ipem.ac.uk

Volume 33 | Issue 03 | Autumn 2023

IPEM
Institute of Physics and Engineering in Medicine

SCOPE

Surface guided radiotherapy: The 100-day journey to offering tattoo-free treatment

THE BIG DEBATE

We ask four experts about the supply of radionuclides

MEMBER PROFILE

Working as a Clinical Lecturer and Senior Radiotherapy Physicist

PROSTHETIC LINERS

Additive manufacturing to tackle comfort in lower limb prosthetics

RESEARCH

Why it is so important to publish negative research results

CHAIR OF IPEM SCOPE EDITORIAL ADVISORY BOARD

Reflecting and reviewing

Usman Lula outlines the content in the latest issue of *Scope*, including revamping clinical services and the implementation of new software.

Welcome to the Autumn issue of *Scope* 2023. As I write this editorial (from Almaty, Kazakhstan), I have been pondering why it took me twice as long to write this editorial as when I'm not on holiday. Reasons (or excuses) could be the hot climate, social distractions, or tiredness from the previous day of climbing on the picturesque Shymbulak mountain. More likely, it could be due to an increase in time spent reflecting.

Reflecting on and reviewing clinical services can provide an impetus for significant change. It can have positive impacts on service users, colleagues, practice and general health and wellbeing. It allows identifying, processing, learning and appreciating positive, negative and challenging experiences. Changes to improve services for the patient are guided by key principles based on core values that underpin the NHS constitution. Earlier this year, Andrew Simpson showcased the development of a new piece of software for an overnight oximetry sleep service, which provided the rationale for change, software design and expected roll out. The new piece of software has since been implemented and is in clinical use. In this issue, Andrew reflects on the successes of the clinical measurement team, including feedback, challenges and related future work.

When we think about career breaks, all sorts of reasons pop up in our minds, including improving health, rediscovery, learning and developing new skills, venturing into new territories and freedom. This of course may or may not have an impact (depending on how we go about it, or how much of a leeway we have) on our finances, feeling we have been left behind those who continue to work, difficulties in finding a new role and just how do you explain this on a CV? Well, rest assured, for those thinking about taking this step now or in the future, we have a feature that will guide you along the way. Matthew Gardner provides deep insights into his own journey of a career break, how he started, his plan, learning and eventually how he felt he became a better scientist.

Reflecting on and reviewing clinical services can provide an impetus for significant change

Finally, we have our regular member profile. In this issue, Georgios Ntentas gives us an insight into his "clinical-academic" role, what he likes most about his job, the biggest challenges in his sector, what he would like to change in the profession, the accomplishments he is most proud of and much, much more.

I hope you enjoy the issue and the rest of your summer.

Usman Lula

Usman Lula
Chair of IPEM Scope EAB

RESEARCH

Knowing what not to do

For a long while, I have felt that journal publications are biased towards pieces of research that, on the whole, were a success, or at least had positive results. This, in itself, I believe, has resulted in a skewed research landscape, with too much focus on impact factors, citations and generally publication of work that has been successful or reinforces what is already in the literature. Clara Ferreira, one of our *Scope* Editorial Advisory Board members, has been thinking about this and why there aren't enough "negative results" published in literature. After all, science is about knowing what not to do. In this issue, she focusses on publication bias, reproducibility, open-source science and the few publications that publish negative results.

IPEM
Institute of Physics and Engineering in Medicine

Scope is the quarterly magazine of the Institute of Physics and Engineering in Medicine

IPEM Fairmount House, 230 Tadcaster Road, York, YO24 1ES
T: **01904 610821** | F: **01904 612279**
office@ipem.ac.uk | **ipem.ac.uk**

Usman Lula
Chair of the IPEM Scope Editorial Advisory Board
Email: **Usman.lula@uhb.nhs.uk**

Clara Ferreira
Commissioning Editor
Email: **clarainesferreira@gmail.com**

Dr Paul Doolan
Commissioning Editor
Email: **paul.doolan@goc.com.cy**

Natasa Solomou
Commissioning Editor
Email: **natasa.solomou@nnuh.nhs.uk**

Helen Chamberlain
Commissioning Editor
Email: **hchamberlain@macmillan.org.uk**

Sean Edmunds
IPEM External Relations Manager
Email: **Sean@ipem.ac.uk**

Scope is published on behalf of the Institute of Physics and Engineering in Medicine (IPEM) by

Redactive Publishing Ltd
redactive.co.uk

redactive

Publisher: Tiffany van der Sande
tiffany.vandersande@redactive.co.uk | +44 (0)20 7324 2728

Editor: Rob Dabrowski

Senior designer: Gary Hill

Picture researcher: Akin Falope

Production: Aysha Miah-Edwards

aysha.miah@redactive.co.uk | +44 (0)20 7880 6241

Advertising sales:

scope@redactive.co.uk | +44 (0)20 7880 7556

 ISSN 0964-9565

Memcom 2021: Highly Commended
Best Magazine Launch or Relaunch
Memcom Membership Excellence Awards 2021

FEEDBACK
Discuss, debate, share.
mycommunity.ipem.ac.uk/login

WEBSITE
News, events, support.
ipem.ac.uk

ARCHIVES
Back issues of *Scope* online.
ipem.ac.uk/scope

CO

THE BIG DEBATE

14/ RADIONUCLIDES
We ask four experts six questions about radionuclides. Topics that are touched on include securing a domestic supply of radionuclides, the cost of diagnostic and therapeutic procedures due to their scarcity and whether there are any successful approaches internationally that we can learn from.

> There is an opportunity for changes to allow the MHRA to assess new radiopharmaceuticals more rapidly, bringing cost savings for those that develop them

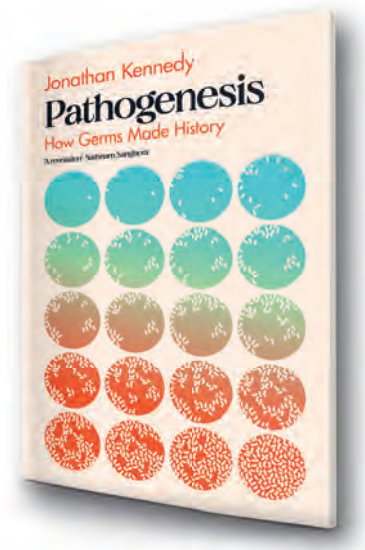
Dr Matthew Walker
Senior Clinical Scientist **page 14**

Volume 33 | Issue 03 | Autumn 2023

NTENTS

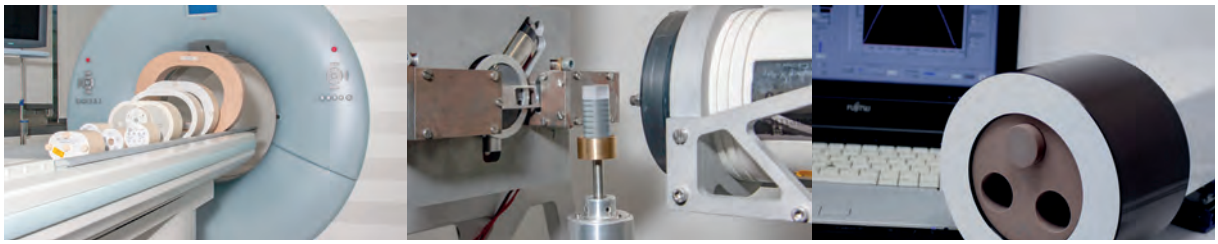
GENERAL

ENDNOTES



PTW THE DOSIMETRY COMPANY

QRM Phantoms

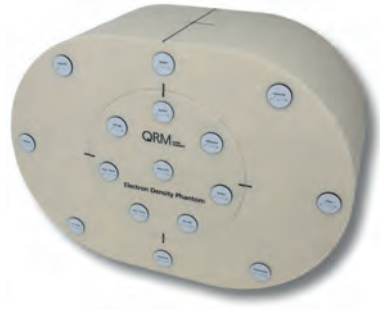


A comprehensive range of phantoms for all situations

Phantoms are specially designed objects that are scanned or imaged to analyse the accuracy and efficiency of a wide range of processes in medical imaging. PTW have teamed-up with QRM to provide a huge range of phantoms for all your needs. Here are a few examples:

The Spectral CT Phantom

The Spectral CT Phantom is used to test different types of CT modalities with dual-energy, multi-energy or photon-counting setups and is available in 4 (QRM-10139) and 8 (QRM-10147) hole versions. The 20 mm inserts are available in a wide range of tissue types and Iodine/ CaHA concentrations



The Comprehensive Electron Density Phantom

The Comprehensive Electron Density Phantom (QRM-90114) is used to calibrate the HU/electron density conversion for CT datasets used for radiotherapy treatment planning. 16 rods mimic a variety of tissue densities and conform to ICRU recommendations. Suitable for photon, electron and proton planning processes

The Cone-Beam Phantom

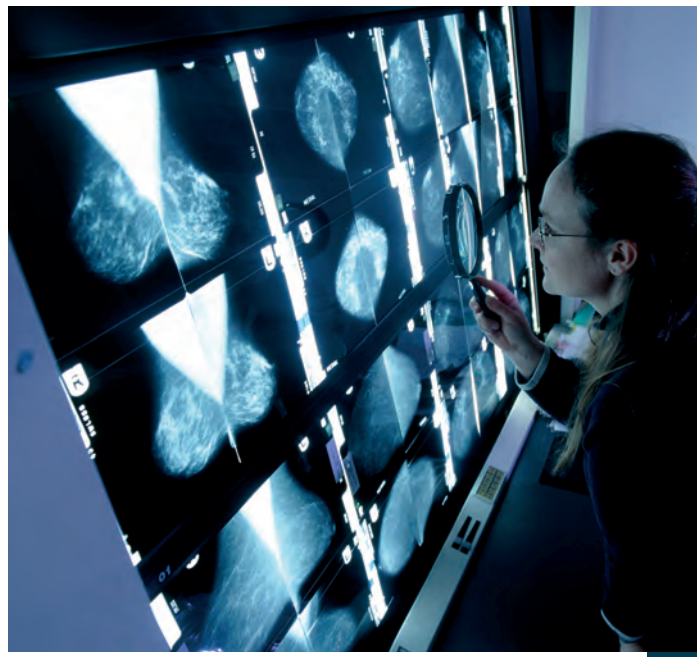
The Cone-Beam Phantom, Expert (QRM-10103), for testing the imaging performance in diagnostic and cone-beam CT, has low contrast sections providing contrasts between 3 and 200 HUs. Spatial resolution line patterns from 4 to 30 lp/cm and an additional edge insert determine the system MTF in different orientations.

In addition to our standard range, we can design bespoke phantoms for medical, industrial and research purposes. For more information on our range of QRM phantoms and to see what PTW can do for you visit https://www.qrm.de/en/, or contact us at PTW-UK: sales2.uk@ptwdosimetry.com

FEEDBACK
Discuss, debate, share
my.community.ipem.ac.uk

WEBSITE
News, events, support
ipem.ac.uk

UPFRONT



MEDICAL IMAGING

Earlier detection of breast cancer

A team of researchers has succeeded in refining mammography – the X-ray imaging technique used to detect tumours in their early stages – to produce more reliable results and be less unpleasant for the patient.

The researchers have extended conventional computed tomography (CT) so that the image resolution is significantly higher for the same radiation dose.

This means that small calcium deposits, known as microcalcifications, which can be a sign of breast tumours, could be detected earlier than before. This would improve the chances of survival for the women concerned.

The team believes that this new technique, which is based on X-ray phase contrast, could be swiftly put to use in clinical settings.

The team includes scientists and researchers from the Paul Scherrer Institute (PSI) and ETH Zurich, together with the Baden Cantonal Hospital (KSB) and the University Hospital Zurich (USZ).

"We need a little bit more time," said Marco Stampanoni, head of the research group at PSI and a Professor of X-ray Imaging at ETH Zurich. "But with our work we have taken an important step on the way."

In 2020, breast cancer was the most commonly diagnosed form of cancer worldwide, with over two million cases. It accounts for 24.5% of cancer cases in women, and 15.5% of cancer-related deaths.

Control studies have found that only 46% of suspected cases detected during mammography screening are confirmed as cancer.

Studies also show that mammography misses an estimated 22% of genuine cases.

The research team used grating interferometry (GI) and the X-rays not only pass through the object being examined, but also through three gratings with a line spacing of a few micrometres, which make additional information visible compared with conventional X-rays.

The X-rays can come from a conventional X-ray source, whereby the radiation dose is roughly equivalent to that in conventional CT scans of the breast.

"We are aiming to reduce the dose by a factor of two to three while maintaining the same resolution or increasing the resolution by 18–45% – in each case compared with conventional X-rays," explains physicist Michał Rawlik, lead author of the paper and a member of the research team supporting Stampanoni.

bit.ly/3OjDgdE

IMAGES: SCIENCE PHOTO LIBRARY/SHUTTERSTOCK/ISTOCK

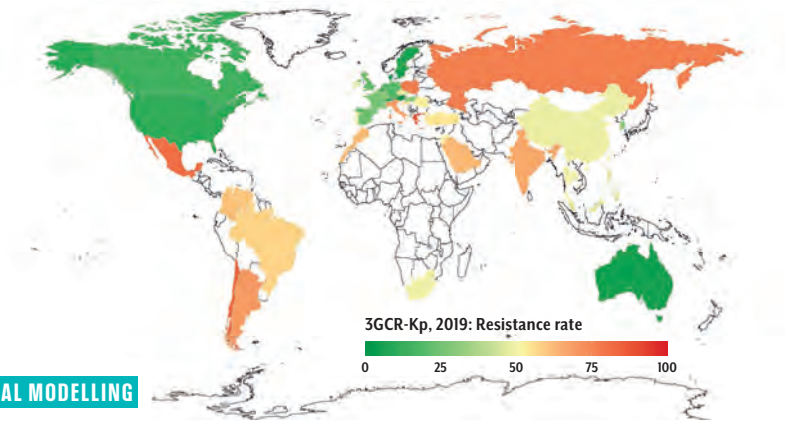
FAST FACTS

1
Breast cancer is the most diagnosed form of cancer worldwide.

2m
There are a total of more than two million cases annually.

24.5%
It accounts for 24.5% of cancer cases in women.

15.5%
It accounts for 15.5% of cancer-related deaths in women.



STATISTICAL MODELLING

A global overview of antibiotic resistance

To understand the main determinants behind worldwide antibiotic resistance dynamics, a team of French scientists developed a statistical model based on a large-scale spatial-temporal analysis.

Using the ATLAS antimicrobial resistance surveillance database, the model revealed significant differences in trends and associated factors depending on bacterial species and resistance to certain antibiotics.

Countries with high quality health systems were associated with low levels of antibiotic resistance among all the gram-negative bacteria investigated, while high temperatures were associated with high levels of antibiotic resistance in Enterobacteriaceae. Surprisingly, national antibiotic consumption levels were not correlated with resistance for the majority of the bacteria tested.

The results suggest that antibiotic resistance control measures need to be adapted to the local context and to targeted bacteria-antibiotic combinations.

First author of the study Eve Rahbé said: "Research teams study how antibiotic resistance emerges in a bacterium in a Petri dish or in an individual, but we are currently lacking a population-level, global overview that can be used to investigate links between resistance and specific factors."

bit.ly/46XXdht

BIOSENSOR

FLUORESCENT NANOTUBES TO DETECT BACTERIA AND VIRUSES

An interdisciplinary European research team has developed a new approach to construct modular optical sensors that are capable of detecting viruses and bacteria.

The researchers used fluorescent carbon nanotubes with a novel type of DNA anchors that act as molecular handles. The anchor structures can be used to conjugate biological recognition units, such as antibodies aptamers, to the nanotubes.

The recognition unit can subsequently interact with bacterial or viral molecules to the nanotubes. These interactions effect the fluorescence of the nanotubes and increase or decrease their brightness.

The team used tubular carbon nanosensors with a diameter of less than one nanometre. They linked DNA bases to the nanotube to create a defect in the crystal structure of the nanotube. As a result, the fluorescence of the nanotubes changed at the quantum level.

They group showcased the concept using the SARS CoV-2 spike protein.

bit.ly/471bkm4

NEWS IN BRIEF

Digital heart replica

Scientists have developed a "genotype-specific digital-twin" strategy (Geno-DT) to create a virtual replica of a patient's heart, providing crucial insights into cardiac health for the diagnosis and treatment of arrhythmogenic right ventricular cardiomyopathy (ARVC). The research is described by the editors as an important study in the field of personalised medicine.

bit.ly/46Qs5AB

Innovative wearable sensor

Wearable sensors make it possible to continuously monitor biomarkers, such as sweat lactate. However, one common problem in such devices is that their microfluidic channels tend to trap air bubbles present in the sweat. If these bubbles cover the sensor's electrodes, the measurements get interrupted. A research team from Tokyo University of Science has come up with a novel microfluidic sweat lactate sensor whose measurements remain unaffected by the air bubbles thanks to a larger-than-usual sweat reservoir.

bit.ly/3Q3cSGa

Robotic liver transplant

A surgical team from Washington University School of Medicine in St Louis recently performed the first robotic liver transplant in the US. The successful transplant, accomplished in May at Barnes-Jewish Hospital, extends to liver transplants the advantages of minimally invasive robotic surgery – a smaller incision resulting in less pain and faster recoveries, plus the precision needed to perform one of the most challenging abdominal procedures.

bit.ly/3O1lI7V

SCAFFOLD PROTEINS

"Copper to create clearer MRI images"

Scientists have found a new use for copper in magnetic resonance imaging (MRI) contrast agent design, which they claim could help to create better images.

The team discovered a novel copper protein binding site, which does not occur in nature, that has the potential for use in MRI contrast agents used to improve the visibility of internal body structures in scans.

Researchers from the Universities of Birmingham and St Andrews, as well as Diamond Light Source, published their findings after creating a highly elusive abiological copper site bound to oxygen donor atoms within a protein scaffold.

The experts found that the new structure displayed highly effective levels of relaxivity – the ability of a contrast agent to influence the relaxation times of protons, which helps create clearer and more informative images during an MRI scan.

Co-author Dr Anna Peacock, Reader in Bioinorganic Chemistry at the University of Birmingham, said: "We prepared a new-to-biology copper-binding site that shows real potential for use in contrast agents and challenges existing dogma that copper is unsuitable for use in MRI.

"Despite copper largely being disregarded for use in MRI contrast agents, our binding site was shown to display extremely promising contrast agent capabilities, with relaxivities equal and superior to the Gd(III) agents used routinely in clinical MRI. Our discovery showcases a powerful approach for accessing new tools or agents for imaging applications."

bit.ly/3q0MimD

UP CLOSE

DNA ORIGAMI

WHAT IS DNA ORIGAMI?

DNA origami involves the folding of DNA to create 2D and 3D objects at the nanoscale.

HOW DOES IT WORK?

Long strands of DNA are folded into a complex scaffold of staple strands (200–300 nucleotides). This leads to formation of a complex structure that has characteristic features because of their nanoscale dimensions.

WHAT ARE THE LATEST DEVELOPMENTS?

The increasing interest in DNA origami has led to the development of rate-zonal centrifugation (RZC) as a scalable, high yield, and contamination-free method for purifying DNA origami nanostructures.

HOW DOES RZC PURIFICATION WORK?

It uses a linear density gradient of viscous media, such as glycerol or sucrose, to separate molecules according to their mass and shape.

IS THERE ANY NEW RESEARCH?

