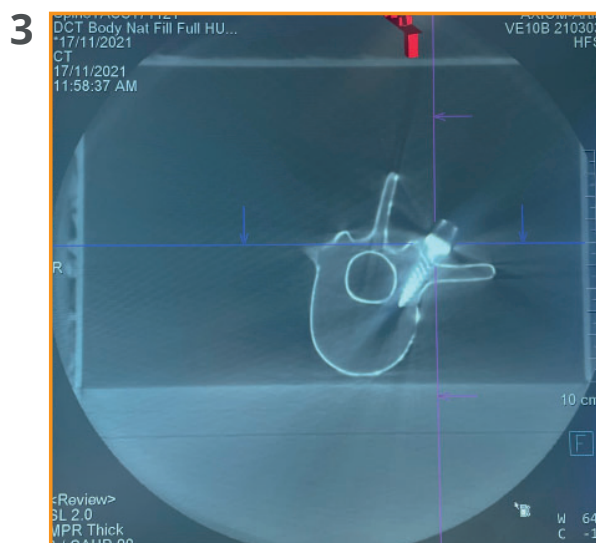
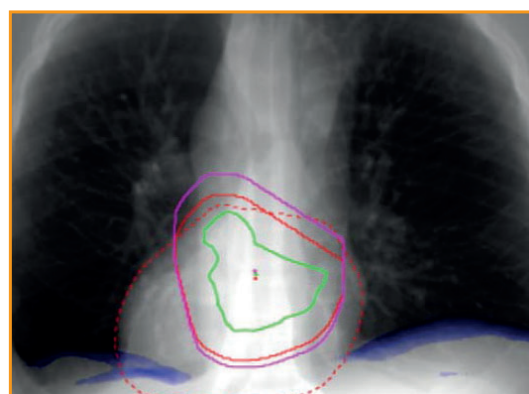
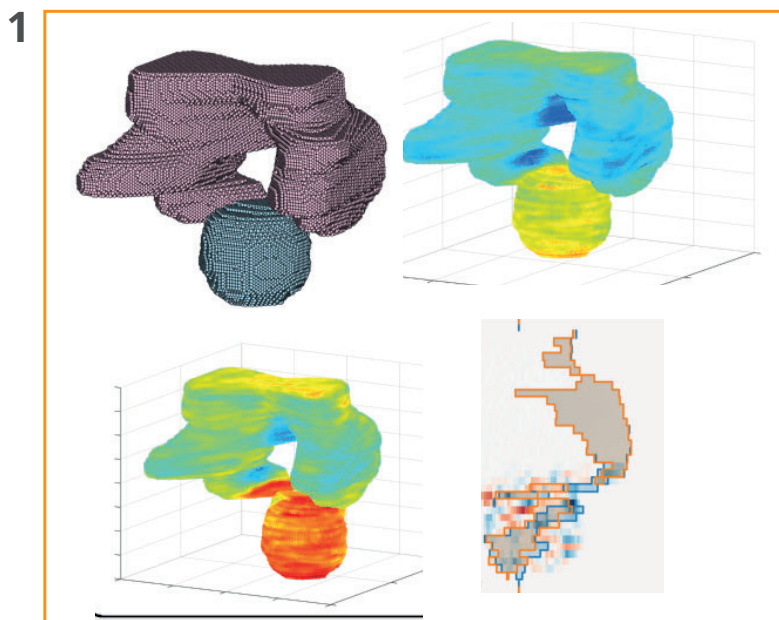
Dr Caterina Brighi was awarded **Early and Mid-Career Research Oral Presentation Prize** at the Sydney Cancer Conference for *Stability of multiparametric MR imaging biomarker-derived dose prescriptions for glioblastoma*.

Emily Hewson was awarded **Best student presentation at MedPhys21**, the Student Research and Education Symposium of the NSW/ACT Branch of the Australasian College of Physical Scientist and Engineers in Medicine, for *Real-time dose-optimized multi-target MLC tracking for locally advanced prostate cancer*.

Nicholas Hindley was awarded the **Worldwide Innovations in Medical Physics Scholarship**, and **Marco Mueller**, winner in the **General Poster Competition** at the **Winter Institute of Medical Physics 2021**.

Dr Chandrima Sengupta was awarded **Best Radiation Oncology Oral Presentation** for *Six Degrees of Freedom Intrafraction Motion Monitoring during Stereotactic Liver Radiation Therapy in TROG 17.03 LARK Trial: Higher accuracy in half the treatment time than the current standard of care*, at the Engineering and Physical Sciences in Medicine (EPSM) conference.

Dr David Waddington was awarded **Siemens Prize for Best ECR presentation** at the ISMRM ANZ Annual meeting for *Accelerating Image Reconstruction for Tumour Tracking with AUTOMAP*.



Pictured: A selection of eye-catching images from the prize-winning presentations

1. Emily Hewson: The new multi-target MLC tracking method calculates dose errors in real time and adapts the MLC leaves to minimise dose error for independently moving targets. These are a few of the models created during the process.
2. Nicholas Hndley: Our technology uses the imaging panels available on any standard radiotherapy machine. In this image, we see the technology adapting to the complex motion of cardiac substructures.
3. Tess Reynolds: 3D-printed surgical guides allow fast and accurate placement of surgical hardware. Here, we see a perfectly placed pedicle screw in a replica human vertebra using our 3D-print guides.
4. Caterina Brighi: This is a comparison of MRI-derived parametric, tumour probability and dose prescription maps between two imaging sessions.

Grants

Commenced in 2021:

Professor Paul Keall, *Cancer Imaging and Targeted Radiation Therapy: From Discovery to Clinical Practice*. NHMRC Investigator Grant (2021-2025), **\$2,114,215**

Dr Owen Dillon, **Quadro RTX 8000 GPU** for machine learning projects. NVIDIA Research Accelerator Grant (Equipment)

Awarded in 2021 and commencing in 2022:

Dr Tess Reynolds. *Improving quality of life for metastatic spine patients*. Cancer Institute NSW Early Career Fellowship (2022-2024), **\$415,000**,

Professor Ricky O'Brien, Professor Andreas Fouras, Professor Paul Keall, Dr Dasantha Jayamanne, Dr Benjamin Harris, Professor Dale Bailey, Dr Hilary Byrne, Dr Tess Reynolds, Dr Nina Eikelis, Dr Robert Jamison. *Lung Ventilation Imaging: A new device to protect the lungs for cancer treatment*. NHMRC Development Grant (2022-2024), **\$1,075,714**

