IMAGE X INSTITUTE | THE UNIVERSITY OF SYDNEY

ANNUAL REPORT

2023

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

SNAPSHOT 2023

$2.7M
Grants commenced

6
Clinical trials active

30
papers published

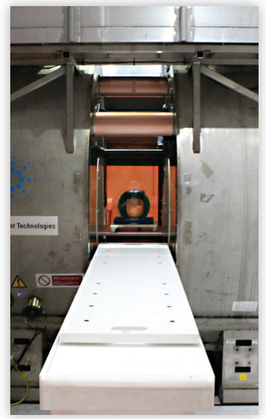
$2M+
grants awarded in 2023

26 **invited talks** presented

83 **Participants** in clclinical trials

4
New **clinical studies approved** for 2023

54
Conference presentations and **invited talks** given



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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. This year saw Robinson and Cancer Institute NSW Fellow, Dr Tess Reynolds, appointed as Deputy Director of Image X. Tess has introduced some great new initiatives and fresh energy to the institute.

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 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, MRFF and the University of Sydney amongst others. Without them, there would not be an Image X Institute. 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 2023

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 (Real-Time Image-Guided Radiation Therapy) 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.

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

IMAGING WITH CARBON NANOTUBE SOURCES
Enabling rapid 3D imaging during radiation therapy treatment.

FUNCTIONAL IMAGING
Visualising and measuring biological processes

MRI
Developing nanoparticle reagents and imaging biomarkers to better image and treat brain cancer.

PET IMAGING
Imaging metabolic processes to improve treatment plans and response predictions.

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

REAL-TIME IMAGE-GUIDED RADIATION THERAPY

KIM
Technologies that track moving tumours using a standard linac and markers.

MARKERLESS
Technologies that track moving tumours using a standard linac, without markers.

MR-GUIDANCE
Enabling real-time tumour tracking on images acquired during MRI-Linac treatment.

TUMOUR TARGETING
Adapting the treatment beam aperture to target the tumour in real-time

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

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: Closeup of the Artis Pheno, Charles Perkins Centre Hybrid Theatre

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.

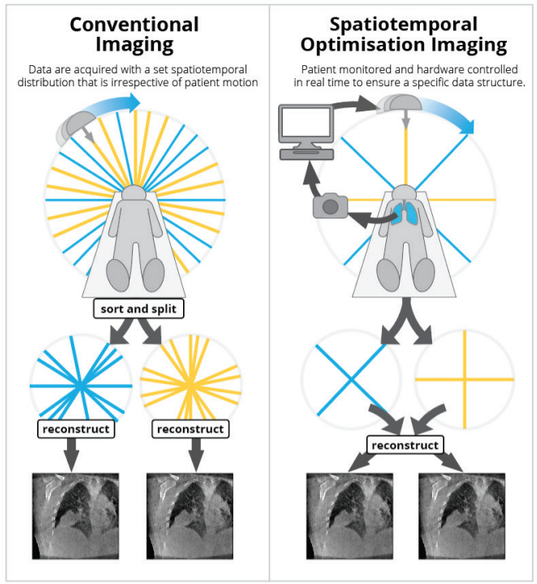
By connecting the patient's physiological signals to imaging acquisition, we can ensure clearer images, lower imaging dose and faster acquisition.

CBCT (Cone-Beam) Imaging

Researchers: Owen Dillon, Ricky O'Brien, Tess Reynolds, Hilary Byrne, Mark Gardner
Students: Benjamin Lau

Project Overview

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.



Highlights of 2023

With 4D-CBCT being increasingly used for image guidance for lung cancer radiotherapy, the problems of the method including inconsistent image quality, streaking artefacts, high imaging dose, as well as long scan times become more pressing. These limitations are largely overcome using a combination of adaptive velocity gantry, x-ray imaging control and motion-compensated reconstruction as demonstrated by the work published in the Medical Physics Journal with Benjamin Lau as first author. Ben presented this work at the AAPM 2023 meeting in Washington and one of his PhD supervisors, Dr Owen Dillon, was an invited speaker to the symposium on CBCT. Ben returned to the US to take up his Fulbright Scholarship at John Hopkins University in Baltimore.

The intellectual property underpinning the ADAPT technology has been licensed to a major radiotherapy system vendor, a critical step for widespread adoption.

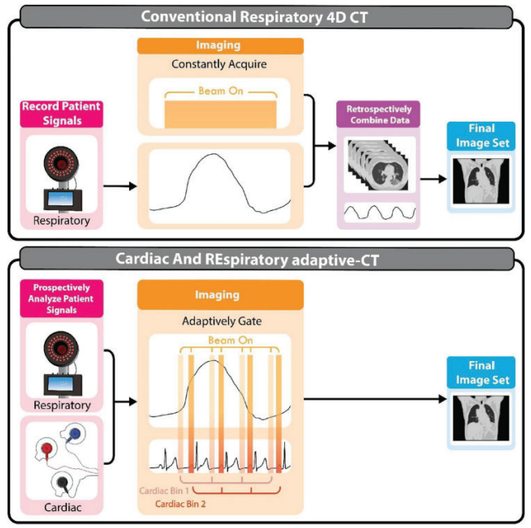
Pictured: By adapting the x-ray hardware to only acquire images at the precise times and locations that reveal the most information, we were able to reduce scan time 63% and scan radiation 85% in the ADAPT clinical trial. The figure shows how we achieved this adaptation and compares to the current standard approach.

CT Imaging

Researchers: Magdalena Bazalova-Carter (Visiting Researcher) , Elshin Mathias, Ricky O'Brien, Tess Reynolds

Project Overview

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 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.



Pictured: Comparison of conventional respiratory 4D CT and CArdiac and REspiratory adaptive CT

Highlights of 2023

In 2023, Dr Natasha Morton's 2022 Physical and Engineering Sciences in Medicine paper titled "CArdiac and REspiratory adaptive Computed Tomography (CARE-CT): a proof-of-concept digital phantom study" was awarded the Kenneth Clarke Journal Award from the Australasian College of Physical Scientists and Engineers in Medicine. Additionally, Elshin Mathias continued work on preparing the REACT Technology for implementation in the REACT clinical trial.

Results of the final phantom studies testing and comparing the REACT technology to current clinical practice prior to the clinical trial being ready to open were shared via a poster presentation at the 2023 American Association of Physicists in Medicine Annual Meeting.

Dr Tess Reynolds was invited to present a Medical Physics Webinar for the American Association of Physicists in Medicine titled "Advances in Cardiac CT and CBCT Imaging".

Interventional Imaging

Researchers Magdalena Bazalova-Carter (Visiting Researcher), Owen Dillon, Ricky O'Brien, Tess Reynolds

Project Overview

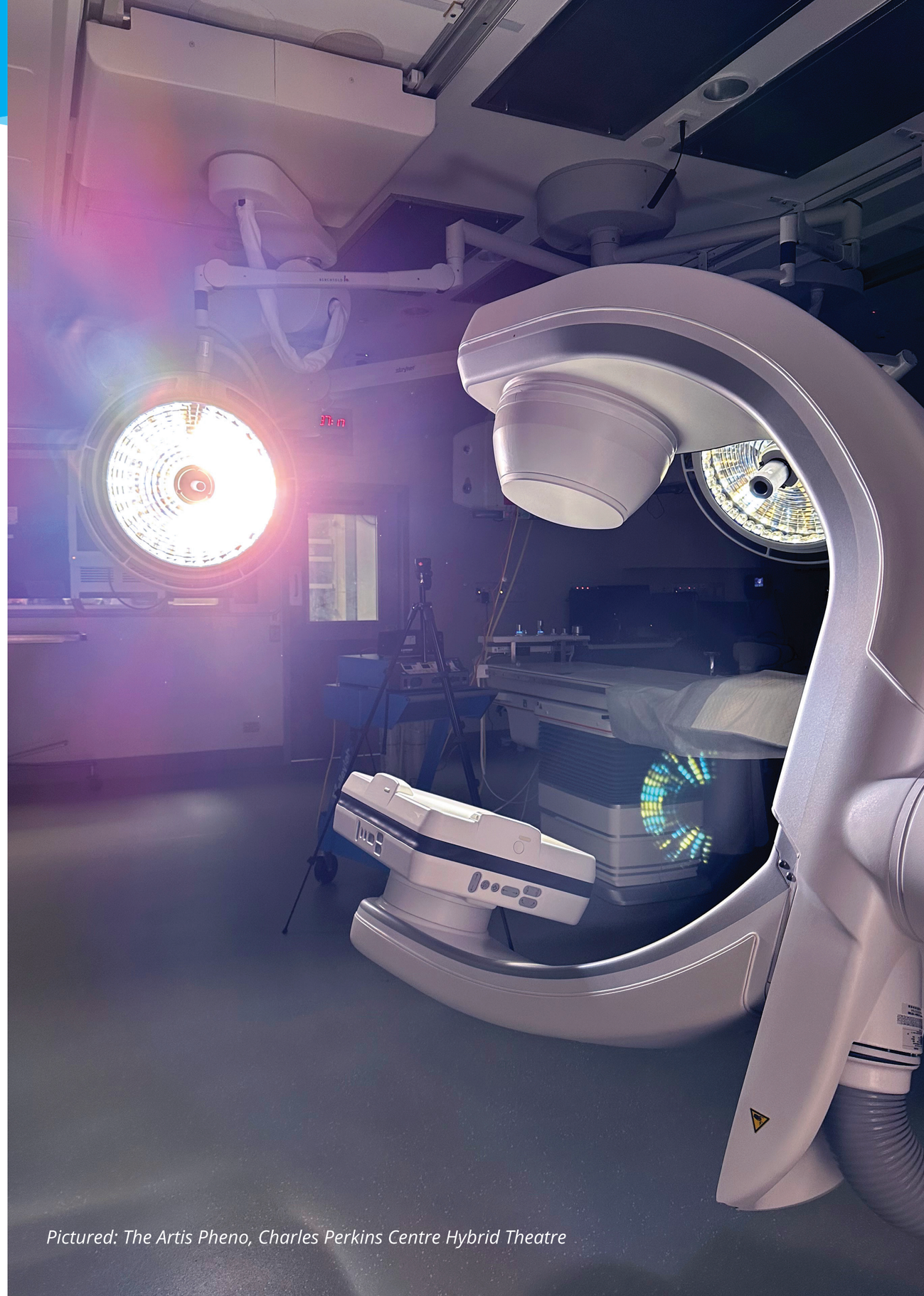
Improving intraoperative imaging and developing novel 3D-printed solutions are key pathways towards safer surgical procedures. We use the state-of-the-art Hybrid Theatre to develop new imaging technologies in the interventional suite. A centrepiece of the theatre is the ACRF-funded Siemens ARTIS pheno 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, reduce metal artifacts from surgical hardware, and reduce blur from cardiac and respiratory motion during imaging. 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 2023

In 2023, Dr Tess Reynolds was invited to present seminars on the Image X Institute's Interventional Imaging Program at leading academic, clinical and industrial institutions, including Harvard University/ Massachusetts General Hospital (Boston, USA), the University of Wisconsin-Madison (Madison, USA), the British Columbia Cancer Center – Victoria (Victoria, Canada), Siemens Healthineers Advanced Therapies (Forchheim, Germany). Dr Tess Reynolds also received one of ten University of Sydney Robinson Fellowships to continue and expand the Image X Institute's Interventional Imaging Program. The Robinson Fellowships were designed to support and retain the University's best early-career academics by creating a pathway towards continuing positions.

In partnership with Siemens Healthineers, Johns Hopkins University (USA), the University of Pennsylvania (USA), the Austrian Center for Medical Innovation and Technology (Austria), and Danube Private University (Austria), Dr Tess Reynolds developed a novel imaging technique that extends the intraoperative field-of-view in both the lateral and longitudinal direction 10-fold. The details of the technique were outlined in a publication in the journal Medical Physics. Targeting improving interventional imaging during thoracic procedures, Dr Tess Reynolds led the expansion of the metal artifact reduction imaging techniques to include motion compensation to remove motion blur due to patient respiration. The results of the study were presented via an oral presentation at the 2023 American Association of Physicists in Medicine Annual Meeting.