Yes, a team of US researchers created a LEGO gradient mixer to purify 3 DNA origami shape. The LEGO gradient mixer was able to purify folded DNA origami nanostructures from excess staple strands, regardless of their aspect ratios. Moreover, the gradient was able to separate DNA origami dimers from DNA origami monomers.

WHERE CAN I READ MORE?

bit.ly/470e4QH

PANCREATIC TUMOURS

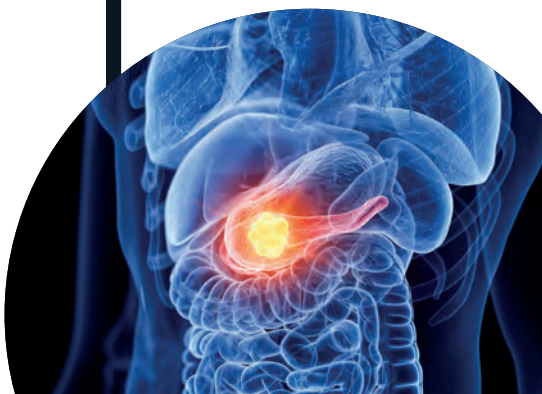
ULTRASOUND ACTIVATION IN IMMUNOTHERAPY

A team of researchers has developed a sonodynamic cancer immunotherapy based on semiconducting polymer nanoparticles that are joined to immunomodulators and activated by ultrasound.

Scientists from Nanyang Technological University in Singapore and Donghua University in China have used ultrasound for the first time for an effective sonodynamic treatment of orthotopic pancreatic cancer in a mouse model.

The team prepared nanoparticles from a specific semiconducting polymer that responds to ultrasound. Activated by ultrasound waves, it transferred its energy to molecular oxygen, from which singlet oxygen was formed in the cells to induce immunogenic cell death and kill cancer cells.

bit.ly/3DkPvQP



IMAGES: SCIENCE PHOTO LIBRARY/SHUTTERSTOCK

IPEM COURSE

Latest cohort successfully completes CTTS

The latest cohort on IPEM's Clinical Technologist Training Scheme (CTTS) have successfully passed their course.

The CTTS has earned a strong reputation in the sector, offering a robust, externally validated education and training framework for clinical technologists, and ensuring a workforce fit to practise.

Successful completion of the CTTS sees graduates awarded IPEM's Diploma in Clinical Technology and opens a route to joining the Register of Clinical Technologists (RCT).

The 17 trainees who recently completed the course and were awarded their Diploma in Clinical Technology included:

- Nathan Britten, NHS Greater Glasgow and Clyde
- Ramsay Clark, NHS Lothian
- Gregory Farooq-Smith, NHS Lothian
- Ryan Feeley, NHS Greater Glasgow and Clyde
- Arran Fernie, NHS Lothian
- Leyla Garibay Quezada, Oxford University Hospitals NHS Foundation Trust
- Jamie Hall, NHS Grampian
- Shazia Khan, NHS Greater Glasgow and Clyde
- Louise Macdonald, NHS Greater Glasgow and Clyde
- Colin Mason, NHS Highland
- Callum Scotford, NHS Lothian
- Juan Carlos Sedeno Tuya, NHS Lothian
- James Stewart, Newcastle upon Tyne Hospitals NHS Foundation Trust
- Ethan Sycamore, Maidstone and Tunbridge Wells NHS Trust
- Caitlin Wilson, Sheffield Teaching Hospitals NHS Trust

Dr Robert Farley, IPEM's President, said: "I would like to congratulate all of the trainees on successfully completing their course and they are now eligible to join the RCT. They can also upgrade to full membership of IPEM and join more than 4700 medical physicists, clinical and biomedical engineers and clinical technologists working in hospitals, academia and industry."

Applications for the next intake of the course are now welcome and the closing date to apply is 30 September.

ipem.ac.uk/learn/ipem-clinical-technologist-training-scheme

ULTRASOUND PHYSICS

"WORKFORCE IS OVERWORKED AND UNDERAPPRECIATED"

Ultrasound services are being provided by an overworked and underappreciated workforce, a new survey has found.

IPEM's Ultrasound Workforce Survey was conducted earlier this year, with some 60 NHS trusts and organisations that provide ultrasound services invited to respond.

It revealed an ultrasound physics workforce that has not grown and is under significant stress, with little capacity or resources for training.

The other main finding was a vacancy rate in ultrasound physics of 23% for clinical scientists and 14% for clinical technologists – a significantly higher figure than for other medical physics specialisms.

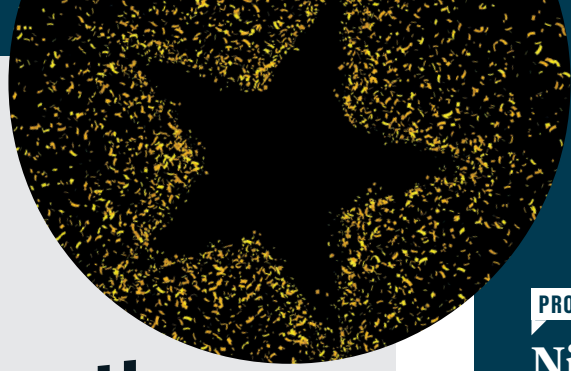
The aim of the survey was to identify the extent of the workforce gap within ultrasound physics to help IPEM's Ultrasound and Non-ionising Radiation Special Interest Group develop a new workforce model.

The workforce issue prompted almost 76% of respondents to say the current staffing provision is insufficient, raising concerns about improving the workforce provision via training due to staff capacity. Without intervention, it is feared this problem will only worsen, as 17% of the workforce are approaching retirement age.

IPEM's survey came hot on the heels of the recent statement on the current workforce shortfalls and recruitment outlook within the wider medical physics and clinical engineering community, which called for urgent action.

There was widespread disappointment that the long-anticipated NHS Long Term Workforce Plan offered little to tackle these critical workforce issues.

Sarah Matthews, of IPEM's Ultrasound and Non-ionising Radiation Special Interest



BEST PRACTICE

IPEM achieves the IiV quality mark

A national quality mark for best practice in volunteer management has been awarded to IPEM.

Investing in Volunteers (IiV) is the UK quality standard for all organisations involving volunteers.

IPEM was assessed against six quality areas and excelled in all aspects of working with its volunteers.

Sandra Adair, Interim IiV Manager on behalf of the awarding body, UK Volunteering Forum (UKVF), said: "UKVF is delighted to announce IPEM's successful achievement of this award; they have demonstrated a real commitment to volunteering, and proven that their volunteer management policies and procedures meet nationally recognised standards."

Eva McClean, IPEM's EDI and Member Networks Manager, said: "IPEM can only achieve its charitable and strategic objectives through our volunteer members and their contributions. Completing the IiV standard process and assessment has allowed us to analyse how we support and interact with our volunteers and how we can best develop and optimise our support.

"Achieving the standard required us to complete a year-long six-step process, which involved an extensive analysis of our processes and systems."

Phil Morgan, Chief Executive Officer of IPEM, added: "Achieving this standard shows how much IPEM values, recognises and supports volunteers. However, because of their pivotal role in delivering our strategy, we will continue to improve our management of volunteer engagement."

investinginvolunteers.co.uk

IMAGE: ISTOCK.SCIENCE PHOTO LIBRARY

Group, said: "The ultrasound physics workforce is in really urgent need of support, in terms of improving training opportunities to fill existing vacancies and develop/consolidate the current workforce, and in justifying the creation of further established posts."

Dr Jemimah Eve, IPEM's Head of Workforce Intelligence and Training, added: "Without swift and effective action, the ultrasound physics workforce will decrease further, thereby stretching an already overworked and underappreciated workforce and further compromising patient safety and care."

bit.ly/ultrasound_workforce

PROFESSIONAL RECOGNITION

Nine new IPEM Fellows

Nine members of IPEM have recently been admitted as Fellows.

The new Fellows are:

- **Dr Emmanuel Akinluyi, a Medical Equipment Engineer at Guy's and St Thomas' NHS Foundation Trust in London.**
- **Dr Fiammetta Fedele, a Consultant Medical Physicist and Head of Non-Ionising Radiation at Guy's and St Thomas' NHS Foundation Trust.**
- **Dr Sam Tudor, Consultant Clinical Scientist and Head of Quality Control and Dosimetry at Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust.**
- **Dr Mark Hill, Head of Radiation Physics at the Gray Institute for Radiation Oncology and Biology at the University of Oxford.**
- **Dr Gordon Waiter, Senior Lecturer at the Aberdeen Biomedical Imaging Centre at the University of Aberdeen.**
- **Dr Bal Sanghera, a Clinical Scientist at the Paul Strickland Scanner Centre, Mount Vernon Hospital, East and North Hertfordshire NHS Trust.**
- **Professor Dean Barratt, Director of Studies in Medical Physics and Bioengineering at University College London.**
- **Dr John Dickson, Head of Clinical Nuclear Medicine Physics at University College London Hospitals NHS Foundation Trust.**
- **Dr Siu Man Lee, Head of Healthcare Engineering & GI Physiology at the Royal United Hospitals Bath NHS Foundation Trust.**

Dr Robert Farley, IPEM's President, said: "I would urge any Full Members to apply for Fellowship to help us make the key decisions that will shape both IPEM and the wider professions we represent into the future."

ipem.ac.uk/get-involved/membership/fellowship

POLICY UPDATE

Workforce crisis point

Sean Edmunds, the Institute's External Relations Manager, outlines recent key policy updates.

It had been a long time in coming, and it was hoped that there would be some recognition of the crisis point being reached in the medical physics and clinical engineering (MPCE) workforce.

When it was published, however – just a few days before the NHS celebrated its 75th birthday – the NHS England Long Term Workforce Plan proved to be a huge disappointment, with virtually no mention of the MPCE community in it.

This came on the back of IPEM's recent statement on the current workforce shortfalls and recruitment outlook within MPCE, which restated calls for urgent action to address shortages in this crucial area.

Speaking after the publication of the plan, Dr Robert Farley, IPEM's President, said: "There is a huge depth of concern among the MPCE workforce about the current state of their provision within Healthcare Science and the publication of the plan does nothing to alleviate that.

"While it's good it recognises there is a workforce issue and something is being done, it needs to be remembered that healthcare requires a multi-disciplinary team, and medical physicists and clinical engineers are a key part of that.

"It is hugely disappointing there was no mention of the MPCE workforce in the plan, other than a pledge to increase training places for all Healthcare Scientists by 13% in five years' time. The reality, though, is this equates to only around 15 additional places a year for MPCE by 2025 and an additional 33 per year from 2028 – woefully short of the 450 MPCE staff posts currently sitting vacant, and those vacancies will likely have increased further by 2028."

Thirty years

Recommended staffing models in fact show the MPCE workforce actually requires at least 900 additional staff to come from additional training opportunities, which will be impossible to achieve by the meagre increase of training places pledged per year. At such a rate it would take close to 30 years to reach the required staffing levels.

IPEM's statement calls for a number of specific measures to be addressed:

- Provide £8m additional funding annually over a five-year period – £40m in total – to NHS Trusts to increase their staffing and training capacity
- Utilise and promote all available training routes
- Include specific 'Clinical Scientist' and 'Clinical Technologist' role titles on the

JOINING FORCES AND STRENGTHENING RELATIONSHIPS

A memorandum of understanding was signed by IPEM with AXREM, the UK trade association representing suppliers of diagnostic medical imaging, radiotherapy, healthcare IT and care equipment in the UK.

This formalised the already strong working relationship between the two organisations and will see joint promotion of events, as well as other opportunities to engage on a range of projects. This includes IPEM's Science Leadership Strategy, with the aim of driving transformative professional development across the sector.

IPEM also joined the Global Clinical Engineering Alliance (GCEA), which empowers and recognises the clinical engineering profession for its unique contribution to improving healthcare delivery outcomes. The GCEA's goal is to educate and advocate for patients and staff, and supports the expansion of education programmes designed to improve systems thinking, standards and regulatory frameworks.

Two consultations were also responded to. Nicky Whilde, as Chair of the Radiotherapy Professional Standards Panel, submitted evidence on behalf of IPEM to the House of Commons Health and Social Care Select Committee's inquiry into Future Cancer, which is looking at innovations in cancer diagnosis and treatment.

IPEM submitted evidence to a white paper by the Department for Science, Innovation and Technology on AI regulation: a pro-innovation approach, with input from members of the Clinical and Scientific Computing Special Interest Group.

IMAGE: ISTOCK

Healthcare requires a multi-disciplinary team, and medical physicists and clinical engineers are a key part of that

IT WOULD TAKE CLOSE TO 30 YEARS TO REACH THE REQUIRED STAFFING LEVELS

- National Shortage Occupation List
- Add 'Clinical Engineer' as an eligible occupation of the Health and Care Worker Visa as a matter of urgency.

IPEM's Workforce Intelligence Unit has routinely surveyed and evaluated issues relating to staffing levels within the MPCE workforce since 2013. The unit, together with IPEM volunteers drawn from across the healthcare science professions, have gone on to develop workforce models for multiple specialisms within MPCE, to provide guidance outlining the essential requirements for a safe and effective workforce. These models have been critical in determining the established workforce shortfall in several areas and have emphasised the need for further funding dedicated to increasing the workforce establishment.

Taking steps

Dr Farley concluded: "IPEM has clearly outlined the scale of the issue and is taking steps itself, including events by our Special Interest Groups looking at overcoming the workforce challenges within their particular areas; the reinstatement of the Heads of MPCE meetings to cover each nation within the UK; and setting up a Workforce Panel.

"We need to address these concerns because, otherwise, the risk is the MPCE workforce will continue to decline."

THE BIG DEBATE

Radionuclides

We ask four experts about the supply of radionuclides, emerging technologies and the future impact on nuclear medicine.

Q ***How critical is a secure domestic supply of radionuclides for the UK's healthcare system, what are the current challenges in ensuring a secure supply?***

HEATHER

At present, the UK is very heavily dependent on production facilities elsewhere in the world for radioisotopes that are key to routine nuclear medicine and research. In particular, routine nuclear medicine imaging relies on an ageing network of reactors across Europe to generate ^{99m}Tc. Downtime (scheduled and otherwise) across this network has severely disrupted supply several times in the last couple of decades, extending waiting times for imaging and delaying the treatment decisions that rely on that information.

GLENN

A domestic supply of radiopharmaceuticals has been discussed since the end of the last century. There are several factors that now make this a necessity if the UK is to compete globally in healthcare. Reactors are ageing, molecular radiotherapy is expanding rapidly and the decision to leave the European Union has brought increased paperwork, delays and delivery costs. Unlike cold chemotherapeutics, radioactive drugs cannot be stored.

MATTHEW

Radionuclides are used across a range of medical applications including diagnostic imaging, targeted cancer therapies and research. Without a reliable supply of radionuclides it would be impossible to deliver and develop clinical services in these areas, putting at risk the quality and range of healthcare provision in the UK.

Aside from some cyclotron-produced radionuclides, the UK is heavily reliant on imports from a few (mostly EU) production facilities. This vulnerability in the supply chain is coupled to the short half-life and transport delays can disrupt patient treatments. Securing a domestic supply would require long-term investment in new infrastructure and in the workforce required to run complex and highly regulated facilities, only possible with significant collective effort and widespread engagement.

JENNIFER

It is extremely important to the UK public that they can have access to nuclear medicine procedures when they need them. The best way to ensure that patients can access these procedures is for the UK to have control of the supply chain and securing its own sovereign supply is ultimately the most effective way to do this. Without sovereign supply the UK will remain at the back of the queue whenever there are global shortages.

Q ***How does the scarcity of radionuclides affect the availability and cost of diagnostic and therapeutic procedures in the UK? What strategies can be employed to mitigate these challenges?***

HEATHER

Not having "home-grown" production facilities means we have very little control over which isotopes are available and when for a wide range of purposes and the associated costs. The costs of importing from the EU

> IT SEEMS MORE FITTING THAT WE ARE MORE PART OF AN ACTIVE PAN-EUROPEAN NETWORK

have also increased significantly since Brexit, reflecting the more complex administration required in the presence of trade barriers. I think there's a lot that could be done to enable smoother transport of materials into the UK, but given how established nuclear medicine and nuclear research is in the UK, it seems more fitting that we are more part of an active pan-European production and supply network rather than consumers of it. Investment in our own facilities is a very strong signal that the UK is seriously committed to such a partnership and active participation in this network of facilities potentially allows us more say in how cross-cover is provided during downtime and less disruption to supply.

GLENN

We have no control over therapeutic drugs supplied by pharmaceutical companies and there are monopoly issues. The suspension of Ra-223 production in 2014 had a significant impact on patient treatments. If a domestic supply is developed, it is essential that it is supported by production, distribution and clinical implementation. A UK roadmap with cost analysis is needed now. A starting point is that since Brexit ~10% of starting material cost is from delivery.

MATTHEW

As supply of radiopharmaceuticals is mainly via the private sector, there is an obvious link between scarcity and cost. Scarcity over the longer term with few competing providers is likely to lead to higher prices for the end users and limited availability. At present, radiopharmaceutical purchase requests are occasionally met with the response from the supplier that quotas have already been filled. Furthermore, the utilisation of radionuclides for imaging in the UK is below that of

IMAGES: SHUTTERSTOCK

MEET THE PANEL

DR HEATHER WILLIAMS

Consultant Medical Physicist and Nuclear Medicine Group Leader
The Christie NHS Foundation Trust

DR GLENN FLUX (IPEM FELLOW)

Head of Radioiostope Physics
Institute of Cancer Research, the Royal Marsden Hospital in Sutton, Surrey

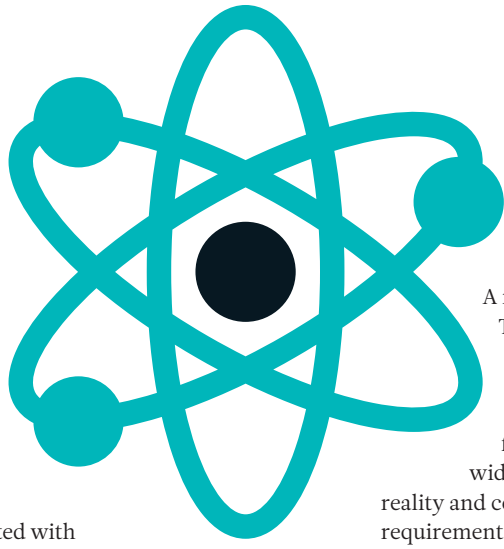
DR MATTHEW WALKER

Senior Clinical Scientist
Oxford University Hospitals NHS Foundation Trust

DR JENNIFER YOUNG

NCITA Imaging QC/QA Team Radionuclides for Health UK, King's College London

many other developed countries. Diversification of supply, including domestic production alongside international collaboration, would mitigate these challenges and boost availability. But we need caution, as the cost of the radionuclide is only one consideration when new (radioactive) drugs are produced by pharmaceutical companies with a need to recoup their extensive development costs.



JENNIFER

The scarcity of radionuclides really impacts the provision of a consistent clinical service, which impacts patient care. The costs associated with import and transport are definitely a big contribution to the price of radiopharmaceuticals, so we should be investing in UK infrastructure allowing radionuclides to be produced in the UK for UK patients. Of course, ideally, a research reactor would be situated here, but that is a long-term option, in the shorter term a high-energy cyclotron could be used to supply a range of novel radionuclides for clinical trials or nuclear waste could be used as a source of radionuclides.