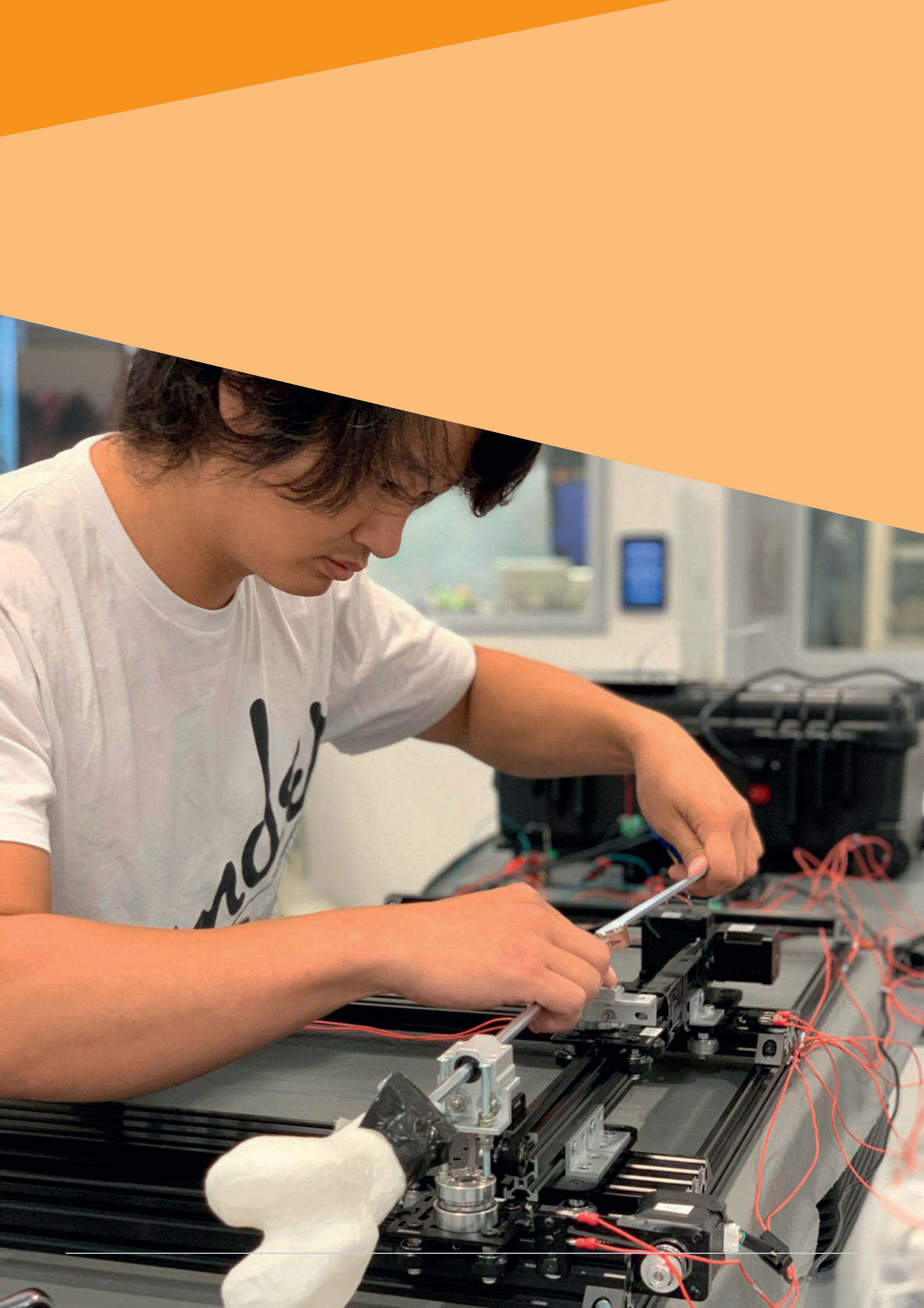
Professor Paul Keall, Professor Ricky O'Brien, Dr Doan Trang Nguyen, Associate Professor Jeremy Booth, Professor Andrew Kneebone. *Dynamic cancer targeting for radiation therapy patients*. Cancer Australia Priority-Driven Collaborative Cancer Research Scheme (2022-2025), **\$581,216**

Dr Doan Trang Nguyen, Associate Professor Jeremy Booth, Professor Paul Keall, Professor Ricky O'Brien, Professor Thomas Eade. *Using artificial intelligence to enhance radiotherapy effectiveness*. Cancer Council NSW Project Grant (2022-2024), **\$449,316**.

Professor Ricky O'Brien. DVCR COVID support scheme, University of Sydney, **\$41,600**.

Dr Suzie Sheehy; Dr Matteo Volpi; Professor Geoffrey Taylor; Associate Professor Roger Rassool; Professor Anatoly Rozenfeld; Professor Michael Lerch; Professor Paul Keall; Dr Brendan Whelan; Dr Elizabeth Hinde; Dr Rohan Dowd. *X-LAB beamline: accelerating applied research with tunable electron beams*. Australian Research Council Linkage Infrastructure, Equipment and Facilities 2022 round 1, **\$391,000**

Pictured: Dr Joseph Prinable works on a robotic knee, for an imaging experiment.





Engagement

The community surrounding the ACRF Image X Institute is made up of a diverse array of individuals and teams. It encompasses undergrad and higher degree students, health professionals, researchers, cancer survivors, consumer advocates, and more. Outside of research collaborations, in 2021 we continued to engage with our community online, via social media and online events.

Summer Lecture Series

At the start of every year, our researchers present weekly lectures on the key building blocks of radiation therapy and cancer imaging. This lecture series is tailored to suit our Summer Research Program students, but also appeals to external guests who are looking to brush up on their knowledge. We provide these lectures for free, as a way to connect and contribute to making scientific knowledge accessible to all. These guests include allied health professionals, staff from commercial radiation therapy vendors, masters students from a range of universities, and other interested members of the community. The lecture series provides an opportunity for guests and students to learn directly from our researchers, and connect with them through Q&A sessions.

The 2021 Summer Lectures were:

Introduction to Radiotherapy with Professor Paul Keall

Anatomy of a Linac with Dr Brendan Whelan

Radiotherapy workflow with Jonathan Hindmarsh

Motion Management in Radiation Therapy with Dr Doan Trang Nguyen

X-Ray Computed Tomography with Dr Owen Dillon

Introduction to MRI with Dr David Waddington

Radiobiology with Dr Paul Liu

Pictured: Kuldeep Makhija explains a project at the ACRF Image X Institute Launch, 2017.



E-Newsletter

The quarterly e-news serves to share our successes with our community. It details major funding successes, staff achievements and scientific advances. Each newsletter also shines the spotlight on a staff member, clinical trial or project. In 2021, our E-Newsletter was distributed to an audience of over 150 subscribers. The subscriber base is a mix of event attendees, past and present collaborators, students and staff, website sign-ups, allied healthcare workers, industry and commercial parties, and consumers.

Social Media

Our social media reach continued to grow in 2021, as we implemented dedicated content strategies devised and managed by Julia Johnson our Design & Communications Officer.