Dr Tess Reynolds's 2022 Investigative Radiology paper title "Extended longitudinal 3D imaging with a multi-turn reverse helical CBCT" was awarded the 2023 Faculty of Medicine and Health Early-Mid Career Researcher Outstanding Publication Award.



Pictured: The Artis Pheno, Charles Perkins Centre Hybrid Theatre

Carbon Nanotube Sources for Radiation Therapy Imaging

Researchers: Owen Dillon, Ricky O'Brien, Tess Reynolds

Project Overview

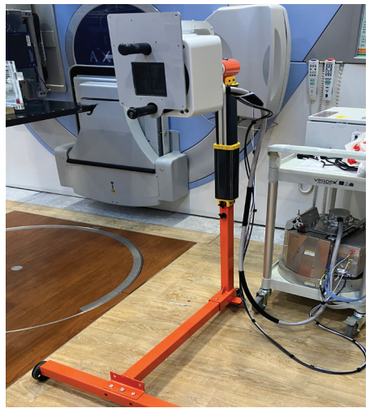
Conventional x-ray sources are large, heavy, and have long warm-up/cool-down times. New Carbon NanoTube (CNT) based x-ray sources can weigh as little as 1 kg, measure 15 cm wide and have effectively instant on/off times, making them well suited to use in arrays.

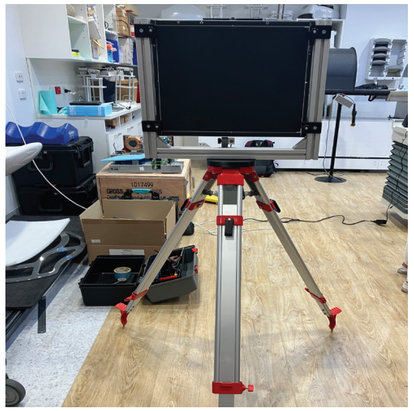
In this project we aim to replace the current slow acquisition method of mechanically rotating a single conventional x-ray source around a patient, to digitally switching CNT sources to acquire 3D images in as little as 1 second.

Highlights of 2023

In 2023 we published a first in world study using simulation results to show how CNT sources could enable 1 second volumetric imaging during radiation therapy. This work was presented in the Scientific Reports journal and presented at American Association of Physicists in Medicine 2023 Annual meeting, the world's largest conference on medical physics.

The implications of this study motivated us to build a unique prototype system with our clinical partner, Nelune Comprehensive Cancer Centre. We have integrated a CNT imaging system with a dedicated research radiation therapy system and are beginning to perform experiments to demonstrate the feasibility and efficacy of the technology. The work will be further boosted by the commencement of a Cancer Council Project Grant in 2024.





Pictured Left : CNT source (on the orange stick), the generator is on the lower deck of the cart, and the control box is on the upper deck.

Pictured Right: The battery powered detector transmits over wifi, making it totally wireless.

The Functional Imaging Program

Program Overview

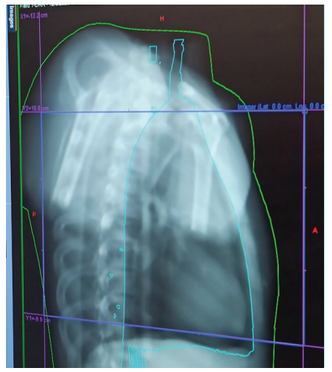
Functional imaging is a branch of medical imaging that captures the activity within the body's organs and tissues. It allows visualisation of physiological processes, such as ventilation and metabolism, providing insight into how the body functions. By mapping these dynamic changes, functional imaging aids in diagnosis and predicting or monitoring treatment effectiveness.

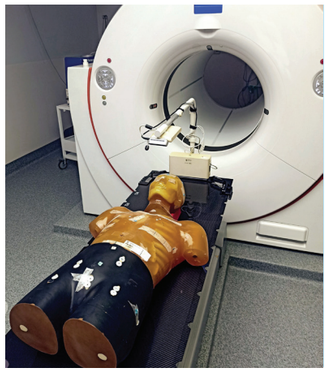
CT Ventilation Imaging (CTVI)

Researchers: Hilary Byrne, Owen Dillon, Mark Gardner, Paul Keall, Hunor Kertesz , Jeremy Lim, Ricky O'Brien, Tess Reynolds. **Students:** Jeremy Lim, Keying Guo.

Project Overview

CT Ventilation Imaging (CTVI), developed by Image X, spatially maps lung function using routine CT images for radiation therapy planning. It produces 3D maps indicating well-functioning and poorly functioning lung areas. Radiation therapy, crucial for 77% of lung cancer patients, can lead to severe radiation pneumonitis in up to 18% of cases. Considering lung function during planning can spare healthy lung tissue, reducing side effects. Image X aims to gather evidence supporting clinical adoption of CTVI to spare healthy lung tissue and explore broader applications beyond radiation therapy.





Pictured: L-R: Imaging quality assurance, a ful body tissue equivalent phantom.

Highlights of 2023

CTVI work has forged ahead this year, with ethics submitted for VENTURE and VITaL and ethics submission for POPPY in Jan 2024.

Jeremy Lim was hosted for 3 months by Image X collaborator Prof. Marcel van Herk in Manchester, UK. His project took advantage of a large dataset to investigate the link between radiation therapy dose to functional lung and overall survival of lung cancer patients. Jeremy will present the results at the main European radiation oncology conference, ESTRO, in 2024.

Image X also hosted student when Keying Guo, a physics undergraduate from The University of Cambridge. Keying applied machine learning to projection images to find alternative ways to identify lung function. Experiences like these are important for undergraduate students in developing research techniques and introducing them to the field of medical physics.

We took delivery of two 3D-printed lung phantoms which highly accurately reproduce inhale and exhale images of a real patient. These will be used to investigate CTVI methods and for quality assurance for upcoming clinical trials.

Magnetic Resonance Imaging (MRI)

Researchers: Caterina Brighi, Phillip Janowicz, Paul Keall, David Waddington

Project Overview

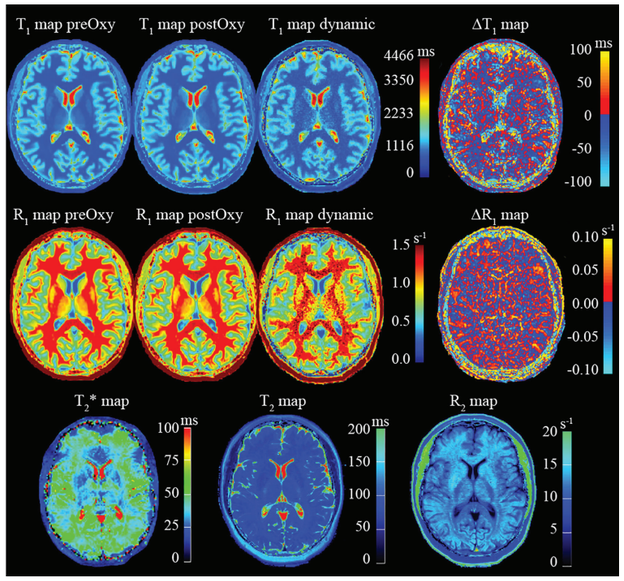
Magnetic Resonance Imaging (MRI) not only provides exquisite anatomical detail but the ability to image markers of tumour biological activity and uptake of metal nanoparticles by tumour cells. These capabilities are utilised in two research projects. Imaging biomarkers associated with hypoxia, a feature of tumour regions with a poorer response to radiation therapy, have been developed using brain images from patients with glioblastoma. The mapping of hypoxic regions will allow radiation dose to be increased where it is needed. Glioblastoma has a very poor prognosis and metallic nanoparticles that are electively taken up by tumour cells have the potential to assist with identification of tumour cells, and also to sensitise them to radiation treatment. These nanoparticles are being tested in preclinical models of glioblastoma.

Highlights of 2023

After 2 years of consistent effort, Dr Caterina Brighi gained ethics approval for a clinical trial of hypoxia imaging in glioblastoma patients through a collaboration with Royal North Shore hospital.

Dr Brighi and Dr David Waddington began work on a successful NHMRC Development Grant with Ferronova Ltd that is aimed at using iron oxide nanoparticles to identify aggressive subregions of brain cancer. Dr Phillip Janowicz established our preclinical brain tumour imaging program in collaboration with Sydney Imaging and gave updates on the progress of his nanoparticle work at national conferences including the International Society of Magnetic Resonance in Medicine – ANZ.

Dr Waddington was awarded a patent from his work on nanoparticle imaging with MRI along with co-inventors at Harvard University. In recognition of the impact of his nanoparticle MRI work, Dr Waddington was also named a Junior Fellow of the International Society of Magnetic Resonance in medicine.



Pictured: Example of quantitative images obtained from MRI protocol acquisition on a healthy volunteer.

Positron Emission Tomography (PET)

Researchers: Caterina Brighi, Paul Keall, David Waddington.
Students: Yuvnk Trada

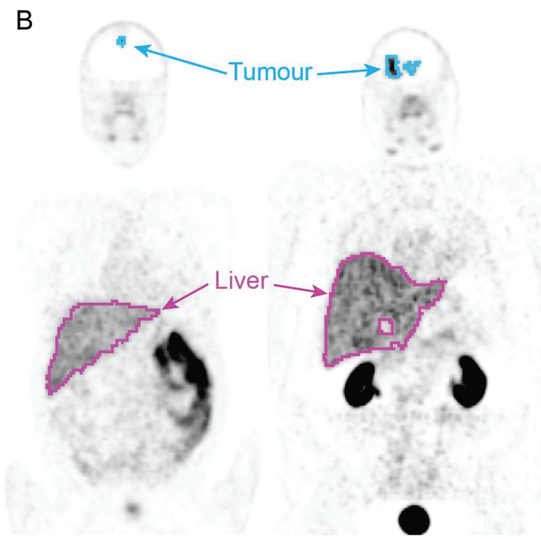
Project Overview

A Positron Emission Tomography (PET) scan uses radiotracers to visualise and measure the metabolic activity of tissues. Tumour cells can have different uptake of tracers and metabolic profiles compared to surrounding normal tissue so PET imaging can provide sensitive and specific detection of tumour spread and characteristics. We have investigated PET imaging biomarkers for glioblastoma and Head & Neck cancer. The goal is to identify imaging biomarkers that have an impact on the clinical management of patients, given the increasing importance and need for more specific, affordable, and widely available molecular imaging biomarkers.

Highlights of 2023

Dr Caterina Brighi led a study demonstrating that 68Ga-PSMA-617 has superior characteristics to 18F-FET as a PET imaging biomarker for recurrent glioblastoma tumour delineation and secondary treatment planning. The clinical data were collected in a study supported by Genesis Care and the findings were published in the International Journal of Molecular Sciences and presented at the European Association of Neuro-Oncology 2023 meeting.

Dr Yuvnik Trada's PhD project focuses on developing methodology and protocols for mid-treatment PET imaging to predict predict later treatment response and toxicity in Head & Neck cancer patients treated with radiation therapy. These predictive models could be used to adapt treatment planning to improve tumour control and reduce side effects. The work has also led to three first author papers for Yuvmik in 2023 in European Radiology, QIMS and Radiotherapy & Oncology.



Pictured: Full body PET images using 68Ga-PSMA-617 biomarker of two patients, with tumour (blue) and liver (purple) segmentations.

Kilovoltage Intrafraction Monitoring

Researchers: Paul Keall , Freeman Jin, Yifan Li, Sam Liang, Chandrima Sengupta
Students: Alicja Kaczynska

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 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 2023

KIM technology has continued to be used to treat prostate cancer patients in the TROG 18.01 NINJA trial and liver cancer patients in the TROG 17.03 LARK trial. The LARK trial has recruited 32 patients and the KIM-guided geometric and dosimetric outcomes showed significant improvements as compared to standard-of-care treatment. Initial results were presented by Dr Chandrima Sengupta at the European Society of Radiation Oncology 2023 meeting and she also led the publication *The first clinical implementation of real-time 6 degree-of-freedom image-guided radiotherapy for liver SABR patients* which was published in the prestigious first-in-human section of the Radiotherapy and Oncology journal.

The trial is closed to recruitment and the data are being collated for publication of the trial results.