Q ***Are there any emerging technologies or alternative approaches being explored that may help to deliver a secure domestic supply of radionuclides? How do these innovations address security concerns and infrastructure requirements?***

HEATHER

There are a number of isotopes that are interesting for research, including clinical research, which could be separated from industrial waste. This sounds unappealing – a bit like digging around in a skip for something valuable that's been accidentally thrown away – but considered logically it makes a great deal of sense to recycle existing materials. Other options include expanding the number of cyclotrons, adding more of those suited to ^{99m}Tc production and building our own reactor specifically to generate isotopes for medical and research purposes as part of the existing pan-European network.

GLENN

The ARTHUR project, a proposal for a nuclear reactor in Wales, offers the greatest hope for a long-term supply of radiopharmaceuticals and will place the UK at the forefront of translational research and development. The potential to use nuclear waste from the National Nuclear Laboratory is also promising.

MATTHEW

A range of options are being investigated. The ARTHUR project, which aims to build a new public sector facility mirroring the technology of Australia's OPAL reactor, already has significant backing including from the Welsh government. It has the wide support base needed to turn vision into reality and could provide many of our domestic requirements. New technologies such as cyclotron-produced Tc-99m could use existing infrastructure to diversify the supply of this radionuclide, but international collaboration with a shared goal of resilient, adequate global supplies of Mo-99 also safeguard this sector. Regarding security, the conversion in Mo-99 production methods from use of high-enriched uranium to low-enriched uranium targets, is now achieved with all major suppliers having adopted use of the lower-risk material.

JENNIFER

It's really exciting that the UK National Nuclear Laboratory has initiated a programme of work that looks to extract lead-212 from nuclear waste. This radionuclide has both beta and alpha emissions in its decay chain and has shown really promising therapeutic results in a US phase 1 neuroendocrine cancer clinical trial. Having a UK source of lead-212 will accelerate R&D, allow UK clinical trials to take place and may attract biotechs to the UK too. The UK government has also just launched the Medical Radionuclides Innovation Programme – it'll be great to see what projects come out of that!

"THIS SOUNDS LIKE DIGGING AROUND IN A SKIP FOR SOMETHING THAT'S BEEN ACCIDENTALLY THROWN AWAY

Q ***What about people – if we do manage to develop a world-leading domestic nuclear medicine capability, do we have the professionals we will need to run it? If not, what needs to be done to secure a talent pipeline?***

HEATHER

There is a huge skills gap in the UK when it comes to the nuclear medicine clinical workforce, whether they be clinical technologists, radiographers, radiologists, nuclear medicine physicians,

radiopharmaceutical scientists, technicians or medical physicists, which has been well-documented. It is also very hard to recruit people with the niche skillset required to run a cyclotron or reactor to create the raw materials. Further investment in training routes for all these staff groups is clearly required. In terms of the NHS workforce, I think many of the issues have already been highlighted during recent strike action. My opinion is that we need adequate staffing and facilities, competitive salaries for all staff groups, and more funded degree-level apprenticeships where this is a good fit for the role.

I also think we need to be more careful about how we present the UK as an attractive place for international talent – news of the current state of our health service, the cost of living crisis and rhetoric from the government regarding immigrants is reported beyond our borders and is certainly not helping.

GLENN

Staffing is an issue across the board and is an early agenda item at every meeting on molecular radiotherapy. The clinical sciences struggle to recruit due to lower pay in the NHS than in the commercial sector and a lack of visibility at the stage at which students are choosing their careers. Intelligent use of radiotherapeutics – particularly treatments informed by imaging and dosimetry – will save costs that can be re-channelled to support staff. It is for UK physics to lead on this.

MATTHEW

There is enormous talent in the UK but working in the NHS I'm aware of major challenges for training, recruitment, and retention of scientific staff. Would similar difficulties be faced by those tasked with developing a domestic production facility? I expect there would be challenges, but the UK has numerous nuclear facilities as well as plentiful high-quality universities with strong nuclear physics departments that can help educate the workforce of the future. With appropriate and targeted investment – to support and entice students to the nuclear sector, as well as giving training opportunities to the local populous – together with funding for national and international recruitment where required, I would hope that staffing difficulties would be avoided.

JENNIFER

People are just as important, if not more important, than infrastructure. We have a shortage of skilled people in this area and it's something that the UK needs to invest in. It probably needs a visionary but also collaborative approach to start the right training programmes to support this growing opportunity, and this training gap is something Radionuclides for Health UK has been encouraging UK universities to consider.

"FURTHER INVESTMENT IN TRAINING ROUTES FOR ALL THESE STAFF GROUPS IS REQUIRED

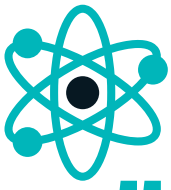
Q ***How might the kind of regulatory reform described in the government's 2021 Life Sciences Vision – removing bureaucratic barriers, while prioritising patient safety – be applied to nuclear medicine? What are the barriers and what would you like to see change?***

HEATHER

There is always a balance to be struck between appropriate regulation to underpin safety and arcane bureaucracy. Nuclear medicine is a highly regulated and regularly inspected area of clinical practice, and I have no issue with that. However, I do think streamlining guidance from multiple bodies overseeing safety to make sure the route to compliance is clear and not overly onerous is an area for improvement. The barriers to research with novel radiopharmaceuticals are particular high, which risks deterring companies who may prefer to conduct initial trials outside the UK due to the regulatory burden.

GLENN

The Prime Minister stated in the introduction to the *Life Sciences Vision* that "the full breadth of our regulatory freedoms from Brexit [will] make the



"REGULATORY REFORM WILL HELP, BUT THERE IS MORE TO CONSIDER

UK the best place in Europe to invest in a life-science business". Nevertheless, there are concerns that industry is investing less in UK research. Post-Brexit limitations of access to EU funding are also having a pronounced effect. Regulatory reform will help, but there is more to consider. The current high regulatory standards must not be compromised.

MATTHEW

There is an opportunity for changes to allow the MHRA to assess new radiopharmaceuticals more rapidly, bringing cost savings for those that develop them, while building on schemes to allow NHS patients early access to novel therapies. I would like to see a streamlined approval process for new radioactive drugs that could take place alongside reforms to ease the sharing of data internationally. These changes could increase the pace of innovation, aiding the development of new radiopharmaceuticals and expanding their uses, but also aiding the creation of new digital technologies. New artificial intelligence (AI), for example, could be applied within nuclear medicine to improve image reconstruction or to assist with image reporting.

JENNIFER

There has already been a fantastic step forward this year with the MHRA announcement that diagnostic radiotracers will no longer be considered investigational medicinal products (IMPs). This will accelerate UK clinical trials by reducing the administrative burden and is well justified due to diagnostic radiotracers' excellent safety record. However, as new radiopharmaceutical-based therapeutics are emerging, it is important to work with the MHRA to ensure they understand the unique aspects of these novel treatments and how they can be fairly and accurately assessed for safety. In particular, I believe we need to emphasise the importance of personalised dosimetry for patient safety.

Q ***Are there successful approaches internationally we can learn from? And could collaborations with international partners and organisations contribute to the UK's objective of establishing a secure domestic supply of radionuclides?***

HEATHER

The UK has historically benefitted from home-grown innovation and the exchange of ideas with international partners. We need to learn from ideas that have worked elsewhere but also tailor them to nuclear medicine in the UK. Personally, I'd like us to learn from established medical and research reactors (and associated processing plants) elsewhere in Europe and beyond, and from medical cyclotron networks, as I think the solution for the UK is a mix of the two. I recently examined a DClinSci thesis discussing cyclotron-produced ^{99m}Tc drawing on data from TRIUMF in Canada, which shows great promise. I would certainly like to see the UK explore the possibility of providing cyclotron-produced ^{99m}Tc alongside cyclotron-produced PET isotopes.

GLENN

Investment from industry will be necessary to build a UK reactor. International collaborations are essential in nuclear medicine where there are fewer patients and a need for multidisciplinary expertise. Collaboration with Australia should be pursued as they lack access to some commercial radiopharmaceuticals but are able to produce their own with the ANSTO OPAL reactor.

MATTHEW

There is already coordination between the main suppliers, for example, facilitated by the European Observatory on the supply of medical radioisotopes. Such collaboration is necessary to avoid breaks in provision from concurrent downtime, to promote reviews of the supply chain and to help shape new policies aimed at securing supplies. While a home-grown supply of medical radionuclides has its benefits, an international outlook will give better variety and stability of supply. If new domestic production facilities are built, these are likely to function more effectively and with greater yields if they can build partnerships with those in the international community that already have expertise with the technology.

JENNIFER

Australia is an excellent example of a country that has invested in its own infrastructure for radionuclides – it has a research reactor and processing facilities at ANSTO and is also investing in a high-energy cyclotron. It also has reduced regulatory requirements for radiopharmaceuticals produced within hospitals and this has allowed it to lead the world in nuclear medicine clinical trials in prostate cancer. In Europe, the PRISMAP initiative is an excellent network for novel radionuclide production that has accelerated R&D programmes.

Member profile: Dr Georgios Ntentas

I work as an NIHR Clinical Lecturer and Senior Radiotherapy Physicist at Guy's and St Thomas' NHS Foundation Trust/King's College London and a Medical Physics Research Fellow at University of Oxford.

Tell us about your typical working day.
Being in a clinical-academic role, I split my time between clinical radiotherapy work (two days a week) and research (three days a week). A typical clinical day involves using patients' scans to create individualised radiotherapy treatment plans, or measuring the radiation dose emitted by the radiotherapy machines to ensure that the amount of radiation delivered to our patients is correct and safe.

There is no such thing as a typical research day, I am currently the Principal Investigator in a clinical trial where I scan cancer patients before and after their radiotherapy treatment using simultaneous cardiac PET/MR imaging to detect chemotherapy- and radiotherapy-related heart disease with the aim to reduce it in current and future patients.

What do you like most about your job?
Combining clinical work with research is by far my favourite part – research can be very exciting and offer you independence but it can also be very daunting and demotivating if you don't see any application of it in real life for prolonged periods of time, which happens all the time by the way.

What are the biggest challenges for yourself or the sector?
More investment in radiotherapy services is needed urgently to try to maintain our treatment targets. Staff morale has been seriously affected during the pandemic and we see NHS colleagues going to the private sector or abroad due to low pay, morale and prospects.

What one thing would you like to change about the profession or your area of specialty?
More combined clinical research roles in radiotherapy physics are needed, and physicists should drive and push innovation and new ideas in the departments. Roles with some protected and funded time for us to utilise our scientific and analytical skills to drive change and innovation are needed in every department.

What accomplishment have you been most proud of?
Securing my current NIHR fellowship to run my own clinical study is definitely one of the things I am most proud of in my career. And that is because it came as a result of many years of hard work and effort.

What do you do in your free time?
I love travelling with my partner and visiting family abroad (we are both originally from Europe), and going on cycling holidays and holidays with friends. I also love spending time with friends in London, exploring the city and going to festivals, gigs and clubs.

Why did you join IPEM?
I joined IPEM as a medical physics trainee back in 2012 as I wanted to engage with other trainees and network. It was the first year of the STP so it was very helpful attending the induction days run by the then IPEM trainee network that guided us through the training.

Which IPEM member benefits do you value or use the most?
IPEM's work with policymakers and standing up for our profession is probably one of its most valuable contributions, we need a strong voice in parliament to ensure our professional rights and workforce planning is taken into consideration in terms of medical physics and clinical engineering needs.

What does (or should) IPEM do to help you in your career?
IPEM has helped me develop my leadership and professional skills through my involvement in the committees and networking opportunities. The last highlight was a recent Healthcare Early Career award I received from the Institute, which was a great honour.

IMAGE: ISTOCK


100
DAYS

A JOURNEY TO TATTOO-FREE RADIOTHERAPY

Dr Jennifer Dobson and **Dr Shelley Taylor** talk us through the process of offering tattooless radiotherapy for breast cancer patients, from conceiving the initial idea to treating the first patients in May this year.

Surface guided radiotherapy (SGRT) has become a rapidly expanding and sought-after technology for radiotherapy centres around the world. It uses a surface map of the patient, obtained using infrared light projections, to aid set up for treatment and can be used to monitor the patient's position during treatment, even gating the beam if required. One benefit to using SGRT is that patients can be set up without the need for tattoos.

Usually, the patient is positioned on every day of their radiotherapy treatment using two or three small permanent tattoos, with the aid of lasers, to the same position they were in at their planning CT scan. This positioning is vital to ensure that the patient receives their treatment as accurately and safely as possible. However, the tattoos can psychologically impact patients as they are a permanent reminder of their cancer treatment.

In 2021, it was proposed that Rosemere Cancer Centre (RCC) introduce SGRT. The big question for a struggling

ILLUSTRATIONS: SPOOKY POOKA

NHS trust was where to find funding. In November 2021, a bid was submitted to Rosemere Cancer Foundation charity to fund six linac-based systems, and one CT simulator-based system. The charity generously agreed to provide funding as part of their 25th anniversary celebrations and an order was made to a radiation oncology technology company in early 2022 for what became their largest single site install in the UK. This is our journey from gaining funding to going tattooless for our first treatment site.

Information gathering

A multidisciplinary project team was assigned and site visits planned as we gathered as much information as possible to make an effective and efficient installation, commissioning and clinical implementation plan. Visits were made to the Queen Elizabeth Hospital Birmingham before install, and The Christie at Macclesfield after install. We are extremely grateful for the insight the two centres gave us into their experiences, which was invaluable in helping us with all aspects of the project.

A core team of four radiographers and four physicists received two days of offsite user training from the equipment supplier in August 2022 – the first group to attend training at the brand-new training facility in Basingstoke. Additionally, two RCC engineers attended an extensive four-day supplier course in November 2022.

Once the offsite training was complete, our mission was to train as many operators as possible in the pre-treatment, treatment delivery and physics teams – this was aided by comprehensive online training packages provided by VisionRT. We also implemented daily QC of the SGRT systems as soon as they were operable, to ensure familiarity of the QC operators with the systems prior to clinical implementation.

We needed licenses from the vendors of the linacs and CT scanners in order to integrate the SGRT systems with the existing equipment. However, these were an unforeseen and considerable additional expense, which had not been included in our original funding bid to Rosemere Cancer Foundation. Thankfully, the charity was able to provide the additional funds.

To get the system installed within the hospital IT network we followed local procedures, including completing a data protection impact assessment and system level security policy. We also required virtual servers to host the application and patient databases. It took a few iterations to provide IT with the necessary information and this was only completed three weeks prior to install.

Figure 1 Rosemere Cancer Centre's core team with the application specialist at the dedicated training facility in Basingstoke.

In August 2022, the manufacturers performed a site survey for all seven systems, which revealed we would need some electrical work for the treatment rooms, as the cameras and monitors required additional power sockets and isolator switches. Building works were not included in our SGRT install contract and a minor works request was submitted to the hospital Estates department, whose contractors completed the work during clinical hours.

The install

Delivery of the systems began in September 2022. Storage of the systems prior to installation required a lot of space, and consideration of where was possible for this was important. Installation of four systems took place in October and November 2022, and the final two systems in January 2023.

The install of each linac-based system was scheduled to take three days and due to installation engineer availability, could not be scheduled for weekends. As we were getting six systems, this resulted in a loss of a total of 18 clinical days. We are fortunate to have a decant linac that was crucial in facilitating installation of the systems with little disruption to the service.

We overcame several issues during installation and acceptance testing of the systems. Notably, the delay to the acceptance of the SimRT system, due to problems with camera stability. This was resolved by the addition of a Unistrut in the ceiling cavity, funded by the trust and carried out by our radiotherapy engineering team. For the linac systems, connectivity to the oncology information management system caused some difficulty that was resolved by having a meeting with all vendors one evening after the department clinical finish.

One of our linacs has a 6-DoF couch, which has a camera mounted on the ceiling in a similar location to the sagittal SGRT camera. It was important to consider how the two systems would work together and ensure that one camera did not occlude the other. The install engineers had previous experience with situations such as this and were able to give us options on how to arrange the systems; we proceeded with two separate ceiling mounts. Following install, extra time was scheduled for recalibrating the 6-DoF couch.

Acceptance and commissioning was based on published reports and advice and documentation kindly shared with us by colleagues from the Queen Elizabeth Hospital, Birmingham. We initially

"LESS THAN 100 DAYS AFTER GOING CLINICAL WITH SGRT, WE STOPPED TATTOOING ALL BREAST PATIENTS

Table ❶ The timeline from first treatment using SGRT to going tattooless for all breast cancer treatments.

January 2023	
4th	Go live with small cohort of 2-field 5# breast treatments
13th	All 2-field 5# breasts treated with SGRT
February 2023	
1st	All 2-field 15# breasts treated with SGRT
6th	Go live with breast boost treatments
March 2023	
7th	Go live with small cohort of 3-field 15# breast treatments
20th	All 3-field breasts treated with SGRT
23rd	Go live with small cohort of 3-field breast with IMC
April 2023	
3rd	All 3-field breasts with IMC treated with SGRT
11th	Go live with small cohort of 2-field 5# left breasts with DIBH
May 2023	
2nd	All 2-field left breasts treated with SGRT in DIBH **All breasts treated tattooless with SGRT**

concentrated our commissioning on two linacs, to ensure we could go clinical with our chosen treatment site in the shortest possible time. Because we had a large multidisciplinary team working on this project, we were able to complete commissioning tasks, documentation and training simultaneously.

Clinical use

We decided to go live with two-field breast treatments, aiming to use SGRT for initial patient setup and to monitor position during treatment. This was a minimal change from our usual technique and only involved small modifications to the pre-treatment pathway.

SGRT went into clinical use at the beginning of January 2023. SGRT applications specialists and engineers arrived the day before going live to do final onsite training with treatment delivery teams and to offer support whilst we treated our first patients. On the first day we successfully used SGRT for five patients, with their set-up data audited immediately afterwards. Within two weeks we had the confidence to treat all two-field breast patients with surface guidance for set-up and monitoring.

Figure ❷ Treatment radiographers with Rosemere Cancer Centre's first patient to be treated using SGRT.

Confidence in the system grew much faster than anticipated. The roll out to more complex breast treatments, including deep inspiration breath hold (DIBH), three-field, bilateral and internal mammary chains (IMC) occurred over the next four months.

Once all breast patients were being treated using SGRT, we began to think about removing tattoos. During the four months the system had been used clinically, patients were still tattooed, but the clinical staff found that they did not need to use them for setup, as they were able to use the SGRT system to position the patient accurately. We proactively audited treatment times, imaging correctional moves versus SGRT deltas, and repeat imaging rates. On average, SGRT set up matched kV imaging to within 1mm, confirming the SGRT set up was as accurate as previous procedures.

Due to the audit data and the confidence gained in the first four months using SGRT, there were no real barriers to going tattooless. At the beginning of May 2023, less than 100 working days after going clinical with SGRT, we stopped tattooing all breast patients.

The set-up is quicker and will improve as we gain more experience with the system. The ability to monitor the patient position in real-time during treatment is giving more confidence that there is minimal intrafractional motion, and if there is, the system uses "beam hold" to automatically gate the treatment beam delivery until the patient is back in the correct position.

What next?

Our next step will be arranging more applications training on two additional linacs and in the autumn, beginning to use SGRT for lung treatments. We are keen to roll out this technology to all possible sites and want to investigate the use of faceless masks for our head and neck, and brain patients, and utilise SGRT in conjunction with our 6-DoF couch.

We were able to complete the implementation of SGRT across the department and remove tattoos for all breast patients in such a short time due to a large team working collaboratively and simultaneously on all aspects of planning, install, commissioning, training, and clinical roll out and with the wider teams working flexibly over the whole period. The success of this project is a testament to the hard work and commitment of the project team and the entire department. We would like to thank Rosemere Cancer Foundation for providing the funding for this fantastic equipment that will make a difference to so many patients.