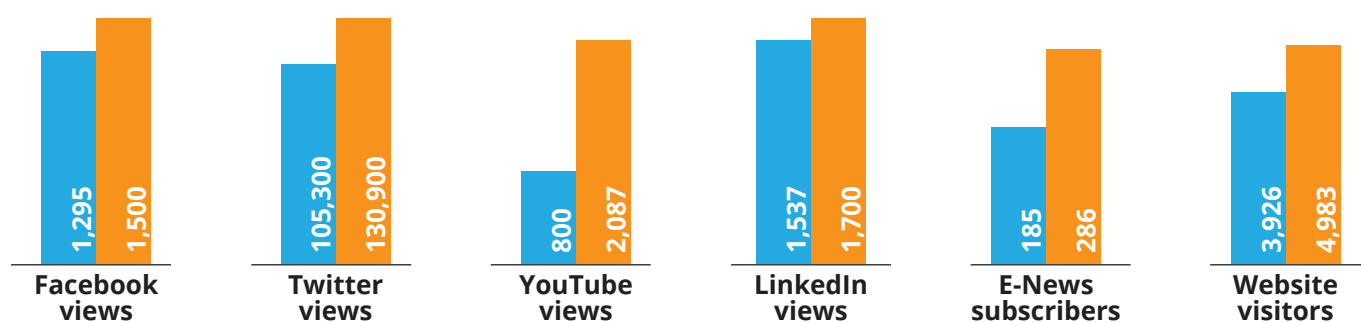
In 2021 we shone the spotlight on impactful papers, and staff achievements, as well as featuring an explainer series which showcased our clinical trials. We ran three month-long content series:

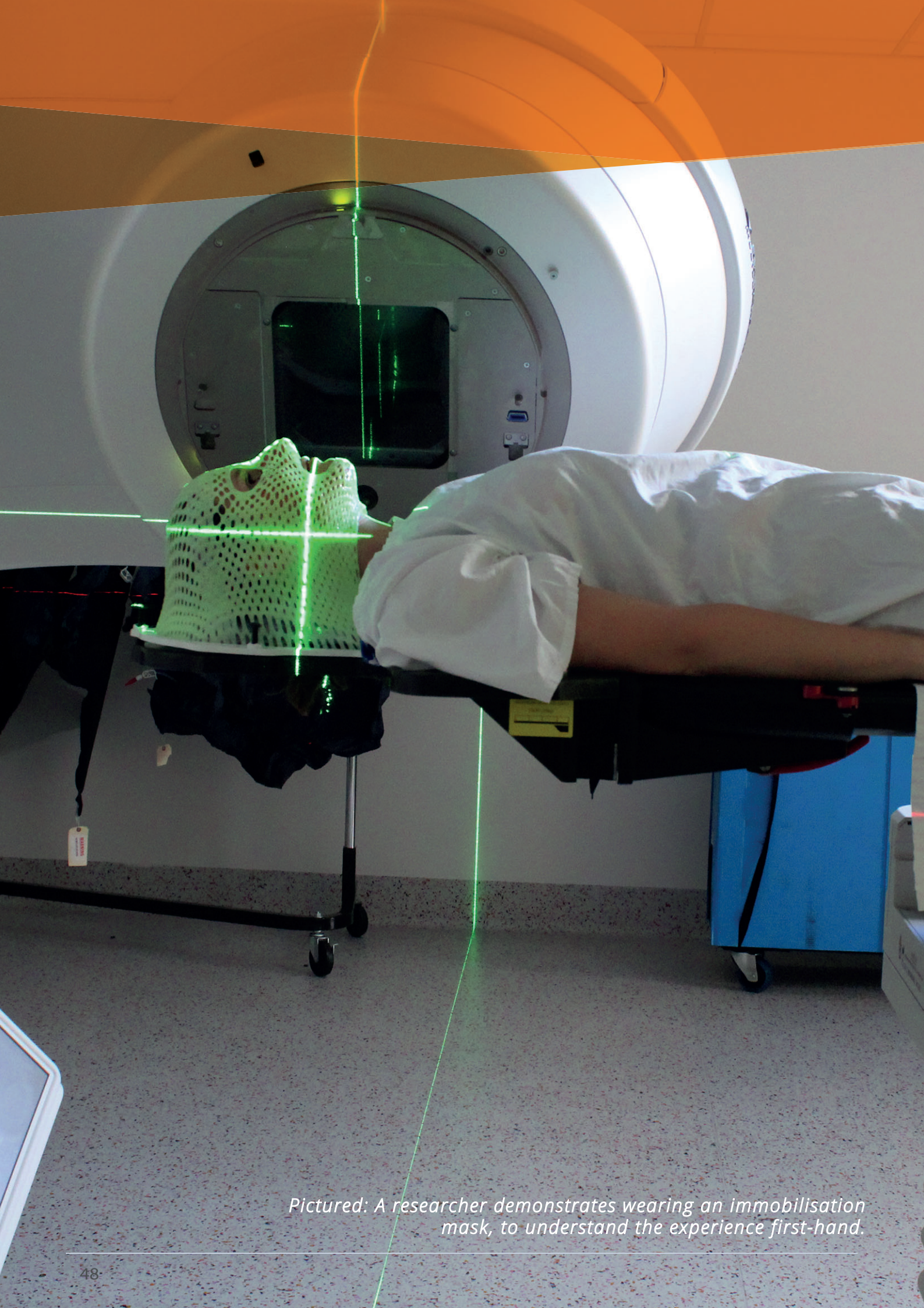
Cardiac research twitter showcase in February for Valentine's Day

AAPM Conference talk showcase in July

'Clinical Trials Files' twitter showcase in October for our trials and studies

Social Media Stats 2020 2021





Pictured: A researcher demonstrates wearing an immobilisation mask, to understand the experience first-hand.

Consumer Involvement

People with a lived experience of cancer (referred to as consumers) have unique insight which can guide research activities. They help us ensure that research projects and clinical trials align with the needs of future patients. On the larger scale, including consumers in projects not only develops trust between the public and the research sector, it increases the relevance of our research to the community. On a smaller scale, it helps our scientists communicate more effectively and strengthens our applications to funding bodies.

We thank our consumers for their involvement in our research program:

Andrew Bowen	Lee Hunt	John Stubbs
Heriberto Bustamante	Julie McCrossin OAM	Marj Salter
Miriam Cavanagh	Dr Lyn Oliver	
Hans Ede	Suzette Regan	



Prof Paul Keall and Julie McCrossin hold an immobilisation mask

Remove the Mask: A Consumer-led Project

Here at the institute, we have seen first-hand the power of embedding consumer advocates and their voices deeply into scientific projects. The Remove the Mask project was first conceived when Paul heard Julie McCrossin OAM presenting at a conference, sharing the terror and anxiety she experienced during her radiation therapy treatments. Paul approached Julie after her presentation and from that conversation, the institute's most high profile project was forged.