KIM was previously tested in the TROG 15.01 SPARK trial for prostate cancer patients which, along with publications, generated terabytes of images and other data types. To provide a resource for the research community, Dr Sengupta and Yifan Li developed tools and documentation to deidentify and upload the data to a publicly accessible repository. Sam Liang continued to build the imaging database tools for making clinical imaging data collected from different trials and sites accessible for researchers.

Pictured: Dr Chandrima Sengupta and the LARK Clinical Trial collaborators.

Associated Studies

LARK (Liver SBRT with KIM guidance)

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 (prostate SBRT with KIM guidance)

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

Markerless Tracking

Researchers: Mark Gardner, Nicholas Hindley, Jonathan Hindmarsh
Students: Adam Mylonas

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.

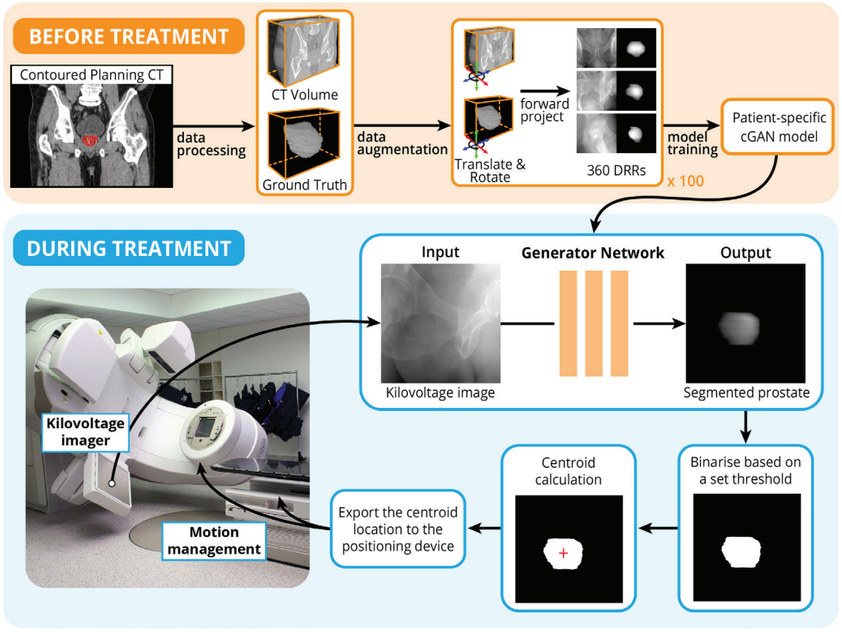
Highlights of 2023

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 leaning model can be used for the simultaneous tracking of lung tumours and the lung. Patients have continued to be recruited to the MAGIK, VALKIM (lung cancer) and ROCK-RT (liver cancer) trials with recruitment reaching completion for the CHIRP (head and neck cancer) trial.

We also established proof-of-principle for the first deep learning framework capable of simultaneously tracking targets and organs-at-risk in three-dimensions in real-time, which led to a publication in the journal Physics in Medicine and Biology, an oral presentation at the AAPM Annual Meeting in Texas, US and was awarded the Faculty of Medicine and Health Bright Ideas Grant.

To create the large datasets needed to train neural networks, we developed a data augmentation method for head and neck cancer patients. This method, which was published in Medical Physics, warps pre-treatment scans with physiologically realistic motion to generate a new set of simulated images. We developed an open-source Contour Alignment Tool that allows users to quickly and easily match contours in images acquired during treatment.

The Contour Alignment Tool is being used in clinical trials to create datasets to train neural networks and led to a presentation at EPSM.



Pictured: Simulated real-time clinical study of patient-specific prostate segmentation in kilovoltage images via deep learning.

Associated Studies

MAGIK - Markerless Image Guidance Using Intrafraction Kilovoltage X-ray Imaging

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

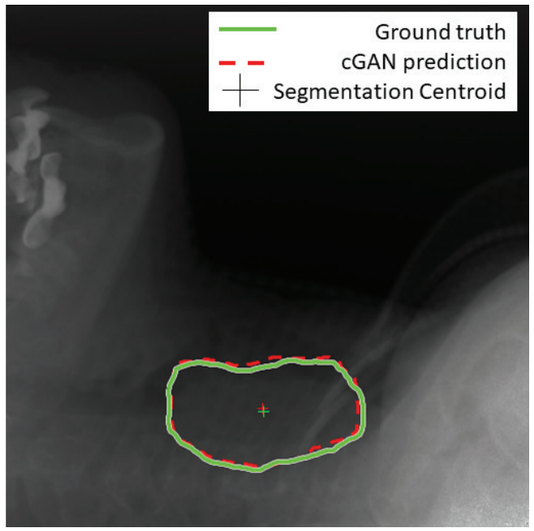
VALKIM is a RNSH led study for lung cancer using our markerless tracking technology.

ROCK RT - Radio-opaque contrast agents for liver cancer targeting with KIM during radiation therapy: An observational feasibility study

ROCK-RT is a non-interventional feasibility study for markerless liver cancer tracking using contrast agents.

CHIRP - The Collection of Head Images during RadiotheraPy

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.



Pictured: An example of the markerless tracking accuracy for a patient in the Collection of Head Image for RadiaotheraPy (CHIRP) dataset.

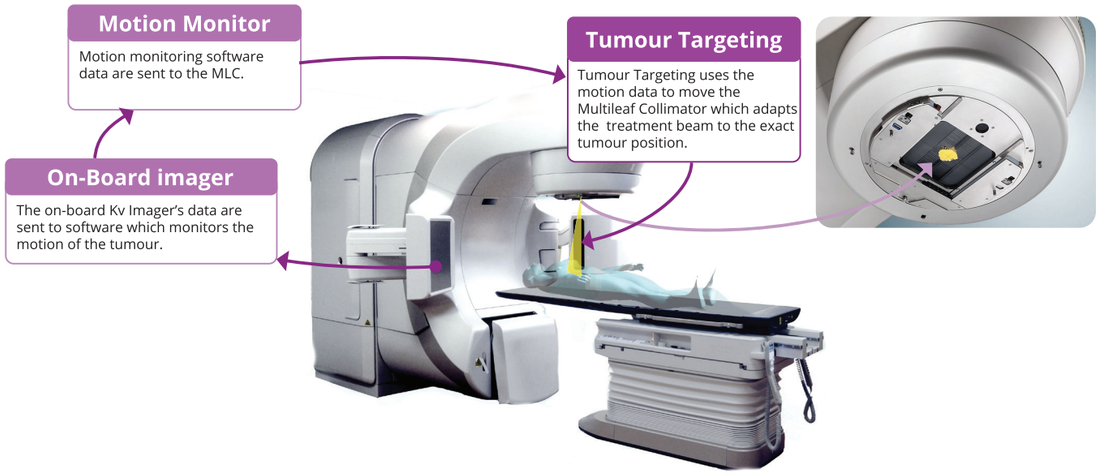
Tumour Targeting

Researchers: Emily Hewson, Paul Keall, Lars Mejnertsen

Overview

Tumour Targeting is a technology 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 on-board imaging equipment to adapt the shape and position of the radiation beam.

Our 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

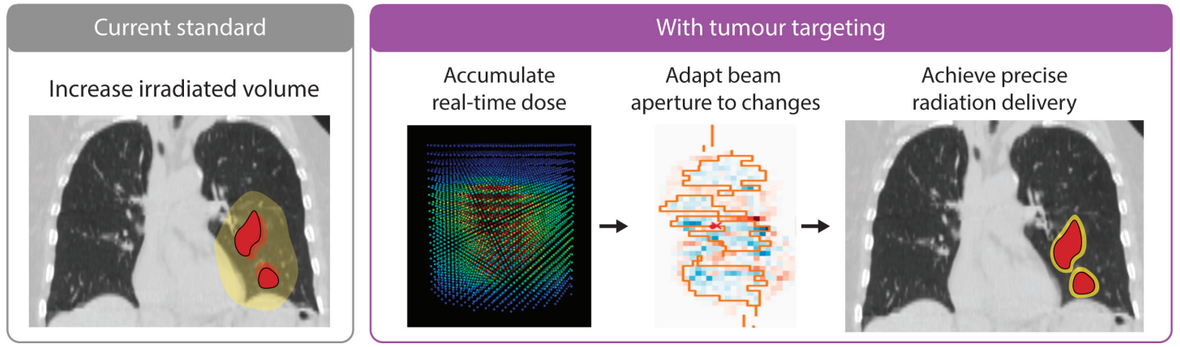
Highlights of 2023

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 and lead to a patent, "Dose-based optimization for multi-leaf collimator ("MLC") tracking during radiation therapy methods and apparatus" filed and licensed in 2023. 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.

Dr Emily Hewson commenced a fellowship funded by the Cancer Institue NSW to extend this tumour targeting technique for patients with multiple tumours in the lung to enable more effective radiation therapy treatment for a high-risk cohort of patients.

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.



Pictured:Tumour targeting can improve the accuracy of radiation delivery for patients with multiple, independently moving targets to control the tumour while minimising harmful side effects.

MRI Guidance

Researchers: Thomas Boele, Paul Liu, Paul Keall , David Waddington, Brendan Whelan
Students: James Grover, Elia Lombardo (Visiting PhD student)

Magnetic Resonance Imaging (MRI) devices produce high resolution images providing detailed anatomical 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. Unlocking the potential of MRI-Linacs for precise targeting requires real-time adaption of the radiation beam to the acquired imaging information. This presents challenges as MRI is a relatively slow imaging modality. Our program utilises machine learning and the Australian MRI-Linac system to develop and test tumour targeting methodology with the goal of implementation on clinical systems.

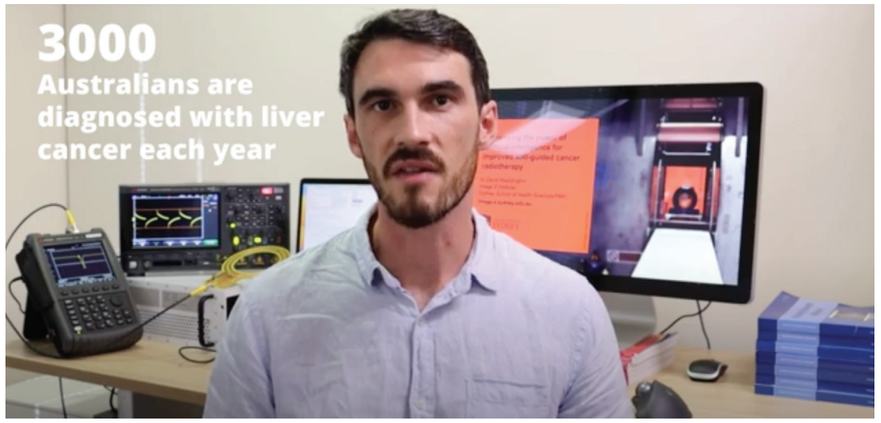
Highlights of 2023

Medical imaging continues to be transformed by the rapid developments occurring in the field of artificial intelligence (AI). Our team have been hard at work through 2023, translating AI advances to improve tumour targeting technologies on MRI-Linacs with AI. Dr David Waddington and James Grover won research grants from Tour de Cure to further their work using AI to target tumours. Dr Thomas Boele is continuing to build our international collaborations as he left to begin a Fulbright Exchange with Massachusetts General Hospital aimed at finding new ways to image cancer with MRI. On the back of her pioneering work in AI and MRI, Image X postdoc Dr Shanshan Shan received and accepted an offer of a continuing academic appointment at the highly respected Shanghai Jiao Tong University. Shanshan's latest work in distortion correction was published in leading MRI journal Magnetic Resonance in Medicine.

Associated Studies

The MANTRA clinical trial. The world first clinical trial of an inline MRI-Linac.

AMPI Trial – 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.



Pictured: Stills from the Tour de Cure videos.

Surface Imaging and Remove the Mask

Researchers: Youssef Ben Bouchta, Mark Gardner
Students: Chen Cheng, Daniel Wang

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.