Dr Jennifer Dobson *and* ***Dr Shelley Taylor*** *are Physicists at the Rosemere Cancer Centre, Lancashire Teaching Hospitals NHS Foundation Trust.*

VIRTUAL VOLUNTEERING

A collaborative prosthetics research project

An international, multi-disciplinary team has demonstrated a low-carbon way for clinicians and scientists in the UK to engage with global health, and how their counterparts in low-resource settings can benefit from these exchanges of expertise.

There have been multiple reports and international agreements since the first Intergovernmental Panel on Climate Change. These have done little to "bend the CO2 emissions curve". As a result, the chances of limiting global warming to 1.5 degrees are now very slim indeed, and to reduce the already alarming risks of runaway catastrophic warming, we need rapid year-on-year reductions in emissions.

A typical UK citizen's annual CO2 emissions are around 12.7 tonnes. Flights (including personal flights, business flights and air freight) are responsible for around 12% of this figure. Despite the hype

surrounding electric aircraft, fundamental problems with range remain unresolved, so long-haul flights will be associated with a substantial carbon footprint for the foreseeable future.

In addition to the volume of individual travel, the NHS has a long-standing interest in global health, with trainee clinical scientists/engineers and clinicians having benefitted from exposure to health systems in low-resource settings, often involving extensive travel. These initiatives have often been encouraged through travel grants and electives, and are seen as a positive feature of training. Global health placements have been shown to play an important role in enabling health workers to reflect positively on their experiences in the NHS, and adopt more systems and context-grounded understandings of policies and practices.

IMAGES: GETTY

> "YOU NEED TO FIRST INTERACT, GAIN TRUST, AND THEN YOU SAY: OK, LET'S HOLD THE VIRTUAL WORKSHOP
>
> **Orthopaedic Technician, Uganda.**

Virtual ways of working

Until recently, the only realistic way for UK-based scientists and clinicians to directly engage with global health issues has been to spend time in a low-resource country. However, during the period of COVID-19-related restrictive travel, internet connectivity in low-resource countries – such as Uganda – improved, and expectations of how it can be used changed. A 2020 survey of global health partnerships found that 94% of respondents were now using virtual ways of working, compared to 38% pre-COVID. Those findings come with an increased acceptability and enthusiasm in low-resource settings for communicating and working online.

In addition to virtual working, as the COVID-19 pandemic also impacted on volunteering efforts, there was a shift towards volunteering online across a number of charity and public sectors, which included the emerging area of "virtual volunteering" in global health. This shift has the potential of widening diversity and inclusion of global health volunteers, as international mobility has historically been the preserve of the privileged for centuries and facilitated the career progression of those involved. People with disabilities, family or caring responsibilities – or those with fewer mobility "windows" in their career paths – have often been excluded. The UN and others recognise the potential of virtual volunteering to widen participation opportunities and enable organisations to access specialist technical expertise from highly-motivated professionals for whom international travel is not an option. Despite positive theorising about the potential for virtual volunteering in global health in the literature, there was to date little evaluation of this concept in practice.

This paper reports on a series of virtual exchanges between teams in the UK, US and Uganda focusing on prosthetics, and their evaluation. It concludes with a discussion of opportunities to re-think how UK scientists and clinicians can continue to engage positively with partners in low-resource settings without air travel. We start with an outline of the project that this virtual working was linked to, then outline the different virtual volunteering activities carried out, and finish with a reflective discussion.

Fit-for-purpose prosthetics

An established collaboration between social scientists at the University of Salford (and Knowledge for Change charity) and biomedical engineers at Makerere University, Uganda supported the development of a collaborative research project, Fit-for-Purpose (F4P) affordable body-powered prostheses, funded through the Global Challenges Research Fund. Other partners were the University of Greenwich, University College London, University of Southampton, and University of Jordan.

The launch meeting in 2018 was conducted with the teams in Uganda, Jordan and UK meeting virtually. The first year and a half of the project involved academics, clinicians, and volunteers aligned to the project taking a number of flights between the UK and Uganda. The volunteers included two trainee clinical engineers on the Scientist Training Programme (STP), who carried out a useful study of repair services in the Ugandan prosthetics service. Other volunteers aligned to the project included two students studying prosthetics and orthotics, and a

group of social work students from Norway. While we tried to minimise the number of trips, the assumption was that knowledge exchange could not easily be achieved without face-to-face contact between research teams and collaborating clinicians in the two countries.

The UK volunteers found their visits to be both interesting and rewarding. The physical exchanges also helped to generate a shared understanding of experiences and backgrounds, and the development of a trust relationship essential for effective co-working. Face-to-face communication, particularly working cross-culturally, is often regarded as a pre-requisite for the development of trust. However, the dramatic impact of COVID-19 travel restrictions offered an opportunity to reassess the necessity of physical co-presence.

In March 2020, almost all international flights across the world stopped and the teams continued their work remotely. At that point, one of the full-time researchers who joined the project in early 2020 was still in Canada, awaiting visa clearance. The other team members were based around the UK, in Uganda and Jordan. We moved to online working, with Zoom being the preferred platform. During 2020 and 2021, the Knowledge for Change team in collaboration with their partner hospital – Fort Portal Regional Referral Hospital – set up a virtual learning suite within the Ninsiima Centre for Rehabilitation of People with Physical Disabilities.

> **"THE CHALLENGES THAT COME WITH WORKING IN A LOWER-INCOME COUNTRY ARE QUITE UNIQUE**
>
> **STP Trainee and Virtual Volunteer**

Virtual working

The virtual work took two forms:

Clinically focused exchanges: Clinicians in Uganda typically use a technique known as (conventional) "draping" to make the socket that fits onto a residual stump following leg amputation. The conventional approach typically involves transporting and storing large sheets of polypropylene, and an excess of waste when the sheets are cut to size.

During discussions about supply chains with Lee Willan – a Salford University Prosthetics Technician – we realised that draping was possible using a different product that came in much smaller sizes (approximately 50cms square), as opposed to 2m/1m for the polypropylene sheets currently used in Uganda. The price of these smaller sheets seemed very competitive, their potential shipping could be easier and, importantly, there was a suggestion that the product may offer a higher quality socket.

Discussions with the team in Uganda suggested that they were aware of this technique but the key reason they were not using it was the lack of a "bubble draping frame" – a simple metal device (valued at about £100) to clamp and support the material whilst it is warming in the ovens.

The first Virtual Workshop involved a demonstration of the draping technique (Figure ❶). The team followed up with the donation of a bubble draping frame and some samples of plastic to the Fort Portal Hospital workshop, followed by a second, hands-on, practical workshop.

Co-design of Assistive Technologies (AT): During 2020 and 2021, the geographically-distributed F4P team collaborated on the development of designs of purely mechanical prosthetic hands. The academic partners were supported by volunteer engineers in a US-based prosthetics and orthotics company, Fillauer TRS. The work was informed by some of the work completed pre-COVID-19, including user needs evaluation, and involved a co-design exercise with people with limb difference, delivered by the Ugandan academic team. This led to simple mechanical designs, one of which is being trialled in a forthcoming study in Uganda. Three volunteer trainees

Figure ❶: Salford prosthetics technician demonstrating the bubble draping technique to technicians in Fort Portal

on the STP participated in this part of the project, but here we will focus on one of the projects.

The process of co-design or co-creation with potential users may lead to better prosthesis designs. To address this, the Uganda-based members of the F4P team ran a face-to-face co-design workshop with people with upper limb loss. The first STP volunteer worked virtually with the Uganda-based members of the team (also biomedical engineers) on structuring the format and delivery of the workshop, and initial analysis of the results. The results then allowed the research team to take forward a narrower set of concept designs.

Discussion

This pilot demonstrated the potential of virtual engagement, but also highlighted the on-the-ground realities of working in this way. Internet connectivity continued to be a challenge at times and a certain amount of behind-the-scenes work was required: planning the sessions across time zones; setting up equipment; and finding a physical space for the virtual workshops to happen. The creation of the virtual learning centre in Fort Portal was stimulated by these necessities and continues to be a valuable resource for virtual interprofessional learning. The involvement of volunteer STP trainees required some preparatory work by the F4P team to identify appropriate roles that could be delivered remotely within the time frame.

Figure ❷: Two of the orthopaedic technicians in Fort Portal using the bubble draping technique during a virtual workshop

The virtual workshops have led to the adoption of bubble draping as the preferred method of socket-making in Fort Portal (Figure ❷), which has lowered costs and enabled a more agile supply chain, which ultimately means more people who need prosthetics in the region can access them.

The work of the STP trainee virtual volunteers has also provided valuable specific, technical expertise to move the co-design work forwards, and the trainees reported that they had benefited hugely from the experience of working with colleagues from low-resource settings. The experience has encouraged them to use their new perspectives in their NHS careers.

Virtual volunteering offers a low-carbon way for clinicians and scientists in the UK to engage with global health, and for their counterparts in low-resource settings to benefit from these exchanges of knowledge and expertise. It is cost effective and widens access to the benefits of volunteering for the NHS workforce. For example, virtual volunteering can potentially attract volunteers who wouldn't be able to participate via the traditional physical approach, therefore widening both diversity and inclusion. People can also "donate" a few hours in a week/month over a long period of time, something that was difficult with physical volunteering across international boundaries. Further work is needed to properly understand the best approaches to implementing and – equally importantly – sustaining the relationships which underpin this type of work. ○

Kenney L, Horder C, Howard D *and* ***Ackers L*** *from the University of Salford,* ***Ssekitoleko R*** *and* ***Mulindwa B*** *from Makerere University,* ***Hussaini A*** *from University of Portsmouth,* ***Kyberd P****, a visiting researcher UCL,* ***Donovan-Hall M*** *from University of Southampton.* *The authors would like to acknowledge funding from: Engineering and Physical Sciences Research Council and National Institute for Health Research, grant number EP/R013985/1, and the Tropical Health and Education Trust.*

IMAGES: UNIVERSITY OF SALFORD MANCHESTER

TOWARDS CLINICAL TRANSLATION OF FLASH RADIOTHERAPY

Challenges for the medical physicist

IMAGES: ISTOCK

A look at the history and developments in the ever-evolving field of FLASH radiotherapy.

For decades, radiotherapy research has successfully pursued two major principles to maximise the therapeutic window: dose fractionation and spatial conformity. Now a third player – the temporal beam structure – has entered the game. A rediscovered idea to modify the biological effect of radiation by delivering the treatment in a fraction of a second has emerged as a possible approach that can expand the traditional radiotherapy paradigm. This concept is today known as FLASH radiotherapy and is generally associated with radiation delivered at ultra-high dose rates (UHDR) above 30-40 Gy/s, which is a factor of 100-1000 higher than that used for conventional (CONV) radiotherapy.

The short beam-on time (on the millisecond timescale) associated with FLASH radiotherapy has the potential to eliminate the impact of motion during treatment, which may allow the use of tighter treatment margins for moving targets – e.g. lung tumours following the patient's breathing pattern – resulting in less healthy tissue being exposed to high doses of radiation. Even more interestingly, preclinical studies have suggested that this type of dose delivery in certain conditions may increase the normal tissue tolerance dose by 10-50% compared to CONV radiotherapy, without compromising the treatment effect.

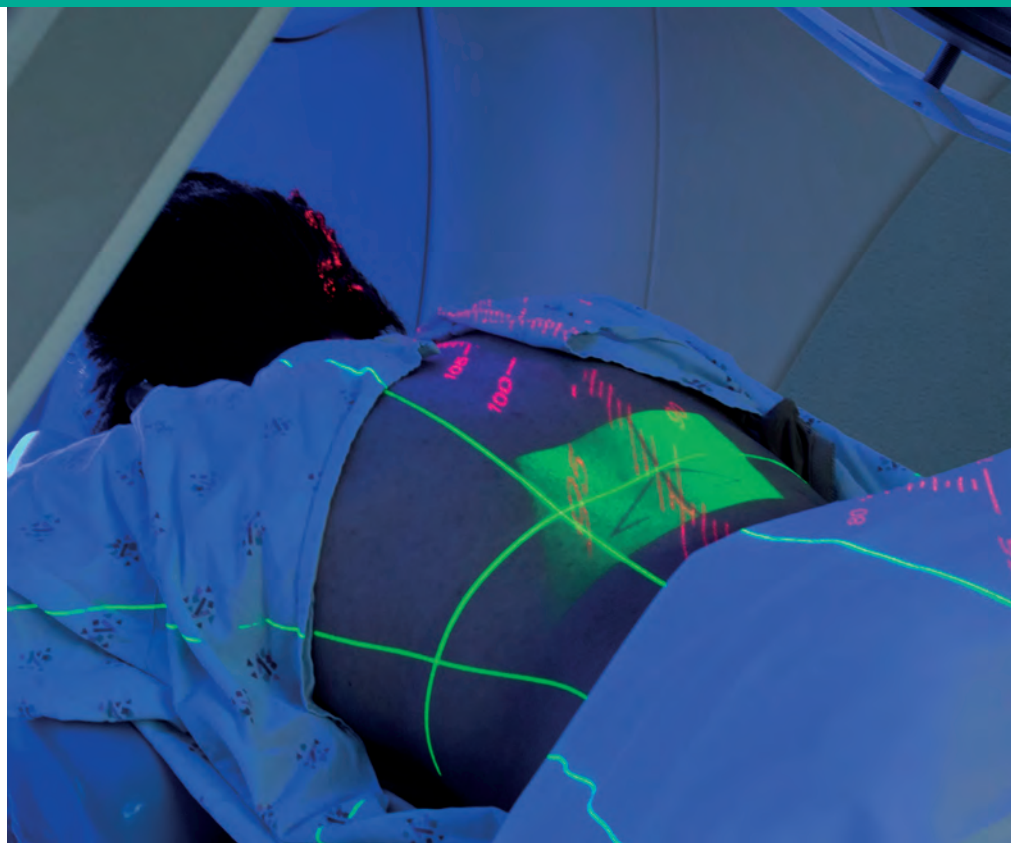
To secure the clinical implementation of FLASH radiotherapy, thorough interdisciplinary research is needed to better understand the physical parameters and biological mechanisms that trigger the protective effect in normal tissues while maintaining therapeutic efficacy.

History

The first observation of an altered biological response following ultra-high dose rate radiation was reported in 1959. Dewey and Boag (after encouragement from Dr. L. H. Gray) conducted an experiment in bacteria that resulted in reduced radiosensitivity when exposed at ultra-high dose rates, using high dose µs electron pulses, as compared to exposures to the same total doses but at traditional dose rates. In 1967, Town et al. demonstrated a protective effect in mammalian cells after single pulse delivery with an average dose rate of ~10^7 Gy/s. And in 1982, Hendry et al. showed an induced resistance to epithelial necrosis in mice tail at average dose rates of ~10^3 Gy/s. Several other studies during that same period observed similar phenomena in various biological systems, but some reported no difference in the biological effect in mammalian cells exposed to ultra-high dose rates compared to CONV dose rates. The conflicting results were one of the reasons why these early observations did not lead to further progress at the time (Figure ❶). Furthermore, it was considered that the total dose required to obtain a sparing effect would be too high to be clinically applicable and that there was a risk of reduced treatment effect in tumours.

Due to a seminal publication by Favaudon et al. in 2014, a renewed interest in radiotherapy with ultra-high dose rates was triggered. They reported on a comparative study where a single dose of

"TOTAL DOSE AND DOSE PER FRACTION SEEM TO HAVE AN IMPORTANT ROLE



radiation was delivered to the thorax of mice, either with FLASH (average dose rate of ≥40 Gy/s) or CONV (average dose rate of 1.8 Gy/min) radiotherapy. A single dose of 17 Gy FLASH resulted in a drastically lower degree of radiation-induced lung fibrosis than 17 Gy CONV. Only after increasing the FLASH dose to 30 Gy, side effects became significant and similar to the CONV 17 Gy group. They also showed that FLASH and CONV were equally effective in inducing tumour growth delay in two different xenograft models (breast cancer HBCx-12A and head and neck cancer Hep-2) growing subcutaneously in nude mice. Normal tissue sparing with maintained tumour response after FLASH compared to CONV was coined the "FLASH effect". In 2017, Montay-Gruel et al. conducted a study to investigate the brain's neurocognitive function after 10 Gy whole-brain electron irradiation as a function of average dose rates (from 0.1 Gy/s to 10^6 Gy/s). The results showed that memory was completely preserved at average dose rates of 100 Gy/s and above. In contrast, no notable protection of memory function was observed for average dose rates of 20 Gy/s and below. To date, the normal tissue sparing effect as well as the similar anti-tumour effect have both been replicated in various preclinical models involving different types of particles. Additionally, research in larger animals has been performed to investigate FLASH in scenarios applicable to human patients. Veterinary clinical trials on companion cats and dogs with spontaneously occurring tumours provide data that are highly relevant for a clinical translation. For instance, some of these studies have added very valuable information about dose limiting late normal-tissue toxicity at high-dose single-fraction treatments, suggesting the need for further studies on hypo-fractionated FLASH radiotherapy.

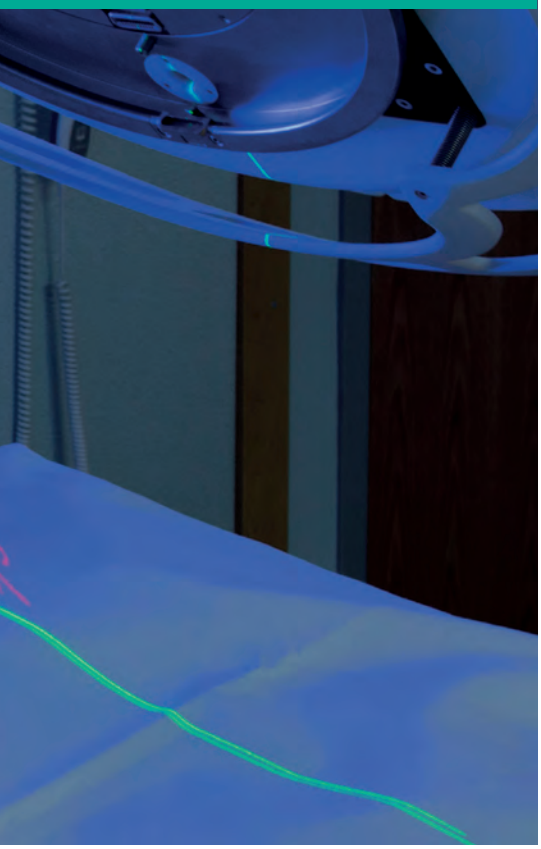
The first human patient to be treated with FLASH radiotherapy was reported in 2019. The patient, a 75-year-old man diagnosed with a CD30+ T-cell cutaneous lymphoma in 1999, had received CONV radiotherapy more than 100 times with good treatment effect but poor skin tolerance. A complete tumour response was achieved 36 days after a single treatment

"PRECLINICAL STUDIES HAVE SUGGESTED THIS TYPE OF DOSE DELIVERY MAY INCREASE TOLERANCE DOSE BY 10-50%

fraction of 15 Gy FLASH radiotherapy (167 Gy/s) administered in 10 electron pulses during a total treatment time of 90 ms. Only grade 1 skin toxicities were observed, which was considered to be far less severe than skin damage from earlier CONV irradiations. In 2021, the same patient was treated for two different tumours on the same day using 15 Gy FLASH (167 Gy/s) and 15 Gy CONV (0.08 Gy/s), respectively (20). Direct comparison found no difference between the two treatments in terms of acute reactions, long-term effects at two years, or tumour control. More recently, the findings from the first clinical trial of human FLASH, FAST-01, were published. Ten patients were treated palliatively for symptomatic bone metastases in the extremities, with the desired therapeutic benefit. Treatments were administered as 8 Gy FLASH (≥40 Gy/s) using a proton transmission beam. In this study, the feasibility and safety of the delivery was demonstrated. Other clinical trials (FAST-02, IMPulse, LANCE) are ongoing.