Julie is now the major consumer advocate in the Remove the Mask project, and has helped us to find more consumers to add their voices to the project too. The consumers provide insight and perspective at Remove the Mask inter-disciplinary meetings. Their insights bring to light priorities and perspectives which couldn't be uncovered by anyone who hadn't undergone treatment themselves, and have directly shaped the solutions our researchers are developing.



Personnel

Academic Staff

Professor Paul Keall, Director

Professor Ricky O'Brien, Deputy Director

Dr Mir Massoud Aghili Yajadda, Postdoctoral Research Associate

Dr Youssef Ben Bouchta, Postdoctoral Research Associate

Dr Samuel Blake, Postdoctoral Research Associate

Dr Caterina Brighi, Postdoctoral Research Associate

Dr Emily Debrot, Postdoctoral Research Associate

Dr Owen Dillon, Postdoctoral Research Associate

Dr Michelle Dunbar, Postdoctoral Research Associate

Dr Mark Gardner, Postdoctoral Research Associate

James Grover, Research Associate

Dr Xiaoshui Huang, Postdoctoral Research Associate

Dr Paul Liu, Cancer Institute NSW Early Career Fellow

Dr Elshin Mathias, Postdoctoral Research Associate

Dr Lars Mejnertsen, Postdoctoral Research Associate

Dr Joseph Prinable, Postdoctoral Research Associate

Dr Tess Reynolds, University of Sydney Postdoctoral Fellow

Dr Chandrima Sengupta, Postdoctoral Research Associate

Dr Shanshan Shan, Postdoctoral Research Associate

Dr David Waddington, Cancer Institute NSW Early Career Fellow

Dr Brendan Whelan, NHMRC Early Career Fellow
20 FTE in 2021

Professional Staff

Dr Helen Ball, Operations Manager
Indrajit Ghosh, Software Engineer
Jonathan Hindmarsh, Clinical Medical Physicist
Julia Johnson, Design & Communications Officer
Kuldeep Makhija, Software Engineer
Amelia Martin, Research Assistant
Natalie Plant, Clinical Trials Lead
Shona Silvester, Clinical Trials Lead
Dr Sara Tomka, Institute Manager
Sebastien Ybert, Project Manager, Research Operations
7.1 FTE in 2021

Students

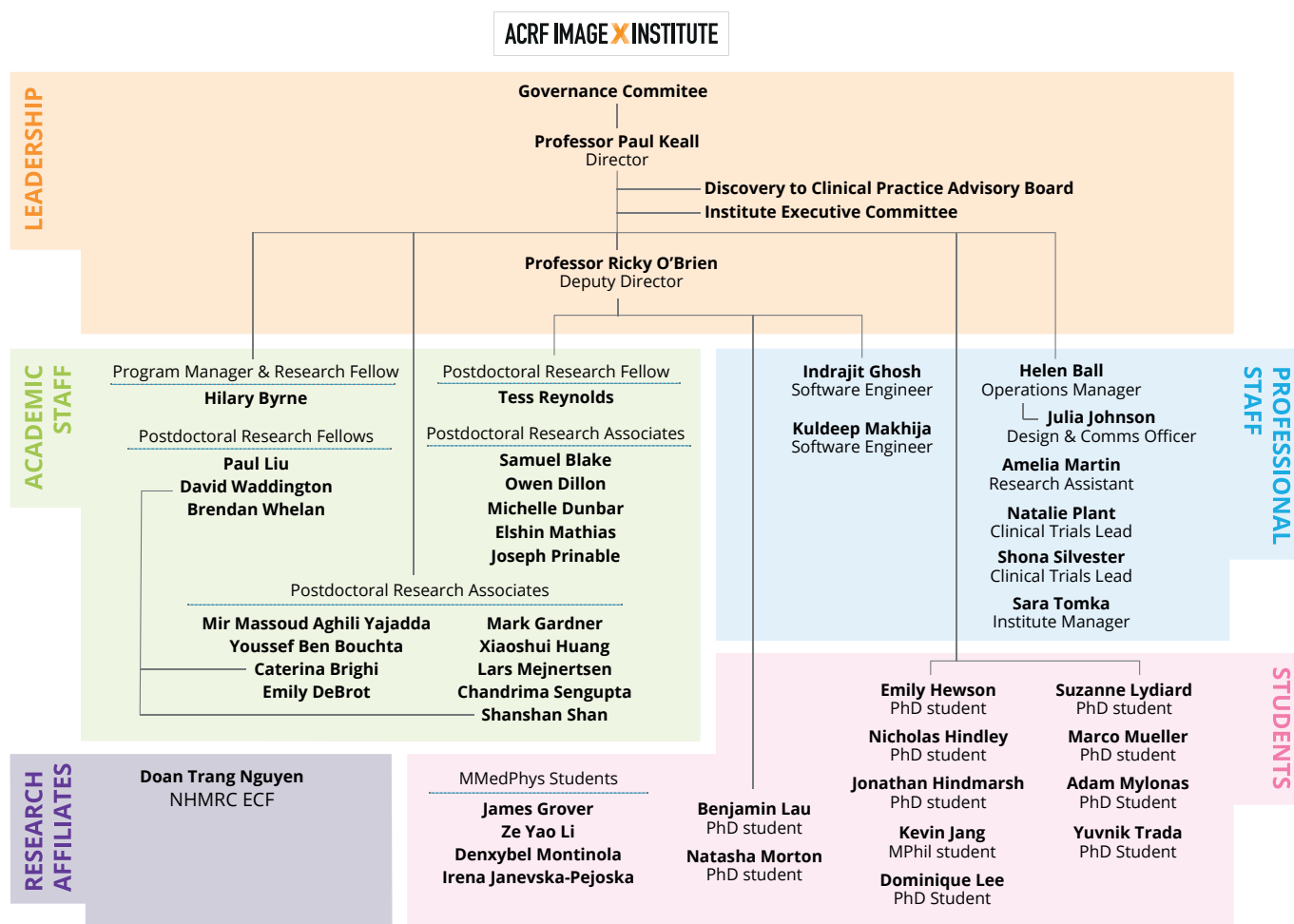
Emily Hewson, Doctor of Philosophy
Nicholas Hindley, Doctor of Philosophy
Jonathan Hindmarsh, Doctor of Philosophy
Benjamin Lau, Doctor of Philosophy
Dr Dominique Lee, Doctor of Philosophy
Natasha Morton, Doctor of Philosophy
Marco Mueller, Doctor of Philosophy
Adam Mylonas, Doctor of Philosophy
Dr Yuvnik Trada, Doctor of Philosophy
7.5 FTE in 2021

James Grover, Masters of Medical Physics
Irena Janevska-Pejoska, Masters of Medical Physics
Dr Kevin Jang, Masters of Philosophy
Ze Yao Li, Masters of Medical Physics
Denxybel Montinola, Masters of Medical Physics