Highlights of 2023

Safe and accurate treatment involves monitoring both surface motion and internal organ motion. Dr Ben Bouchta has developed a surface monitoring software to accurately track a person's face as they move. The accuracy and reliability of this software was tested in volunteers as part of the VISION study which completed recruitment this year. Preliminary results were presented at the European Society for Radiotherapy and Oncology (ESTRO) meeting in May 2023 and a paper describing the development of the technology was submitted for publication in the Physics and Imaging in Radiation Oncology (PHIRO) Journal. This technology's acceptance and feasibility is being tested in the SMART clinical trial which recruited 16/20 patients in 2023.

Dr Gardner has been developing methods to monitor the internal organ motion during treatment. Dr Gardner's method for detecting the tumour location in simulated head and neck x-ray images has been published in the Medical Physics Journal in March 2023. His head and neck motion simulation method was presented at the Engineering in Medicine and Biology Conference in July 2023. Dr Gardner is completing the analysis of the CHIRP trial which finished recruitment in late 2023. Data from the CHIRP trial will be used to help guide the safe implementation of mask-free radiotherapy and further development of his tumour localisation method.

Associated Studies

CHIRP

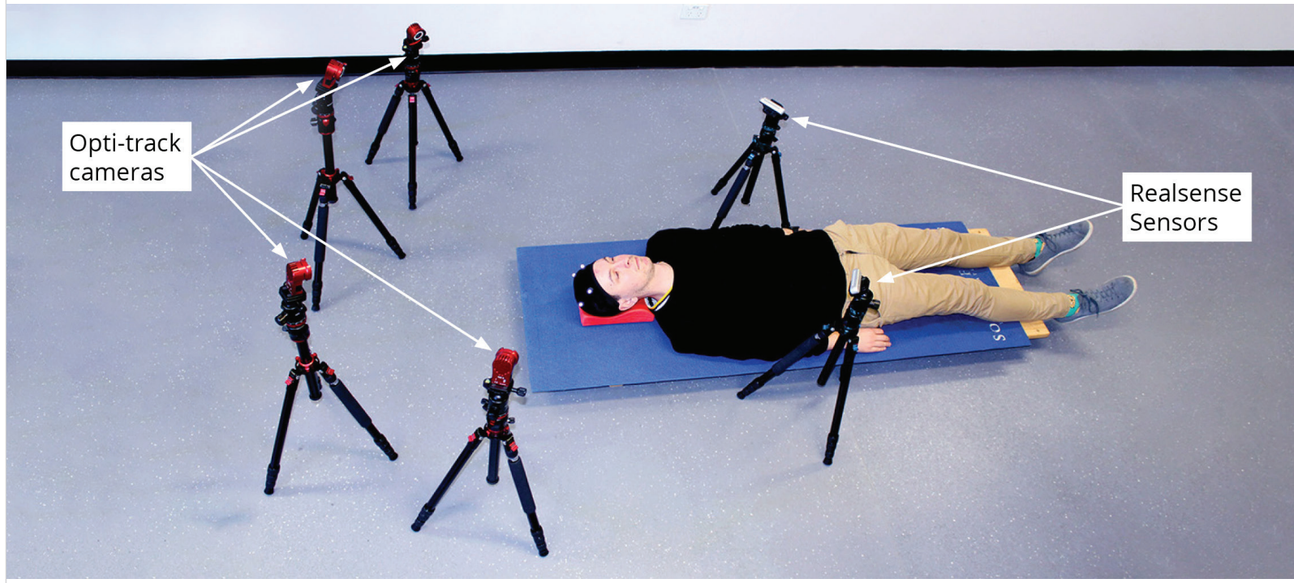
The Collection of Head Images during RadiotheraPy: Clinical trial that is collecting the images acquired during radiotherapy for head and neck cancer patients, including X-ray images.

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.



Pictured: The VISION Study setup.

Clinical Studies

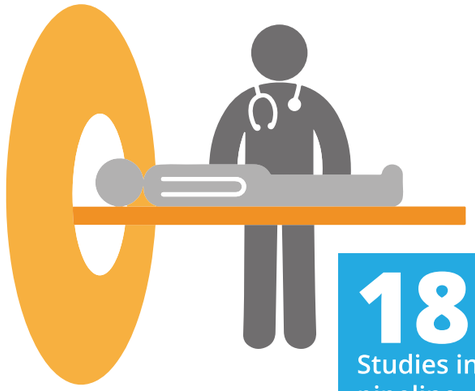
In 2023 we had 9 clinical trials open and actively recruiting participants. In total we recruited 83 participants to our trials. This was our best recruitment year at Image X to date. Two studies – CHIRP and VISION, reached their recruitment targets and the results are now being analysed.

In addition to the actively recruiting trials, we had a further 7 studies in various stages of development. These trials cover the whole trial development process from concept design right through to ethics submissions and site start up activities. Three of these studies received ethics approval in 2023 and are expected to open to accrual later in 2024.

Clinical Trial Leads

Natalie Plant

Shona Silvester

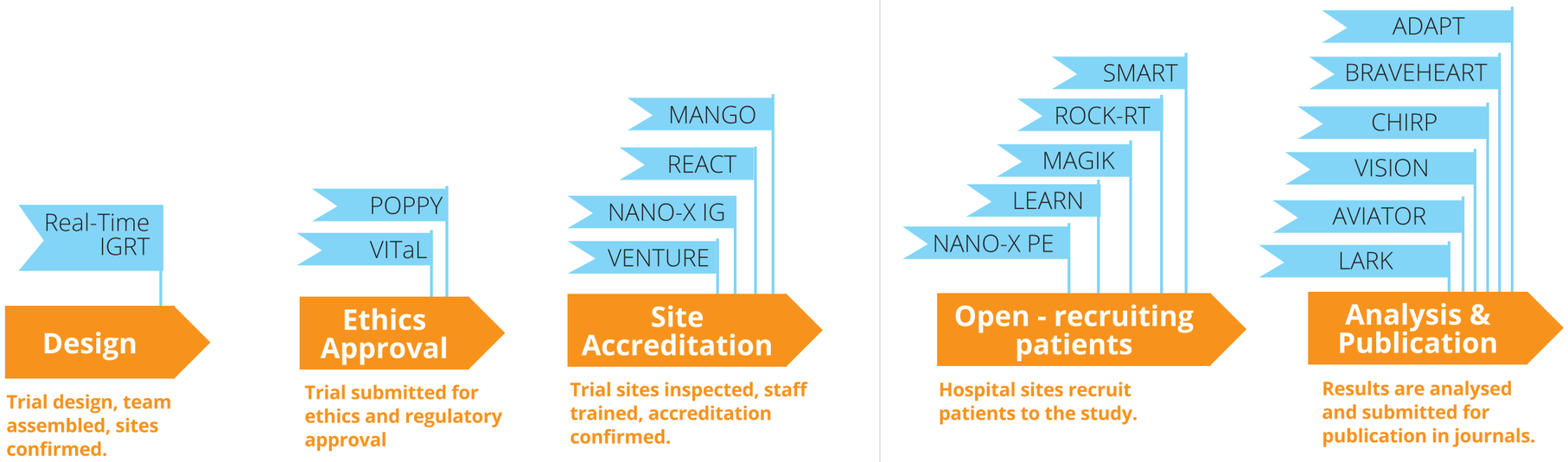


18 Studies in our pipeline.

5 Trials open and recruiting patients

83 Participants recruited

STUDY STATUS IN 2023



Open Science

Sharing of clinical trial data has great potential to accelerate scientific progress and ultimately improve public health by generating better evidence on the safety and effectiveness of therapies for patients. (USA National Institute of Health)

The FAIR principles define a set of characteristics for data and tools to be Findable, Accessible, Interoperable and Reusable. In accord with these principles, the data from the **TROG 15.01 SPARK** prostate cancer clinical trial were published on the University of Sydney eRepository. While this achievement involves contributions from the entire TROG 15.01 SPARK team, including patients on the trial, Dr Chandrima Sengupta and Yifan Li led the checking, collation, organising and documentation for this endeavour. Since its publication, the 3 terabyte dataset has been downloaded over 200 times.

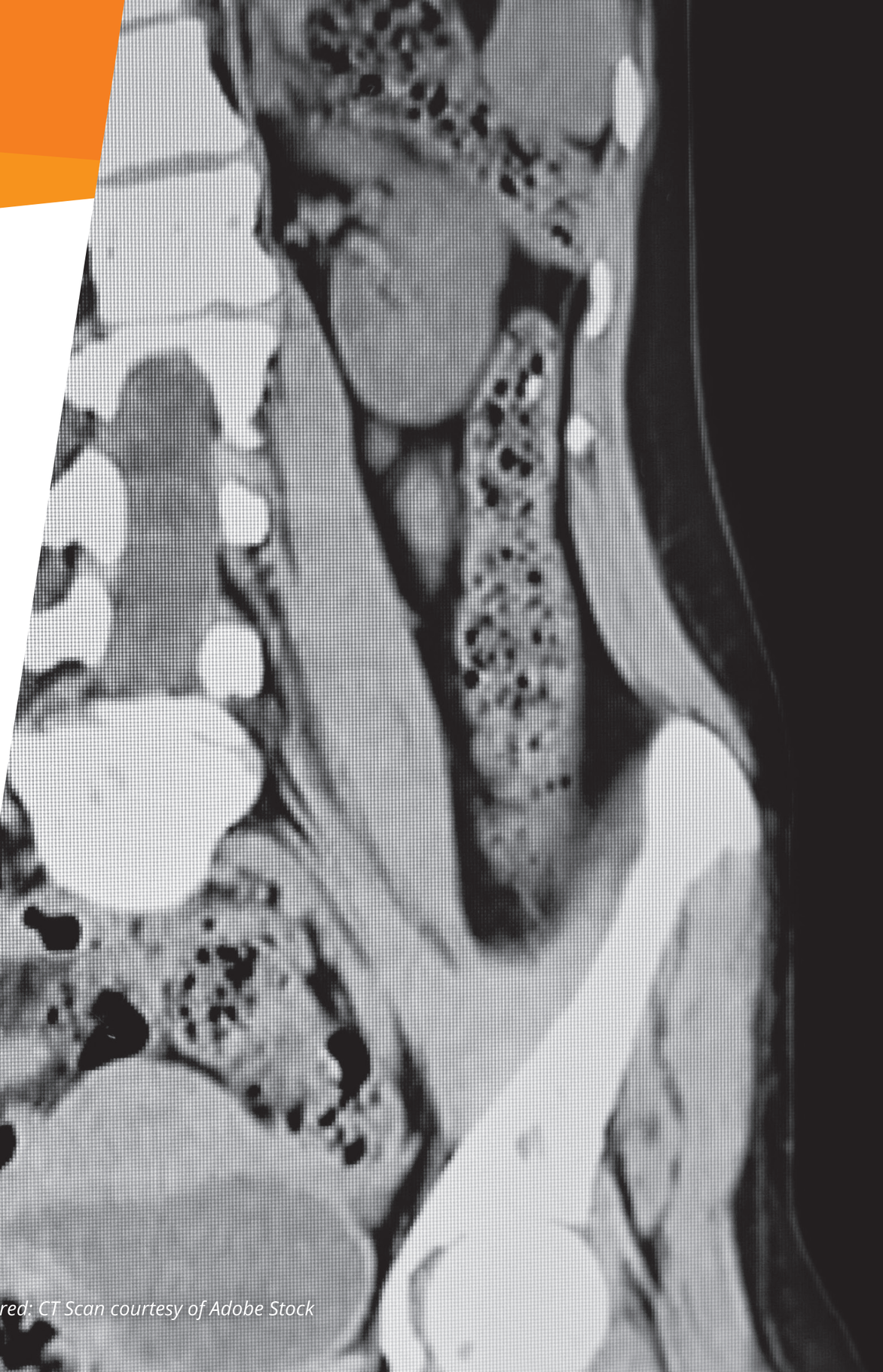
To support the scientific community, we can maximise the utility and impact of the tools we create and the data we collect by making them available to other researchers.

Open-source software tools through our github site include:

Contour-Alignment tool developed by Adam Mylonas. This tool is employed on imaging data in the ROCK-RT and LEARN clinical studies.

ParticlePhaseSpace: A python package for streamlined import, analysis, and export of particle phase space data developed by Dr Brendan Whelan and Dr Leo Esnault was published in the Journal of Open Source Software. This tool provides an open source and extensible framework for the import, analysis, and export of particle phase space data, which historically exists in very fragmented and incompatible formats.