FLASH effect beam parameters

One important line of current research focuses on determining the optimal temporal beam structure for FLASH radiotherapy. So far, FLASH studies have involved different types of particles (electrons, protons, X-rays, heavy ions) produced by various radiation sources (dedicated electron accelerators, modified medical linear accelerators, cyclotrons, synchrotrons). The macro- and micro-pulse structure of these beams differ substantially from each other, which may be part of the explanation for the variations in the magnitude of the observed (or not observed) FLASH effect between studies. Some of the techniques also rely on scanning the beam (or sample/target) to fully cover the target, which adds a dimension to the dynamics of the



radiation delivery. Initially, the average dose rate was the main parameter identified for modulating the FLASH sparing effect. However, as more preclinical data have become available, several authors have reviewed the key temporal beam parameters for obtaining a FLASH effect and suggested that pulse dose rate, dose-per-pulse (DPP), pulse repetition frequency, and total delivery time may also be important (Table ❶ and Figure ❷). The latter is closely linked with the average dose rate and is highlighted as "the key beam parameter" in a study by Ruan et al., reporting that the shorter the total delivery time, the larger the FLASH effect. The total dose and the dose per fraction also seem to have an important role. To ensure a robust comparison between FLASH studies, authors should report detailed information about the beam, including the pulse characteristics.

Data on how the values of these parameters influence the FLASH effect are still limited, and more studies are required to narrow the options, find optimal values, and to set the requirements for (future) clinical FLASH radiation sources. According to the current published data, a FLASH effect generally requires average dose rates ≥30–40 Gy/s, total irradiation time ≤100–200 ms, and total doses of ≥5–10 Gy.

Figure ❶ Timeline describing the history of ultra-high dose rate (UHDR) and FLASH radiotherapy (Konradsson, 2023).

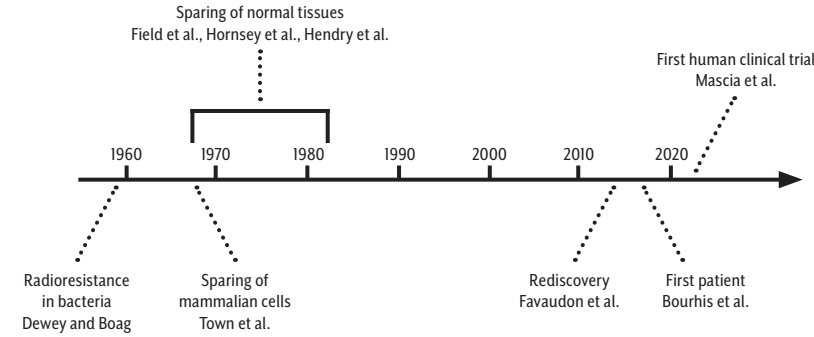
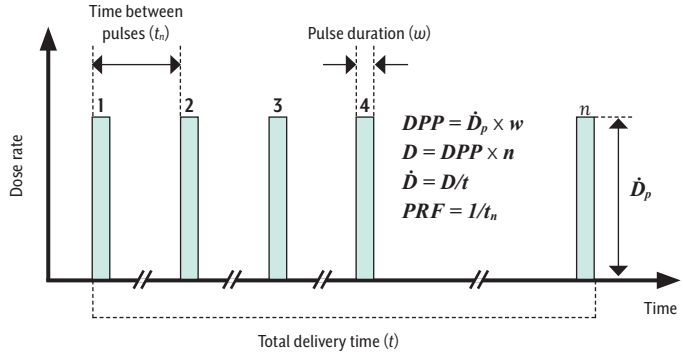


Table ❶ Beam pulse parameters and their typical values for (linear accelerator based) conventional (CONV) and ultra-high dose rate (UHDR) irradiations.

Beam parameter	Description	CONV	UHDR
Average dose rate ($\dot{D}$)	Mean dose rate for multi-pulse delivery	~10^{0}-10^{1}Gy/min	≥30-40 Gy/s
Pulse dose rate ($\dot{D}_p$)	Dose-rate within a single pulse	~10^{2} Gy/s	≥10^{5}-10^{6} Gy/s
Number of pulses (n)	The total number of pulses in a treatment fraction	~10^{3}-10^{4}	~10^{0}-10^{2}
Dose-per-pulse (DPP)	The dose delivered in a single pulse	~10^{-4}-10^{-3} Gy	≥1 Gy
Pulse duration (w)	Irradiation time for each pulse	~10^{-6}-10^{-5} s	~10^{-6}-10^{-5} s
Pulse repetition frequency (PRF)	Number of pulses delivered if the total delivery time is exactly 1 s	~Hz-kHz	~Hz-kHz
Time between pulses (t_n)	Time from the start of one radiation pulse to the start of the following radiation pulse	~10^{-3}-10^{-2} s	~10^{-3}-10^{-2} s
Total delivery time (t)	Irradiation time from the start of the first pulse to the end of the last pulse in a treatment fraction	~10^{0}-10^{1} min	≤0.1-0.2 s
Total dose (D)	Total dose delivered in a treatment fraction	~2 Gy	≥5-10 Gy

Figure ❷ Terminology and pulse structure. Adapted from Wilson JD, Hammond EM, Higgins GS, Petersson K (2020).



Magnitude of the FLASH effect

The required/optimal values of beam parameters discussed above could have been influenced by the assays used in the reported preclinical experiments; what end-point was used, what tissue type was irradiated, what dose was required to distinguish an induced toxicity, and what dose saturated that toxicity. The magnitude of the observed effect seems to further depend on the tissue type, e.g. no observed difference in tumours (mainly data from subcutaneous tumours in mice), a slight (≈10% dose modifying factor) sparing effect in crypts of the small intestine (in mice), and a large (≈50% dose modifying factor) sparing effect seen for skin. One can speculate that this depends on the microenvironment, e.g. oxygen content in that tissue, as we know that oxygen is a vital radiotoxicity modifier/sensitiser, and as it has been shown that oxygen modulates the FLASH effect *in vivo*, *in vitro* and *ex vivo*.

Clinical procedures

The road towards clinical translation of FLASH radiotherapy also entails the development of safe and effective tools and procedures to plan and deliver radiotherapy at ultra-high dose rates. To some extent, this can be achieved by adapting existing methods, but in some cases, it requires development of new technology. One area where currently available techniques can be used, although adapted to the very short treatment times in FLASH radiotherapy, is motion management. Even though detrimental patient motion during beam-on can be avoided, it is now more important than ever that the patient is in the correct position at the exact time of the exposure. Recent work has shown that conventional surface-guided motion management techniques can be utilised to monitor patient position in a FLASH radiotherapy setting, until the moment when it is deemed safe to enable beam-on. Another area where it has been found necessary to reinvent existing technology is treatment planning. Again, due to the short treatment times, sufficient dose conformity and homogeneity cannot be achieved with intensity modulation using moving parts. In electron FLASH radiotherapy, however, an alternative intensity-modulation technique utilising a static grid of metal pins partially blocking the beam in an optimised pattern, has recently been shown to give promising results. Finally, one area where development of novel technique is required is beam monitoring during treatment delivery. Today's standard employment of transmission ion chamber dosimetry fails at ultra-high dose rates due to the poor ion collection efficiency. Recent work has demonstrated that it is possible to overcome this problem by modifying the ion chamber design with increased polarisation voltage and reduced electrode gap.

> **"RUAN ET AL. REPORTED THE SHORTER THE TOTAL DELIVERY TIME, THE LARGER THE FLASH EFFECT**

Conclusion

Preclinical studies are trying to establish the radiobiological mechanism responsible for the FLASH effect and how the size of the effect depends on tissue type, microenvironment, and immune system. While there is still some way to go before we have these answers, understand how FLASH works, and have the technical ability to fully utilise FLASH-RT clinically, clinical trials are already up and running, albeit in few institutions, with small patient numbers and, so far, limited to early-phase (I and II) trials.

For the medical physicist, the ultra-fast delivery of FLASH radiotherapy brings many unique technical and physical challenges that remain to be solved before considering a large-scale adoption of the technique. This includes developing treatment machines that are capable of delivering radiotherapy with the required temporal beam structure in a clinical setting, with high safety and good dosimetric and geometrical accuracy, and establishing robust procedures for the delivery of FLASH in the preclinical and clinical setting.

Further work in this area is still needed to ensure a safe and accurate delivery of the prescribed dose to the patient, and to guide the continued efforts towards clinical translation of FLASH radiotherapy.

Elise Konradsson *PhD and* ***Professor Crister Ceberg*** *work in Medical Radiation Physics at Lund University, Sweden, and Research Group Leader* ***Kristoffer Petersson*** *works in Radiation Physics at Skåne University Hospital, Lund, Sweden and the Oxford Institute for Radiation Oncology at the University of Oxford.*

PART II

IMPROVING A SLEEP SERVICE THROUGH TECHNOLOGY

After outlining the development of a new suite of software and hardware for an overnight oximetry service in our Spring cover feature, we now look at its implementation at the James Cook University Hospital.

The new sleep system that was developed by the clinical measurement team was implemented on 31 May 2023 and, to date, has managed 308 new appointments for 307 new patients. The new system consisted of:

- A sleep desktop (SleepTalk) application that allowed healthcare science assistants to register the clinic to the new database.
- A web application (SleepWeb) to manage the clinic, the appointment and the issuing of equipment.
- A barcode scanner system to track the return of equipment that has been issued in the clinic.

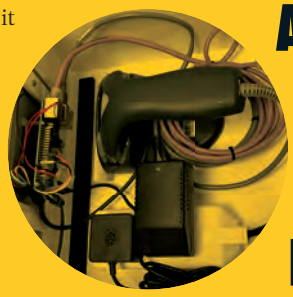
The sleep desktop application is the tool that was developed to communicate with the hospital's patient administration system (PAS) CaMIS, which is used to

IMAGES: IKON

organise patient's appointments. The tool extracts the patient's demographics and appointment data from CaMIS and loads it into the SQL Server 2008 R2 Database, which stores the new normalised tables for the new system. After the clinic has been registered, it then appears on the Sleep Web application.

The patient's appointment can then be managed, including the issuing of equipment for tracking. The system also allows staff to enter appointment comments, and automatically generates comments for SMS consent and equipment issuing.

The patient takes the equipment home, wears it for two nights and returns it back to the hospital's main reception. At the reception, there is now a barcode scanner that allows the patient to scan their equipment back before placing the equipment into the collection box. This scanning then notifies staff the equipment has been returned and is ready for downloading. The system also shows equipment that is still outstanding.



> "THE GOAL IS TO CREATE A COMPLETE SLEEP MANAGEMENT SYSTEM COVERING ALL DIAGNOSTIC TESTS

A success

Technical implementation was overall a success. However, we had some concerns around the barcode scanner overheating. This led to us delaying the roll-out of the barcode scanner by one week. We ran the barcode scanner for one week within the department, with extra cooling to monitor the heat. After we were satisfied, we moved the barcode scanner to the hospital's main reception where it has remained operational.

Darren, a Healthcare Science Assistant who prepares and issues the oximeters to our patients, commented: "The introduction of the new sleep website has made noticeable improvements to my workload. I can now immediately see the current status of our pulse oximeters, such as whenever a box is returned ready for downloading. It also provides me with a traceable chain as we now electronically issue the devices in clinic, which are then flagged as in use until the patient scans the device back in at reception. This means it is much easier to notice whenever a box is not returned so that we can attempt to contact the patient. Prior to the website, some of these may have been missed as we were very reliant on paper records. The site also helps to link the entire oximetry pathway together as I can both issue boxes and upload results through the same site, without having to use a variety of systems."

Sleep consultant feedback

The primary use case for the sleep clinicians is to review the results.

The feedback from the sleep consultants on accessing the results has so far been positive. The Clinical Lead for Sleep said: "It is very helpful to be able to see the list of clinician clinics by date, I am now able to see what other clinics are happening on the same day as mine."

The Clinical Lead for Sleep provided some useful feedback on how she uses the system, which has informed the next iteration of the sleep database, particularly the way that she prepares for her clinic.

Challenges

A major challenge is that the PAS CaMIS locks the clinic on the day of the appointment. This means that SleepTalk (the desktop application) cannot register patients on the same day if they are added to the clinic. Fortunately, this was picked up during testing prior to going live. To resolve this, we created a method of manually registering patients and creating a random appointment code. This then later syncs with the database to update the appointment code to the one stored in the PAS. For new same-day patients, they continue to be registered manually and there is no current resolution for this.

Despite this challenge, Clinical Scientist Alistair, who is responsible for performing quality checking of results, said: "I was able to intuitively register a new patient with the on-screen instructions guiding me through the process, allowing me to register a same-day urgent patient for oximetry."

Another challenge was communicating with information governance (IG). We completed all the appropriate IG documentation (such as the Data Protection Impact Assessment). However, we did not receive any response or feedback.

Conclusions

Despite some challenges, the feedback from all the users has been positive. There is some feedback which will help inform the next

iteration. The system has remained operational and has processed over 300 appointments. It has also improved several workflows for clinical measurement. We have focused on automating some of the work and creating a task-driven system. For example, once a Clinical Scientist has performed quality control of a study, it now creates a task for the healthcare science assistant to send a text message to a patient to notify that we have received their equipment and passed the results on to the consultant. Previously, the Clinical Scientist would need to email the healthcare science assistant to do this. It now also automatically notifies the healthcare science assistant to rebook an appointment should an oximetry test fail, or to upload results to clinical noting systems where necessary.

Furthermore, the system provides an overview of activity that can be used as key performance indicators (KPIs) – see graphic, left.

Future work

A future improvement for the barcode scanner is to include a 'heartbeat' feature, allowing the barcode scanner to send its latest IP to a server so that the web application can monitor the device's network uptime and alert us if the device loses connection, or is turned off. Interestingly, we have noticed that the 24/7 reception is not staffed 24/7 and sometimes patients do not scan the equipment back in. There is a way to manually return the equipment in the system should a patient not scan the equipment back in themselves. However, it would be useful to know if the barcode scanner is either losing connection or is being turned off at certain times on an evening or weekend. A heartbeat and logging feature could help with this.

Furthermore, I would like to perform a contextual inquiry study of how the clinicians are using the system to inform further design work of the system, which will include the ability for consultants to assign tasks to other staff.

We would also like to take advantage of the Gov.uk Notify API to allow automatic text messaging of patients, completing automating the text messaging workflow.

Due to the success of the system and the changes in the local sleep service, we are considering adding more functionality to manage other sleep diagnostics tests such as the home respiratory sleep studies. The goal is now to create a complete sleep management system covering all diagnostic tests.

Andrew Simpson *is a Clinical Scientist and* ***Tony Alton*** *is a Clinical Technologist. Both are based at The James Cook University Hospital.*

SMART PROSTHETIC LINERS

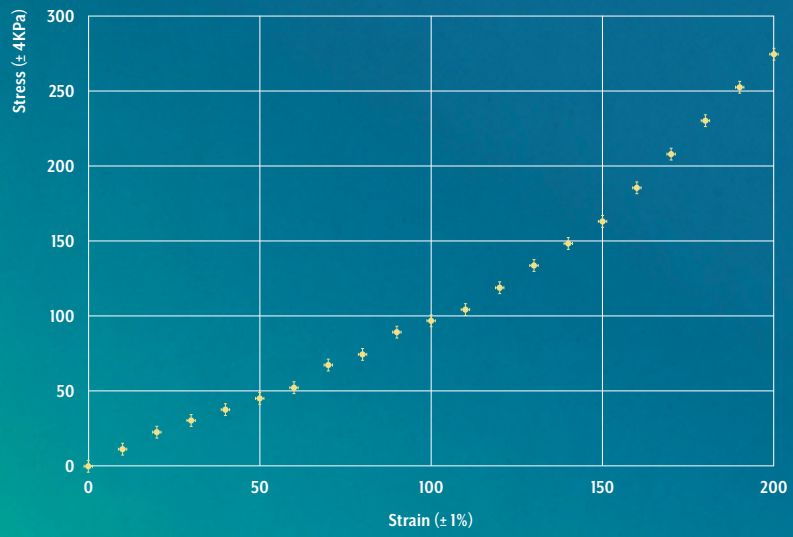
Exploring additive manufacturing techniques

Ben Oldfrey discusses his team's proof-of-concept experiments to tackle comfort in lower limb prosthetics, which won the Jack Perkins Prize for Best Paper in Medical Engineering and Physics.

Elastomeric liners are commonly worn between socket and limb by lower and upper limb prosthetic wearers. This is due to their superior skin adhesion, load distribution and their ability to form a seal. Laboratory tests suggest that elastomeric liners allow reduced shear stress on the skin and give a higher cushioning effect on bony prominences, since they are soft in compression and similar to biological tissues. However, they also increase perspiration, reducing hygiene and increasing skin irritations. Lower limb prosthetic users often particularly face a myriad of dermatological problems such as ulcers, cysts, and contact dermatitis, which are exacerbated by the closed environment of a fitted socket where perspiration is trapped and bacteria can proliferate.

To combat these problems, overheating needs to be addressed. Previous work has shown that for effective thermal management of the socket environment, an active heat removal system is required, yet this is not available. Added to this, liners are not currently designed specifically to fit an individual; it is thought a smart liner that could conform to the residuum

Figure 1 Stress-Strain Curve of Liner Sensor



more accurately, may improve the skin health at the stump-socket interface, and improve topological tracking potential.

A smart liner that can monitor stress states at the stump-socket interface could also help inform re-fit schedules, especially for children. This could be used as a diagnostic tool for monitoring the changes that occur across the day for all users, which depend on activity level, position, and the interaction forces of the prosthetic socket with the limb. To retain the comfort properties of the liner, this would require sensors to be mechanically similar to the liner body, i.e. flexible and pliable, and also thin.

Additive manufacturing is a promising technology to develop a smart liner. It has seen great advances over the past few decades, addressing the need for customisation and efficient one-off production. Printing of soft materials, however, lags behind those developed for rigid materials. One reason for this is that layer-by-layer printing requires the printed object and its support structure to bear the weight of the following layers. This simply does not work for the very low-modulus elastomers we require without warping of the geometry. Another problem with this approach for elastomers is that the cure time of elastomer resins are measured in minutes, even for the most rapid. This would mean long waits between layers to allow for the molecular cross-linking required to maintain elasticity.

This article overviews a set of proof-of-concept experiments that aim to address these various challenges.

3D printed nanocomposite stretch sensor

Stretch sensors here are defined as measuring the in-plane strain of a desired surface. Two common ways to achieve stretch sensing is through measurement of resistance or capacitance as it changes with strain. The advantage of resistive flexible sensors are their relative simplicity and stability for large strain in excess of 100%. However, they tend to be highly non-linear and hysteretic. The two most common complex behaviours being relaxation time and the resistance spikes associated with fast changes in strain rate. There are two major mechanisms by which piezoresistive behaviour is useful for stretch sensing to be achieved. These are: (1) by doping an elastomer matrix with a conductive filler of some kind – this is primarily a nanoscale effect; and (2) by constructing a conductive pathway which undergoes a significant enough geometrical change under stretch that the resistance also changes - this is primarily a macroscale effect.

