

A photograph of a person lying inside an MRI scanner. The person is positioned horizontally, with their head at the bottom of the frame. The scanner's large, circular gantry is visible, with various mechanical components and labels. The lighting is warm and yellowish. A large orange triangle is on the left side of the image.

IMAGE X INSTITUTE |  **THE UNIVERSITY OF SYDNEY**

ANNUAL REPORT

2022



Pictured: A volunteer undergoes a scan in the Australian MRI Linac, Ingham Intitute.

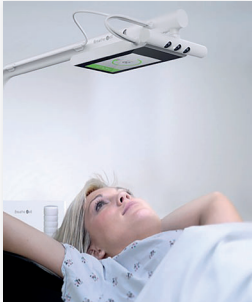
A person wearing a light-colored lab coat and dark trousers stands on the left side of the frame, facing away from the camera. They are positioned next to a large, complex medical imaging machine, possibly an MRI or CT scanner. The machine has a large, curved, metallic structure. The entire image is covered with a semi-transparent orange overlay. The text "Our mission is to improve lives by inventing and advancing new ways to image and treat disease." is written in white, bold, sans-serif font across the middle of the image.

**Our mission is to improve
lives by inventing and
advancing new ways to
image and treat disease.**



\$3M

Grants
commenced



7

Clinical
trials active

33

papers
published

\$6.8M+

grants awarded in 2022

SNAPSHOT 2022

50

Patients
participated in
clinical trials

48

Conference
presentations and
invited talks given

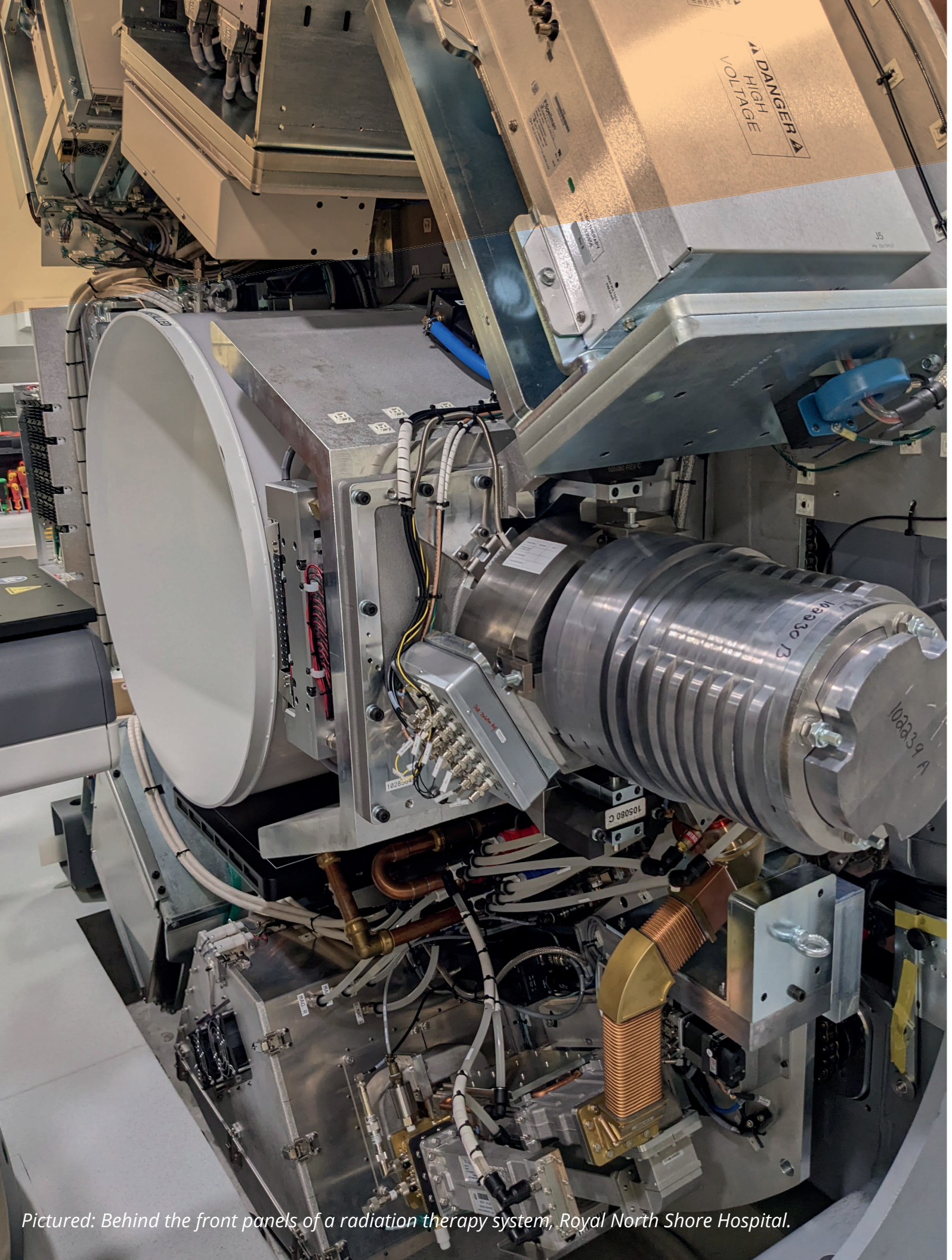
28

invited talks
presented

6

New **clinical studies**
approved for 2023





Pictured: Behind the front panels of a radiation therapy system, Royal North Shore Hospital.

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Director's Message

It has again been an honour and a pleasure to lead Image X through another year of amazing achievements amidst local and global challenges. This annual report will highlight many of our milestones. We are fortunate that our research spans the length of the translational spectrum from basic scientific discovery through to clinical trials and clinically used products to improve patient outcomes. Our project breadth spans nanoparticle research to improve imaging and targeting cancer, building multimillion dollar treatment machines to adapt to changing patient anatomy and physiology to software that can improve treatment accuracy, thorough and the patient experience.

Our work requires people and funding. These people are the Image X professional and academic staff and students, consumer advisors, the many areas of University support, our industry partners, our collaborators and particularly our clinical trial partners. So much time, effort and goodwill from health professionals goes into clinical trials to maximise the short and long term patient outcomes and treatment experience. It is humbling, inspiring and comforting to have this support and to know the virtues of the people caring for patients in our communities.

Coming by money is never easy, and medical research funding is no exception. We acknowledge our funding sources, and the extensive network of people and reviewers behind them, who have chosen to support our research. These funders include the NHMRC, Cancer Institute NSW, Cancer Australia, Cancer Council NSW, ARC, MRFF and the University of Sydney amongst others. Without them, there would not be an Image X Institute.

In addition to the scientific and clinical achievements, with World Pride being held in Sydney in 2023, it is pleasing that at least for different Image X team members have been invited to talk about Diversity, Equity and Inclusivity at different forums over the past year. These invitations say a lot about the Image X team members, and our team culture. Embrace differences, and bring these differences to solve major problems, which for us is to improve lives by inventing and advancing new ways to image and treat disease.

Enjoy the report, and thank you to Julia, Helen and others at Image X for putting this together.

Sincerely

Professor Paul Keall

Director, Image X Institute
Faculty of Medicine and Health
University of Sydney

Research Themes 2022

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 patient's respiratory motion.

● 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.
- **KIM**
Technologies that track moving tumours using a standard linac and markers.
- **MARKERLESS**
Technologies that track moving tumours using a standard linac, without markers.
- **TUMOUR TARGETING**
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.
- **NOVEL BEAM SHAPING**
Developing mechanisms and devices to shape radiation beams with no moving parts.

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 2022

CT IMAGING

4DCT acquires multiple 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, for example, the tumour can appear a different shape, larger or smaller than it actually is. These errors can propagate throughout the radiotherapy treatment process. Respiratory Adaptive Computer Tomography (REACT) aims to reduce both the number and size of these imaging errors, by accounting for changes to a patient's breathing and gating (halting) the CT beam automatically during the imaging process.

In 2022, Natasha Morton demonstrated the benefit of accounting for both respiratory and cardiac motion with a digital phantom study in *CARDiac and RESpiratory adaptive Computed Tomography (CARE-CT): a proof-of-concept digital phantom study*. She also outlined the system

requirements for future respiratory adaptive 4DCT imaging in *System requirements to improve adaptive 4-dimensional computed tomography (4D CT) imaging*. Elshin Mathias continued work on extending REACT to reduce artifacts in the helical mode of 4DCT imaging which led to a poster presentation in American Association of Physicists in Medicine 2022 conference.

Researchers

Elshin Mathias

Ricky O'Brien

Joseph Prinable

Tess Reynolds

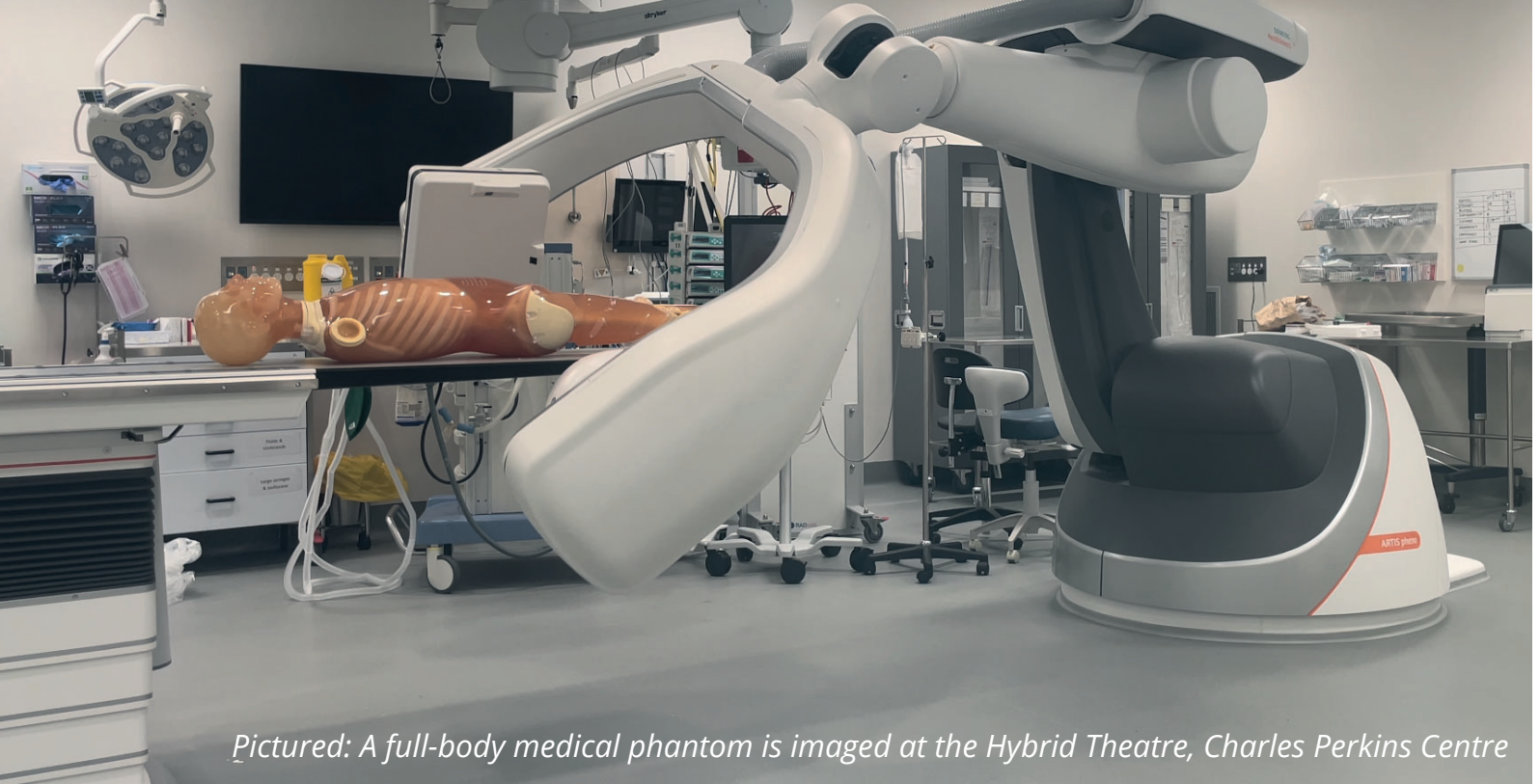
Students

Natasha Morton



Pictured:

A lung phantom experiment at the Hybrid Theatre, Charles Perkins Centre



Pictured: A full-body medical phantom is imaged at the Hybrid Theatre, Charles Perkins Centre

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. PhD student

Benjamin Lau used the imaging data acquired in the ADAPT trial to investigate how much further this technology could be pushed to most improve patient care in *Reducing 4DCBCT imaging dose and time: exploring the limits of adaptive acquisition and motion compensated reconstruction*. The adaptive reconstruction technology pioneered in ADAPT has been applied to new generation radiotherapy systems to enable 20 second 4D imaging in *Thoracic motion-compensated cone-beam computed tomography in under 20 seconds on a fast-rotating linac: A simulation study*.