The Real Time Imaging Database developed by Indrajit Ghosh with contributions from Professor Ricky O'Brien, Dr Chadnrima Sengupta and Sam Liang. The package is a cloud-based mechanism for managing clinical trial data into a central searchable service, which can be used to analyse and create deep-learning models for predicting various features of interest. The learning system allows ease of integration with existing and new applications that produce or require access to the de-identified patient data to researchers, clinicians, and other health professionals who want to use the available clinical data.



Pictured: CT Scan courtesy of Adobe Stock

Translation and Commercialisation

SeeTreat - Image X Spinoff

Founded by Professor Paul Keall and NHMRC & Cancer Institute NSW Early Career Fellow, Dr Doan Trang Nguyen, the mission of SeeTreat Pty Ltd is to build cutting-edge medical software, to equip clinicians with powerful tools to deliver precise radiotherapy, improving treatments for millions patient. Significant investment from a major vendor for radiation therapy systems has led to the establishment of the company headquarters at Haymarket Terminal.

The team are developing software solutions that will transform standard radiotherapy to one capable of adaptive personalised therapy for any patient, anywhere. Several Image X institute alumni including Dr Trang Nguyen, Dr Brendan Whelan, Dr Paul Liu, Indrajit Ghosh, Dr Lars Mejnertsen and Dr Sean Pollock are developing Image X technologies into commercial products that can be deployed in the clinic.

Industry Partnerships

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

Our partnership with Siemens Healthcare has provided unique access to the control system (TACS) of a C-arm robotic imaging system, resulting in publications, international collaborations, further research funding and a Eureka prize. Dr Tess Reynolds leads a new agreement which maintains the unique access to the TACS of the imaging system and formalises inclusion of John Hopkins University and the University of Pennsylvania in the partnership.

TibaRay is a spin-off company from Stanford University developing FLASH or ultra-high-dose-rate radiation therapy. Dr Brendan Whelan formed an industry-funded agreement with TibaRay to model and optimise beamline components, entailing both the fundamental accelerator physics, as well as dose calculation and optimisation in patients.

Patient-connecting Imaging Technology License

Cone Beam CT images acquired immediately prior to radiation therapy can be of poor quality, impacting the accuracy of treatment delivery. Our patient-connected imaging technology uses the patient's breathing to control when and how images of the patient are acquired, effectively synchronising imaging and breathing.

This problem and solution became part of an Australian Government NHMRC grant application that ended up being the top-ranked project grant of 2011. Professor Ricky O'Brien developed a complex real-time optimisation solution that would work, as demonstrated in computer simulations. We collaborated with Prof Jan-Jakob Sonke who had access to a research cancer radiotherapy system in Amsterdam, developing the hardware and software to obtain the first experimental evidence that the solution could be realised.

We partnered with Prof Shalini Vinod and team at Liverpool Hospital to develop an NHMRC-funded clinical study and worked with radiotherapy equipment provider Elekta to maximise safety and risk management for the technology's patient use. The trial was very successful, demonstrating that patient images could be acquired in one minute instead of four, with one-sixth of the imaging dose and better image quality. The magnitude of these improvements led to the technology being licensed to a large global radiation oncology equipment provider.

The current license does not commit our partner to a product, but also allows other potential partners to work with us to build improved devices that image patients more quickly, with less dose, and higher quality images.

Pictured: CT Scanner courtesy Adobe Stock

Awards

Dr David Waddington
Junior Fellowship of the International Society of Magnetic Resonance in Medicine

Based on his past contributions and society service, as well as future potential for outstanding achievements to the field of magnetic resonance, Dr David Waddington was made a Junior Fellow of the International Society of Magnetic Resonance in Medicine (ISMRM). The Junior Fellowship supports attendance at ISMRM events, participation in committee and working group activities and mentoring. David received the award at the ISMRM 2023 meeting in Toronto where he gave an invited talk and an oral presentation for a submitted abstract. David completed his CINSW Early Career Fellowship this year and commenced his NHMRC Emerging Leadership Investigator Grant.

Dr Brendan Whelan
Farrington Daniels Award for Best Paper published in the Medical Physics Journal

Dr Brendan Whelan and collaborators from Stanford University were awarded the American Association of Physicists in Medicine (AAPM) Farrington Daniels Best Paper Award. This award is for an outstanding paper on radiation therapy dosimetry, planning or delivery, published in the Medical Physics journal in 2022. The paper is Bayesian optimization to design a novel x-ray shaping device. It wraps a formal optimisation framework, in this case a Bayesian approach, around a Monte Carlo modelling problem. Typically, Monte Carlo modelling has been trial and error. The optimisation framework allows the best solution to be found. For this application, the problem was to optimise the design and output characteristics of a novel device with no moving parts that could replace the complicated multileaf collimator.

Natasha Morton
Kenneth Clarke Award for Best Paper published in the Physical and Engineering Sciences in Medicine journal

The article CArdiac and REspiratory adaptive Computed Tomography (CARE-CT): a proof-of-concept digital phantom study received the Kenneth Clarke award for the best 2022 paper published in the Physical and Engineering Sciences in Medicine journal. The paper is authored by graduated PhD student Natasha Morton and her PhD supervisors, Ricky O'Brien, Paul Keall and Tess Reynolds. It outlines a new CT imaging technique to simultaneously account for both cardiac and respiratory motion. CARE-CT has the potential to reduce artifacts in key thoracic structures, improving treatment planning and dose calculations for thoracic radiotherapy and emerging cardiac radioablation treatments. As image artifacts have been linked to poorer patient outcomes, this approach has significant clinical potential.

Dr Tess Reynolds
Faculty of Medicine & Health Outstanding Publication Award

Dr Tess Reynolds received a University of Sydney Early-Mid Career Researcher (EMCR) Outstanding Publication Award (Faculty of Medicine and Health) for her 2022 publication in Investigative Radiology, Extended Intraoperative Longitudinal 3-Dimensional Cone Beam Computed Tomography Imaging with a continuous Multi-turn Reverse Helical Scan. The award aims to provide recognition of EMCR's contribution to publication excellence within the faculty.

Benjamin Lau and Dr Thomas Boele
Fulbright Awards

The Australian-American Fulbright commission provides prestigious scholarships and fellowships to foster interdisciplinary research and promote diverse perspectives to address pressing global challenges.

PhD student Benjamin Lau was awarded a scholarship for developing the next generation of 4D imaging systems for radiotherapy. This technology aims to reduce radiation exposure and imaging time whilst improving patient outcomes. As a Fulbright Scholar, Benjamin Lau joined the Advanced Imaging Algorithms and Instrumentation Laboratory at Johns Hopkins University in mid 2023. Ben's application was assisted by the mentoring of past Fulbright recipients, Dr David Waddington and Dr Nicholas Hindley, and the collaboration Dr Tess Reynolds has developed with the JHU group.

Dr Thomas Boele, a postdoctoral research associate, was awarded a Fulbright Fellowship at the Athinoula A. Martinos Center for Biomedical Imaging at Massachusetts General Hospital to explore how the application of novel quantum sensors in medical imaging can enable new imaging modalities for improved disease diagnosis and treatment.

Pictured: University of Sydney, Courtesy Adobe Stock

Competitive Grants and Funding

Commenced 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

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

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

Dr Tess Reynolds. Delivering the Future of Interventional Medical Imaging with Robotic Systems. University of Sydney Robinson Fellowship, salary support and $177,415 project costs

Dr Nicholas Hindley. University of Sydney FMH Bright Ideas Grant. $20,000

Dr David Waddington. University of Sydney FMH Rewarding Research Success. $40,000

James Grover. PhD Research Training Program Stipend, Australian Government Department of Education

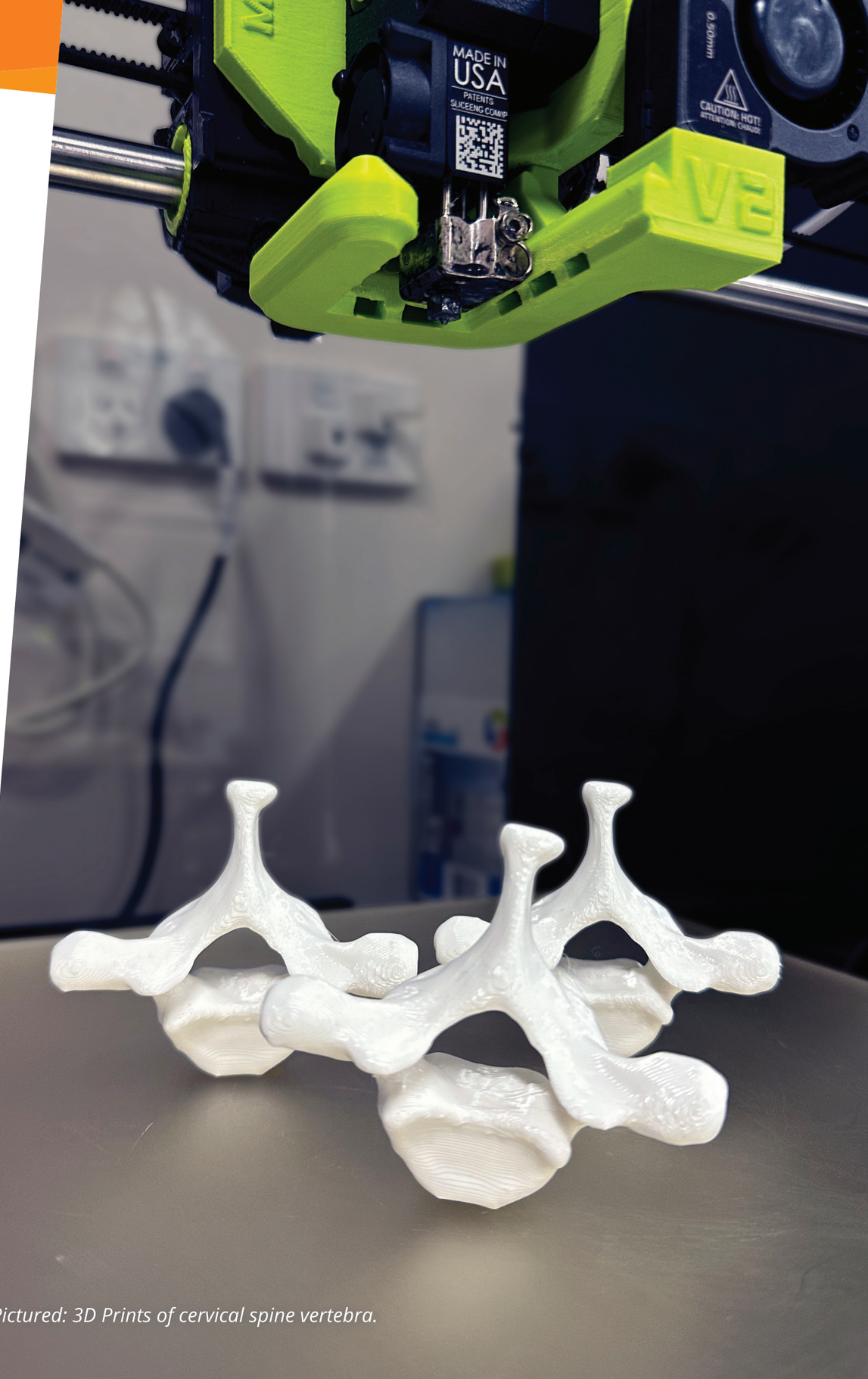
Researchers also received funding from:

Sydney Cancer Partners (**Dr Caterina Brighi, Dr Emily Hewson and Dr Chandrima Sengupta**),

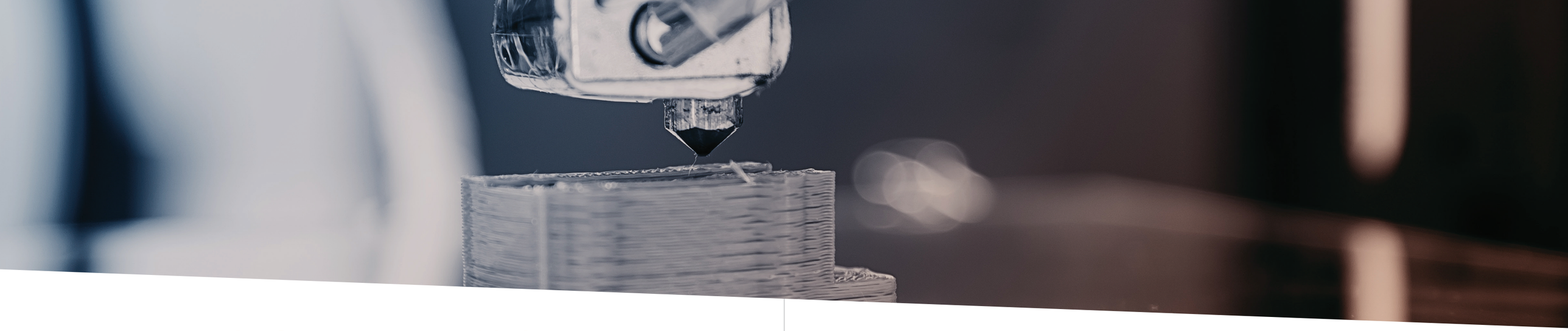
Cancer Institute NSW (**Dr Hilary Byrne and Adam Mylonas**) and

FMH Showcase Travel awards (**Dr Youssef Ben Bouchta, Dr Mark Gardner and Dr Chandrima Sengupta**) to present their work at international conferences.