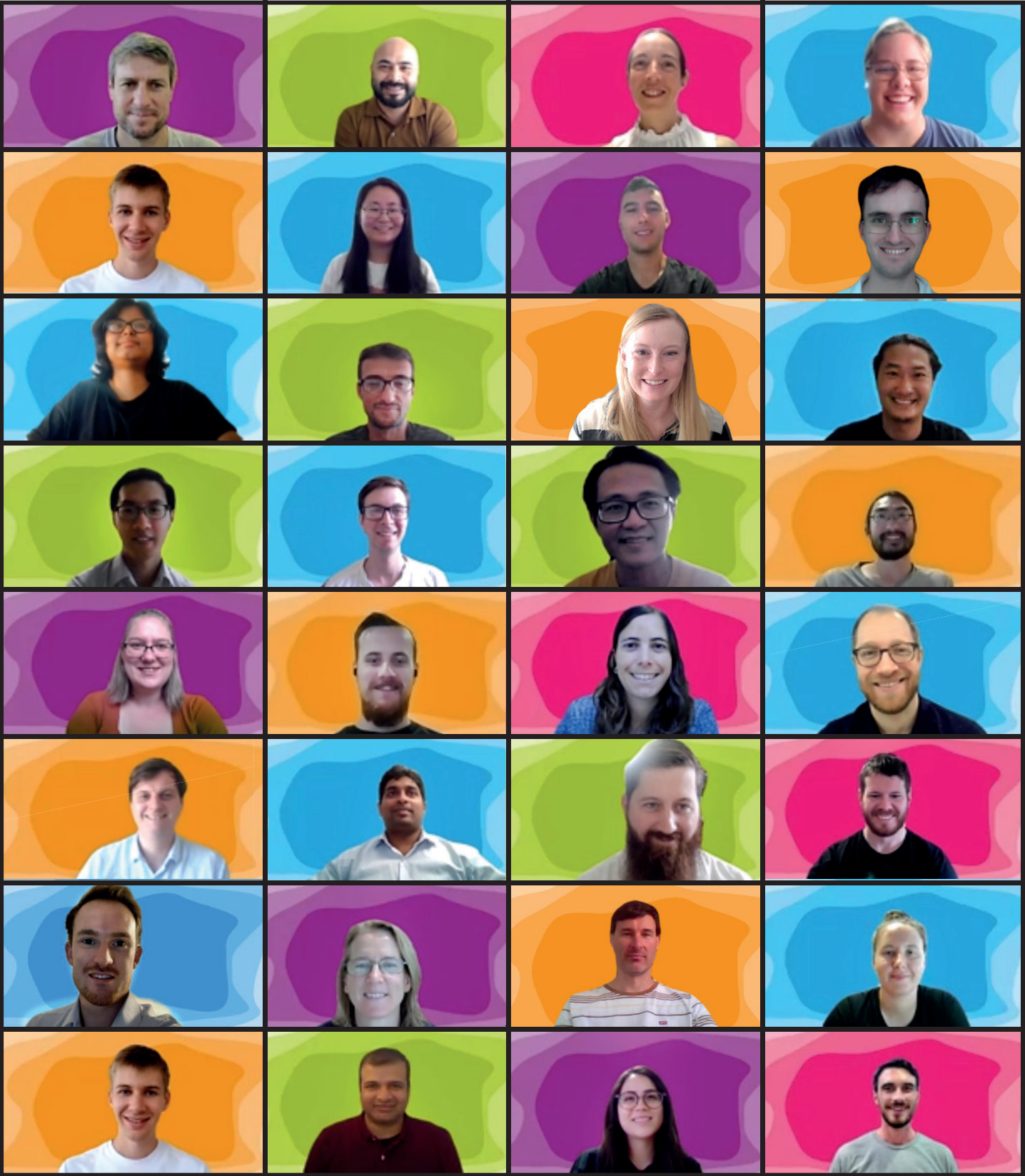
Biomedical Engineering Honours projects

Sophie Yu Wei, Fanyi Zhao, Ashika Hettitanti, Qiting Huang

Organisational Chart



2021 Staff Zoom Portrait





Governance

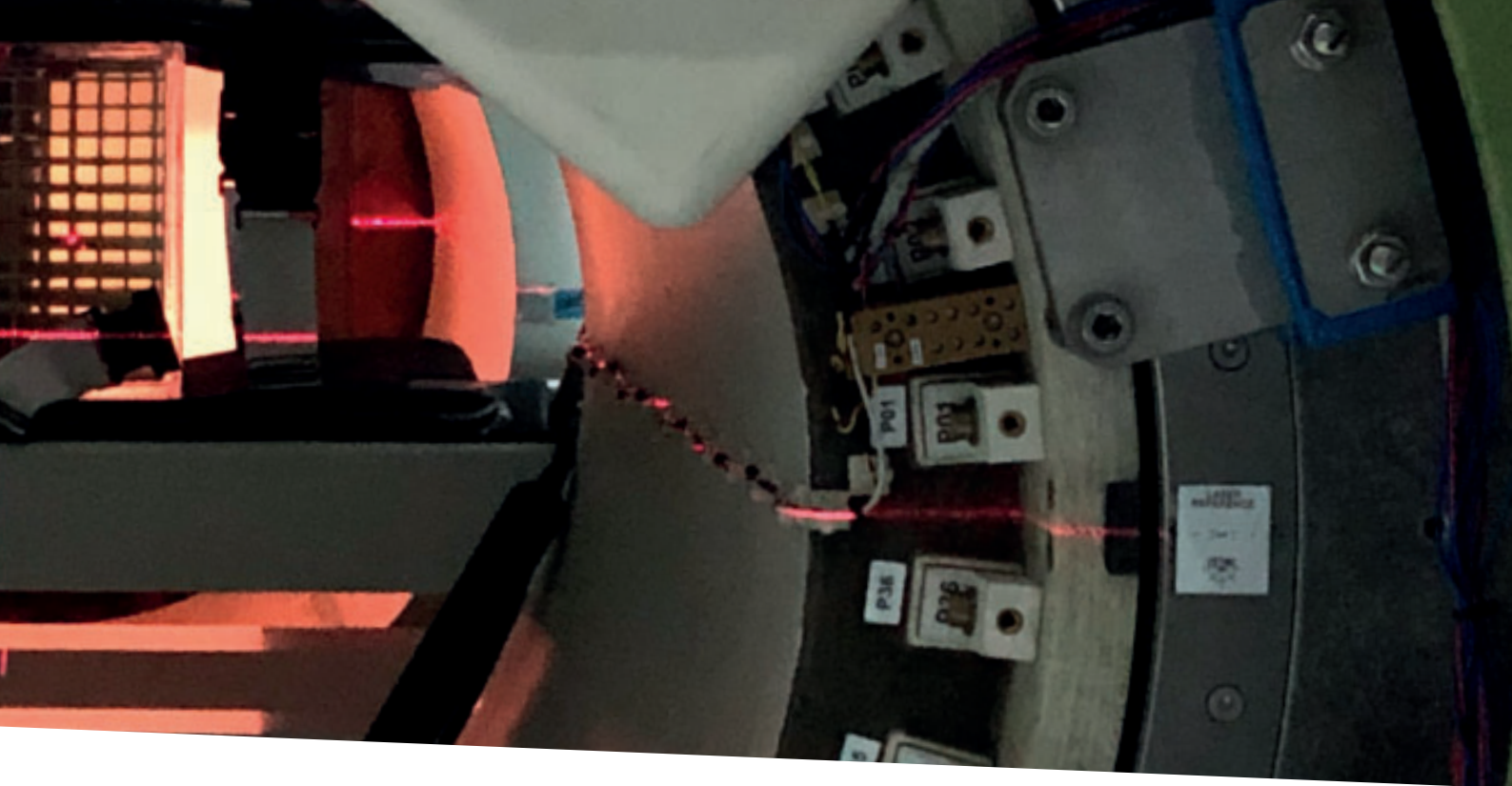
Governance Committee

Our Governance Committee oversees the governance and progress of the Institute and provides direction and support in helping us to achieve our goals through the removal of barriers. The ACRF Image X Institute sits within

the Clinical Imaging node of the Sydney School of Health Sciences and Faculty of Medicine, and the committee has representation from the institute, school and faculty levels as well as Research Operations and Finance.

- Professor Sarah Lewis (Chair), Associate Dean (Research Performance), Faculty of Medicine and Health
- Dr Helen Ball, ACRF Image X Institute Operations Manager
- Professor Paul Keall, ACRF Image X Institute Director
- Professor Ricky O'Brien, ACRF Image X Institute Deputy Director
- Dr Tess Reynolds, ACRF Image X Institute Early Career Fellow
- Professor Laurent Rivory, Pro Vice Chancellor Research
- Mina Tang, Finance Manager, Faculty of Medicine and Health
- Dr Andrew Tindell, Executive Director, Research Operations
- Professor Martin Ugander, Head of Clinical Imaging, Sydney School of Health Sciences

Pictured: Running tests at the MRI Linac



Executive Committee

Our Executive committee provides direction on key issues and operations of the institute.

Its membership includes senior/ early career research academic, student and professional staff representation; Paul Keall, Ricky O'Brien, Helen Ball, Owen Dillon, Tess Reynolds, Sebastien Ybert (Research Operations) and Benjamin Lau.

Discovery to Clinical Practice Advisory Panel

The Discovery to Clinical Practice Advisory Panel provides clinical advice, guidance and recommendations on all three stages of the translational pathway, i.e. discovery, clinical trials into clinical practice, to optimise the clinical, consumer and commercial relevance of our research program.

- Associate Professor Verity Ahern, Radiation Oncologist, Crown Princess Mary Cancer Centre (Westmead Hospital), Director of the Sydney West Radiation Oncology Network
- Professor June Corry, Radiation Oncologist, GenesisCare
- Professor Jarad Martin, Radiation Oncologist and Departmental Director of Research at the Calvary Mater Newcastle Hospital
- Julie McCrossin OAM: Freelance journalist and facilitator, Ambassador for Targeting Cancer
- Associate Professor Peter O'Brien, Chief Medical Officer for Oncology, GenesisCare
- Dr Peter Spencer, Medtech commercialisation consultant, Peter Spencer & Associates
- Dr Kathryn Sunn, Head of Commercialisation, Post-Award Team, University of Sydney

Publications