Researchers

Samuel Blake

Owen Dillon

Michelle Dunbar

Ricky O'Brien

Tess Reynolds

Students

Benjamin Lau

Associated Studies Occuring in 2022

ADAPT

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



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 2022, Dr Tess Reynolds received the 2022 Australian Museum Eureka Prize for

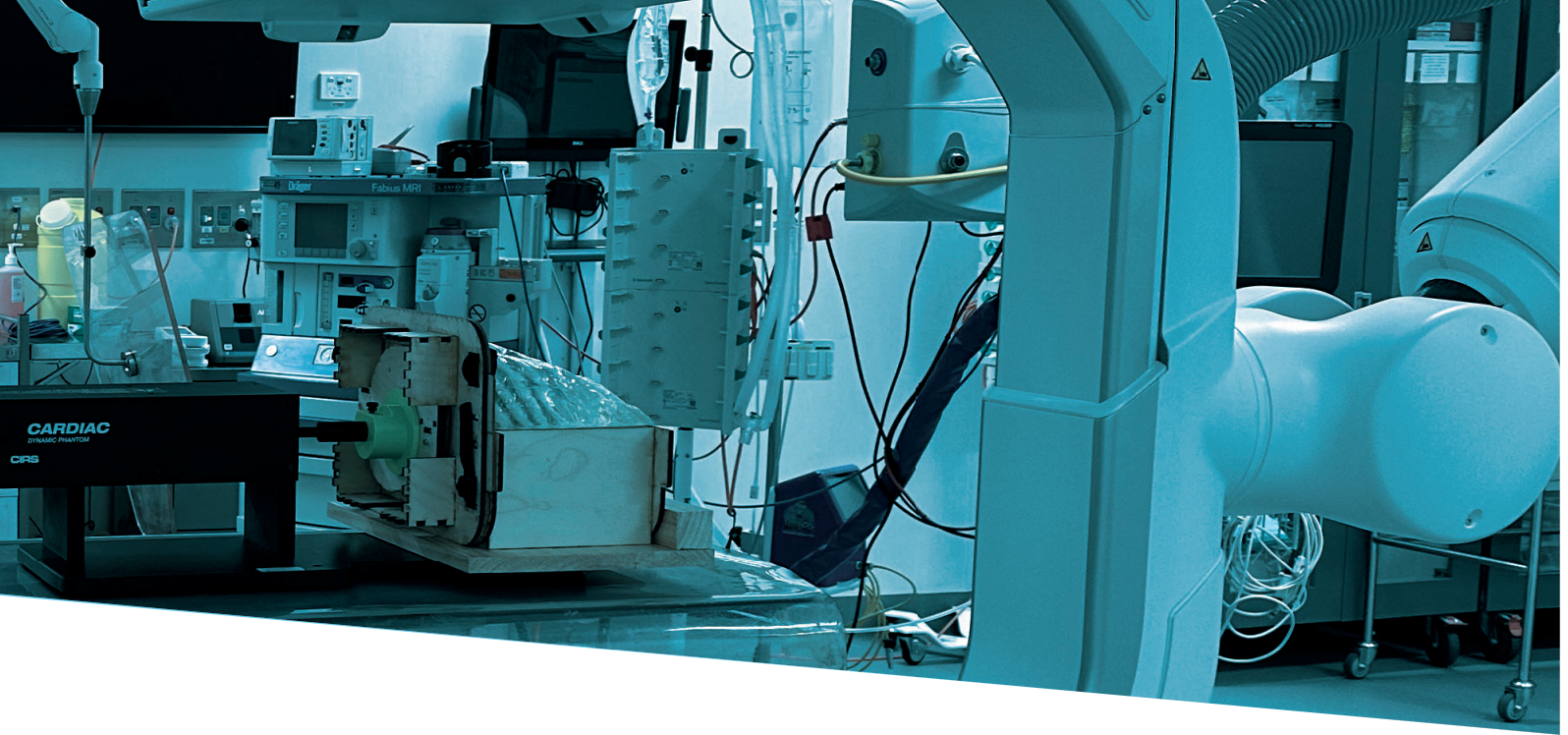
Outstanding Early Career Researcher in part for developing ACROBEAT. The technology will be implemented on a linear accelerator as part of an NHMRC Synergy grant awarded in 2022 to use radioablation to treat cardiac arrhythmias.

Researchers

Owed Dillon

Ricky O'Brien

Tess Reynolds



Pictured: Dr Tess Reynolds works on a pelvis medical phantom at Johns Hopkins University.

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 2022

In 2022, Dr Tess Reynolds was invited to host and speak in a Symposium at the 2022 American Association of Physicists in Medicine Annual Meeting and received the 2022 Australian Museum Eureka Prize for Outstanding Early Career Researcher. 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. 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 in 2022, we collaborated to produce 3 international conference proceedings on the implementation of metal artifact reduction imaging techniques.

Partnering with Dr Andrew Kanawati (Westmead Hospital), Dr Reynolds used 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.

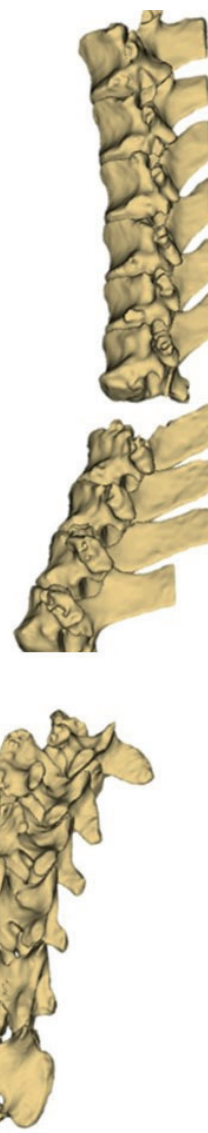
Researchers

Owen Dillon

Ricky O'Brien

Tess Reynolds

Pictured: A 3D-rendering of a sheep spine for procedural planning derived from a CBCT image.



CT Ventilation Imaging

Project Overview

CT Ventilation is a software technique developed by Image X for spatially mapping the function in patients' lungs. Using CT images routinely acquired as part of the radiotherapy planning process, 3D maps can be produced identifying which parts of the lung are functioning well, and which poorly.

Radiotherapy is an essential, life-saving therapy recommended for 77% of lung cancer patients. However, up to 18% of lung cancer patients experience severe radiation pneumonitis following radiotherapy treatment. Taking lung function into account during radiotherapy planning can allow clinicians to spare high

functioning lung and reduce radiation side effects for patients.

Image X are working to gather the evidence needed to support clinical uptake of this technology to spare healthy lung during radiotherapy, and investigate wider use outside radiotherapy.

Highlights of 2022

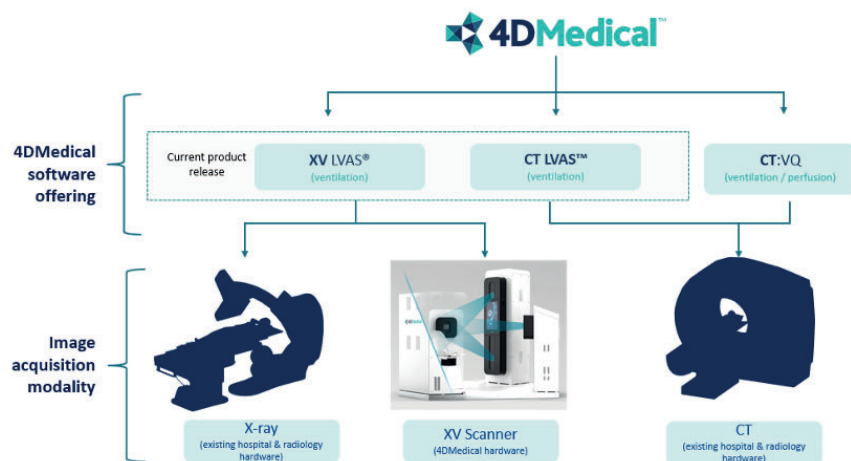
The CT Ventilation team have had an exciting year with the announcement by our industry partner 4D Medical of a commercial CT Ventilation product (CT LVAS). This success stems from a strong, ongoing collaboration. An MTPConnect REDI fellowship has seen Dr Hilary Byrne work closely with the company over the last year during the product development stage. The collaboration will continue through Prof Ricky O'Brien's NHMRC Development Grant researching the implementation of CT Ventilation in lung radiotherapy, and the opportunity to use ventilation imaging in other applications.

Dr Hilary Byrne was part of running a TROG planning study – an open international challenge calling on participants to develop radiotherapy plans to spare high functioning lung. With 98 participants from 12

countries, this was an important opportunity to raise awareness and check technical limitations of the technique.

Jeremy Lim carried out a project in fulfilment of his Master of Medical Physics degree, characterising the stability of CT ventilation technology to input parameter variations. This work is currently being drafted for publication.

Jeremy also presented his research at the EPSM2022 conference. Dr Byrne presented at AAPM2022 on CT ventilation applied to high-quality daily CT images obtained in the recent ADAPT trial, and spoke on trial design for testing CT Ventilation efficacy at the University of Maryland and the University of Sheffield/Weston Park Hospital.



Pictured: 4D Medical's product pipeline.

Researchers

Hilary Byrne
Owen Dillon
Paul Keall
Ricky O'Brien
Tess Reynolds

Students

Jeremy Lim

Kilovoltage Intrafraction Monitoring

Project Overview

During radiotherapy, tumours in the prostate, abdomen and thorax can move up to a few centimetres from the planned treatment position. If the precise position of a tumour during a treatment is not known, it may significantly deteriorate the treatment outcomes.

Kilovoltage intrafraction monitoring (KIM) is a novel 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 any motion beyond the treatment

tolerance by either 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 easily accessible to all cancer patients.

Highlights of 2022

KIM technology has expanded rapidly in the last year. It has been used to treat 20 liver cancer patients and 10 prostate cancer patients in the TROG 17.03 LARK trial and the TROG 18.01 NINJA trial respectively. In the LARK trial, the KIM-guided geometric and dosimetric outcomes showed significant improvements as compared to standard-of-care treatment. We used trial data from prostate cancer treatments to quantify the dosimetric error that can occur due to uncorrected tumour rotation in a paper published in the Medical Physics journal. Offline, the feasibility of using KIM for pancreatic cancer patients in the SPAN-C trial has been assessed.

We have extended KIM to track cylindrical and arbitrarily shaped fiducial markers, as well as smaller markers using deep-learning approaches. This will allow KIM to track smaller and easier-to-implant markers while maintaining the same exceptional sub-millimetre and sub-degree treatment targeting. We have extended the marker segmentation algorithm in KIM to track markers in the Megavoltage images (beams-eye-view) aiming to reduce the imaging dose to the patients.

Our researchers have presented these results at AAPM 2022, EPSM 2022, and two invited presentations at ACPSEM Motion Management Workshops. The presentation on the LARK trial won the 'Best Imaging Oral Presentation' award in EPSM 2022.

Funded by a Cancer Australia grant that commenced in 2022, we will extend KIM to other tumour sites such as spine, treat multiple targets including organs-at-risk to fully account for the differential motion and use smaller markers to reduce risk of marker implantation and toxicity, ultimately move towards marker-less approaches, where possible.



Pictured: The team at Peter MacCallum Cancer Centre in Melbourne oversee the first liver cancer patient treatment in the LARK Trial.



Pictured: Dr Chandrima Sengupta and medical physicist Dr Nick Hardcastle set up an experiment using a lung phantom and linear accelerator, Peter MacCallum Cancer Centre.

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.

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

KOALA

Use Kilovoltage Intrafraction Monitoring to track multiple targets simultaneously. KIM images are used to monitor the prostate via markers, as well as the pelvic bone, for patients with locally advanced prostate cancer.

Pictured: Chandrima Sengupta and a staff member of Peter MacCallum Cancer Centre conduct quality assurance using a lung phantom.

Researchers

Indrajit Ghosh

Jonathan Hindmarsh

Paul Keall

Yifan Li

Ricky O'Brien

Chandrima Sengupta

Students

Alicja Kaczynska

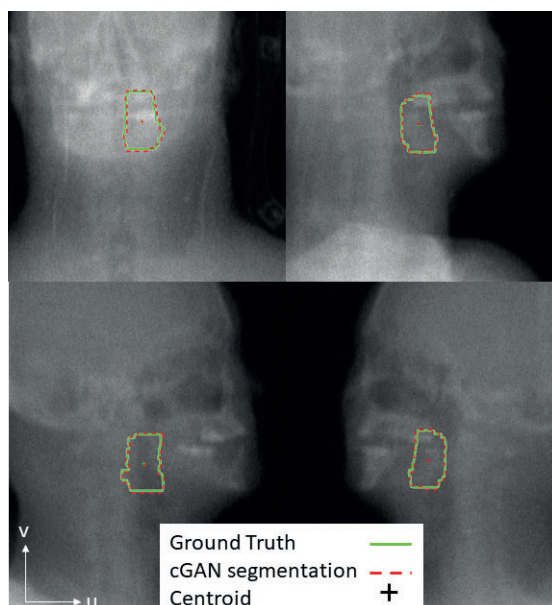
Markerless Tumour Tracking

Project Overview

In an effort to keep track of the tumour location, 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

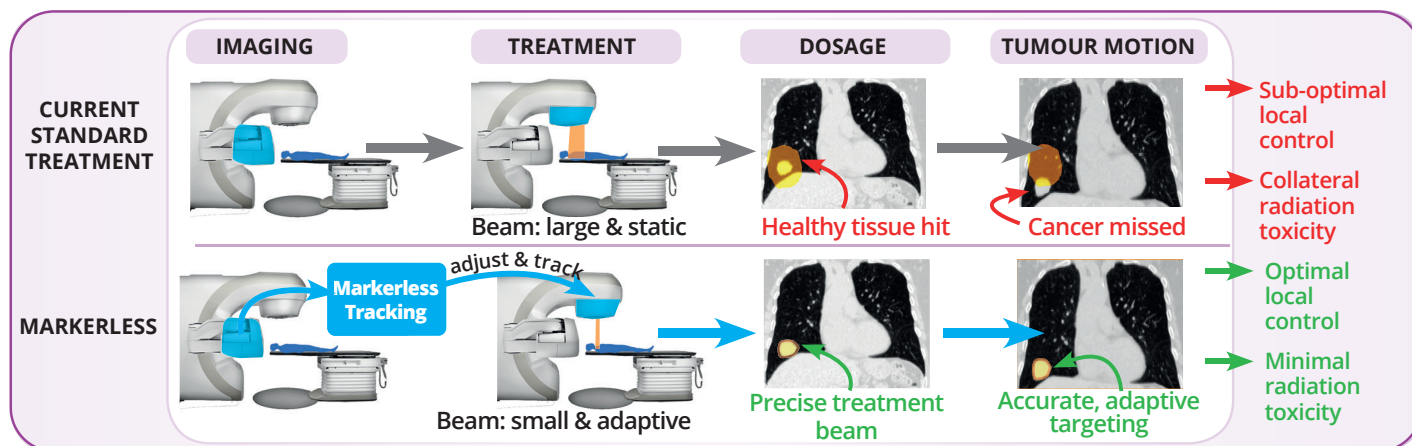
our advanced algorithms. This solution eliminates the invasive surgical implantation of markers and allows the tumour to be accurately targeted. The collateral damage to healthy tissue is minimised, thus improving the outcomes for cancer patients.



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 2022

We have expanded our markerless technology 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. We coordinated a Grand Challenge through the American Association of Physicists in Medicine in which international research groups benchmarked their lung tumour tracking methodology, published in the Medical Physics journal. The protocol of the upcoming MAGIK clinical trial for lung tumour tracking was also published and patients have been recruited to the VALKIM (lung cancer) and ROCK-RT (liver cancer) trials.



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

Associated Studies

MAGIK

Markerless Image Guidance Using Intrafraction Kilovoltage X-ray Imaging (MAGIK). MAGIK aims to determine the feasibility of markerless image guidance using intrafraction kilovoltage imaging.

VALKIM

Markerless Image Guidance Using Intrafraction Kilovoltage X-ray Imaging for Lung Cancer Radiotherapy (VALKIM). VALKIM is a RNSH led study for lung cancer using our markerless tracking technology.

ROCK RT

Radio-opaque contrast agents for liver cancer targeting with KIM during radiation therapy: An observational feasibility study (ROCK-RT). ROCK-RT is a non-interventional feasibility study for markerless liver cancer tracking using contrast agents.