Designs & Communications Officer, **Julia Johnson**, received funding from the USYD Professional Staff Development Fund to attend the Semi Permanent design conference.



Pictured: 3D Prints of cervical spine vertebra.

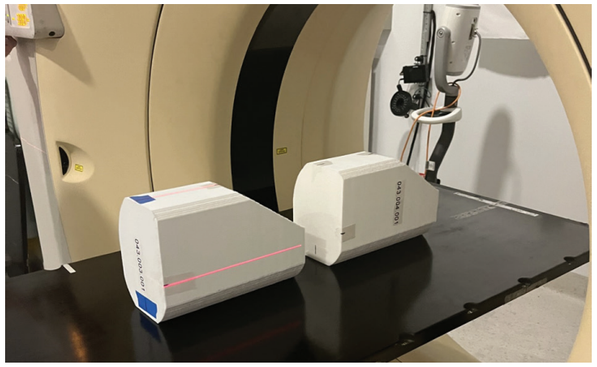


Equipment and Infrastructure Highlights

Head and Neck Phantom

The Remove the Mask team acquired a custom 3D printed head phantom, based off of a real patient CT scan.

"The phantom is made from tissue equivalent materials, so when we scan it, the images will look exactly like a scan of a real human head. We will be attaching the phantom to the robot arm and simulating real patient treatments, incorporate our cancer tumour software for the Remove the Mask project."- Dr Youssef Ben Bouchta



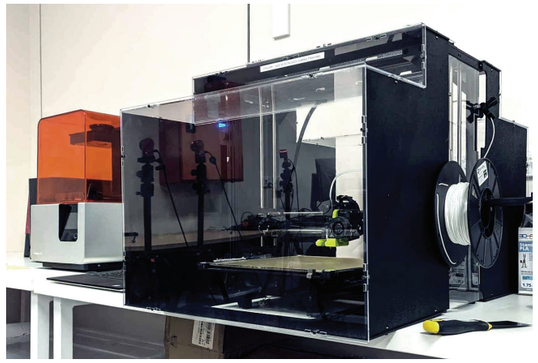
PixelPrint: 3D printed lung inhale/exhale pair of phantoms

Dr Hilary Byrne and the CT Ventilation team acquired two lung phantoms were 3D printed from two CT images of a patient, at full breath in and full breath out. PixelPrint use a custom printing technique to accurately reproduce the density of the source image of the patient's lung, so we end up with a phantom that looks exactly like the patient when we scan it again on a CT machine.

Hilary and team are using these phantoms to improve our technique to produce a 3D map of lung function from inhale and exhale scans of a patient. "We have proven the technique works with scans of patients in a clinical trial, but we can only scan these trial participants once. With a phantom we can scan again and again to investigate the parameters that affect our lung function mapping. " - Hilary

3D Printer

The workshop gained a Fused Deposition Modelling (FDM) 3D printer thanks to Dr Tess Reynolds, which facilitated rapid prototyping capabilities for our researchers. The printer was used to produce medical phantom components, model bones, replacement parts for existing equipment, and even moulds for creating phantoms from other materials.



UR16 Robotic Arm

This year we acquired a new robotic arm with higher weight ratings than our previous robotic arm. The UR16 is for use in the clinic, reproducing patient motion. This motion will initially be translational (left-right, up-down, forward-back) but will eventually include rotational in (yaw, pitch and roll). We will use the robot to hold and move tumour phantoms, to test technologies that track and/or adapt to moving targets in real-time.

The UR16 was taken up to the Radiation Oncology department of Royal Brisbane and Women's Hospital where PhD Candidate Jonathan Hindmarsh used it to assess the accuracy of the Radixact Synchrony when delivered to a moving target. The phantom used consited of a custom Perspex frame, designed in-house by Julia Johnson, plus a 2D array. The frame held a 2D array that measured radiation dose, which Jonathan used to simulate a lung and a prostate treatment delivery.

Engagement

Image X Institute actively engages with a broad range of individuals and groups. This includes undergraduate and postgraduate students, fellow researchers within the Faculty of Medicine and Health, healthcare professionals, researchers, cancer survivors, consumer advocates, and various other stakeholders.

In the media

First-author PhD student, Benjamin Lau, was featured in a PhysicsWorld article "Can state-of-the-art linacs boost the uptake of 4D-CBCT in radiotherapy?". This article is fantastic recognition and icing on the cake for Ben, who spent much of the year undertaking his Fulbright Fellowship in the US: https://physicsworld.com/a/can-state-of-the-art-linacs-boost-the-uptake-of-4d-cbct-in-radiotherapy/

FMH Media

We were able to share some major achievements with our colleagues in the Faculty of Medicine and Health, by securing coverage in the FMH News. These articles help make our researchers visible to their peers in the faculty, and give Image X the opportunity to celebrate our contributions towards achieving the FMH and the University's strategic goals.

The fruits of Prof Paul Keall and Dr Hilary Byrne's partnership with company 4DMedical were featured in the staff news in February, when the commercial product CT LVAS (based on Image X technology) was publicly announced: https://intranet.sydney.edu.au/medicine-and-health/news-events/news/2023/02/fmh-researchers--project-transformed-to-globally-available-clini.html

Dr Chandrima Sengupta's career-highlight first-in-human paper was celebrated in the FMH Wins article in December: https://intranet.sydney.edu.au/medicine-and-health/news-events/news/2023/december/fmh-wins-11-december.html

Consumer Advocates

We thank our consumer advocates for their unique perspectives, representing the priorities and insights of the end users of our technology. Advocates generously provide their time to provide feedback on grant applications, research proposals and study design.

Summer Research Program

Every summer, the Image X headquarters gets an injection of enthusiasm and excitement as we welcome a cohort of summer students for the Summer Research Program. Students spend their summer break working on projects outlined by our researchers, receiving mentorship and support along the way. Summer students come from a range of areas including biomedical engineering, software development, mathematics, physics and more. The program, co-ordinated by Dr Youssef Ben Bouchta, has resulted in many ongoing projects and relationships. Summer students have gone on to become research assistants, undertake masters projects, and even become PhD candidates and Fulbright Fellows.

Undergraduate and Postgraduate Teaching

Part of the institute's strategy to engage with students (and identify possible future Image X students) has been to take on more speaking and teaching opportunities. In 2023 a bigger cohort of our researchers took up teaching and public outreach opportunities:

Dr Hilary Byrne lectured the Master of Medical Physics students on the subject of Radiation Physics, PHYS5012.

Dr Youssef Ben Bouchta taught a lecture for the Medical Radiation Science III course.

Prof Paul Keall and Dr Brendan Whelan lectured on MRI in Radiation Therapy in the Masters of Medical Imaging Sciences MRTY5141 unit on Hybrid Imaging.

Alicja Kaczynska gave several lectures for the Physics Bridging Course as well as providing several tutorials and demonstrations. Alicja also lead some second year physics comp labs for the Bachelor of Science.

Dr Owen Dillon lectured on CT imaging to Masters of Medical Physics students for the course "Medical Imaging Physics"

Dr Phillip Janowicz lectured in Physics PHYS5006 - Image Quality as well as taking part in marking and designing and marking the exams.

Dr Tess Reynolds and Dr David Waddington lectured for Medical Radiation Technology 3123, Radiography Work Integrated Learning 4.

General Public Outreach

Dr Mark Gardner mentored and presented to science extension year 12 students on their Science Extension networking day at the University of Sydney.

As part of National Science Week, Dr Hilary Byrne took part in 'Meet a Scientist' at Centennial Park. This was an open event for the public that had several hundred or more attend. Hilary spent the day showing people of all ages how we use science and technology to look inside the human body.

Pictured: Dr Tess Reynolds gives Summer Students a tour of the Hybrid Theatre.

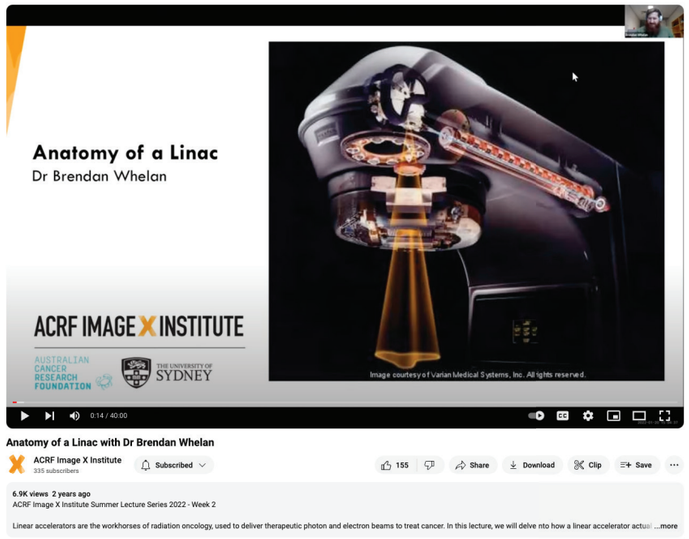
Social Media

With the reach and effectiveness of X (Twitter) dwindling, in 2023 we focussed on other platforms that could engage our wider community more reliably. Most impressively, our Youtube views went up over 10 times their 2022 numbers thanks to the addition of long-form lecture videos, and our LinkedIn presence increased six-fold. Website views continued to rise steadily as well.

Online Reach in Numbers

	Facebook views	X (twitter) views	YouTube views	E-News subscribers	LinkedIn visitors	Website visitors
2023	**600**	**34,716**	**9,100**	**379**	**3,011**	**4,933**
2022	1,295	67,247	800	335	598	3,926

Top Video of 2023



Comments left for our our top viewed video in 2023, 'Anatomy of a Linac with Dr Brendan Whelan':

"Thank you very much for this presentation. What is most impressive is your physics montage where you succeeded to explain things without writing a single equation!"

"A fascinating topic, and we all owe our thanks to physicists like Brendan without whom cancer would still be death sentence."

Selected Tweets of 2023

2023 Staff Photos

Image X Staff and students enjoy some gelato to celebrate the team's successful abstract submissions to the EPSM conference.

L-R: Youssef Ben Bouchta, Hunor Kertesz, James Grover, Owen Dillon, Jonathan Hindmarsh, Paul Keall, Tess Reynolds, Thomas Boele, Julia Johnson, Emily Hewson, Keying Guo, Hilary Byrne, Chandrima Sengupta, and Ann Yan.

Image X Staff and students celebrate the end of a great year by 'Bowling with sub-mm accuracy' (and optional 70's dress up theme).

Squatting L-R: Youssef Ben Bouchta, Chen Cheng, Ann Yan, Alicja Kaczynska, Vicky Chin, Paul Keall, Tess Reynolds, David Waddington, Helen Ball, Julia Johnson, Hilary Byrne. **Standing L-R**: Freeman Jin, Yifan Li, Emily Hewson, Hunor Ketesz, Shona Silvester, Adam Mylonas, Owen Dillon, Jonathan Hindmarsh, Phillip Janowicz, Sam Liang.