The following peer-reviewed articles were published or accepted for publication in 2021.

Booth J, Caillet V, Briggs A, Hardcastle N, Angelis G, Jayamanne D, Shepherd M, Podreka A, Szymura K, Nguyen DT, Poulsen P, O'Brien R, Harris B, Haddad C, Eade T, Keall P. *MLC tracking for lung SABR is feasible, efficient and delivers high-precision target dose and lower normal tissue dose*. *Radiotherapy and Oncology*. 2021;155:131-137. doi: 10.1016/j.radonc.2020.10.036

Buckley JG, Dowling JA, Sidhom M, Liney GP, Rai R, Metcalfe PE, Holloway LC, Keall PJ. *Pelvic organ motion and dosimetric implications during horizontal patient rotation for prostate radiation therapy*. *Medical Physics*. 2021;48(1):397-413. doi: 10.1002/mp.14579

Buckley JG, Smith AB, Sidhom M, Rai R, Liney GP, Dowling JA, Metcalfe PE, Holloway LC, Keall PJ. *Measurements of human tolerance to horizontal rotation within an MRI scanner: Towards gantry-free radiation therapy*. *Journal of Medical Imaging and Radiation Oncology*. 2021;65(1):112-119. doi: 10.1111/1754-9485.13130

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Conference Presentations

The presenting author is denoted by the asterisk

American Association of Physicists In Medicine 2021 Annual Meeting (Virtual)

E Hewson*, D Nguyen, J Booth, P Keall, L Mejnertsen. Real-Time Dose-Optimized Multi-Target MLC Tracking for Locally Advanced Prostate Cancer. Best in Physics Oral presentation

T Reynolds*, Y Ma, G-J Gang, O Dillon, T Russ, W Wang, T Ehtiati, C Weiss, N Theodore, J Siewerdsen, R O'Brien, J Stayman. Imaging from the cervical to the lumbar spine with a continuous multi-turn reverse helical 3D cone-beam CT scan. Jack Fowler Early Career Investigator Award, Oral presentation

P Liu*.Next-Generation Target Tracking Using MRI Guidance. Invited talk

S Lydiard*.Research Opportunities from Academia: A Summary of the State-of-the-art Cardiac Radioablation Medical Physics Research and Future Opportunities. SAM Invited talk

D T Nguyen* (mage X affiliate).AI for intrafraction motion monitoring: Are we there yet?. SAM Invited talk

T Reynolds*. Adaptive Imaging - Syncing with Patients for Safer and Smarter 3D imaging. Invited talk

S Blake*, O Dillon, R O'Brien.A Method for 4D Cone-Beam CT in Under 20 Seconds with New Generation Linacs. Oral presentation

O Dillon*, B Lau, T Reynolds, P Keall, S Vinod, A Wallis, S Smith, J Sonke, R O'Brien. Faster Safer Clearer 4DCBCT: Results of the ADAPT Clinical Trial. Oral presentation

Q Hoang, J Booth, V Caillet, P Keall, D Nguyen*. One-Second Into the Future: A Deep Learning Method to Predict 3D Lung Cancer Target Motion to Account for Adaptation Latency. Oral presentation

B Lau*, O Dillon, T Reynolds, P Keall, J Sonke, S Vinod, R O'Brien. Rapid Low Dose 4DCBCT.Oral presentation