Researchers

Mark Gardner

Jonathan Hindmarsh

Students

Marco Mueller

Adam Mylonas

Tumour Targeting

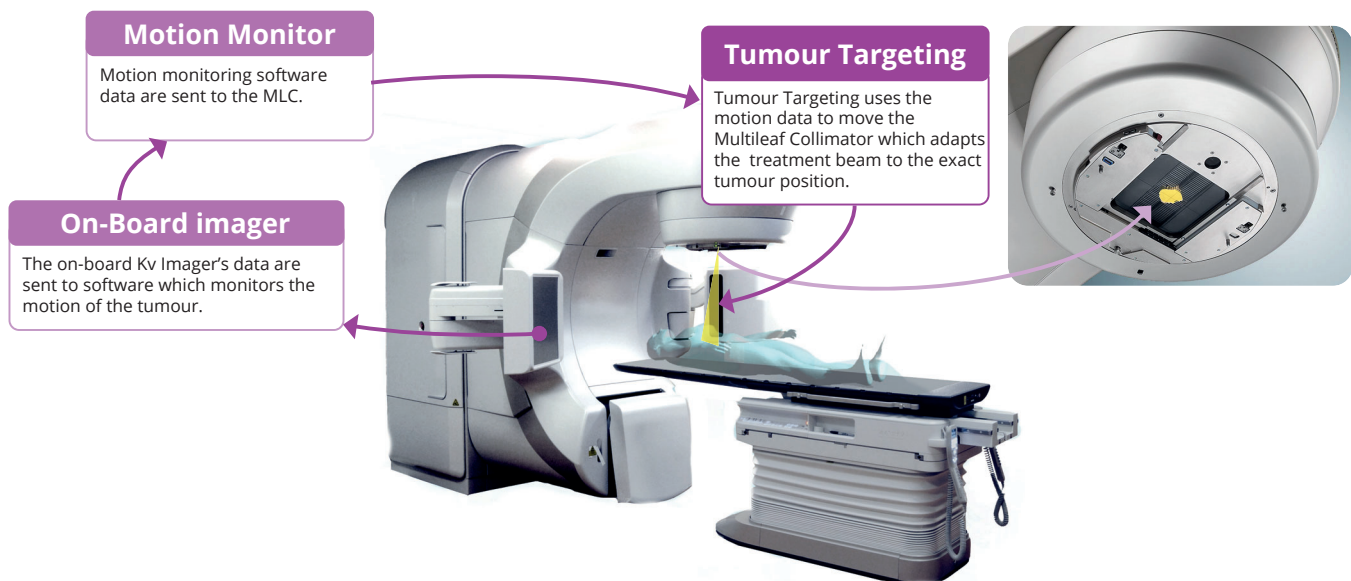
Project Overview

Tumour Targeting is a system that changes the shape and position of the radiation beam during treatment to follow the movement of the tumour. It dynamically shapes the radiation to target the tumour as it moves, ensuring the radiation beam always hits the tumour and while sparing the surrounding healthy tissue. It uses the real-time

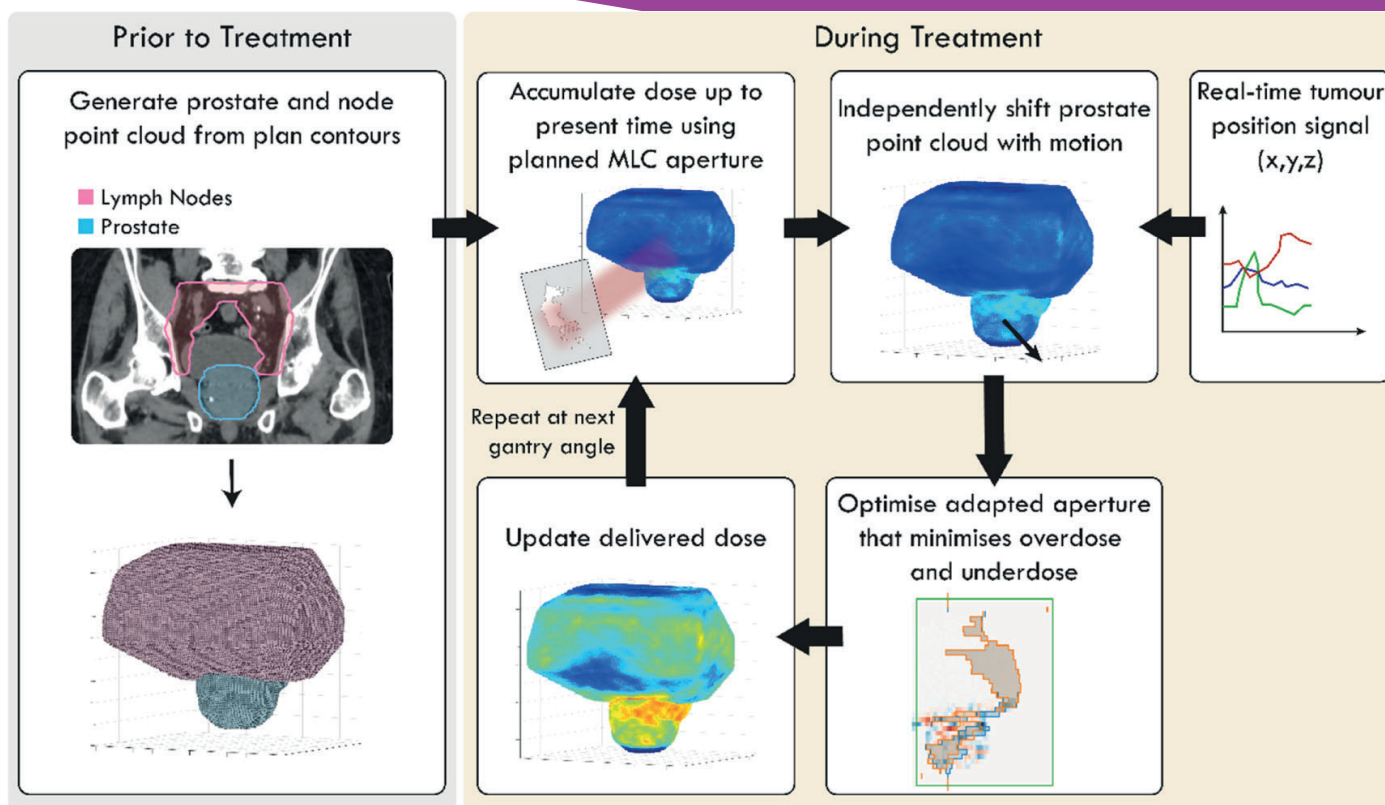
information from the radiation therapy system's existing on-board imaging equipment to adapt the shape and position of the radiation beam.

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 Tumour Targeting 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 tumour targeting works



Pictured: The process of targeting multiple tumours using real-time tumour targeting.

Highlights of 2022

Tumour Targeting has seen some exciting improvements throughout the previous year. With the field of adaptive radiotherapy moving toward adapting treatments based on the radiation dose deposited during treatment, our team is pioneering dose-based tumour targeting. A proof of concept was published in early 2021, demonstrating the ability to move and shape the beam based on previously delivered dose in real-time, providing significant improvements to the efficacy of the treatment.

Since then, this method has been extended to include multiple targets, allowing two treatment sites to be treated simultaneously while accounting for their individual motions. These findings were published in *Optimising multi-target multileaf collimator tracking using real-time dose for locally advanced prostate cancer patients* in the Physics in Medicine & Biology journal.

Furthermore, improvements to the dose-based targeting method are being actively 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 but to reduce radiation dose to healthy tissue while maintaining dose to the target tumour.

Researchers

Emily Hewson
Paul Keall
Amelia Martin
Lars Mejnertsen

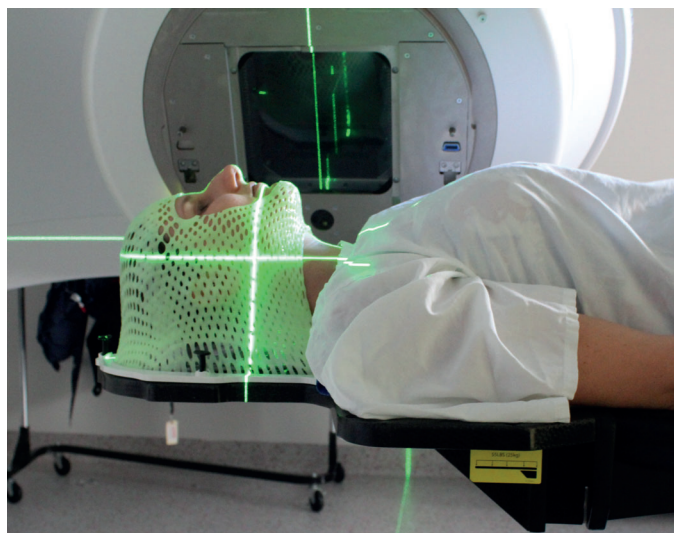
Remove the Mask

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.



Pictured: A researcher experiences the immobilisation mask.

Highlights of 2022

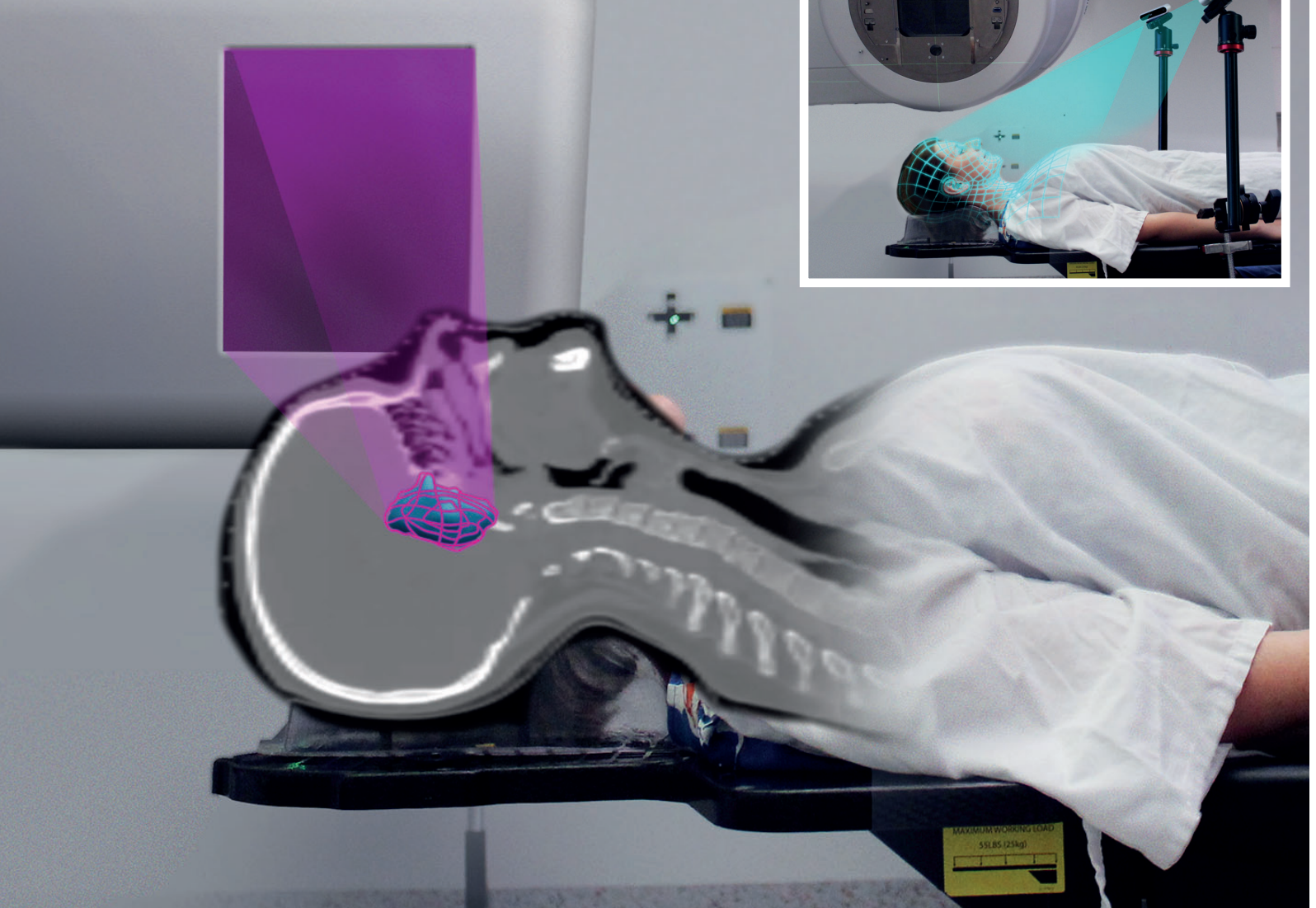
Safe and accurate treatment involves monitoring both surface motion and internal organ motion. Dr Youssef Ben Bouchta has been developing the surface monitoring technology, engineering software to accurately track a person's face as they move. He has published an open-source surface monitoring code and presented preliminary results at the American Association of Physicists in Medicine (AAPM) conference in Washington DC. He is also leading the VISION study, a volunteer study which aims at testing the accuracy of his surface monitoring technology.

The VISION study has recruited 30 volunteers and is expected to meet its recruitment target of 50 volunteers by July 2023.

Dr Mark Gardner has been developing methods to monitor the internal organ motion during

treatment. Dr Gardner has completed and is publishing a method for detecting the tumour location in simulated head and neck X-ray images, the results of which he also presented at the AAPM annual meeting.

Dr Gardner is overseeing the CHIRP trial, which is collecting X-ray images of patients during radiation therapy. Currently 12 participants have been recruited to the CHIRP study. These X-ray images will be used to determine if the methods used in the simulated study can be applied to actual patient images. Dr Gardner has also released an open software repository which allows for simulating realistic head and neck deformations in CT scans.



*Pictured: The onboard imager sees the position of the tumour.
Inset: The external sensors are used to calculate the position and motion of the patient.*

Associated Studies

CHIRP

The Collection of Head Images during RadiotheraPy: Clinical trial that is collecting the images acquired during radiotherapy for head and neck cancer patients, including X-ray images.

VISION

Volunteer study that aims at collecting surface images of volunteer to test the accuracy of novel head motion monitoring methods and to estimate the expected patient motion during a radiotherapy treatment.

SMART

Surface Monitoring technology to Remove The mask – Stage 1 (SMART): Clinical trial that aims at testing the feasibility of the Remove the Mask technology in the clinic and to assess the impact of this technology on patients' mask anxiety.