Personnel

Academic Staff

Professor Paul Keall, Director, NHMRC Leadership Fellow

D Tess Reynolds, Deputy Director, Cancer Institute NSW and Robinson Fellow

Dr Youssef Ben Bouchta, Research Associate

Dr Thomas Boele, Research Associate

Dr Caterina Brighi, Research Fellow

Dr Vicky Chin, Research Associate

Dr Owen Dillon, Research Fellow

Dr Mark Gardner, Research Fellow

Dr Emily Hewson, Cancer Institute NSW Early Career Fellow

Dr Nicholas Hindley, Research Associate

Dr Phillip Janowicz, Research Associate

Yifan Li, Research Associate

Jeremy Lim, Research Associate

Dr Paul Liu, Cancer Institute NSW Early Career Fellow

Dr Elshin Mathias, Research Associate

Dr Lars Mejnertsen, Research Associate

Dr Chandrima Sengupta, Research Associate

Dr David Waddington, NHMRC Emerging Leadership Fellow

Dr Brendan Whelan, Senior Research Fellow

Ann Yan, Research Associate

Professional Staff

Dr Helen Ball, Operations Manager

Indrajit Ghosh, Software Engineer

Jonathan Hindmarsh, Clinical Medical Physicist

Freeman Jin, Software Engineer

Julia Johnson, Design & Communications Officer

Alicja Kaczynska, Research Assistant

Sam Liang, Software Engineer

Natalie Plant, Clinical Trials Lead

Shona Silvester, Clinical Trials Lead

Students

Chen Cheng, Doctor of Philosophy

James Grover, Doctor of Philosophy

Jonathan Hindmarsh, Doctor of Philosophy

Benjamin Lau, Doctor of Philosophy

Adam Mylonas, Doctor of Philosophy

Dr Yuvnik Trada, Doctor of Philosophy

Alicja Kaczynska, Masters of Medical Physics

MD, Bachelor of Biomedical Engineering or Bachelor of Diagnostic Radiography Honours

Nabeeha Chowdhury, Maya Cohen, Wai Haang Leung, Laeticia Pajanacci, Mohommed Fathi Syed, Daniel Wang, Cooper Wray

Visitors

A/Prof Magdalena Bazalova-Carter, Victoria University, Canada

Keying Guo, University of Cambridge, United Kingdom

Georgia Stevens, University of Newcastle, United Kingdom

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

Professor Paul Keall, Image X Institute Director

Dr Helen Ball, Image X Institute Operations Manager

Ishan Pratap Kakkar, Finance Manager, Sydney School of Health Sciences

Mark Kay, Director Post Award, Research Portfolio

Dr Tess Reynolds, Image X Institute Deputy Director

Dr David Waddington, Image X Institute Early Career Fellow

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

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, Lars Mejnertsen, Hilary Byrne, David Waddington and Adam Mylonas.

Publications

The following peer-reviewed articles were published or accepted for publication in 2023.

Ahmed AM, Gargett M, Madden L, Mylonas A, Chrystall D, Brown R, Briggs A, Nguyen DT, Keall P, Kneebone A, Hruby G and Booth J (2023). "Evaluation of deep learning based implanted fiducial markers tracking in pancreatic cancer patients." Biomed Phys Eng Express 9(3). DOI: 10.1088/2057-1976/acb550.

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Brighi C, Puttick S, Woods A, Keall P, Tooney PA, Waddington DEJ, Sproule V, Rose S and Fay M (2023). "Comparison between [(68)Ga]Ga-PSMA-617 and [(18)F]FET PET as Imaging Biomarkers in Adult Recurrent Glioblastoma." Int J Mol Sci 24(22). DOI: 10.3390/ijms242216208.

Brighi C, Waddington D, Keall P, Booth J, O'Brien K, Silvester S, Parkinson J, Mueller M, Yim J, Bailey D, Back M and Drummond J (2023). "The MANGO study: A prospective investigation of oxygen enhanced and blood-oxygen level dependent MRI as imaging biomarkers of hypoxia in glioblastoma." Frontier Oncol 13. DOI: 10.3389/fonc.2023.1306164.

Byrne HL, Steiner E, Booth J, Lamoury G, Morgia M, Richardson K, Ambrose L, Makhija K, Stanton C, Zwan B, Bromley R, Atyeo J, Silvester S, Plant N and Keall P (2023). "BRAVEHeart: a randomised trial comparing the accuracy of Breathe Well and RPM for deep inspiration breath hold breast cancer radiotherapy." Trials 24(1): 132. DOI: 10.1186/s13063-023-07072-y.

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Dillon O, Reynolds T and O'Brien RT (2023). "X-ray source arrays for volumetric imaging during radiotherapy treatment." Sci Rep 13(1): 9776. DOI: 10.1038/s41598-023-36708-x.

Gardner M, Bouchta YB, Mylonas A, Mueller M, Cheng C, Chlap P, Finnegan R, Sykes J, Keall PJ and Nguyen DT (2023). "Realistic CT data augmentation for accurate deep-learning based segmentation of head and neck tumors in kV images acquired during radiation therapy." Med Phys 50(7): 4206-4219. DOI: 10.1002/mp.16388.

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Lombardo E, Liu PZY, Waddington DEJ, Grover J, Whelan B, Wong E, Reiner M, Corradini S, Belka C, Riboldi M, Kurz C, Landry G and Keall PJ (2023). "Experimental comparison of linear regression and LSTM motion prediction models for MLC-tracking on an MRI-linac." Med Phys 50(11): 7083-7092. DOI: 10.1002/mp.16770.

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Sengupta C, Nguyen DT, Moodie T, Mason D, Luo J, Causer T, Fan Liu S, Brown E, Inskip L, Hazem M, Chao M, Wang T, Lee YY, van Gysen K, Sullivan E, Cosgriff E, Ramachandran P, Poulsen P, Booth J, O'Brien R, Greer P and Keall P (2023). "The first clinical implementation of real-time 6 degree-of-freedom Image-guided radiotherapy for liver SABR patients." Radiother Oncol: 110031. DOI: 10.1016/j.radonc.2023.110031.

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Yamamoto T, Kabus S, Bal M, Keall PJ, Moran A, Wright C, Benedict SH, Holland D, Mahaffey N, Qi L and Daly ME (2023). "Four-dimensional computed tomography ventilation image-guided lung functional avoidance radiation therapy: A single-arm prospective pilot clinical trial." Int J Radiat Oncol Biol Phys 115(5): 1144-1154. DOI: 10.1016/j.ijrobp.2022.11.026.

Pictured: Jonathan Hindmarsh sets up an experiment with the 6DoF Robot

Conference Presentations

The presenting author is denoted by an asterisk.

Accuray Australasian Symposium 2023 (Brisbane, QLD)

J Hindmarsh*, S Crowe, J Booth, S Dieterich, P Keall. A 6 Degree-of-Freedom Robot for Adaptive Radiation Therapy Quality Assurance. *Oral Presentation*

American Association of Physicists in Medicine Annual Meeting 2023 (Houston, TX, USA)

H Byrne*. Invited speaker in the symposium on Functional lung sparing radiotherapy clinical trials: outcomes and future concepts. *Oral Presentation*

O Dillon*. Invited speaker in the symposium on Cone Beam CT: Interventional and Specialty Applications. *Oral Presentation*

E Hewson*. Invited speaker in the symposium on Target Tracking in Radiation Therapy. *Oral Presentation*

B Lau*, O Dillon, T Reynolds, R O'Brien. Fast Motion Compensated Reconstructions for Adaptive 4DCBCT. *Oral Presentation*

E Lombardo, P Liu, D Waddington, J Grover, E Wong, M Reiner, C Belka, C Kurz, M Riboldi*, Ge Landry, P Keall. Experimental Investigation of AI Motion Prediction for MLC-Tracking at an MRI-Linac. *Oral Presentation*

M Ramish Ashraf*, L Skinner, B Whelan, S Melemenidis, R Manjappa, A Shu-Jung Yu, M Surucu, E Elliot Graves, P Maxim, B Loo. Development of a Real-Time Beam Control System and Accurate Monte Carlo Modeling in Preparation for an Electron Flash Clinical Trial. *Oral Presentation*

T Reynolds*, O Dillon, Y Ma, R O'Brien, J W Stayman, G Gang. Reducing moving metal artefacts during interventional thoracic cone-beam CT: motion compensated non-circular orbits. *Oral Presentation*

M Bazalova-Carter, T Reynolds*, E Mathias, J Laidlaw, N Earl, N Shavdia, R Davis, S Mayer, D Karaman, D Richtsmeier, P-A Rodesch, P Keall. First Clinical Verification of Low-Cost 4D-CT Anthropomorphic Breathing Thorax Phantom with Deformable Lungs. *Oral (SNAP) Presentation*

N Hindley*, C-C Shieh, P Keall. A Patient-Specific Deep Learning Framework for 3D Thoracic Motion Estimation during Lung Cancer Radiotherapy. *Oral (SNAP) Presentation*

X Nie*, B Whelan. A SCAMP Project: Identifying Sources of Research Funding in Medical Physics. *Oral (SNAP) Presentation*

E Mathias*, T Reynolds, J Hindmarsh, J Barber, J Sykes, P Keall, R O'Brien. The Future of 4DCT: An Evaluation of Advanced Methods versus Standard of Care. *Blue Ribbon ePoster Presentation*

H Byrne*, N Eikelis, J Dusting, A Fouras, P Keall, P Pirakalathanan. Direct Comparison of CT-Ventilation Imaging Methods. *ePoster Presentation*

O Di*llon*, T Reyn*olds, R O'Brien. Subsecond CBCT with Field Emission Sources and Modern Linac Gantries. *ePoster Presentation*

M Gardner*, O Dillon, H Byrne, P Keall. Rapid 4D Cone-Beam CT for New Generation Linacs. *ePoster Presentation*

M Gardner*, A Mylonas, M Mueller, Y Ben Bouchta, J Sykes, P Sundaresan, P Keall, D T Nguyen. Towards Removing the Mask: A Real-Time Method for Accurate Segmentation of Head and Neck Tumors in kV Images. *ePoster Presentation*

American Thoracic Society 2023 International Conference (Washington, DC, USA)

N Eikelis*, P Pirakalathanan, H Byrne, J Kirkness, J Dusting, E Castillo, P Keall, A Fouras. Performance of CT:V Quantitative Ventilation Imaging Against PET Ventilation Imaging. *Poster Presentation*

Asian Forum for Accelerators and Detectors 2023 (Melbourne, VIC)

B Whelan*. Bayesian optimization to design a novel x-ray shaping device. *Invited Talk*

Australian Institute of Physics 2023 annual meeting (Canberra, ACT)

N Hindley*. How Einstein's general relativity enables motion adaptive radiotherapy. *Invited Talk*

Australian Society for Medical Research (ASMR) National Scientific Conference (Melbourne, VIC)

M Gardner*, A Mylonas, Y Ben Bouchta, J Sykes, P Sundaresan, P Keall, D T Nguyen. Using deep learning to track tumours during head and neck radiation therapy: Can we improve the patient experience by removing the immobilisation mask. *Oral Presentation*

Cancer Research Network AI in Cancer Care symposium (Sydney, NSW)

D Waddington*. How we have deployed AI-powered imaging tools to clinical systems and enabled radiotherapy treatments with improved accuracy. *Keynote Speaker*

9th Charles Perkins Centre EMCR Symposium (Sydney, NSW)

P Janowicz*, C Brighi, D Waddington. Towards detecting infiltrative brain cancer using novel superparamagnetic iron oxide nanoparticles and magnetic resonance imaging. *Oral Presentation*

European Association of Neuro-Oncology Meeting 2023 (Rotterdam, Netherlands)

C Brighi*, S Puttick, A Woods, P Tooney, D Waddington, P Keall, V Sproule, M Fay. Evaluation of 68Ga-PSMA-617 PET as a diagnostic agent in recurrent glioblastoma patients: results of the Genesis GBM 001 phase I/II study. *Poster Presentation*