The printed sensors we discuss here, made from carbon nanotubes and ecoflex silicone (CNT-Ecoflex) are a development from our previous work calibrating sensors made from commercially-available sensors. Materially, the CNT-Ecoflex is most similar to the Adafruit rubber (also being made of carbon nanoparticles and rubber) tested in a previous paper, however, the CNT-Ecoflex sensors had two key differences. These were: (a) the active pathway was printed in a serpentine wave pattern as opposed to just a straight line, and (b) it was encapsulated in an elastic substrate of lesser stiffness. The wave pattern results in a reduction of the overall molecular strain across the entire sensor by allowing transverse strain to occur in place of strain parallel to the bulk strain direction. It is assumed that

Figure ❷ Fabrication of an embedded active cooling system

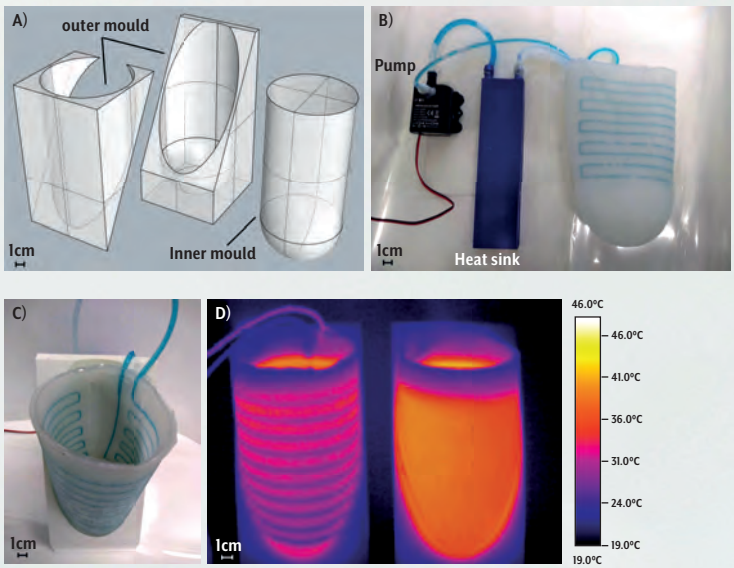


Figure ❸ The inner and removable outer sections of the liner mould

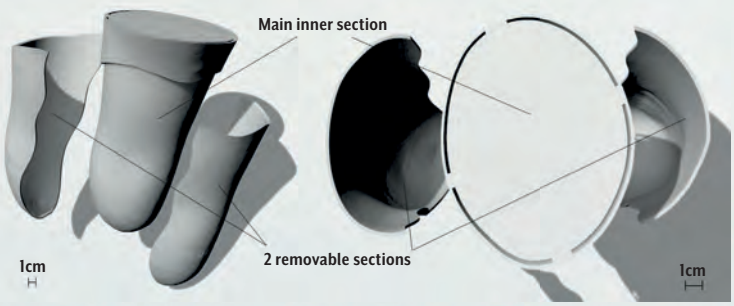
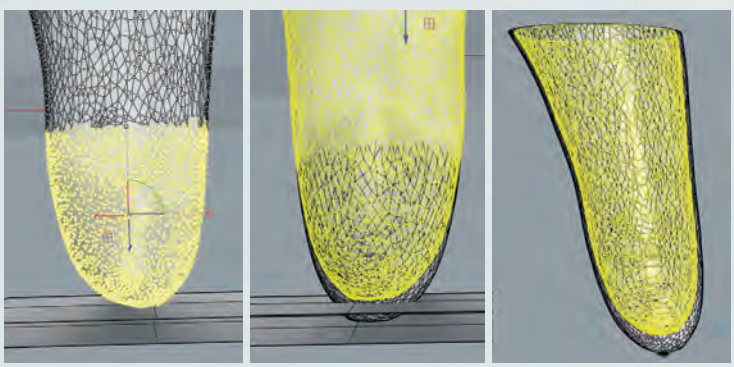


Figure ❹ 3D scan data used to produce 3D-printed mould for bespoke socket liner



this overall reduction in bulk strain to the active sensor body reduces the nonlinearity of the sensor, which we show by comparing between the Pearson Correlation Coefficient of the raw training results of the Adafruit rubber – our CNT-Ecoflex sensors have an average of 0.73 compared to 0.60. The macrostructural simplicity of the sensor still allows good learning of behaviour, even at much larger strains compared to the commercial materials. The CNT-Ecoflex sensors show themselves to be superior to when we look at the Full Scale Error, the lowest achieved was 4.68% range, compared to 7.17% range achieved with the Techniktex 1D Sensor and 9.53% range for the Adafruit rubber sensor. The wave pattern is assumed to have aided this accuracy over an extended range.

The calibration method uses Long Short Term Memory Recurrent Neural Networks (LSTMs), which were chosen in part due to their ability to learn behaviour in the time domain, and therefore the time-dependent hysteresis found in these materials. A full description of this calibration method can be found in our previous paper by Oldfrey et al., where we developed the method using commercially-available materials. The datasets were used to train the LSTM architecture for around 14 hours following an automated training schedule.

3D-printed mould from 3D scan data

A 3D scan of the user's residual limb was taken using a handheld 3D scanner at Stanmore Royal National Orthopaedic Hospital. Using the Rhino CAD software package, the scan file was then sliced to isolate the leg portion, and some artefacts present in the mesh from a fabric covering the residual limb were removed. The fabric sleeve was used to improve the reflective properties of the surface of the leg. It is this digital shape that is used to produce a bespoke fitting liner that conforms perfectly to the user's leg on the inner surface. The outer surface of the liner is defined by 2mm thick in the transverse plane, smoothly expanding to 10mm thick at the distal end. The thicknesses of commercially-available non-bespoke socket liners vary and are chosen by personal preference, these values were suggested by the prosthetist team at Stanmore, as well as being scaled down by 5% in the transverse plane of the limb, with no scaling in the longitudinal direction, to aid in fit. It is clear, however, that this liner is very basic in its structure; modern liners generally comprise multiple materials adding various structural and mechanical properties. The liner produced represents a starting point to creating bespoke liner geometries for the future.

Embedding a growth/volume sensor

A pre-fabricated 1D stretch sensor was then embedded in the bespoke liner by placing it in the mould prior to

"THE FLUIDIC CHANNEL PRINTING METHOD IS NOVEL AND COULD BE APPLIED TO OTHER APPLICATIONS

recasting the liner. This was done by drilling holes through the outer mould, at points measured to match the sensor length. The connecting elastic ribbon wires from the sensors were then pushed through the holes and sealed over with putty to stop the silicone from leaking out during the process. The mould was then filled, and left to set for four hours, producing the growth tracking liner. Once the sensor-embedded liner was created, the calibration process was completed following the same method as previously used for the 1D sensor experiments. The sensor was manually stretched and relaxed for up to 15 minutes under the webcam, producing a large set of data points of strain vs resistance. The sensor stretching is done by hand, well representing real-world strain behaviour.

The sensor was successfully embedded in the liner, however, improvements need to be made to make this a useful approach for outside the lab. The electrode placement still presented noise and could be improved to stabilise the sensor signal. When filling, the moulding method resulted in bubbles being trapped in the liner (only for the sensor-embedded liner), so improving the insertion method for pouring the silicone into the mould and degassing in a state that would allow trapped air to escape more effectively is needed. What we have shown is the potential use of this system to measure circumferential change in a liner, which could be applied to any sensor placement. The sensor placement here is an estimation of the midpoint of the longitudinal axis of the liner; future alternative positioning may be beneficial. The study has shown the potential advantages in the use of pre-trained neural network models as the starting point for various applications. The liner sensor embedded here – as it was the same geometry as the previous 1D CNT-Ecoflex sensors produced – re-trained in a significantly reduced timeframe. Further experiments can be done to explore the nature of this transfer-learning approach. Transfer learning could also be applied to re-training liners after damage, as the stresses placed on socket liners is high, and their robustness must be considered. The liner CNT-Ecoflex stretch sensor showed a potential range of stress measurement of 0–274kPa over a strain range of 0–200%.

Embedded active cooling system

Previous work has shown the need for active cooling in the socket, as opposed to passive cooling, where simple material choices attempt to improve heat transfer out of the socket. We have demonstrated the fabrication of an embedded active cooling system for socket liners. It comprises a single unbroken fluidic channel that enters the liner from the proximal edge and travels directly to the distal end of the cylindrical section of the liner and then traverses the circumference of the liner back and forth, rising until it exits the liner adjacent to the entry point. For this proof-of-concept prototype, we have used a scaled down mini-liner. The control and cooling liner were placed in front of a thermal camera to show the thermal behaviour of the device. A snapshot of this cooling can be seen in figure 1. The intake to the liner is seen to be blue, leading to the lower cooling rings being coolest, increasing in temperature as the cooling fluid flows upwards and the out-take is seen as bright pink, indicating the active removal of heat from the system.

This is an early stage of development of this system and it needs more in-depth testing, particularly inside a socket, however, we believe that the potential for active heat removal can be seen. The fluidic channel printing method is novel and could be applied to other applications, both inside liners or in other soft devices. Investigation into optimum channel geometries and how they will affect the integrity of the liner is further work. The placement and connection to the heatsink is a difficult problem that also needs to be addressed. Finally, further investigation into the potential robustness of the cooling system needs to be addressed, given the challenging in-socket environment.

IMAGES: GETTY/ALAMY

The next stages

We hope that this ensemble of methods and results using soft materials to create active technologies encourages further exploration of embedded functions in prosthetic liners. Currently, our group is working on creating a user-testable version of the cooling liner and novel methods for stiffness-graded elastomer interfaces between socket and limb, with optimisation of the design via finite element modelling of an upper limb prosthesis user. Updates on these will be hopefully be in publication towards the end of this year.

Ben Oldfrey *is a Research Fellow working between the Global Disability Innovation Hub and the Institute of Making at UCL. The paper on which this article is based was awarded the Jack Perkins Prize for Best Paper in Medical Engineering and Physics at IPEM's Science Technology and Engineering Forum (STEF), held in Glasgow earlier this year. Ben's co-authors on the paper were* ***Ania Tchorzewska****, Institute of Making, UCL;* ***Dr Richard Jackson****, Institute of Making, UCL;* ***Mark Croysdale****, Royal National Orthopaedic Hospital, Stanmore, UK;* ***Prof Rui Loureiro****, Aspire Create, UCL;* ***Prof Cathy Holloway****, Global Disability Innovation Hub, UCL; and* ***Prof Mark Miodownik****, Institute of Making, UCL.*

ALPHA DART

Using alpha particles to treat solid tumours

A team from Cambridge looks at setting up Diffusing Alpha-emitters Radiation Therapy (Alpha DaRT) for Vulva Cancer.

Carcinoma of the vulva is rare. It makes up just 3–5% of gynaecological cancers and generally occurs in the elderly. Most are squamous cell carcinoma (85–90%). The current treatment option is surgery, often followed by concurrent chemo-radiotherapy. There is high morbidity associated with radiotherapy. Acute toxicity of radiotherapy has been reported by van Triest et al in 2021.

- Skin ≥ Grade 2 92%
- Skin ≥ Grade 3 54%
- Pain ≥ Grade 3 37%

Emerging evidence from a new study published by the Alpha Tau Medical team using alpha particles – Alpha DaRT – was of significant interest to try to improve the options for patients with vulva cancer. The potential benefits being:

- To downstage the primary with minimal morbidity resulting in less extensive (or no) surgery
- To improve local control
- Abscopal effect on distant disease (nodes/metastases)
- Less post-operative radiotherapy and associated morbidity.

Alpha particles are known to be very destructive to tumour cells. They cause direct, irreparable damage to the cell DNA and lead to cell death. However, the range of alpha particles in tissue is very limited. Therefore, until now, it was not possible to use alpha particles as a locally delivered treatment for solid tumours.

Technology and technique

The Alpha DaRT technology relies on the diffusion of atoms that emit alpha particles within the tumour tissue, in order to overcome the short-range limitation of the alpha particles themselves. The extended range that the alpha radiation can reach enables the potential treatment of the entire tumour.

Alpha DaRT technology is based on small quantities of Radium-224 (^{224}Ra) affixed to metal sources that are inserted directly into the tumour. When ^{224}Ra decays, it releases further radioactive progeny with short half-lives that diffuse through the tumour. These atoms emit additional short-range alpha radiation that damages and kills cancer cells within a short period of time.

The surgical insertion technique:

- The Alpha DaRT source is made of stainless steel
- The ^{224}Ra is embedded on the source surface
- The Alpha DaRT sources are strung on a biocompatible suture.

Alpha needle applicators are used to place sources. Fixation of the suture at the skin surface is simple and fast.

The distribution of radioactive atoms inside the tumor has direct correlation with the necrotic areas they cause.

A feasibility study for 10 patients at Cambridge University Hospitals NHS Foundation Trust (CUH), with the primary end-point being tolerability (treatment completed as planned) was accepted by the MHRA in March 2023. The first clinical patient was treated in May 2023.

Radiation safety, regulatory compliance and commissioning

There are a number of novel aspects to Alpha DaRT that impact on its introduction into clinical use from a physics perspective.

Alpha DaRT starts as a sealed source device and is only considered unsealed once applied inside the tumour, when the radioactive progeny are able to diffuse. While the methodology of inserting the applicators is similar to a brachytherapy technique, the mechanism of action of DaRT is completely distinct from that of brachytherapy.

> THESE ATOMS EMIT SHORT-RANGE ALPHA RADIATION THAT DAMAGES AND KILLS CANCER CELLS

Therefore, clinical introduction required the involvement of three teams of medical physicists:

Radiation protection to ensure compliance with UK regulations.

Nuclear medicine to provide expertise on unsealed source therapy: radioassay of the applicators and patient blood and urine samples, and systems of control for theatre and ward.

Radiotherapy to provide expertise on brachytherapy and commissioning and planning using alpha dosimetry.

It was important for us all to first understand the physics of the decay scheme of the DaRT sources.

The ^{224}Ra is produced in a ^{228}Th generator. No ^{228}Th is present in the ^{224}Ra sources.

^{220}Rn is a short-lived gas, so highly dispersible. Depending on the trajectory of the emitted alpha particle, either ^{220}Rn, ^{216}Po or ^{212}Pb daughters can "escape" from surface of source. As the half-lives of the progeny are much shorter than that of ^{224}Ra, the daughter products remain in secular equilibrium with ^{224}Ra. The only significant half-life in the decay chain is that of ^{212}Pb (10.6 hrs). Once daughters are released from the source into the body, ^{212}Pb therefore becomes the head of the decay chain and is the dominant radionuclide in any samples such as blood and urine. The radioactive progeny emit a range of α, β and γ radiation, so contamination is readily detectable.

Regulatory compliance

Radiation protection physicists began the process of ensuring compliance with UK regulations for this first application of Alpha DaRT in the UK. There are three sets of regulations applicable to the introduction of DaRT: the Environmental Permitting Regulations 2016 (EPR16), the Ionising Radiations Regulations 2017 (IRR17) and the Ionising Radiation (Medical Exposure) Regulations 2017 (IRMER17).

EPR16 governs the keeping and use of radioactive material and the accumulation and disposal of radioactive waste, with the aim to protect the public and the environment from hazards associated with radioactive material/waste. EPR permits are issued for sealed and unsealed sources.

IMAGES: SHUTTERSTOCK

EPR16 actions specific to DaRT were identified as:

Source designation: Alpha Tau ships the sources in airtight applicators, as *sealed sources*. They become *unsealed sources* when removed from applicators. Agreement was obtained from the Environment Agency (EA) that designation should be in accordance with the CUH *unsealed* EPR permit.

The CUH permit's "any other" category for holding radioactive material prior to and during source use allows up 6 GBq of miscellaneous radionuclides. Nuclear medicine had already allocated 4 GBq of this for ^{223}Ra, ^{75}Se and ^{125}I. This left adequate capacity for ^{224}Ra. The shipment of sources for the first clinical patient totalled 191 sources, and a total of less than 30 MBq.

The CUH permit allows for the accumulation of solid waste (unused applicators, removed sources and contaminated items) to decay for a maximum of 14 days for up to 100 GBq of ^{212}Pb ($T_{½}$ = 10.6 hours) and six months for up to 10 GBq of ^{224}Ra ($T_{½}$ = 3.6 days). In practice, two months is sufficient to ensure all ^{224}Ra products have become inert.

If ^{224}Ra from opened applicators is present in the waste, it must be stored in water in an airtight container to contain any potentially dispersible ^{220}Rn. Unopened, spare applicators are considered sealed, hence can be stored to decay without water. If ^{224}Ra is not present, it is stored as ^{212}Pb and there is no risk from ^{220}Rn.

Patient urine contains ^{212}Pb and its daughters, but should not contain any ^{224}Ra. As ^{212}Pb is a beta emitter, this aqueous waste is managed under the *Any Other Beta* allowance of 2 GBq per month.

Nuclear medicine uses IPEM excretion factors for common diagnostic and therapeutic radiopharmaceuticals. Factors depend on the radiopharmaceutical and patient physiology, and can be determined analytically and/or experimentally.

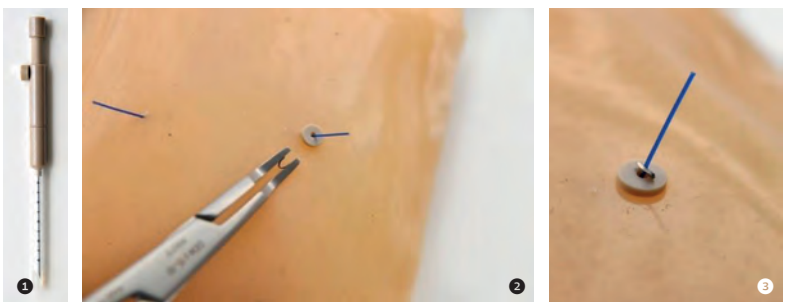
It was necessary to determine a conservative estimate of the excretion factor from Alpha Tau data, and then seek EA approval because ^{224}Ra / ^{212}Pb excretion factors are not included in the IPEM list. Using a default of 100% would have caused issues, due to the already high environmental impact on the CUH site from ^{177}Lu, ^{223}Ra and ^{131}I therapies.