Researchers

Youssef Ben Bouchta

Mark Gardner

Paul Keall

Kuldeep Makhija

Students

Daniel Wang

Wanying Zhang

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

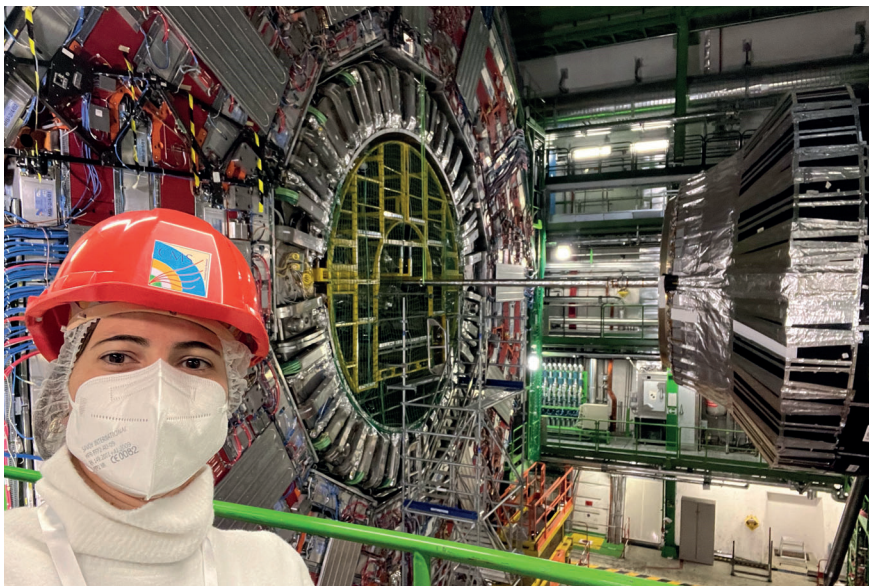
is a \$30M multi-institutional collaboration that spans building a prototype MRI-Linac system, one of four unique designs globally, to developing software and functional techniques that can also be deployed on commercial MRI-Linac systems.

Highlights of 2022

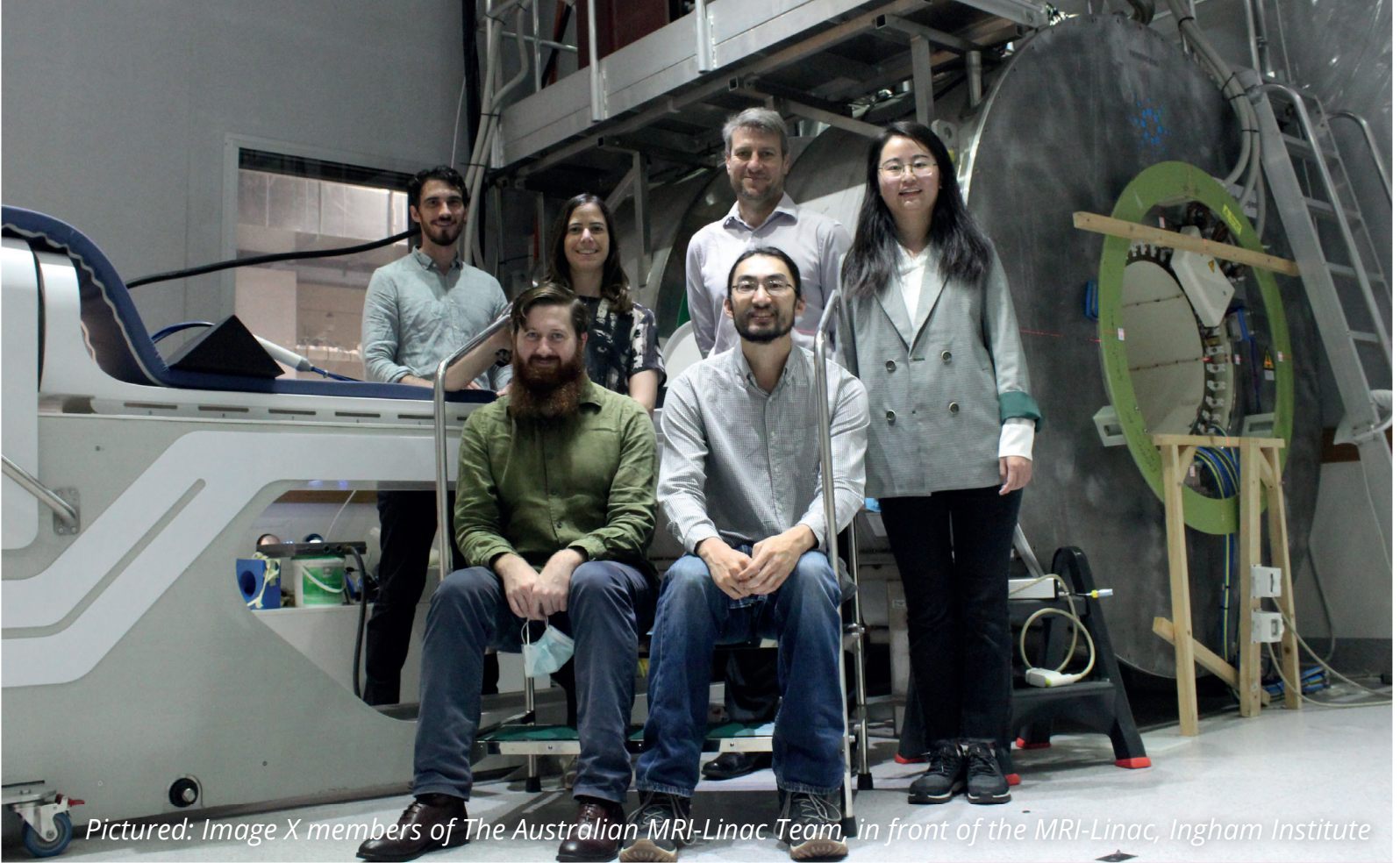
It was another big year for the MRI-Linac team with the easing of COVID restrictions allowing clinical work to resume. Artificial intelligence (AI) has transformed medical imaging and its application to MRI-Linacs will improve the accuracy of radiation delivery on MRI-Linacs.

Dr Shanshan Shan's work integrating AI reconstruction into lung imaging won 'Best in Physics' at the American Association of Physicists in Medicine Annual Meeting. Dr Paul Liu's AMPI trial saw the first patient study begin on the MRI-Linac system at Liverpool. Dr David Waddington won a prestigious NHMRC Investigator Grant to continue his work on the MRI-Linac for the next 5 years with a project titled "Advancing Dynamic MRI to enable adaptive lung radiotherapy."

The team is excited to have James Grover transitioning from a research associate role to beginning his PhD after winning a valuable Research Training Program Scholarship. Dr Caterina Brighi has helped to further our international impact, beginning a sabbatical at Politecnico di Milano investigating the use of MRI in carbon ion radiotherapy.



Pictured: Dr Caterina Brighi visits the Large Hadron Collider at CERN, Switzerland.



Pictured: Image X members of The Australian MRI-Linac Team, in front of the MRI-Linac, Ingham Institute

Dr Phillip Janowicz has been a welcome addition to the team, furthering Image X's brain cancer work via a research agreement with Imagination Biosystems Ltd. Several members of the MRI-Linac team were authors on an article published in Nature Reviews Clinical Oncology - the world's highest impact journal in Clinical Oncology. Dr Waddington and Dr Brighi were awarded an NHMRC Development Grant with Uni SA, investigating new platforms for imaging and treating glioblastoma.

Associated Studies

MANTRA

The world first clinical trial of an inline MRI-Linac was approved to begin in Q3 2021 but was delayed by the COVID lockdown. First in human treatments will begin in 2023.

AMPI

The Australian MRI-Linac Patient Imaging trial is testing the feasibility of treating different types of cancers on an inline MRI-Linac. Patients are imaged in the treatment position verifying the capability of the system to deliver radiation targeted with MRI. The first patients were recruited to this study in 2022.

Pictured: MRI The Linac team in front of the MRI-Linac.

Researchers

Caterina Brighi

James Grover

Paul Keall

Paul Liu

Shanshan Shan

David Waddington

Brendan Whelan

Students

James Grover

Monique Leadbitter

Win Lynn

Novel Beam Shaping

Project Overview

The process of delivering high quality external beam radiotherapy requires some means to shape and modulate X-ray dose to closely conform to tumour geometry. In modern RT, this is achieved with a multileaf collimator; a complex mechatronic device utilising over 100 independent motors, encoders, and tungsten leaves to dynamically modulate the beam in time and space.

In this project, we are collaborating with Stanford University to develop mechanisms and devices to

shape radiation beams with no moving parts. By doing this we hope to achieve two things:

1. Enable much faster treatment delivery by leveraging fundamental advances in accelerator science enabling up to a 15 x increase in the intensity of a radiation beam.
2. Increase the robustness of beam delivery by eliminating moving parts.

Highlights of 2022

Traditionally, the design of new devices/equipment in radiotherapy involves the manual iteration/tweaking of parameters in advanced computer simulations of radiation transport. For this project, we completely changed this paradigm by wrapping our simulations in a formal optimisation framework, which allows the computer to automatically and efficiently find the best solution to a problem.

This framework has been published in Medical Physics, and also as open source software called TopasOpt. Using this approach, we were able to generate several designs for a beam shaping concept with no moving parts. This paper also demonstrated the feasibility of this concept to deliver therapeutic radiation at least as fast as traditional approaches, and much faster under some circumstances.

This work was also published in Medical Physics, and was featured in the editor's picks.

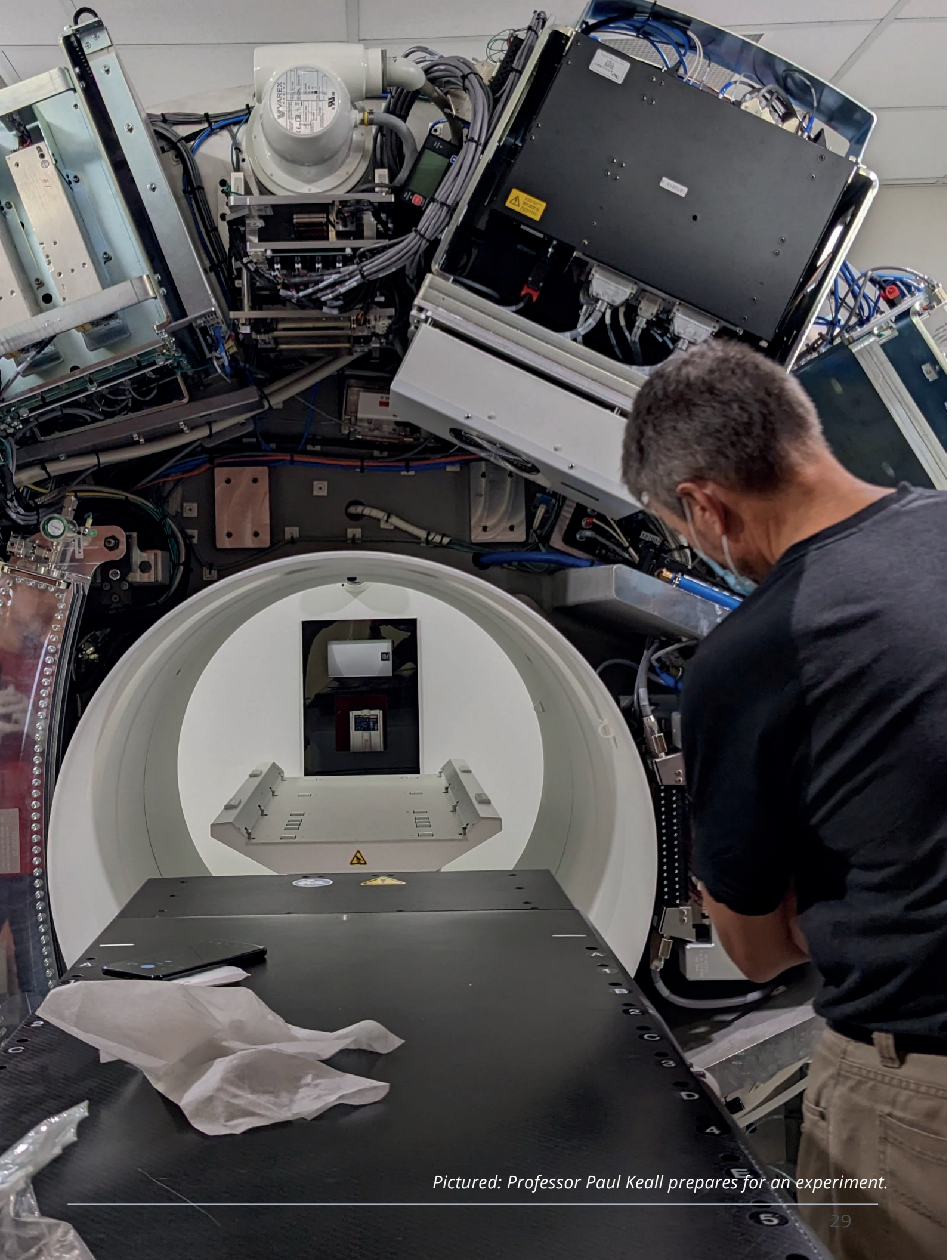
The next steps for this project are to continue to refine and optimise the beam delivery concept, and to carry out treatment planning studies to assess and refine the ability of this approach to deliver high quality dose in patients.

Researchers

Paul Keall

Lars Mejnertsen

Brendan Whelan



Pictured: Professor Paul Keall prepares for an experiment.

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 2022 we had 7 clinical trials open and actively recruiting participants. In total, we recruited 50 participants to our trials in 2022.

In addition to the actively recruiting trials, we had a further 7 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

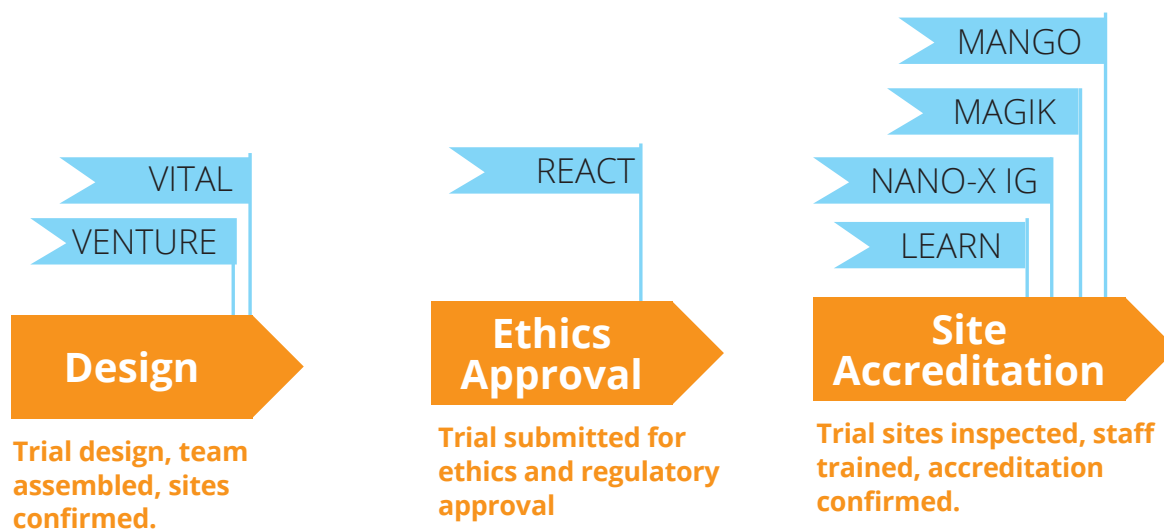
activities. Two of these studies received ethics approval in 2022 and are expected to open to accrual later in Q2, 2023.