C Brighi*, B Moffat, A Whitehead, O Cook, A Moore, A Grose, A Rossi, R Dykyj, E Lau, G Fitt, H Gan, A Scott, E-S Koh. Preliminary findings from the MRI quality assurance programme for the prospective multi-site Australian FIG ([FET-PET in Glioblastoma) TROG 18.06 study. *Poster Presentation*

European Association of Nuclear Medicine 2023 Annual Congress (Vienna, Austria)

M. Lyngby Lassen*, H. Kertész, I. Rausch, A. Kjaer, V. Panin, D. Bharkhada, R. deKemp, T. Beyer, and P. Hasbak, Positron Range Correction for 82Rb myocardial PET: Validation in a healthy cohort. *Oral e-poster presentation*

European Society of Radiation Oncology 2023 meeting (Vienna, Austria)

Y Ben Bouchta*, M Gardner, P Keall. A novel low-cost open-source surface-guided radiation therapy system for head and neck radiotherapy. *Oral Presentation*

C Sengupta*, D Nguyen, T Moodie, S Skouboe, T Rakvilde, P Poulsen, R O'Brien, J Booth, T Wang, YY Lee, P Keall. Dosimetric impact of tumour rotation in real-time adaptive liver stereotactic body radiation therapy. *Poster Presentation*

Engineering and Physical Sciences in Medicine conference 2023 (Christchurch, New Zealand)

D Chrystall*, C Sengupta, E Hewson, A Mylonas, Y Li, T Wang, D Lee, P Poulsen, T Moodie, N Hardcastle, C Jones, SF Liu, J Chu, DT Nguyen, P Keall, J Booth. Beam's-eye-view tracking for liver SBRT enabled by deep-learning: A multi-institutional analysis. *Oral Presentation*

D Chrystall*, M Stewart, M Mueller, N Hindley, J Hindmarsh, D Jayamanne, P Keall, J Booth. Markerless tumour tracking for lung SBRT: First results of the VALKIM clinical trial. *Oral Presentation*

E Hewson*, O Dillon, P Poulsen, J Booth, P Keall. Monitoring intrafraction pelvic motion in six-degrees-of-freedom for multi-target tracking on a standard linac. *Oral Presentation*

J Hindmarsh*, S Crowe, J Booth, S Dieterich, P Keall. A 6 Degree-of-Freedom Robot for Adaptive Radiation Therapy Quality Assurance. *Oral Presentation*

J Hindmarsh*, S Crowe, J Booth, S Dieterich, P Keall. Application of System Theoretic Process Analysis to MLC tracking in Radiation Oncology. *Oral Presentation*

A Kaczynska*, DT Nguyen, T Moodie, E Hewson, Y Ben Bouchta, T. Wang, P Keall, C Sengupta. Developing a real-time 6DoF target tracking system for liver SABR using sparse kilovoltage x-ray imaging and a continuous external signal. *Oral Presentation*

Y Li, P Keall, DT Nguyen, R O'Brien, E Hewson*, H Ball, V Gebski, J Booth, P Greer, T Moodie, N Hardcastle, P Poulsen, S Arumugam, J Martin, A Kneebone, S Siva, K-H Tai, S Turner, T Eade, A Hayden, G Hruby, R Bromley, P Hunter, L Wilton, J Kipritidis, C Sengupta. An open-source initiative for the TROG 15.01 Stereotactic Prostate Adaptive Radiotherapy utilizing Kilovoltage Intrafraction Monitoring (SPARK) trial results. *Oral Presentation*

J Lim, H Kertesz*, H Byrne, J Kipritidis, N Eikelis, S Roderick, M Crispin, D Bailey, J Booth, P Keall, D Jayamanne, R O'Brien. VENTURE: Ventilation using radiographic examination - an upcoming cross-disciplinary clinical trial. *Oral Presentation*

J Lim*, H Byrne, J Kipritidis, J Booth, P Keall. Validating a Patient-Specific Quality Metric for CT Ventilation Images. *Oral Presentation*

A Mylonas*, P Ramachandran, V Seshadri, C-C Shieh, P Keall, DT Nguyen. Contour Alignment Tool: An open-source application for visualising and aligning 3D contours in 2D x-ray projections. *Oral Presentation*

IEEE Engineering in Medicine and Biology Society (EMBS) International Annual Conference 2023 (Sydney, NSW)

M Gardner, Y Ben Bouchta*, J Sykes, P Keall. A kinematics-based method for creating deformed patient-derived head and neck CT scans. *Oral Presentation*

International Conference of Medical Physics 2023 (Mumbai, India)

C Sengupta*, DT Nguyen, T Moodie, A Kaczynska, D Mason, T Causer, S Liu, T Wang, YY Lee, K Gysen, R O' Brien, P Keall. Accuracy of external tumour motion monitoring in liver SABR: Results from the TROG 17.03 LARK trial. *Oral Presentation*

International Society for Magnetic Resonance in Medicine & European Society for Magnetic Resonance in Medicine and Biology 2023 Annual Meeting (Toronto, Canada)

D Waddington*, E Shimron, S Shan, N Koonjoo, S Shen, M Rosen. Accelerated Imaging at Ultralow Magnetic Fields: A comparative study of traditional and neural-network-based reconstruction approaches. *Oral presentation*

D. Waddington*. Invited speaker in the education symposium on Nuclei & Magnetization: From Classical Physics to Quantum Mechanics.

J Grover*, P Liu, B Dong, S Shan, B Whelan, P Keall, D Waddington. Super-resolution imaging on an MRI-linac to improve real-time MRI used in MRI guided radiation therapy. *Poster Presentation*

S Shan*, Y Gao, M Ma, H Gan, DEJ Waddington, B Whelan, P ZY Liu, C Liu, M Gao, F Liu. B0 Inhomogeneity Distortion Corrected Image Reconstruction with Deep Learning on An Open Bore MRI-Linac. *Poster Presentation.*

International Society for Magnetic Resonance in Medicine ANZ 2023 meeting (Brisbane, QLD)

J Grover*, S Shan, P Keall, D Waddington. Towards real-time high spatiotemporal resolution multi-slice MRI for real-time adaptive MRI-guided radiation therapy using deep learning. *Datablitz (short talk and poster) Presentation.*

P Janowicz*, C Brighi, D Waddington. Towards detecting infiltrative brain tumours using novel superparamagnetic iron oxide nanoparticles and MRI. *Datablitz Presentation.*

MedPhys2023 (Sydney, NSW)

C Cheng*, M Gardner, O Dillon, Y Ben Bouchta, P Sundaresan, P Keall. Head and neck 3D motion estimation with a single x-ray imager using a Kalman filter framework. *Oral Presentation*

A Kaczynska*, DT Nguyen, T Moodie, E Hewson, Y Ben Bouchta, T. Wang, P Keall, C Sengupta. Developing a real-time 6DoF target tracking system for liver SABR using sparse kilovoltage x-ray imaging and a continuous external signal. *Oral Presentation*

Alicja Kaczynska received the Best MSc/undergraduate student presentation at the MedPhys 23 meeting.

9th MR in RT meeting (Los Angeles, CA, USA)

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*

B Oborn, P Keall* A comprehensive quantitation of the dosimetric impact of electron streaming for MRI-guided proton therapy. *Oral Presentation*

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

2023 Society of Brain Mapping and Therapeutics meeting (Los Angeles, CA, USA)

C Brighi*, Invited speaker in the session on Neuro-Oncology: New Radiation Technologies

SPIE Medical Imaging 2023 (San Diego, CA, USA)

T Reynolds*, Ma Y, Wang T, Mei K, Noël PB, Gang GJ, Stayman JW. Revealing pelvis structures in the presence of metal hip prosthesis via non-circular CBCT orbits. *Oral Presentation*

Symposium for Noninvasive Radioablation 2023 (St Louis, Missouri)

P Keall*. Imaging and targeting the beating heart in a breathing patient. *Invited talk*

Invited Talks

Dr Mark Gardner, ***Remove The Mask: Improving the radiation therapy experience for head and neck cancer patients***. Medical Device Research Institute, Flinders University

Dr Mark Gardner, ***Remove The Mask: Improving the radiation therapy experience for head and neck cancer patients.*** Stanford University

Dr Nicholas Hindley, ***How Einstein's general relativity enables motion adaptive radiotherapy.*** British Columbia Cancer Agency, Canada

Jonathan Hindmarsh, ***System Theoretic Process Analysis and Radixact Synchrony.*** British Columbia Cancer Agency, Canada

Jonathan Hindmarsh, ***System Theoretic Process Analysis and Radixact Synchrony.*** Tom Baker Cancer Centre, Canada

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

Professor Paul Keall, ***Building and clinically translating new technology in radiation therapy***. University of Malaya, Malaysia

Professor Paul Keall, ***Building and clinically translating new technology in radiation therapy.*** Washington University School of Medicine, USA

Professor Paul Keall, Dr Tess Reynolds and Dr Owen Dillon, ***Virtual clinical trials are central to bench to bedside research: The Image X Institute Experience.*** Center for Virtual Imaging Trials webinar

Dr Hunor Kertész, ***Positron Range Correction for PET Imaging. Institute of Medical Physics and Masters of Med Phys program,*** University of Sydney

Jeremy Lim, ***CT Ventilation Imaging in Radiotherapy. Radiotherapy Related Research Department,*** The Christie, United Kingdom

Jeremy Lim, ***CT Ventilation Imaging: Impact of Key Algorithm Parameters and Correlating Dose to Functional Lung with Survival.*** POLARIS, Department of Infection, Immunity & Cardiovascular Disease, The University of Sheffield, Sheffield, United Kingdom

Dr Tess Reynolds, ***Advances in Cardiac CT and CBCT imaging.*** American Association of Physicists in Medicine (AAPM) webinar.

Dr Tess Reynolds, ***Expanding the capabilities of robotic cone beam CT imaging systems.*** Department of Medical Physics, The University of Wisconsin-Madison, USA

Dr Tess Reynolds, ***Advances from the pheno down under.*** Advanced Therapies, Siemens Healthineers, Germany

Dr Tess Reynolds, ***Delivering the future of robotic Cone Beam CT imaging,*** British Columbia Cancer Center, Victoria, Canada

Dr Tess Reynolds, ***Delivering the future of robotic CBCT imaging,*** IMPACT Research Seminar Series, University of Sydney

Dr Tess Reynolds, E***xpanding the capabilities of robotic CBCT imaging systems.*** Massachusetts General Hospital, USA.

Dr Caterina Brighi, ***Clinical Benefits of Multiparametric MRI-Guided Dose Painting Radiotherapy in Glioblastoma,*** 20th Annual World Congress of Society for Brain Mapping and Therapeutics, Los Angeles, California, USA

Dr Chandrima Sengupta, ***Patient motion tracking on standard linear accelerators.*** GenesisCare, Sydney

Dr Chandrima Sengupta, ***Clinical translation of tumour tracking technologies.*** Aarhus University, Denmark.

Dr Chandrima Sengupta, ***Motion management in radiotherapy.*** Department of Physics, University of Calcutta, India

Dr Chandrima Sengupta, ***Motion Monitoring on standard linear accelerators.*** Indian Institute of Technology, India

Dr Chandrima Sengupta, ***Motion Monitoring on standard linear accelerators***. Apollo Hospital, India

Dr David Waddington. ***Harnessing the power of AI for improved MRI-guided cancer radiotherapy.*** Sydney Precision Data Centre, University of Sydney

Dr David Waddington, ***Real-time deployment of open-source tools for image reconstruction.*** MRI Together (global online event)

Other presentations

Dr Caterina Brighi was a panellist for the Women in Imaging Event 2023, organised by the Centre for Advanced Imaging at the University of Queensland. The event's theme was Cracking the code for a diverse, equitable and inclusive workplace #EmbraceEquity.

Dr Tess Reynolds was a panellist for the USYD Researcher Development Unit workshop on Prizes – Why they matter and how to apply (and win).

Professor Paul Keall argued for the negative in the debate In five years from now, SABR will mostly be single-day plan-and-treat at the SABR Symposium in Melbourne.

Pictured: Observations from behind the Linear Accelerator.

Contact

Image X Institute
Level 2, 1 Central Avenue
Eveleigh NSW 2015
Email: image-x.contact@sydney.edu.au

image-x.sydney.edu.au