S Lydiard*, B Pontre, N Hindley, B Lowe, G Sasso, P Keall. Cardiac Radioablation: MRI-Guided Tracking of Cardiac-Induced Target Motion. Oral presentation

E Mathias*, N Morton, R O'Brien. Respiratory Adaptive Computed Tomography (REACT) to Reduce Artifacts in Helical 4DCT Scans. Oral presentation

M Mueller*, A Mylonas, P Keall, J Booth, D Nguyen. Simultaneous Segmentation of Target and Organ at Risk in Thoracic Kilovoltage Images. Oral presentation

D Nguyen*, T Moodie, C Sengupta, E Sullivan, T Blacketer, R O'Brien, J Booth, Y Lee, T Wang, P Keall. Motion Management During Breath-Hold SBRT Liver Treatments: External Optical Monitoring Is Not Adequate – First Results of the TROG 17.03 Liver Ablative Radiotherapy with KIM (LARK). Oral presentation

T Reynolds*, Owen Dillon, Ricky O'Brien. Head, Shoulders, Knees, and Toes: Towards Full Body Upright Cone-Beam CT imaging. Oral Presentation

C Sengupta*, S Alnaghy, D Nguyen, A Kyme, K Makhija, T Moodie, D Mason, V Caillet, K Shi, R O'Brien, J Booth, S Tomka, P Keall. 6-DoF Robotic Motion Phantom: An Open-Source Project for Quality Assurance of Real-Time Image-Guided Radiotherapy Technologies. Oral presentation

S Shan*, D Waddington, P Liu, B Dong, J Buckley, D Elwadia, T Pham, G Liney, P Keall. Correcting Image Distortion for Brain Tumor Treatments On An MRI-Linac. Oral presentation

S Blake*, O Dillon, R O'Brien. Correcting Cone-Beam CT for Patient-Generated Scatter Using Bayesian Monte Carlo Extrapolation. Interactive ePoster

H Byrne*, J Kipritidis, O Dillon, J Booth, P Keall. Investigation of the Sensitivity of Ventilation Accuracy to the Deformable Image Registration Regularization Parameter. Interactive ePoster

B Lau*, O Dillon, T Reynolds, P Keall, J Sonke, S Vinod, R O'Brien. Reducing Scan Time and Dose: Motion Compensated Reconstruction for Adaptive 4DCBCT. Interactive ePoster

P Liu*, D Waddington, S Shan, B Dong, P Keall. Enabling Upright Radiotherapy Through the Deformation of Horizontally Acquired Images. Interactive ePoster

N Morton*, T Reynolds, P Keall, R O'Brien. CARE-CT: CARDiac and RESpiratory Adaptive Computed Tomography .Interactive ePoster

M Gardner*, A Mylonas, M Mueller, Y Ben Bouchta, J Sykes, P Keall, D Nguyen. Automatic Segmentation of Head and Neck Tumors During Treatment: Can We Remove the Mask Yet?. General ePoster

A Mylonas*, M Mueller, P Keall, J Booth, D Nguyen. Towards Real-Time Markerless Prostate IGRT During VMAT Treatment. General ePoster

C Sengupta*, S Skouboe, D Nguyen, T Ravkilde, P Poulsen, T Moodie, P Keall. Performance Characterization of a Real-Time Dose Reconstruction Algorithm for Prostate Stereotactic Radiotherapy Treatment. General ePoster

Australia and New Zealand Chapter of the International Society for Magnetic Resonance in Medicine (Virtual)

D Waddington*. Accelerating Image Reconstruction for Tumour Tracking with AUTOMAP. Oral presentation

Australian Institute of Physics Summer Meeting (Blended)

P Keall*. Building and clinically translating new technology for cancer imaging and targeted radiation therapy. Keynote Speaker

Cooperative Trials Group for NeuroOncology Annual Scientific Meeting (Virtual)

C Brighi*, S Puttick, S Li, P Keall, D Waddington, P Bourgeat, A Gillman, M Fay. Standardisation of 18F-FET PET imaging quantification in neuro-oncology: a semiautomated method for background activity and biological tumour volume definition. ePoster

Engineering and Physical Sciences in Medicine (Blended)

H Byrne*, C Stanton, B Zwan, M Gargett, E Steiner, K Makhija, J Atyeo, K Richardson, L Ambrose, R Bromley, J Booth, M Morgia, G Lamoury, P Keall. Comparing patient monitoring and biofeedback methods for breast radiotherapy: the BRAVEHeart trial. Oral presentation

B Whelan*, J Wang, R Fahrig, M Shumail, S Trovati, S Tantawi, J Perl, P Keall, B Loo. Towards IMRT with no moving parts: Bayesian optimization of a novel X-ray collimation concept. Oral presentation

M Mueller*, A Mylonas, P Keall, J Booth, DT Nguyen. Simultaneous segmentation of tumour, organ-at-risk and diaphragm in thoracic kV-projections using machine learning. Oral presentation

C Sengupta*, D T Nguyen, T Moodie, T Wang, Y Y Lee, R O' Brien, J Booth, P Keall. Six Degrees of Freedom Intrafraction Motion Monitoring during Stereotactic Liver Radiation Therapy in TROG 17.03 LARK Trial: Higher accuracy in half the treatment time than the current standard of care. Oral presentation

J Selvaraj*, C Sengupta, P Keall. KIMView: An open-source real-time tumour motion, dose, and anatomy visualisation tool for radiotherapy. Oral presentation

Z Y Li*, A Mylonas, R Brown, J Booth, D T Nguyen. A novel real-time IGRT method to track the prostate without fiducial markers .ePoster

J Hindmarsh*, J Booth, S Dietrich, P Keall. Hazard analysis in radiation therapy: Applying System-Theoretic Process Analysis to MLC tracking. ePoster

I Ghosh*, C Sengupta, A Mylonas, P Keall, D T Nguyen. Development of a Cross-Institutional Centralised Database to Leverage Radiotherapy Clinical Trial Data for Deep Learning Applications. ePoster

J Luo*, C Sengupta, D Mason, D Nguyen. Tumour Motion-inclusive Dose Reconstruction for Pinnacle Treatment Planning System (TPS) for the TROG 17.03 LARK clinical trial. ePoster

H Byrne*, O Dillon, S Blake, J Kipritidis, R O'Brien, P Keall. Lung ventilation imaging from low-dose 4DCBCT for daily function adaptation: a proof of concept study. ePoster

S Blake*, O Dillon, H Byrne, R O'Brien. Rapid 4D cone-beam CT in under 20 seconds with new generation linacs: a simulation study. ePoster

European Society for Therapeutic Radiology and Oncology Annual meeting 2021 (Blended)

C Brighi*, E-S Koh, L Holloway, A Walker, F Aly, P Keall, D Waddington. Stability of multiparametric MR imaging biomarker-derived dose prescriptions for glioblastoma. Oral presentation