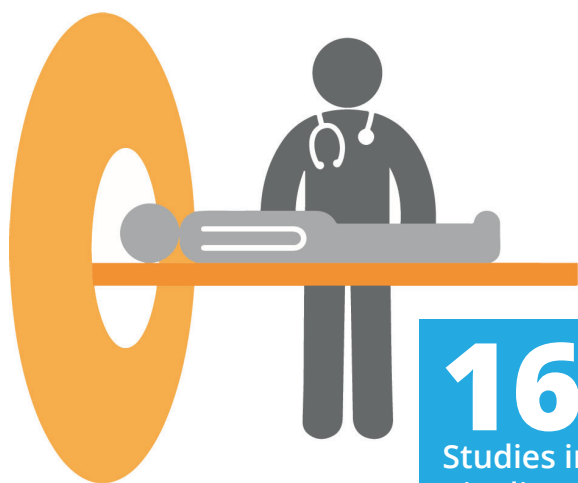
Clinical Trial Leads

Natalie Plant

Shona Silvester

STUDY STATUS IN 2022





16

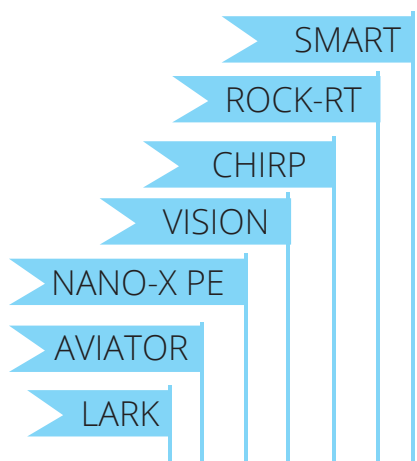
Studies in our pipeline.

7

Trials open and recruiting patients

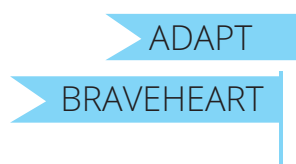
50

Patients recruited



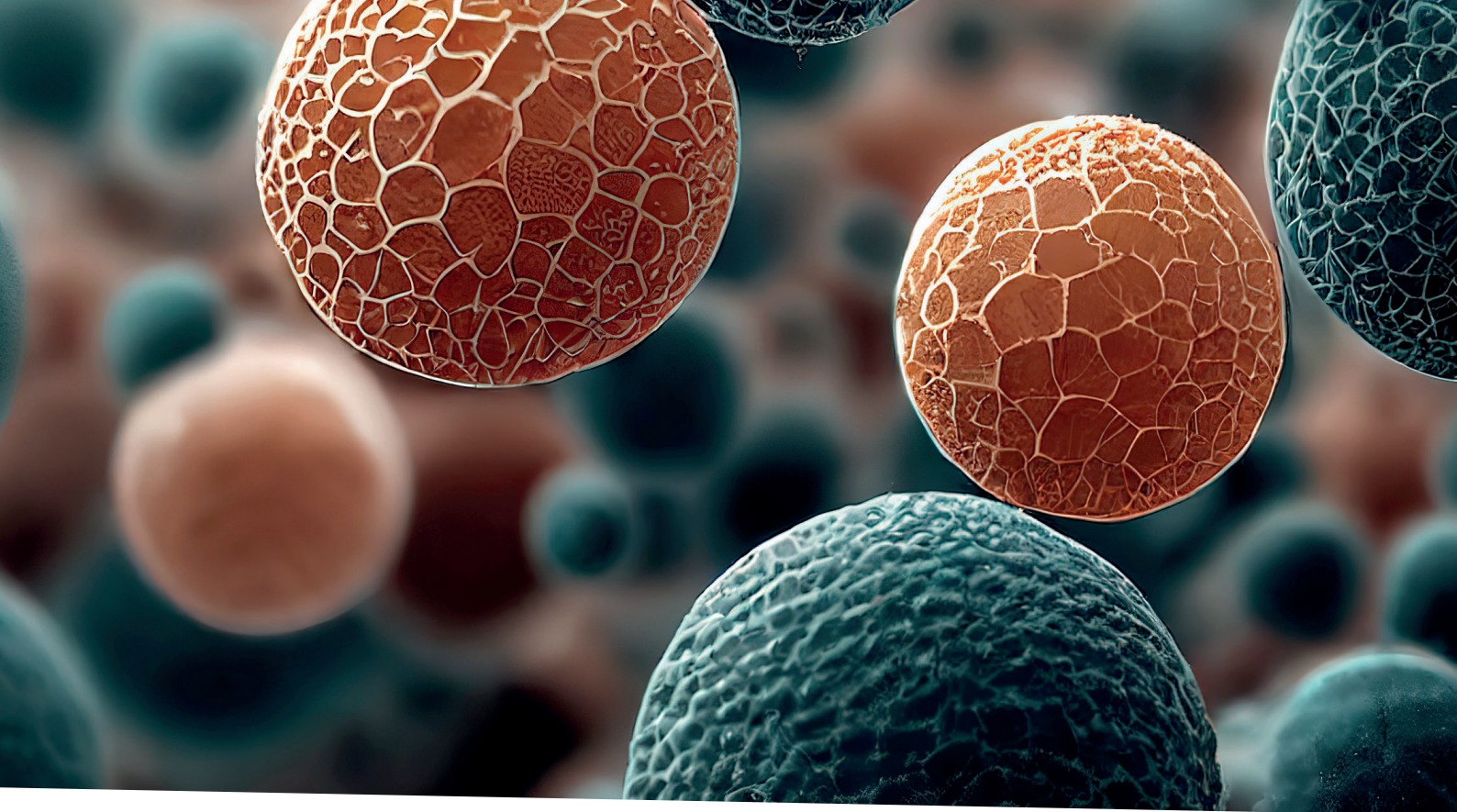
Open - recruiting patients

Hospital sites recruit patients to the study.



Analysis & Publication

Results are analysed and submitted for publication in journals.



Translation and Commercialisation

Intellectual Property

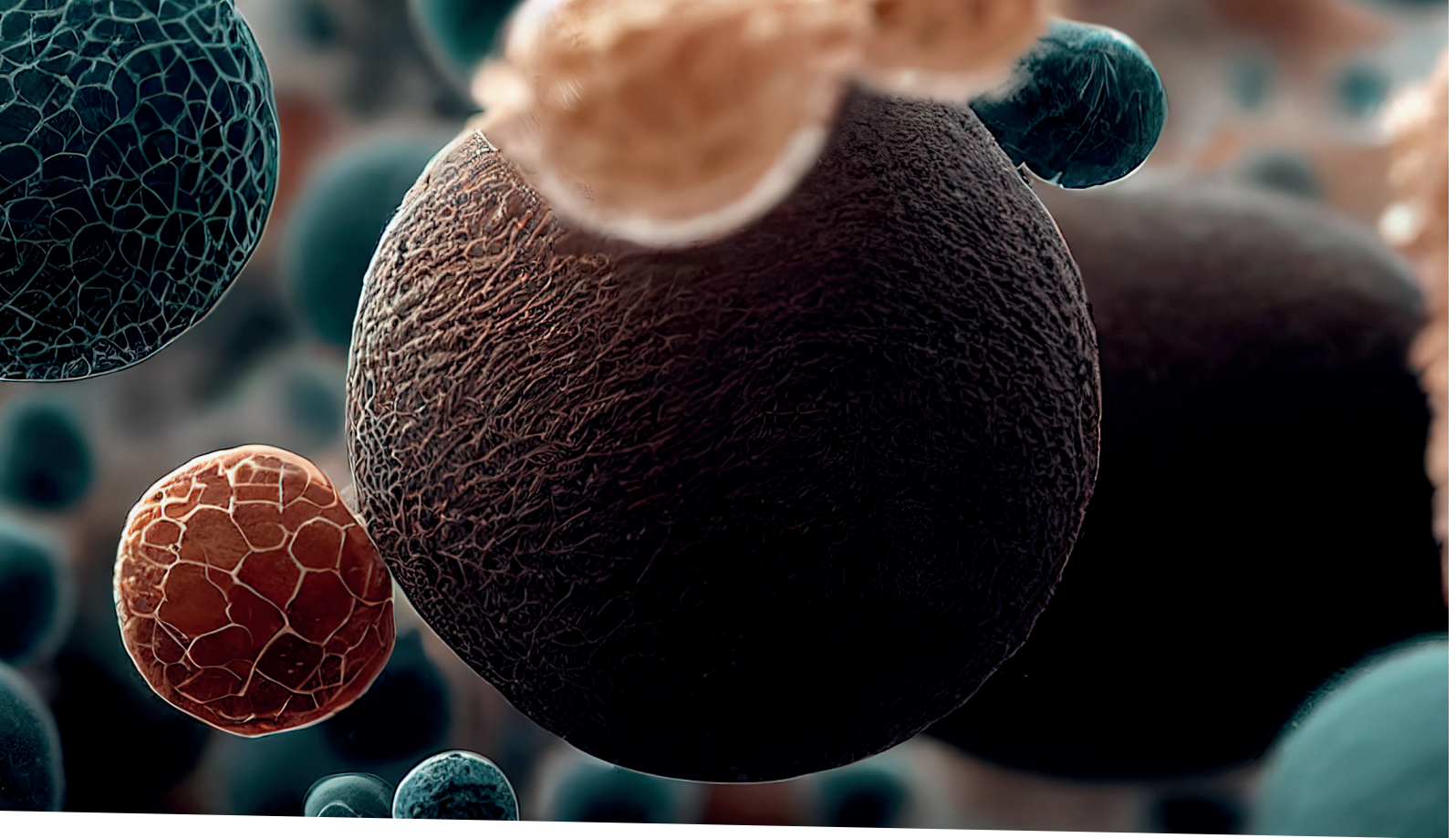
To ensure that our technologies are developed for the benefit of the University and community, we work with the Commercialisation team of the Research Portfolio, to protect and commercialise intellectual property.

We have been working on CT ventilation for over a decade, and it is wonderful to see this research lead to a product to potentially help the diagnosis and management of patients across multiple lung diseases. 4D Medical, our NHMRC Development grant and REDI Fellowship partner, have released a CT ventilation product in Australia, broadening the accessibility of functional lung imaging for Australians living with lung disease.

Partnerships

Forming partnerships with industry is key to widespread adoption of our innovations.

Dr David Waddington leads a new industry research agreement with industry partners Imagion Biosystems and Nucleus Therapeutics and researchers, Prof Zdenka Kuncic (School of Physics) and Dr Caterina Brighi. The industry partners will provide nanoparticle and targeting reagents for enhanced imaging and treatment of brain tumours in a preclinical studies and funding for a researcher to perform the work.



Open Source Tools

We create some devices and tools 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 tools by making the technology open-source and available to other researchers.

SpyGRT (Surface Guided Radiation Therapy (SGRT) with Python (py)) is an open-source toolkit developed by Dr Youssef Ben Bouchta that allows rapid development of an SGRT application that can be used to test novel applications of surface guidance or develop novel SGRT algorithms. It was presented at the American Association of Physicists in Medicine 2022 annual meeting.

Dr Brendan Whelan led the development of TopasOpt: An open-source library for optimization with Topas Monte Carlo. It puts a formal optimisation framework around the very powerful Monte Carlo particle transport tool for answering important cancer imaging and targeting questions. It was published in the Medical Physics journal.



Awards

Dr Tess Reynolds wins the Eureka prize for Outstanding Early Career Researcher

Dr Reynolds received the award for her large body of innovative work, summarised as: By developing technology to better guide robotic imaging during surgery, Dr Reynolds is improving the view for surgeons as well as outcomes for patients. Partnering with the world's largest medical device company, her pioneering techniques offer clearer, more complete images for complex cardiac and spinal surgery. This prize is a reward for the years of scientific effort that have led to high-impact publications, award-winning presentations, invited talks, grants and international collaborations. Dr Reynolds Some of the credit should also go to Dr Reynolds's supervisor and mentor, Prof Ricky O'Brien, who recruited Dr Reynolds in 2017 after she completed her PhD at the University of Adelaide.

The Australian Museum Eureka Prizes are the country's most comprehensive national science awards, honouring excellence across the areas of research & innovation, leadership, science engagement, and school science. Presented annually in partnership with some of the nation's leading scientific institutions, government organisations, universities and corporations, the Eureka Prizes raise the profile of science and science engagement in the community by celebrating outstanding achievement.

Pictured: Dr Tess Reynolds receiving her award at the Australian Museum, Sydney

Dr Shanshan Shan & Dr David Waddington

Dr Shanshan Shan (first author) and **Dr David Waddington** (senior author) along with other MRI-Linac team members were awarded BEST IN PHYSICS (top 0.5% of abstracts submitted) at the American Association of Physicists in Medicine annual meeting for their abstract Motion-corrected image reconstruction with unrolling networks on an MRI-Linac.

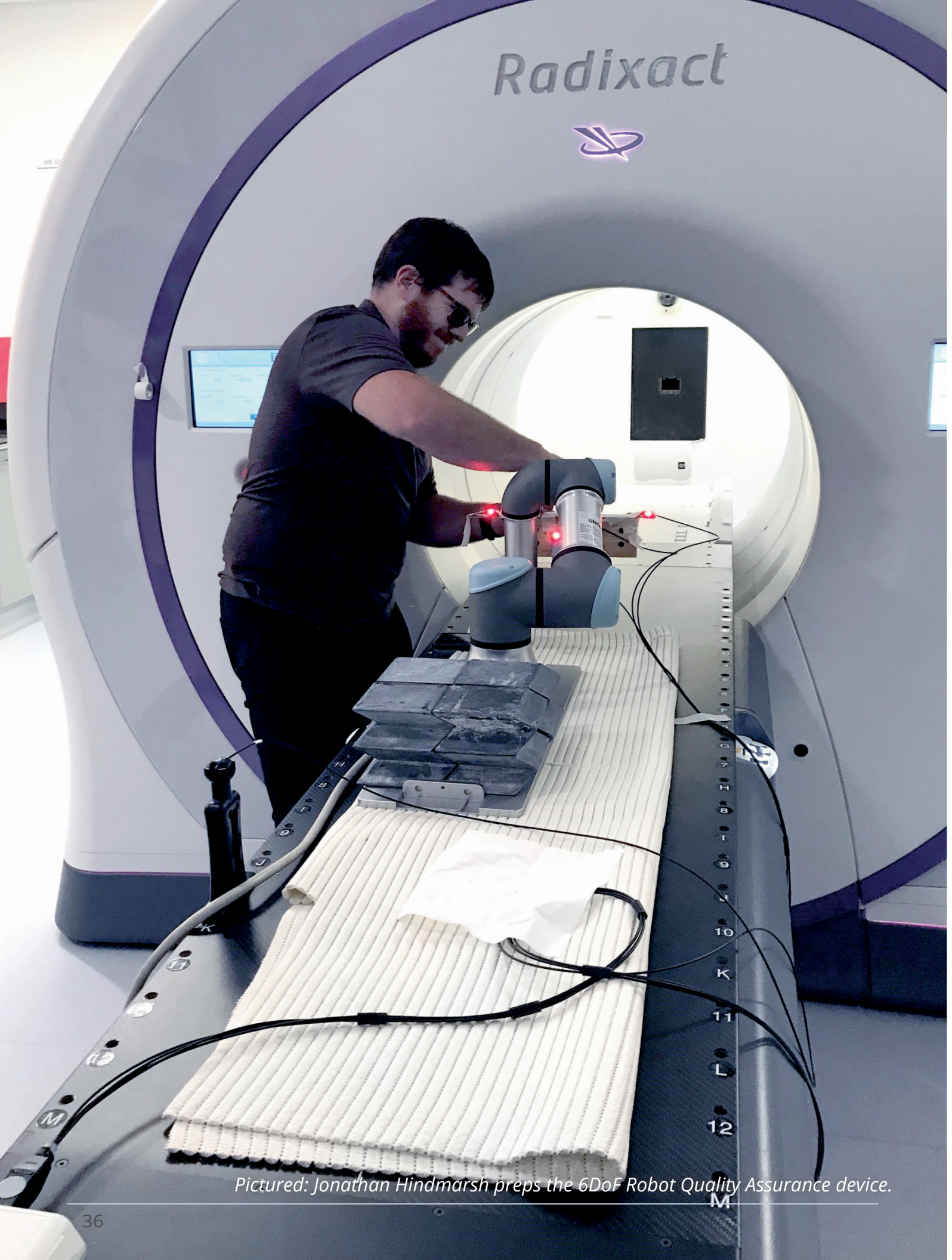
Jeremy Lim

Jeremy Lim received the Dean's Honours List prize at as the highest performing Masters of Medical Physics student at the University of Sydney.