Based on the analytic methodology used initially, a very conservative figure of 4% was agreed with the EA:

Fraction of ^{212}Pb excreted in urine	=	Administered ^{224}Ra activity A_0	*	probability decay will result in ^{212}Pb atom escaping source [0.6] f_d	*	probability ^{212}Pb leaks from tumour into blood stream [0.6] f_t	*	probability of ^{212}Pb transferring from blood plasma into urine

This was confirmed with subsequent Alpha Tau

Figure ❶ An Alpha DaRT needle applicator. **Figure ❷** Suture in situ under the skin
Figure ❸ Fixation of the suture at the skin surface using micro clips and buttons



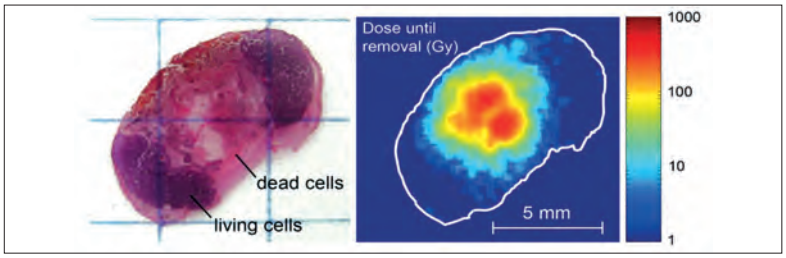


Figure ❹ (left) Hematoxylin-eosin (H&E) stained 5µm section taken from a SCC tumor treated with a 224Ra Alpha DaRT source. Darker (purple) regions in are composed of viable cells, lighter (pink) regions are necrotic. (right) The radiation pattern of the same section. (Lior Arazi and Tomer Cooks – courtesy of Alpha Tau)

Figure ❺ The ^{224}Ra decay chain. Data taken from the NuDat3 database website

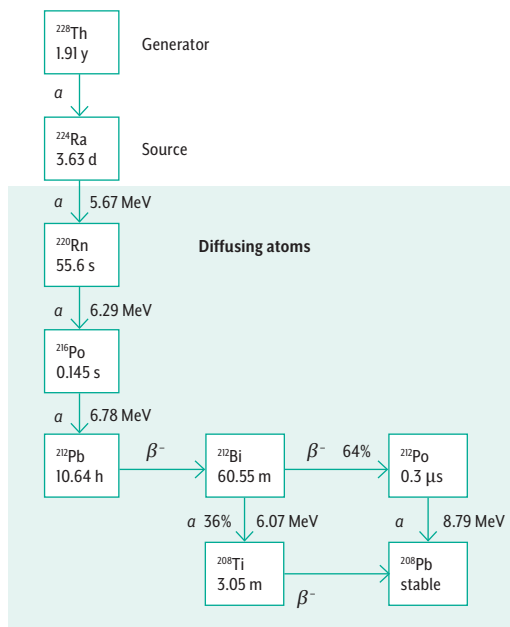


Figure ❻ The radioassay calibration jig and applicator holder

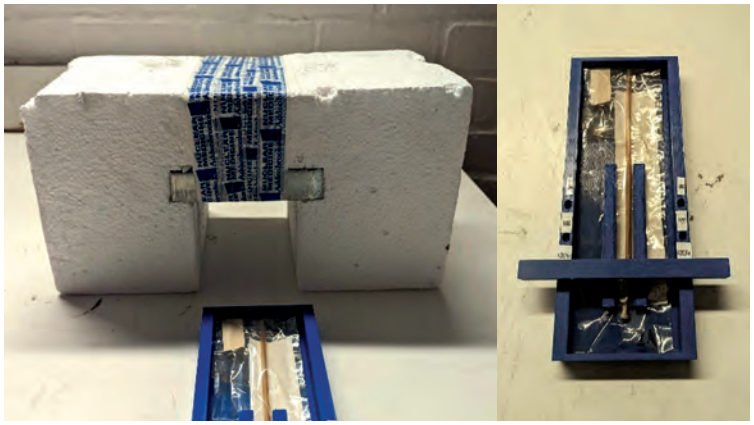
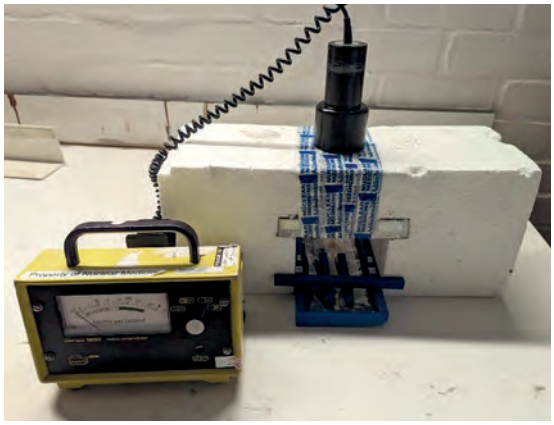


Figure ❼ Monitor set-up for the radioassay calibration jig



experimental data from urine measurements, estimating 0.005 kBq ^{212}Pb per litre of urine per kBq of ^{224}Ra inserted to the tumour. Assuming 1–2 litres of urine output per day, this is 0.5-1%.

IRR17 governs all work with ionising radiation, including work in high-radon areas, with the aim to minimise radiation exposures to staff and public.

IRR17 actions specific to DaRT were identified as:

- Confirmation that HSE consent for radioactive administrations were already in place for nuclear medicine and brachytherapy.
- Radiation risk assessments identified a number of action points: that local rules with RPSs were required, that some staff monitoring was required, that theatre should be designated a controlled area until post-implant/removal monitoring confirms no lost sources or contamination present. Contamination monitoring to be performed using alpha and gamma detectors. During their hospital stay, in-patients should be kept in a side room with en suite and designated as controlled areas. In-patient hospitalisation is not always required and appropriate radiation advice will be given to patients returning home.

Specific contingencies were identified which required contingency plans referenced in the local rules. These included sources coming loose, spills of patient blood and urine, lost sources, and sources left inside the patient following the removal procedure.

IR(ME)R17 governs exposures of ionising radiation associated with medical uses including research, and aims to optimise radiation exposure to patients and volunteers.

IR(ME)R17 actions specific to DaRT were identified:

- Ethics approval was obtained for the Participant Information Sheet.
- ARSAC study approval, with CUH as sponsor.
- ARSAC employer licence for CUH updated to specify "^{224}Ra-148-149 ^{224}Ra seeds for the Treatment of Squamous Cell Carcinoma of the Vulva".
- ARSAC practitioner licence updated to include the study.
- Confirmation that appropriate IRMER employer's procedures were in place in radiotherapy.

Commissioning for clinical use

With regulatory permissions in place, commissioning could proceed. This involved:

- Calibration for the radioassay of applicators.
- Calibration for the radioassay of patient samples.
- Commissioning the planning system.

Radioassay of applicators: Applicators are calibrated prior to delivery. They arrive encased in sterile plastic packaging that should not be opened prior to use in theatre. Hence, the local assay is not a definitive calibration. The aim is to verify that the activity received matches the label to within a reasonable tolerance, i.e. that the number of sources indicated is correct. This is done by measuring the gamma

"IRR17 GOVERNS ALL WORK WITH IONISING RADIATION, INCLUDING WORK IN HIGH-RADON AREAS

emissions: ^{224}Ra: 241 keV (4.1%) and ^{212}Pb: 239 keV (43.6%).

To calibrate the radioassay system, three applicators containing one, three and six sources were measured and a plot of cps vs kBq was drawn. This was repeated for all available contamination monitors. The plot equation was used to verify applicator activity prior to implantation.

Radioassay of patient blood and urine samples: Patient blood and urine are assessed for radioactivity during the treatment period. Data from other DaRT trials indicated activity concentrations in the Bq/g range that were suitable for measurement in a local sample counter. As ^{212}Pb has a short half life (10.6 hours), it is not possible to obtain a calibration source of pure ^{212}Pb. The assay method is to use a ^{224}Ra source and calculate how much ^{212}Pb there is. Alpha Tau provided a sealed calibration source in resin.

The calibration source reached secular equilibrium

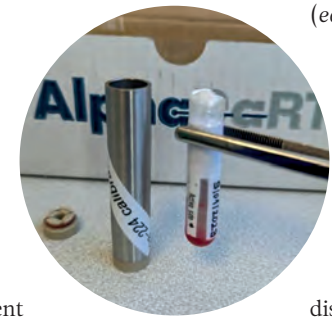


Figure ❽ Sealed calibration source ^{224}Ra in resin

(*equal amounts of ^{224}Ra and ^{212}Pb*), such that:

$A_{212Pb} = 1.138 \times A_{224Ra}$

The calibration source has an accurate ^{224}Ra activity, allowing calculation of ^{212}Pb activity [Bq]

The relationship between ^{224}Ra activity and detected cps:

$CPS_{224Ra} = [0.041 + (0.435 \times 1.138)] \times A_{224Ra} \times \epsilon_{detection}$

where 0.041, 0.435 = branching fractions (^{224}Ra for 241 keV, ^{212}Pb 239 keV γ respectively)

$\epsilon_{detection}$ = detection efficiency [cps/radioactive disintegrations per sec]

Count ^{224}Ra source to find $\epsilon_{detection}$

For a sample containing only ^{212}Pb, the relationship would be:

$CPS_{212Pb} = 0.435 \times A_{212Pb} \times \epsilon_{detection}$

By using the detection efficiency and the CPS of the measured source, one can extract the activity of ^{212}Pb. Then, the conversion factor from CPS to Bq can be easily inferred (CPS measured divided by the calculated ^{212}Pb activity).

Commissioning the MIM Symphony Alpha DaRT planning system: In order to commission any treatment planning system (TPS) comparison should be made between the performance of the TPS with measured data, with known uncertainties associated with the measured data and with assessed inaccuracies in the planning algorithm. The performance is then assessed relative to criteria of acceptance, i.e. limits of accuracy. It is necessary to observe and record under what conditions the system is acceptable or not acceptable (specifically for DaRT, this requires assessing cold spots).

The dosimetry of a brachytherapy planning system generally relies on TG-43 formalism.

However, for DaRT alpha particles this formalism does not make sense for multiple reasons: There is no TG43 data for alpha-particles; A decay constant (with exponential decay of the dose-rate) cannot be applied for the alpha-sources with various decay products. Reference air kerma Rate (RAKR) which is numerically identical to the air-kerma strength 1 U= 1 μGym^2/h = 1 cGycm^2/h with a reference point, usually referred to 1m from the source, is impractical for DaRT treatment, as the dose is negligible there.

The DaRT tumour dose model was adapted to the TG43 formalism and incorporated into the MIM software. The details of how the DaRT model was cast into the TG43 formalism will be described in a separate future publication by Alpha Tau.

Commissioning of the planning system dosimetry, therefore, relied not on checking TG43 data, but on validation of the MIM axial and radial profile output against published data.

Figure ❾ Tests specific to brachytherapy, Table 4.4 IPEM81

Test	Range	Analysis
A. Source data		
Basic source data	(a) **Activity**	**Comparison** against manufacturers and published data
	(b) **Air kerma**	
	(c) **Tissue attenuation** and scatter factors	
	(d) **Half-life**	
B. Point doses and distributions		
	(a) **Single source**	**Dose or dose rate** along a line normal to the axis of the source at distances from centre of the source or sources of 0.5, 1.0, 2.0, 5.0, 7.0 cm. Dose distribution compared with publiched distributions
	(b) **Multiple sources**	
	(c) Standard source arrangements e.g. Manchester, Paris,dosimetry	
C. Source reconstruction		
Phantom with dummy sources	(a) **6 line sources**	**End-point coordinates** and source length
	(b) 12 seed/pellets	
	Manual and auto matching	
D. Coordinate translation and rotation		
	(a) **Sagittal and coronal planes**	Dose distributions compared with published distribution. Repeat of test B (oblique plane only)
	(b) 30° oblique plane through a source inclined at 30° to the normal plane in test B	

Figure 10 Plot to determine equation activity measured by Alpha Tau @ implant time (kBq) vs counts measured in site detector calibration jig.

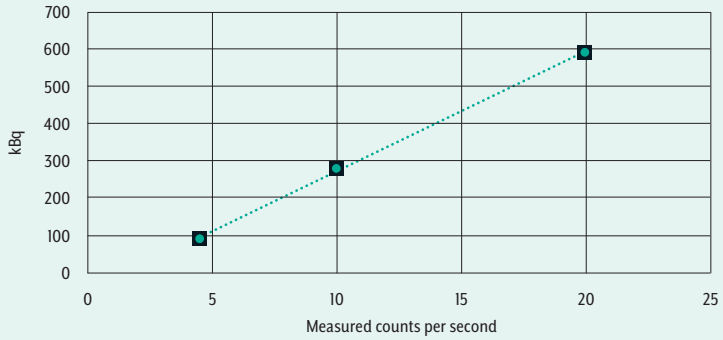


Figure 11 MIM treatment planning system versus COSMOL, radial profiles.

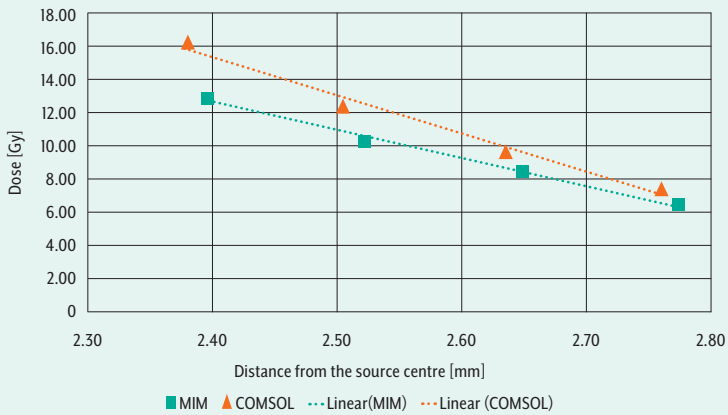
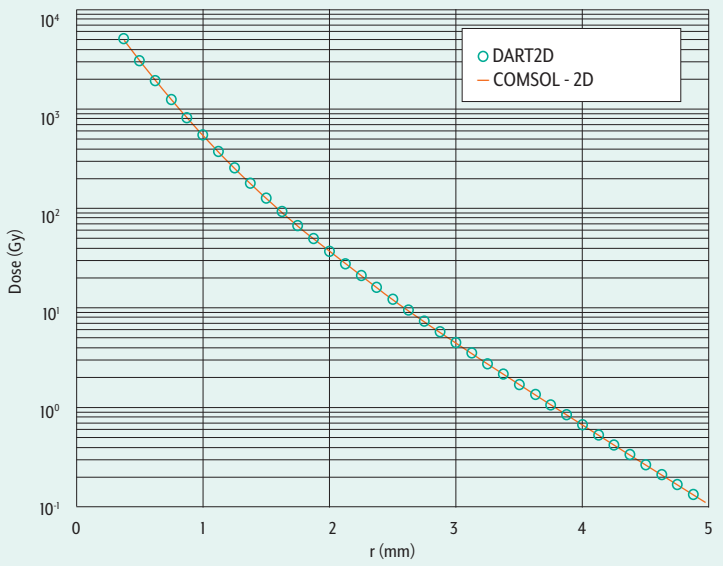


Figure 12 Total alpha particle dose calculated using DART2D and a 2D calculation in COMSOL MultiphysicsTM for the high-diffusion "lead-dominated" case.



Dose resolution and 10 Gy norm point

Distance of the 10 Gy point from the source centre was calculated using 1D data profiles from MIM with distances normalised to match 1 Gy point in COMSOL (radial profile). A 2nd order polynomial fit to 4 points around 10 Gy was applied and solved to estimate the 10 Gy point :

The calculated values for 10 Gy point (distance from the source centre) are MIM 2.53 mm and COSMOL 2.60 mm. The 1D line source dose calculation in MIM begins at the centre of the source – assuming the "surface" is located at the centre (origin is at r=0), whereas Heger *et al.* Med Phys 22 takes into account the actual source's radius (r=0.35 mm).

The current status of the dosimetry as presented in MIM therefore provides a slight underestimation of the spatial distribution of the dose in comparison to the latest 2D calculations. In practice, the dose overlap we apply is thus clinically slightly higher, providing us extra clinical reassurance that we will not have cold spots.

Results and conclusion

The first patient was recruited to the DaRT feasibility study for vulva cancer and successfully treated at CUH May 2023.

GTV ~3.5 cc and CTV~13.3 cc were outlined on diagnostic MR. 141 DaRT sources were inserted in theatre. The treatment plan was produced on CT, fused to MR and indicated excellent dose coverage to the GTV on Day 0, V100 =89%, D90 = 95% (9.5Gy), and minimal cold spot 0.06 ml, not deemed to be clinically significant.

Repeat CT planning on day 7 showed improved coverage with the reduction of postoperative oedema GTV V100 =97%, D90 ~200 % (20 Gy). No cold spots were identified.

Initial clinical response is very encouraging.

The newness of this technology and its first use in the UK and in the vulva gave the CUH physics team an exciting challenge. We hope we have now forged a path and identified a safe and comprehensive set-up method that will make it an easy and straightforward task for other UK centres to emulate.

***Dr Sarah Heard**, Head of Nuclear Medicine Physics; **Evelyn Shin**, Senior Nuclear Medicine Physicist; **Graham Whish**, Lead Clinical Scientist-Radiation Protection; **Diane Whitney**, Head of Brachytherapy Physics; **Dr Magdalena Klodowska**, Radiotherapy Physicist; **Dr Li Tee Tan**, Consultant Clinical Oncologist. All are based at Cambridge University Hospitals NHS Foundation Trust.*

For further information on DaRT and its implementation, visit bit.ly/DaRT

DIGITAL HEALTHCARE TECHNOLOGY

Imaging Systems Manager **Navinah Nundlall** discusses her role and work in the Digital Healthcare Technology Directorate.

In my 14 years of working in the NHS, I have developed and gained a multitude of skills and exposure across clinical, scientific and technology divisions. I'm a registered Clinical Scientist in Radiotherapy Physics/Clinical Computing, trained at Queen Elizabeth Hospital Birmingham (QEHB) and have now moved into the role of Imaging Systems Manager at University College London Hospitals (UCLH).

My team provides support and service within Imaging for different Imaging systems; mainly PACS (Picture Archiving and Communication System), VNA (Vendor Neutral Archive), transfers and receives images from different institutions, implements and supports post-processing imaging software, as well as AI tools, for research and trial purposes.

We play a major role in dealing with complex, high quantities of data that are readily available for research and development. The demand on the Imaging Systems team has been synonymous with the rate of referrals for cancer treatment and new sharing agreement between trusts across the North Central London (NCL) Hub. Previously managed by Imaging Division, as complexity of imaging devices and advancement in applications and services developed, the division required increased technical expertise and guidance. The team was fittingly transitioned to the Digital Healthcare Technology (DHCT) Division.

Risk management

We are a team that acts as a bridge between imaging demands and clinical system deployment. We help translate clinical and technological imaging requests/issues/impact between divisions and boards.

Whenever a new service or product arises that relates to imaging, we are consulted and are part of the process to ensure that they are clinically safe and effective for use. As part of the assessment and validation, DHCT use the two safety standards published by NHS Digital: DCB0129: Clinical Risk Management: Its Application in the Manufacture of Health IT Systems and DCB0160: Clinical Risk Management: Its Application in the Deployment and Use of Health IT Systems.

DCB0129 is the standard that manufacturers must comply to and are expected to share with the health organisation their clinical risk management assessment. This will provide the health organisation an insight into the safety controls the manufacturer has put in place to manage risks associated with the Health IT System (HIT). In addition to complying to this standard, manufacturers must also share their Digital Technology Assessment Criteria (DTAC). The DTAC (developed by NHSX and now known as NHS Transformation Directorate) is the national minimum baseline criteria that healthcare organisations use to assess suppliers in the procurement phase or, in this case, part of a due diligence process of implementing an HIT into the clinical workflow. It gives the healthcare organisation reassurance that the manufacturer is meeting the clinical safety, data protection, technical security, interoperability, usability and accessibility standards for this HIT.

DCB0160 is the standard that provides a set of requirements for the health organisation to establish a clinical safety management system within which clinical risks associated with the

IMAGES: SHUTTERSTOCK

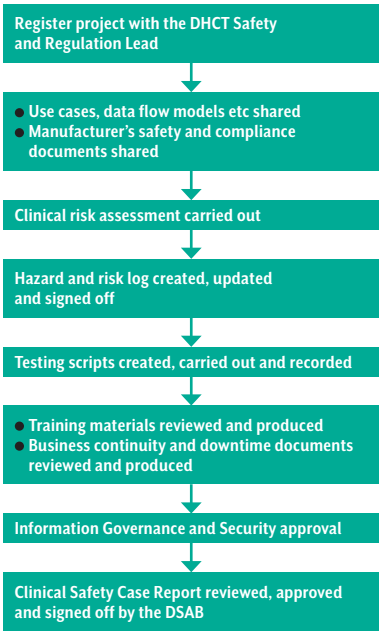
deployment, implementation, use and decommissioning of a new or modified HIT are appropriately managed.