M Mueller*, P Poulsen, W Verbakel, L Ren, L Wang, S Mori, R Berbeco, P Zhang, J Roeske, R Hansen, P Keall. The MArkerless Lung target Tracking CHallenge (MATCH). Oral presentation

X Huang*, S Vinod, P Keall, M Field, V Batumalai, L Holloway. Real world radiotherapy protocol compliance for patients with Stage I-III Non-Small Cell Lung cancer .ePoster

International Society for Magnetic Resonance in Medicine Annual meeting 2021 (Virtual)

David Waddington*. High-Contrast Imaging at Low Magnetic Fields. Invited talk

MedPhys2021 (Virtual)

E Hewson*. Real-time dose-optimized multi-target MLC tracking for locally advanced prostate cancer. Oral presentation

J Hindmarsh*. Applying a new hazard identification method, system theoretic process analysis, to quality assurance for multileaf collimator tracking. Oral presentation

Z Y Li*. A novel real-time IGRT method to track the prostate without fiducial markers. Oral presentation

J Grover*. Machine Learning Applied to CT Ventilation Imaging. Oral presentation

The Royal Australian and New Zealand College of Radiologists Annual Scientific Meeting (Virtual)

C Chiu*, N Hindley, T Reynolds, P Keall, D Waddington. Transfer learning with deep neural networks using YouTube videos for real-time MRI reconstruction in radiation oncology and interventional radiology. Oral Presentation

Sydney Cancer Conference (Virtual)

C Brighi*, E-S Koh, L Holloway, A Walker, F Aly, P Keall, D Waddington. Stability of multiparametric MR imaging biomarker-derived dose prescriptions for glioblastoma. Oral presentation

H Byrne*, C Stanton, B Zwan, M Gargett, E Steiner, K Makhija, J Atyeo, K Richardson, L Ambrose, R Bromley, J Booth, M Morgia, G Lamoury, P Keall. Comparing patient monitoring and biofeedback methods for breast radiotherapy: the BRAVEHeart trial. ePoster and mini-oral presentation

D Waddington*. Career-building and grant applications – Research Funding Workshop. Invited talk

Invited Talks

Dr Caterina Brighi, *Mapping the tumour heterogeneity with multiparametric MRI: changing the paradigm of radiotherapy treatments of brain cancer*. UQ Centre for Advanced Imaging.

Dr Caterina Brighi, *Quantitative imaging biomarkers in neuro-oncology – overcoming the barriers to effective clinical implementation*. Melbourne Brain Cancer Imaging Unit group at the University of Melbourne.

Suzanne Lydiard, *Cardiac radioablation: An introduction, an overview, and how medical physicists could shape its future*. Australasian College of Physical Scientists & Engineers in Medicine webinar.

Marco Müller, *The MARKerless Lung Target Tracking CHallenge (MATCH): An AAPM Grand Challenge*. AAPM Webinar Series: Advances in Medical Physics.

Dr Tess Reynolds, *Near Clinical Imaging in the Hybrid Theatre*, Medical Physics Graduate Program Seminar Series, University of Wisconsin (Madison, USA).

Dr Tess Reynolds, *Twitter for Professional Use*. Ingham Institute of Applied Medical Research.

Dr Tess Reynolds, *Near-clinical hybrid theatre imaging*. Clinical Imaging Summit, University of Sydney

Dr Chandrima Sengupta, *Liver Ablative Radiotherapy Utilizing Kilovoltage Intrafraction Monitoring: TROG 17.03 LARK Trial*. International Clinical Trials Day event organised by the USYD Clinical Trials Support Office.

Dr David Waddington, *MRI: Expanding the accessibility of MRI*. Ingham Institute of Applied Medical Research

Professor Paul Keall gave the following invited presentations.

MLC Tracking: Clinical rationale, clinical experience, guidelines and future directions. Australasian College of Physical Scientists and Engineers in Medicine webinar.

MRI-guided Radiation Therapy: See what you treat. University of Pennsylvania

MRI-guided Radiation Therapy: See what you treat. German Cancer Research Centre, Heidelberg.

Physiologically-gated radiotherapy. Clinical Imaging Summit, University of Sydney

Building Teams for Real World Impact, Keynote speaker, Winter Institute of Medical Physics meeting.

The Australian MRI-Linac system: How to arrive at the first patient treatment? 8th MR in RT Satellite Symposium, German Cancer Research Centre, Heidelberg

Building and clinically translating new technology for cancer imaging and targeted radiation therapy. Plenary speaker, 17th National Annual Meeting of Medical Physics (CSMP2021), Wuhan, China.

Confounding factors due Motion management strategies in SBRT. 2021 European Society for Therapeutic Radiation Oncology Physics Workshop

MRgRT systems: a precommercial device – the Australian system and Next generation of MRgRT systems for the American Association of Physics in Medicine Summer School on Modern Applications of MR in Radiation Therapy.

Intellectual Property

Records of Invention

Online Geometric Calibration with External Markers. Owen Dillon, Ricky O'Brien, Tess Reynolds

Multi-turn reverse helical 3D cone-beam CT imaging. Tess Reynolds, Ricky O'Brien

Upright weight bearing 3DCBCT imaging. Tess Reynolds, Ricky O'Brien, Owen Dillon

REACT. Natasha Morton, Ricky O'Brien, Jonathan Sykes, Paul Keall, Jeff Barber

Kilovoltage Intrafraction Monitoring (KIM)- clinical implementation development and liver cancer treatment. Doan Trang Nguyen, Trevor Moodie, Ricky O'Brien, Sankar Arumugam, Daniel Mason, Paul Keall

Method and system for efficient 2D to 3D image registration and volumetric imaging during image-guided radiotherapy. Nicholas Hindley, Chun-Chien Shieh, Paul Keall

USYD-based MLC Tracking Intellectual Property Update 2021. Doan Trang Nguyen, Paul Liu, Emily Hewson, Paul Keall

Kilovoltage Intrafraction Monitoring Update 2021. Paul Keall, Doan Trang Nguyen, Ricky O'Brien, Chen-Yu Huang, Jin Aun Ng, Jung-Ha Kim and Emma Colvill

Patents filed

Method for tracking respiratory motion during x-ray guided cardiac radioablation. Nicholas Hindley, Paul Keall, Chun-Chien Shieh, Suzanne Lydiard

Dose-based optimization for multi-leaf collimator (MLC) tracking during radiation therapy. Lars Mejnertsen, Paul Keall, Doan Trang Nguyen, Emily Hewson

Licence agreements and assignments

There were six license agreements or assignments in 2021 however they are not listed in more detail as some are confidential.

A photograph of a radiotherapy treatment room. In the foreground, a large white plastic phantom of a human head and neck is positioned on a treatment table. In the background, a large white banner for the ACRF Image X Institute is visible, featuring the institute's name, mission statement, and logos for the Australian Cancer Research Foundation and The University of Sydney. The banner is partially framed by the large, curved gantry of a linear accelerator.

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