Jeremy also won the Masters Student Presentation Prize at the MedPhys22 meeting for *Impact of Key Algorithm Parameters on the Accuracy of CT Ventilation Imaging*.

Chandrima Sengupta

Chandrima Sengupta won the Best Radiation Oncology presentation at the Engineering & Physical Sciences in Medicine (EPSM) 2022 Annual meeting for *First in-human use of real-time tumour tracking for liver SBRT on a standard Elekta linear accelerator*.



Pictured: Jonathan Hindmarsh preps the 6DoF Robot Quality Assurance device.

Post Graduate Students

We congratulate our four PhD students and two Masters of Medical Physics student who graduated or had their degrees conferred in 2022.

Dr Emily Hewson (Thesis title – Enabling real-time adaptive radiotherapy for multiple targets) continues to work at the Image X Institute as a postdoctoral research associate and was awarded a Cancer Institute NSW Early Career Fellowship to commence in 2023.

Dr Natasha Morton (Thesis title - Improving thoracic imaging for radiation therapy: The development and translation of patient adaptive computed tomography) has a position as a healthcare data analyst at Prospecion.

Dr Marco Mueller (Thesis title – Direct tumour tracking during radiation therapy) has a position as an MRI applications research scientist at Siemens Healthcare

Dr Nicholas Hindley (Thesis title - Making the cutting-edge common: Methods for real-time motion management and volumetric imaging on standard radiotherapy systems) completed his Fulbright Fellowship in 2022 at Harvard University and is working at the Image X Institute as a postdoctoral research associate. Nick was also awarded the Faculty of Medicine and Health Ph.D. Thesis Excellence Prize.

Jeremy Lim (Project title – Investigation of parameters affecting deformable image registration for lung ventilation imaging) was awarded the Dean's Honour List prize as the highest performing Masters of Medical Physics student. He is working at the Image X Institute as a research associate.

Ibtisam Almajnooni (Project title - Time-resolved dosimetric evaluation of breast Deep Inspiration Breath Hold (DIBH) radiotherapy treatment) is teaching in the medical physics program at Al-Baha University, Saudi Arabia.

Grants

Commenced in 2022:

Prof Ricky O' Brien, Prof Andreas Fouras, **Prof Paul Keall**, Dr Dasantha Jayamanne, Dr Benjamin Harris, Prof 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, **\$1,075,714** (2022-2025)

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

Dr Hilary Byrne. *Bringing CT ventilation imaging to the wider world*. MRFF REDI Fellowship with 4DMedical as the sponsor organisation. **\$164,728**. (2021-2023)

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

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** (2022)

Prof Paul Keall. FMH Rewarding Research Success. **\$100,000** (2022)

Prof Ricky O'Brien. FMH Rewarding Research Success. **\$100,000** (2022)

Dr Brendan Whelan. FMH Rewarding Research Success. **\$75,000** (2022)

Dr Tess Reynolds. FMH EMCR Next Steps Funding. **\$32,000** (2022)

Grants awarded in 2022 to commence in 2023

Dr David Waddington. *Advancing dynamic MRI to enable adaptive lung radiotherapy*. NHMRC Investigator Grant EL1. **\$628,000** (2023-2027)

Prof Ricky O'Brien, **Prof Paul Keall**, A/Prof Saurabh Kumar, A/Prof Shankar Siva, Dr Doan Trang Nguyen, A/Prof Lois Holloway, Dr Tess Reynolds. *Reducing the impact of radiation on the heart for cancer and cardiac disease patients*. NHMRC Synergy Grant. Administering Institution RMIT. **\$5,000,000** (2023-2027)

Dr Emily Hewson *Enabling precise radiotherapy to improve outcomes for advanced lung cancer patients*. Cancer Institute NSW Early Career Fellowship, **\$393,250** (2023-2025)

Prof Benjamin Thierry, Prof Eva Bezak, A/Prof Hien Le, Dr Lisa Ebert, A/Prof Ivan Kempson, A/Prof Ross Berbeco, **Dr David Waddington**, **Dr Caterina Brighi**. *Preclinical Validation of a Targeted Theranostic Agent for MRI Guided Radiotherapy and Radiosensitisation of Aggressive Brain Tumours*. NHMRC Development Grant. Administering Institution University of South Australia **\$837,678** (2023-2024)

Dr Chandrima Sengupta *High precision low-cost radiotherapy to cancer patients: A technology for tumour motion detection during radiotherapy treatment*. Sydney Cancer Partners Seed grant. **\$13, 593** (2023)

Infrastructure

Equipment, computational and data resources underpin our research and development with some exciting additions to the Institute in 2022.

Upgrade of a research linear accelerator

Before modifying the operation of a clinical device, the modifications must be extensively tested in a research setting. Operating a linac accelerator (linac) requires significant shielding, only available in a purpose-built clinical facility. Research access to linacs in treatment centres is limited because they are prioritised for clinical treatments and any modifications of linac operation must be by agreement of the manufacturer

Through our partnership with the Nelune Comprehensive Cancer Centre and funding from the ARC, ACRF and NHMRC we are fortunate to have access to a linac available solely for research. In 2022 we applied ARC LIEF funding to upgrade the multileaf collimator head on the Elekta research linac. This improvement will allow us to implement and test advanced beam adaptation techniques that were previously not possible.

Development of an Imaging database

Image-guided radiation therapy technologies can be developed by applying statistical techniques and machine learning to the data generated from radiation therapy clinical trials. A challenge is to extract useful features from the files produced in clinical trials and store them in a well-organised, secure and readily usable database. Indrajit Ghosh developed an imaging database which allows collection of deidentified patient data from treatment sites without involving third party data sharing platforms. It provides a flexible platform to utilise existing clinical trial data for machine learning, quality assurance and enables a secure interface to add new data.

Robot for quality assurance in image-guided radiation therapy

We have previously developed a robotic quality assurance device that accurately mimics tumour motion in 6 degrees of freedom, ensuring safe implementation of image-guided radiotherapy technologies in the clinic. With the purchase of a robotic arm with a higher load capacity, we are extending the capabilities of the device to reproduce motion using an imaging phantom with a closer resemblance to patient anatomy and dimensions.

Engagement

The community surrounding the 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 2022 we continued to engage with our community online, via social media and in traditional media.

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 2022 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 Youssef Ben Bouchta

X-ray Computed Tomography with Dr Owen Dillon

Introduction to MRI with Dr David Waddington

Radiobiology 101 with Dr Paul Liu



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 2022, our E-Newsletter was distributed to an audience that grew from 286 to 335 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 2022, as we implemented dedicated content strategies devised and managed by Julia Johnson, our Design & Communications Officer.

In 2022 we shone the spotlight on impactful papers and staff achievements.

Social Media Stats



1,295

Facebook
views



67,247

Twitter
views



800

YouTube
views



335

E-News
subscribers



598

LinkedIn
visitors



3,926

Website
visitors

Pictured: Professor Paul Keall sets up the 6DoF Robot for an experiment.



In the Media

The Remove the Mask project was featured in both mainstream and specialist media.

James Joyce's article 'Anxiety Unmasked' was nationally syndicated through Australian Community Media in Newspapers including the Canberra Times, Newcastle Herald, The Examiner, The Border Mail, The Courier and the Illawarra Mercury. James' article covered his experience being treated for cancer, and the Remove the Mask technology.

The SCOPE magazine published by the Institute of Physics and Engineering in Medicine featured the Remove the Mask project on the cover, and in an article featuring Drs Youssef Ben Bouchta, Mark Gardner and Paul Keall, as well as visualisations by Julia Johnson.

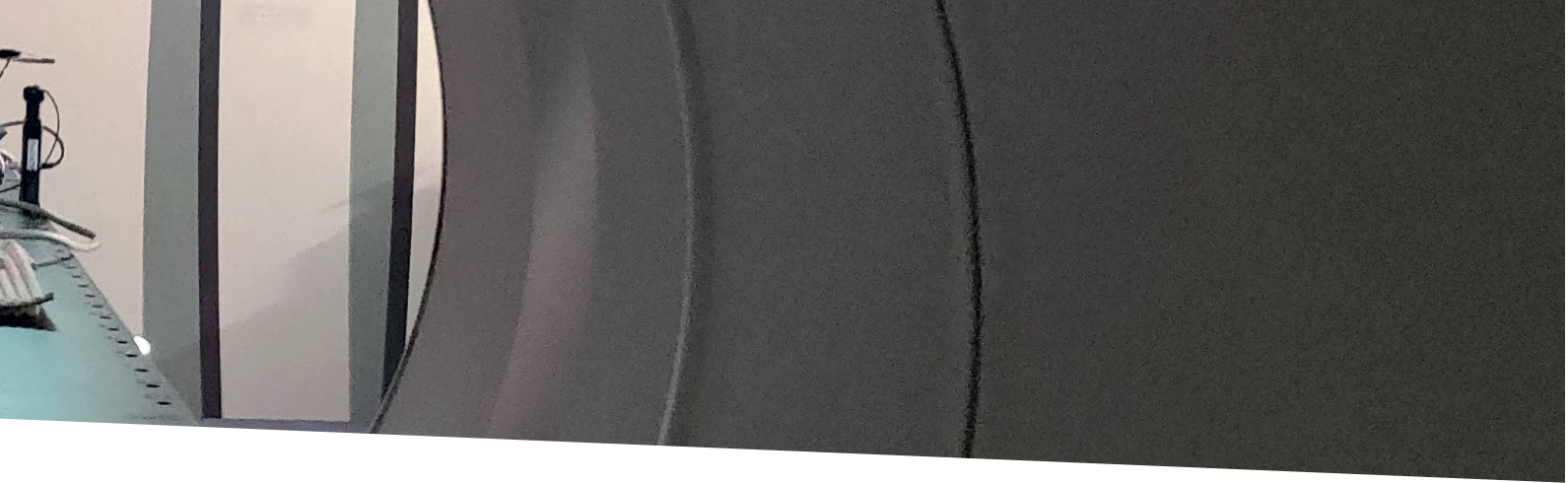
Tess Reynolds was interviewed by ABC TV, ABC Radio Sydney, as well as features in the University news after her Eureka Prize win.

Other media highlights

Remove the Mask featured in a world head & neck cancer day video by Julie McCrossin for Head & Neck Cancer Forum.

Dr Chandrima Sengupta was interviewed for the University of Sydney's Clinical Trials Support Office newsletter.

James Grover's first paper on machine learning for ventilation imaging was featured in science news website Physics world.



Professional Service

In addition to developing and implementing innovative research ideas, members of Image X institute make significant contributions to the medical physics and radiation oncology communities through professional service.

Diversity and Inclusion in Medical Physics

Women and minorities are underrepresented in the medical physics field and a goal of our institute is to provide a diverse and inclusive environment. Dr Hilary Byrne has contributed to the Science in Australia Gender Equity (SAGE) project at the University of Sydney for several years. Building on this work, she has been invited to contribute to two additional professional roles encouraging Diversity, Equity and Inclusion, the American Association of Physicists in Medicine (AAPM) Diversity and Inclusion Subcommittee and the Australasian College of Physical Scientists and Engineers in Medicine ACPSEM Diversity, Equity and Inclusion (DEI) Working Group. Dr Byrne presented at the Engineering and Physical Sciences 2022 meeting on DEI in the medical physics profession and she and Dr Chandrima Sengupta were panel member on the discussion that followed. Dr Brendan Whelan is a co-author on a 2023 publication reporting on diversity of the American Association of Physics in Medicine membership.

Clinically implementing new technologies

For medical research and technologies to have impact they must be translated to the clinic. An important step in this process is for clinical staff to understand the benefits of a new technology, its applications and how it might safely implemented in a clinical setting. Examples of this outreach include workshops on advanced motion management strategies delivered to the Australasian College of Physical Scientists and Engineers in Medicine and the Asia-Oceania Federation of Organisations for Medical Physics by Dr Chandrima Sengupta, Dr Emily Hewson and Prof Paul Keall.

Guidance on clinical implementation is also provided through reports and guidelines. After several years of meeting and writing, an international author team led by Prof Paul Keall completed the ICRU Report 97 MRI-Guided Radiation Therapy Using MRI-Linear Accelerators. The International Committee of Radiation Units has for 90 years developed and promulgated internationally accepted recommendations on radiation related quantities and units, terminology and measurement procedures. The focus of this report is a growing area of radiation therapy, MRI-guidance. Key differences with MRI-guidance over standard care were detailed, along with clinical potential, clinical examples, technical requirements, staffing, safety, recommendations and a future outlook.

Pictured: The 6DoF Robot positioned and ready for use.

Academic Staff

Professor Paul Keall, Director
Professor Ricky O'Brien, Deputy Director (until July 2022)
Dr Youssef Ben Bouchta, Postdoctoral Research Associate
Dr Samuel Blake, Postdoctoral Research Associate
Dr Caterina Brighi, 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 Emily Hewson, Postdoctoral Research Associate
Dr Nicholas Hindley, Postdoctoral Research Associate
Dr Xiaoshui Huang, Postdoctoral Research Associate
Dr Phillip Janowicz, Postdoctoral Research Associate
Jeremy Lim, 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, Cancer Institute NSW Early Career 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
Ann Yan, Research Associate

Professional Staff

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

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
Jeremy Lim, Masters of Medical Physics
Ibtisam Almajnooni, Masters of Medical Physics
Jonathan Hindmarsh Doctor of Philosophy

Bachelor of Biomedical Engineering and Bachelor of Diagnostic Radiography Honours projects

Hongrui Zong, Tianni Ma, Huijie Jane Xu, Nabeeha Chowdhury and Monique Leadbitter

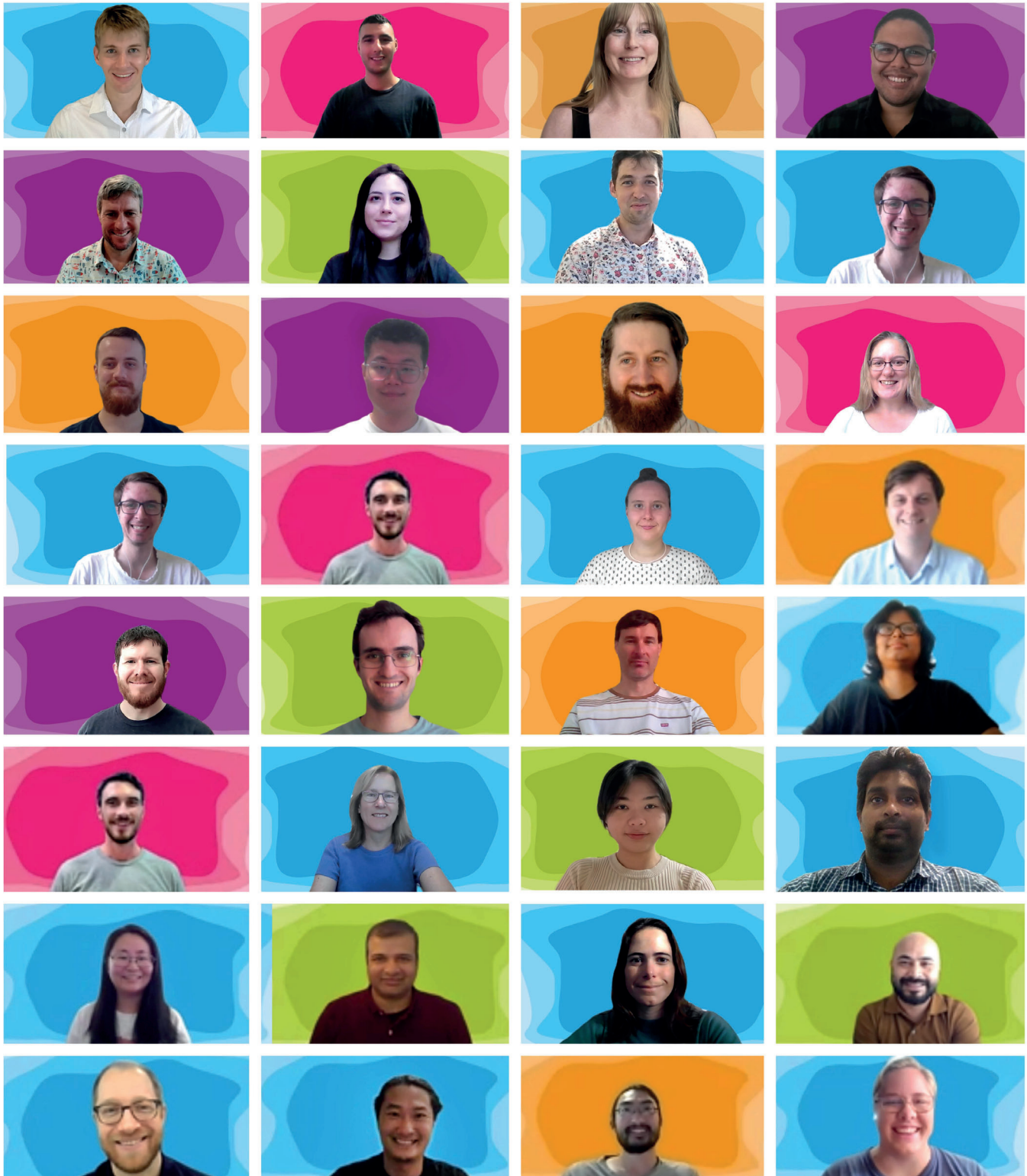
Visiting Researchers

A/Prof Magdalena Bazalova-Carter, Victoria University, Canada
Elia Lombardo, München Comprehensive Cancer Center, Germany

Summer Research Students

Alicja Kaczynska
Win Lyn
Daniel Wang

2022 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 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, Image X Institute Operations Manager

Professor Paul Keall, Image X Institute Director

Dr Tess Reynolds, Image X Institute Early Career Fellow

Rekha Ravi-Indran, Finance Manager, Faculty of Medicine and Health

Dr Andrew Tindell, Executive Director, Research Operations

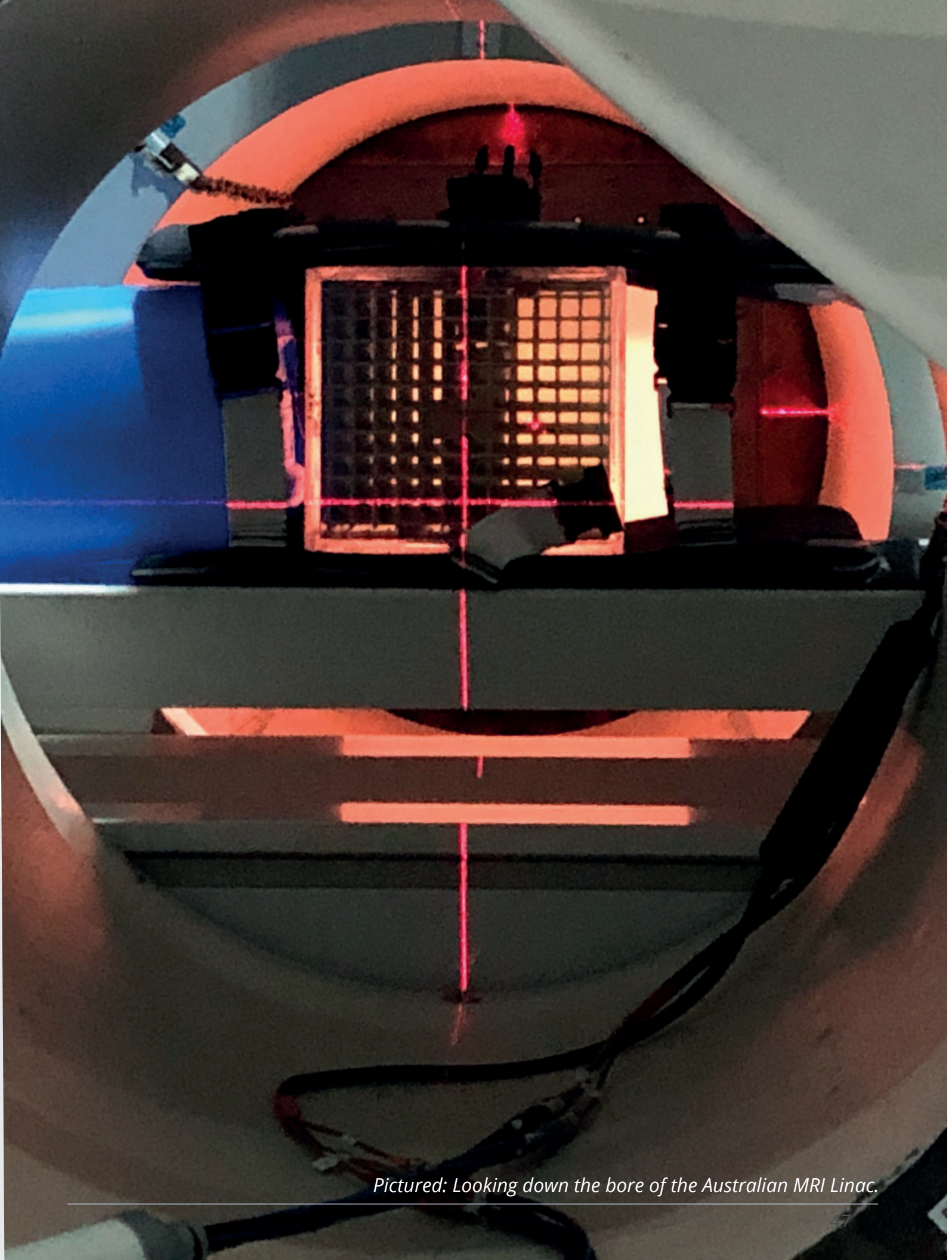
Professor Martin Ugander, Head of Clinical Imaging, Sydney School of Health Sciences

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, Helen Ball, Tess Reynolds, Owen Dillon, Hilary Byrne, and Benjamin Lau.



Pictured: Looking down the bore of the Australian MRI Linac.

Publications

The following peer-reviewed articles were published or accepted for publication in 2022.

Ball HJ, Santanam L, Senan S, Tanyi JA, van Herk M and Keall PJ (2022). "Results from the AAPM Task Group 324 respiratory motion management in radiation oncology survey." *J Appl Clin Med Phys* 23(11): e13810. DOI: 10.1002/acm2.13810.

Begg J, Jelen U, Keall P, Liney G and Holloway L (2022). "Experimental characterisation of the magnetic field correction factor, k_B , for Roos chambers in a parallel MRI-linac." *Phys Med Biol* 67(9). DOI: 10.1088/1361-6560/ac66b8.

Begg J, Jelen U, Keall P, Liney G and Holloway L (2022). "Ion chamber magnetic field correction factors measured via microDiamond cross-calibration from a conventional linac to MRI-linac." *Front Phys* 10 DOI:10.3389/fphy.2022.925890.

Brighi C, Keall PJ, Holloway LC, Walker A, Whelan B, de Witt Hamer PC, Verburg N, Aly F, Chen C, Koh ES and Waddington DEJ (2022). "An investigation of the conformity, feasibility, and expected clinical benefits of multiparametric MRI-guided dose painting radiotherapy in glioblastoma." *Neurooncol Adv* 4(1): vdac134. DOI: 10.1093/noajnl/vdac134.

Brighi C, Puttick S, Li S, Keall P, Neville K, Waddington D, Bourgeat P, Gillman A and Fay M (2022). "A novel semiautomated method for background activity and biological tumour volume definition to improve standardisation of (18)F-FET PET imaging in glioblastoma." *EJNMMI Phys* 9(1): 9. DOI: 10.1186/s40658-022-00438-2.

Brighi C, Salimova E, de Veer M, Puttick S and Egan G (2022). "Reply to Letter from Price et al, re: Translation of focused ultrasound for blood-brain barrier opening in glioma." *J Control Release*. DOI: 10.1016/j.jconrel.2022.06.042.

Brighi C, Salimova E, de Veer M, Puttick S and Egan G (2022). "Translation of focused ultrasound for blood-brain barrier opening in glioma." *J Control Release* 345: 443-463. DOI: 10.1016/j.jconrel.2022.03.035.

Brighi C, Verburg N, Koh ES, Walker A, Chen C, Pillay S, de Witt Hamer PC, Aly F, Holloway LC, Keall PJ and Waddington DEJ (2022). "Repeatability of radiotherapy dose-painting prescriptions derived from a multiparametric magnetic resonance imaging model of glioblastoma infiltration." *Phys Imaging Radiat Oncol* 23: 8-15. DOI: 10.1016/j.phro.2022.06.004.

Goodburn RJ, Philippens MEP, Lefebvre TL, Khalifa A, Bruijnen T, Freedman JN, Waddington DEJ, Younus E, Aliotta E, Meliadori G, Stanescu T, Bano W, Fatemi-Ardekani A, Wetscherek A, Oelfke U, van den Berg N, Mason RP, van Houdt PJ, Balter JM and Gurney-Champion OJ (2022). "The future of MRI in radiation therapy: Challenges and opportunities for the MR community." *Magn Reson Med* 88(6): 2592-2608. DOI: 10.1002/mrm.29450.

Grover J, Byrne HL, Sun Y, Kipritidis J and Keall P (2022). "Investigating the use of machine learning to generate ventilation images from CT scans." *Med Phys* 48(8): 5258-5267. DOI: 10.1002/mp.15688.

Hatamikia S, Biguri A, Herl G, Kronreif G, Reynolds T, Kettenbach J, Russ T, Tersol A, Maier A, Figl M, Siewerdsen JH and Birkfellner W (2022). "Source-detector trajectory optimization in cone-beam computed tomography: a comprehensive review on today's state-of-the-art." *Phys Med Biol* 67(16). DOI: 10.1088/1361-6560/ac8590.

Hewson EA, Nguyen DT, Le A, Booth JT, Keall PJ and Mejnertsen L (2022). "Optimising multi-target multileaf collimator tracking using real-time dose for locally advanced prostate cancer patients." *Phys Med Biol* 67(18). DOI: 10.1088/1361-6560/ac8967.

Kanawati A, Constantinidis A, Williams Z, O'Brien R and Reynolds T (2022). "Generating patient-matched 3D-printed pedicle screw and laminectomy drill guides from Cone Beam CT images: Studies in ovine and porcine cadavers." *Med Phys* 49(7): 4642-4652. DOI: 10.1002/mp.15681.

Keall PJ, Brighi C, Glide-Hurst C, Liney G, Liu PZY, Lydiard S, Paganelli C, Pham T, Shan S, Tree AC, van der Heide UA, Waddington DEJ and Whelan B (2022). "Integrated MRI-guided radiotherapy - opportunities and challenges." *Nat Rev Clin Oncol*. 19(7):458-470. DOI: 10.1038/s41571-022-00631-3.

Keall PJ, Glide-Hurst CK, Cao M, Lee P, Murray B, Raaymakers BW, Tree A and van der Heide UA (2022). "ICRU REPORT 97: MRI-Guided Radiation Therapy Using MRI-Linear Accelerators." *Journal of the ICRU* 22(1): 1-100. DOI: 10.1177/14736691221141950.

Keall R, Keall P, Kiani C, Lockett T, McNeill R and Lovell M (2022). "A systematic review of assessment approaches to predict opioid misuse in people with cancer." *Support Care Cancer* 30(7): 5645-5658. DOI: 10.1007/s00520-022-06895-w.

Lau BKF, Reynolds T, Keall PJ, Sonke JJ, Vinod SK, Dillon O and O'Brien RT (2022). "Reducing 4DCBCT imaging dose and time: exploring the limits of adaptive acquisition and motion compensated reconstruction." *Phys Med Biol* 67(6). DOI: 10.1088/1361-6560/ac55a4.

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Conference Presentations

The presenting author is denoted by an asterisk.

Trans-Tasman Radiation Oncology Group Annual Scientific meeting (Gold Coast, QLD)

P Keall*. Trial Development 21.08 VITaL: The Ventilation Imaging for Thoracic Lung cancer radiation therapy trial. Oral Presentation

International Society for Magnetic Resonance in Medicine & European Society for Magnetic Resonance in Medicine and Biology 2022 Annual Meeting (London, UK)

C Brighi*, D E J Waddington, F Aly, E-S Koh, A Walker, P C de Witt Hamer, N Verburg, L C Holloway, B Whelan, C Chen, P J Keall. Implementation of a Multiparametric MRI Model of Glioma Infiltration for Dose Painting Radiotherapy. Digital Poster

S Shan*, P Liu, D Waddington, B Dong, M Li, F Tang, G Liney, F Liu, P Keall, B Whelan. B0 Inhomogeneity Characterization and Correction on an open bore MRI-Linac. Digital Poster

S Shan*, Y Gao, P Liu, B Whelan, H Sun, F Liu, P Keall, D Waddington. Distortion Free Image Reconstruction using a Deep Neural Network for an MRI-Linac. Digital Poster

D Waddington*, C Chiu, N Hindley, N Koonjoo, T Reynolds, P Liu, B Zhu, C Paganelli, M Rosen, P Keall. Learning motion correction from YouTube for real-time MRI reconstruction with AUTOMAP. Digital Poster

D Waddington*, E Shimron, N Hindley, N Koonjoo M S Rosen. Accelerating Ultra-Low Field MRI with Compressed Sensing. Digital Poster

M Li, E Weber*, D Waddington, S Shan, P Liu, B Dong, S Crozier, F Liu. An 8-element torso RF coil array for the Australian inline MRI-Linac: Initial imaging results. Oral Power Pitch

American Association of Physicists in Medicine Annual Meeting 2022 (Washington, DC, USA)

S Shan*, Y Gao, P Liu, T Reynolds, B Dong, H Sun, M Li, G Liney, F Liu, P Keall, D Waddington. BEST IN PHYSICS (MULTI-DISCIPLINARY): Motion-Corrected Image Reconstruction with Unrolling Networks on an MRI-Linac. Oral Presentation

H Byrne*, C Stanton, B Zwan, M Gargett, E Steiner, K Makhija, J Atyeo, K Richardson, L Ambrose, M Carr, R Bromley, J Booth, M Morgia, G Lamoury, P Keall. Primary Outcomes of the BRAVEHeart Clinical Trial – a Prospective Randomised Comparison of Chest Surface and Abdominal Block Monitoring Systems for Deep Inspiration Breath Hold Breast Cancer Radiotherapy. Oral Presentation

O Dillon*, R O'Brien. Evaluating X-ray Source Arrays for Tomography and Tomosynthesis in Lung Cancer Radiotherapy. Oral Presentation

J Hindmarsh*, S Dieterich, J Booth, P Keall. Using System Theoretic Process Analysis to Design a Commissioning Procedure for MLC Tracking. Oral Presentation

B Lau*, O Dillon, S Vinod, R O'Brien, T Reynolds. Sensitivity Analysis of Acquisition Precision in Fast Low Dose 4DCBCT. Oral Presentation

T Reynolds*, S Hatamikia, O Dillon, Y Ma, A Kanawati, J Stayman, R O'Brien. Continuous dual-isocenter imaging: simultaneously extending the longitudinal and lateral intraoperative 3D CBCT field-of-view for assessing musculoskeletal trauma. Oral Presentation

B Whelan*, B Loo, P Keall. TopasOpt: An Open-Source Library for Optimization with Topas Monte Carlo. Oral Presentation

B Whelan*, P Keall, J Perl, J Wang, S Trovati, S Tantawi, R Fahrig, P Maxim, M Shumail, B Loo. Bayesian Optimization of a Novel Intensity Modulated X-ray Source. Oral Presentation

J Grover*, P Liu, B Dong, S Shan, B Whelan, P Keall, D Waddington. Implementation of Super-Resolution Imaging on an MRI-Linac. Blue Ribbon ePoster

H Byrne*, O Dillon, S Blake, J Kipritidis, R O'Brien, P Keall. Investigating the Feasibility of CT Ventilation Imaging on Fast, Low-Dose 4DCBCT to Enable Daily Adaptive Lung Function Sparing. Interactive ePoster

D Chrystall*, E Hewson, C Sengupta, A Mylonas, T Wang, R O'Brien, Y Lee, P Poulsen, D Nguyen, P Keall, J Booth. A Deep Learning Fiducial Marker Detection Algorithm for Beam's-Eye-View Marker Tracking for Liver Cancer Patients. Interactive ePoster

M Gardner*, A Mylonas, M Mueller, Y Ben Bouchta, J Sykes, P Keall, D Nguyen. Deep-Learning Method for Segmenting Head and Neck Tumours in kV Images Acquired During Radiotherapy. Interactive ePoster

E Hewson*, D Nguyen, A Le, J Booth, P Keall, L Mejnertsen. Investigating a Real-Time Dose Calculation to Guide Multi-Target MLC Tracking. Interactive ePoster

P Liu*, D Waddington, J Grover, P Keall. Improving Tumor Tracking Accuracy During MR-Guided Radiotherapy Using Pre-Trained Super-Resolution Neural Networks. Interactive ePoster

E Mathias*, R O'Brien. Respiratory Adaptive Computed Tomography (REACT) Helical Imaging for Reducing Artifacts in 4DCT Scans. Interactive ePoster

L Mejnertsen*, E Hewson, J Booth, P Keall. Simultaneous Temporal and Dose Optimization for MLC Tracking: Cutting Dose Errors in Half. Interactive ePoster

A Ahmed*, A Mylonas, M Gargett, L Madden, D Chrystall, R Brown, A Briggs, D Nguyen, P Keall, A Kneebone, G Hruby, J Booth. Evaluation of Deep Learning-Based Algorithms for Tracking of Implanted Fiducial Markers in Pancreatic Cancer Patients. General ePoster

Y Ben Bouchta*, C Sengupta, M Gardner, T Reynolds, P Keall. SpyGRT: An Open-Source Low-Cost Surface Guidance System for Radiotherapy Research. General ePoster

M Gardner*, Y Ben Bouchta, J Sykes, P Keall. Simulating Head Motion in a Planning CT for Data Augmentation of Head and Neck Based Deep-Learning Networks. General ePoster

M Gargett*, A Ahmed, A Briggs, T Ravkilde, S Skouboe, P Poulsen, G Hruby, A Kneebone, P Keall, J Booth.

Evaluation of a Real-Time Method for Motion-Induced Dose Error Reporting for Pancreas Stereotactic Body Radiotherapy. General ePoster

J Hindmarsh*, S Dieterich, J Booth, P Keall. A Critical Analysis of Adaptive Therapy Guidelines for Patient Safety, Treatment Quality and System Safety Tests. General ePoster

B Lau*, O Dillon, T Reynolds, R O'Brien. Generating a Phantom with a Motion Ground Truth. General ePoster

Engineering and Physical Sciences in Medicine conference 2022 (Adelaide, SA)

J Lim*, J Kipritidis, J Booth, P Keall, H Byrne. Impact of Key Algorithm Parameters on the Accuracy of CT Ventilation Imaging. Oral Presentation

P Keall *, H Ball, L Santanam, S Senan, J Tanyi, M van Herk. Results from the AAPM Task Group 324 Respiratory Motion Management in Radiation Oncology Survey. Oral Presentation

C Sengupta*, DT Nguyen, B Perrett, SF Liu, E Brown, D Mason, T Causer, J Luo, R O'Brien, JT Booth, YY Lee, W Wang, PJ Keall. First in-human use of real-time tumour tracking for liver SBRT on a standard Elekta linear accelerator. Oral Presentation

J Hindmarsh*, S Dieterich, J Booth, P Keall. A Quality Program for MLC Tracking. Oral Presentation

C Sengupta*, S Skouboe, T Ravkilde, P Poulsen, DT Nguyen, R O'Brien, J Booth, P Greer, T Moodie, N Hardcastle, A Hayden, S Turner, S Siva, K-H Tai, J Martin, P Keall. Dosimetric impact of tumour rotation during real-time adaptive prostate stereotactic body radiation therapy. Poster Presentation

2022 Society for Neuro-Oncology Annual Scientific Meeting (Tampa, FL, USA)

C Brighi*, D Waddington, P Keall, J Booth, K O'Brien, J Parkinson, J Yim, D Bailey, M Back, J Drummond. Magnetic resonance hypoxia imaging for radiation treatment guidance in glioblastoma multiforme - a diagnostic/prognostic clinical imaging study. Poster Presentation

MedPhys2022 (Sydney, NSW)

J Lim*, J Kipritidis, J Booth, P Keall, H Byrne. Impact of Key Algorithm Parameters on the Accuracy of CT Ventilation Imaging. Oral Presentation

J Hindmarsh*, S Dieterich, J Booth, P Keall. Using System Theoretic Process Analysis to Design a Commissioning Procedure for MLC tracking. Oral Presentation

Australian Magnetic Resonance in Radiation Therapy (AusMRinRT) 2022 (Noosa, QLD)

S Kumar*, J Begg, B Dong, E Wong, D Elwadia, A Wallis, D Miller, J Spicer, G Liney, P Liu, P Keall, T Pham. Implementation of workflows for Australian MR Linac – radiation therapy perspective. Oral Presentation

D Waddington*, E Shimron, S Shan, N Koonjoo, M Rosen. Advanced Reconstruction with Deep Learning for ultraflow field MRI. Oral Presentation

S Shan*, Y Gao, P Liu, T Reynolds, B Dong, H Sun, M Li, G Liney, F Liu, P Keall, D Waddington. Motion-corrected image reconstruction using an unrolling network on an MRI-linac. Oral Presentation

J Grover*, P Liu, B Dong, S Shan, B Whelan, P Keall, D Waddington. Super-resolution imaging on the Australian MRI-Linac. Oral Presentation

P Liu*, D Elwadia, J Begg, S Kumar, B Dong, D Miller, J Spicer, A Wallis, E Hewson, P Keall, T Pham. In silico demonstration of MRI-guided multi-leaf collimator tracking of multiple lung cancer targets. Oral Presentation

M Li*, E Weber, D Waddington, S Shan, P Liu, B Dong, P Keall, F Liu, S Crozier. Imaging results using the 8-element torso coil array for the Australian MRI-Linac system. Oral Presentation

P Keall*, S Sheehy, M Barton, T Pham, S Crozier, A Rozenfeld. Towards MRI-guided proton therapy: The ultimate cancer treatment. Oral Presentation

P Keall*, C Glide-Hurst, A Tree, P Lee, B Murray, B Raaymakers, U van der Heide, M Cao. ICRU report on MRI-guided radiation therapy using MRI-Linacs. Oral Presentation

P Martin*, P Metcalfe, C Brighi, E-S Koh, E Chan, F Aly, L Holloway. Repeatability of quantitative MRI Radiomics in glioblastoma. Oral Presentation

E Lombardo*, Y Xiong, M Rabe, L Nierer, D Cusumano, L Placidi, L Boldrini, S Corradini, M Niyazi, M Reiner, C Belka, M Riboldi, C Kurz, P Liu, D Waddington, J Grover, P Keall, G Landry. Offline and online LSTM networks for respiratory prediction at MR Linacs. Oral Presentation

B Whelan*, P Liu, S Shan, D Waddington, B Dong, M Jameson, P Keall. Open source toolkit for quantification, reporting, and correction of geometric distortion in MRI. Oral Presentation

Invited Talks

Dr Caterina Brighi, *Magnetic Resonance Imaging, the MANGO study*. Sydney Clinical Imaging Summit, University of Sydney, Sydney, NSW

Dr Hilary Byrne, *VITaL – TROG New Trial Proposal – shifting the treatment paradigm*. Trans Tasman Radiation Oncology Group Technical Research Workshop, Gold Coast, QLD

Dr Hilary Byrne, *Survey results from the Australasian College of Physical Scientists and Engineers in Medicine Diversity, Equity, and Inclusion working group*. Engineering & Physical Sciences in Medicine Annual meeting, Adelaide SA

Dr Hilary Byrne, *CT ventilation imaging*. Sydney Clinical Imaging Summit, University of Sydney, Sydney, NSW

Dr Emily Hewson, *Advanced MLC tracking applications*. Asia-Oceania Federation of Organisations for Medical Physics (AFOMP) workshop on motion management, Webinar

Dr Emily Hewson, *Advanced MLC tracking applications*. Australasian College of Physical Scientists and Engineers in Medicine (ACPSEM) workshop on motion management, Webinar

Julia Johnson, *Creating Great Posters*. Australasian College of Physical Scientists and Engineers in Medicine (ACPSEM), Webinar

Dr Tess Reynolds, *Expanding the capabilities of robotic cone beam CT imaging systems*. Medical Image Optimisation and Perception Group, University of Sydney, Sydney, NSW

Dr Tess Reynolds, *Expanding the capabilities of robotic cone beam CT imaging systems*. 3D Sync group from Siemens Healthineers, Virtual

Dr Tess Reynolds, *Expanding the capabilities of robotic cone beam CT imaging systems*. John Hopkins University, Baltimore, MD

Dr Tess Reynolds, *Integrating interventional CBCT imaging into the treatment workflow of traumatic musculoskeletal injuries*. American Association of Physics in Medicine Annual meeting 2022, Washington, DC

Dr Tess Reynolds, *The future of cone beam CT for orthopaedic interventions*. Sydney Clinical Imaging Summit, University of Sydney, Sydney, NSW

Dr Chandrima Sengupta, *Marker-based real-time IGRT on conventional linear accelerators*. Asia-Oceania Federation of Organisations for Medical Physics (AFOMP) workshop on motion management, Webinar

Dr Chandrima Sengupta, *Marker-based real-time IGRT on conventional linear accelerators*. Australasian College of Physical Scientists and Engineers in Medicine (ACPSEM) workshop on motion management, Webinar

Dr David Waddington, *Deploying Neural Networks for Real-time MRI guidance*. Sydney Clinical Imaging Summit, University of Sydney, Sydney, NSW

Professor Paul Keall gave the following invited presentations

Building and clinically translating new technology for cancer imaging and targeted radiation therapy. Memorial Sloan Kettering Cancer Center Medical Physics Grand Rounds, Virtual

Building and clinically translating new technology for cancer imaging and targeted radiation therapy. Plenary speaker at the International Union for Physical and Engineering Sciences in Medicine (IUPESM) World Congress 2022 on Medical Physics and Biomedical Engineering, Singapore

Grant writing and publishing in today's competitive world. Invited speaker at the IUPESM World Congress 2022 on Medical Physics and Biomedical Engineering, Singapore

Multileaf Collimator (MLC) Tracking: Clinical rationale, clinical experience, guidelines and future directions. Invited speaker at the IUPESM World Congress 2022 on Medical Physics and Biomedical Engineering, Singapore

Real-time adaptive radiation therapy using tumour tracking. European Society for Therapeutic



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