Safety assurance

The safety assurance process at UCLH is overseen by a Digital Healthcare Safety Assurance Board (DSAB). The remit of the DSAB is to regularly review and approve safety case outputs developed during the implementation stages of DHCT projects. Having completed the NHS Digital safety training, I have reviewed Clinical Safety Case Reports (CSCR) as a Clinical Safety Officer (CSO). This involves providing an independent review of the report and raise any safety risks to the DSAB.

Our Information Governance and Security teams are involved in the latter stage of the process to review the Data Protection Impact Assessment (DPIA) form and data security management practice respectively. The DPIA form helps the manufacturer identify and show their action of minimising the data protection risks of implementing this HIT, where personal information is likely to result in a high risk to an individual. The requirement for such an assessment is a mandatory obligation under the General Data Protection Regulation (GDPR). Data security checks, such as encryption methods for data storage and transmission, access control and authentication mechanisms, incident response and disaster recovery plans in case of security breach or system failure, are all part of the validation. Presenting all these evidence on top of relevant certifications and compliance helps towards the trust in providing the assurance that they are practising good data security and that personal information is handled correctly. The Data Security and Protection Toolkit (DSPT) is an online assessment tool for trusts to measure their performance against the National Data Guardian's 10 data security standards.

Figure 1 Main stages of safety assurance process for new/modified HIT that is followed at UCLH



Working together

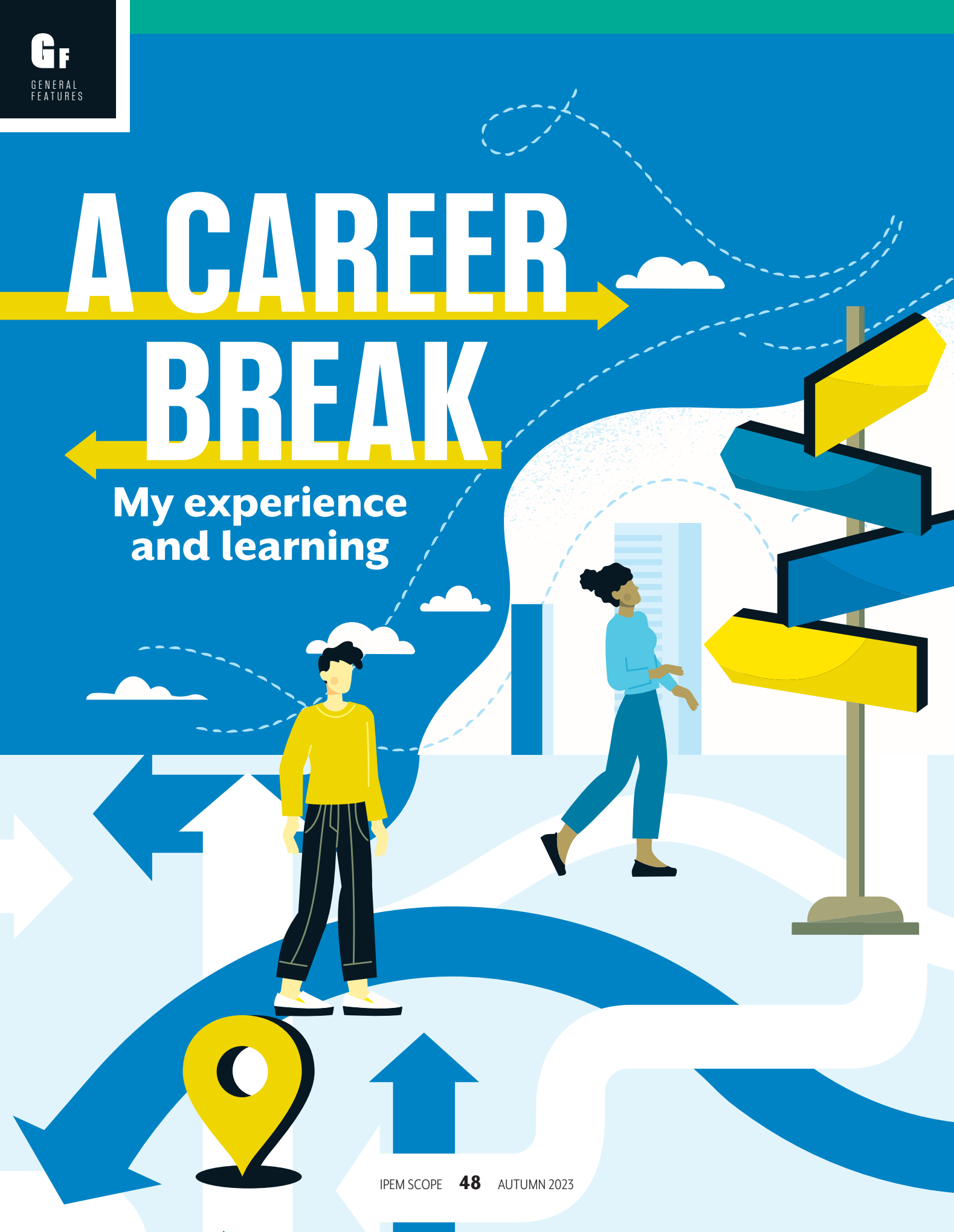
Our involvement in the process does not end there. Every project will require input and resource from our technical team within DHCT and our IT supplier. As a Subject Matter Expert (SME), I get heavily involved in working with our Business Engagement team and Technical Architect to understand the Imaging Department's requirement and vision of new development/projects. We all work together with the stakeholder who submits an SBAR-style (Situation Background Assessment Recommendation) document, which we review with a solution before submitting a work request to our IT supplier. Depending on the level of involvement, I either write the work request or review for the stakeholder. While all projects have a Project Manager, there is always the need for support from the SME. With the extra knowledge, understanding and impact of the service, I am involved in submitting change requests and supporting them in Change Advisory Board (CAB). My team are an integral part of end-to-end testing, communicating, and supporting the clinical stakeholders to an agreed level.

With more and more data accessible within trust systems, I am aware of the increased demand and profile of Digital Healthcare to deliver these requests. I understand the benefit of the data that resides within our systems and how it can improve patient treatment and experience. Throughout training as a Clinical Scientist and within my current post, I understand and ensure that I comply by the various statutory provisions and legislation to aid information governance framework. I follow the best practices while handling sensitive and personal information. I have a good understanding of the Standards of Proficiency for Clinical Scientists and I incorporate its ethos and guidelines into my professional ethics.

Navinah Nundlall *is Imaging Systems Manager and a Clinical Scientist in the Digital Healthcare Technology Directorate at University College London Hospitals NHS Foundation Trust*

A CAREER BREAK

My experience and learning



Matthew Gardner talks through putting his NHS career on hold to work on other projects and the impact it has had on his career and work as a scientist.

Having a couple of years to work on some different projects has refreshed my career and aspirations in a big way. I'm aware of how blessed and privileged I am to be able to experiment with my job roles. Following the pandemic and with better attitudes to flexible/hybrid working perhaps becoming the norm, maybe it's a good time to think about portfolio careers and the benefits they might bring. It likely wouldn't appeal to or work for everyone, but here I seek to share my experience of the benefits/consequences it's brought to myself and my employers.

Where I started

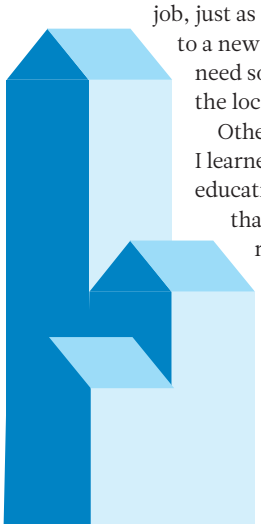
My first career started in a very standard way – I was part of the first cohort of medical physics trainees on the Scientist Training Programme (STP). Before that I did undergraduate physics and an MSc in medical physics. While I did then and still do agree wholeheartedly with what the STP seeks to achieve, I felt there were issues with the national and local implementations and a trainee voice should be heard in making improvements. This led to my joining IPEM's Trainee Panel and ending up as a trainee representative to the National School of Healthcare Science (NSHCS). It's from this early professional involvement that I first became interested in contributing to educational projects. After completion of the STP I worked as a Clinical Scientist in a radiation protection team for five years.

I also gradually became involved in voluntary side projects close to my heart, which I was finding increasingly rewarding. These included organising healthcare science outreach events in schools, becoming a Trustee of a local mental wellbeing charity and delivering events exploring the interface of science and faith in local churches (as for a couple of years I had wanted to do something combining my faith and scientific work). These projects needed more of my time and and I wasn't able to negotiate a part-time working arrangement that would give me enough time to develop external projects. So, to put it bluntly – I quit!

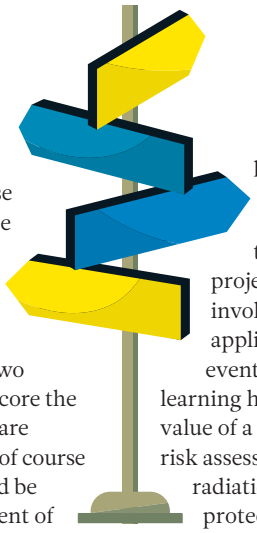
Taking a career break

I started my career break with a plan to work on a portfolio of educational projects. This was a combination of freelance work and setting up a social enterprise – specifically a Community Interest Company (CIC) – to run larger programmes. On the freelance side I started consulting with an exam board on the writing/review of curricula and examinations for technical qualifications in healthcare science. I also did similar work on the STP curriculum review. I found this fascinating. I had to be trained and learn about educational concepts I'd never really considered before. For example, threshold competence, I found, actually a very helpful concept. At first, it seems like the idea that a qualification or course should produce someone just about able to do the job i.e. meet the minimum standard. "Just about" and "minimum standard" doesn't sound good enough – surely we must aim for higher than that? But it really helped me focus on essentials. Anyone completing a qualification or course will need local training in their first job, just as anyone moving to a new workplace will need some time to learn the local practices.

Other useful concepts I learned about in the educational world are that of valid and reliable assessments. A good assessment will be both, but



IMAGES: ISTOCK



they often work against each other. Valid assessments are those that measure what is needed to be measured, i.e. they realistically reflect the role or work the qualification should prepare the learner for. Reliable assessments are consistent, i.e. two equally capable learners should score the same mark, even if the assessors are different. Once we get there, we of course have to consider logistics. It could be argued that a very valid assessment of work-based competence would be some sort of probationary period – if you can do the job for a time and not get dismissed then you must be able to do the job. But it might not be very reliable, because someone has to decide if you can do the job and that person might bring their personal opinions, they might consider the personal friendship or dislike of the learner or any other combination of factors.

Social enterprise

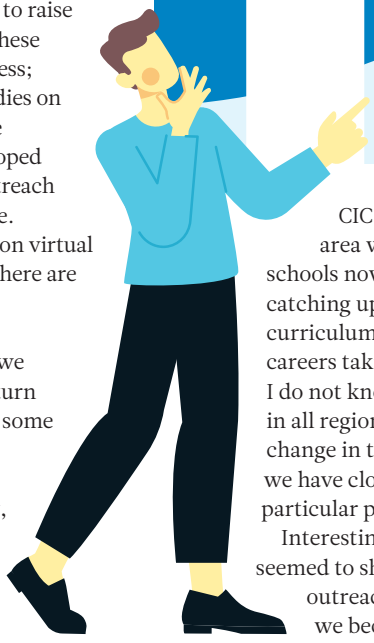
Beyond my freelance work there was also a social enterprise I co-founded, which had two quite distinct programmes to start with. The first was a programme of healthcare science careers workshops for schools. We worked with healthcare science staff and were helped by university students aspiring to a career in the sector. We were partially motivated by the very competitive nature of the STP recruitment process, for which having work experience is a major advantage. This is often (as I myself did as a student) an unpaid work experience placement – so we wanted to try and help by paying the students an hourly rate at the living wage for their involvement in outreach work. We hoped this would open the doors to work experience for those who wouldn't be able to work unpaid.

The other social enterprise programme was delivering science outreach for churches, and providing discussion-based explorations of the interface of science and faith. This can sometimes be seen as a challenging topic, but as a Christian and a scientist it's been important to me since the very start of my journey with faith. Using the lens of my experience in healthcare science we have been able to open very positive conversations about science and faith. Running this was full of valuable experiences that will affect how I think about projects going forward. I was involved in writing funding grant applications to deliver the first few events and pay for start up costs, learning how to convince funders of the value of a piece of work. We had to write risk assessments (not too bad for a former radiation protection physicist), data protection policies and safeguarding policies and put in place intellectual property protections. I tried marketing but still haven't got the hang of it.

Failure! Or a different approach?

I chose the time to start a new career path poorly. After a few months, as the momentum started to build, the COVID-19 pandemic struck. Freelance work quickly moved to remote working but with churches and schools closing, the social enterprise struggled to regain momentum. The science outreach work for churches was designed to be highly interactive, so didn't translate to virtual delivery that well. For schools we started work on a YouTube channel with videos featuring healthcare scientists. We did not know what we were doing at first, but learned and improved along the way, and gave some opportunities for aspiring healthcare scientists to raise their profile by hosting videos. These videos were met with some success; some are now hosted as case studies on the NSHCS website. The YouTube channel is still active and I developed some guidance on producing outreach videos which I am happy to share. Others also did innovative work on virtual outreach during the pandemic; there are now a few healthcare science YouTube channels.

As COVID restrictions eased, we were able to begin a cautious return to in-person events. We trained some students and delivered a few healthcare science sessions in local schools and colleges. Sadly, the social enterprise model no longer seemed sustainable, with the number of events not being enough to keep the CIC going. In our local area we found many schools now had to prioritise catching up on disrupted curriculum work, meaning careers taking a lower priority. I do not know if this is the case in all regions, and it will likely change in time. But, for now, we have closed down this particular programme.



Interestingly, the momentum seemed to shift towards science outreach for churches, as we became encouraged

with the responses from church communities seeking to engage positively with scientists. I am excited to see how this programme grows in the coming few years.

Returning to practice

In total I was out of the NHS for around two years. I started to think about how the momentum was shifting – was being freelance and running a small social enterprise what I was cut out for? As I had become accustomed to a portfolio of projects, I wondered if being a part-time Clinical Scientist could be one of them – especially now that times have changed in favour of more flexible and hybrid working.

While on my career break I maintained my CPD record (turns out it is a hard habit to break!) and passed a random CPD audit, so my portfolio of healthcare science education projects allowed me to keep my HCPC registration. I'd also attended a couple of virtual conferences and over lockdown had some time to write up/publish some research work I'd previously been involved in. This all helped keep me in the loop.

So I went back to my original employer, and asked if they might benefit from a bank Clinical Scientist. The answer was "yes" so I went back on the staff bank. After about a year a permanent contract became available. I'm now a part-time Clinical Scientist, Radiation Protection Adviser (RPA) and STP Training Officer. The rest of the time I still undertake some freelance work and focus my social enterprise work on engaging local churches with science.

Thoughts and things I learned

When first starting back in the NHS I found that I had missed being a scientist. I'd learned a huge amount from the challenges of the projects I'd worked on, but to me it seems there is something uniquely rewarding about working in healthcare science. Now it's part of my life again I rediscovered the excitement I had for the subject when I first started applying for the STP. I do hope this new enthusiasm continues as time moves on. What I learned from my educational roles will be greatly beneficial as an STP Training Officer. I returned to the NHS with insight into how educational programmes are developed and the rationales for some of the oddities built into them. I'm confident this will make me much more effective in helping STP trainees complete the programme than I would have been had I not worked on a portfolio of relevant projects.

This is not meant as a brag, but when I tell people that I quit my job and started a small business career they often say what a brave move it is. In reality, it was a very managed risk – both financially and professionally. My wife was extremely supportive of this endeavour and before starting we worked out that we would get by on her income if we needed to. The other thing I knew is that return to practice was possible if all ended badly. The HCPC actually has very helpful guidance on return to practice even if registration has lapsed. RPA2000 also has a career break scheme to extend certifications held by them, though admittedly it's not as clear as the HCPC system.

Also given the current workforce situation I always strongly suspected that it would not be difficult to find a job somewhere if I ever needed to come back.

> "I LEARNED MANY NEW THINGS AND I BELIEVE RETURNED A BETTER SCIENTIST

A better scientist

I'm very blessed to have back what I sought at the start of this whole journey. I work part-time for the NHS using my skills as a scientist, with a renewed interest. The rest of my time I am able to dedicate to other work and projects in which I can learn new skills and contribute to causes close to my heart. Along the way I learned many new things and I believe returned a better scientist. I have no regrets and now have a portfolio career.

These are my insights into how my particular career has taken shape from STP trainee to scientist to freelancer and social enterprise director to a mix of the previous. I'm very grateful for the opportunities I've had to do all this and look forward to what comes next. I hope this raises some helpful or interesting points on how career breaks and flexible working might benefit a career and improve the service we provide.

Matthew Gardner *is a Clinical Scientist and Radiation Protection Adviser working in Medical Physics at University Hospitals Birmingham NHS Foundation Trust*

PUBLISH NEGATIVE RESULTS

Science is about knowing what not to do

Nuclear Medicine Technologist **Clara Ferreira** argues that publishing negative research results is as important as publishing positive results.

I was 18 years old when I started my life in research. On the first day, it was explained to me that rather than knowing what to do, science is about knowing exactly what not to do.

I was helping some part-time PhD students develop their activities. The first set of results that I helped acquire was negative – they were presented in the team meeting and people were disappointed because it would be difficult to publish them. I did not understand everyone's frustration. We knew exactly what not to do – that is science. Let's tell the world about it and we can save everyone else time, we will all try something else, and it is only a matter of time until we find the answer.

I was a young and innocent researcher, who knew nothing about publishing, scientific journals, and impact factors.

Publishing negative results

Scientific research involves testing a hypothesis through the implementation of an experiment: if the results support the hypothesis, they are positive; if the results do not support the hypothesis, it means that the hypothesis was wrong and the results are negative. Unfortunately, most of the journals do not publish negative results; but all researchers know that most of the results that we are going to produce during our working lives will be negative.

The publication of negative results also saves time and effort because they prevent other researchers from working on a similar project. This will allow people to try different paths and progress further in the field. This way, the publication of negative results can help the scientific community to avoid repeating a failed procedure.

A good example of a negative result which is worth publishing is the Michelson-Morley experiment. The researchers measured the speed of light in different inertial frames, in the same and opposite direction of the Earth's orbit. They concluded that the speed of light was the same in all directions, which means that based on their hypothesis, they obtained a negative result. However, this definitely does not mean that their research was not important. They were awarded the Nobel Prize in Physics in 1907 and their work is considered one of the most famous non-confirmatory experiments. This marked the beginning of the "second scientific revolution" and proves that obtaining negative results is not bad or the end of your career, it is only a result.

Publication bias

According to some authors, 50% of the results obtained in clinical trials funded by the National Health Service never see the light. And in 2007, more than 85% of the

❶ **Left.** Albert Abraham Michelson FFRS HFRSE (December 19, 1852 - May 9, 1931) was a German-born American physicist known for his work on measuring the speed of light and especially for the Michelson-Morley experiment. In 1907 he received the Nobel Prize in Physics, becoming the first American to win the Nobel Prize in a science

❷ **Below.** American scientist Edward Williams Morley (1838 – 1923)

IMAGES: ALAMY

published studies indicated to present positive results.

The publication of only experiments with positive results leads to publication bias because it does not include contributions that do not fit with the "positive" result. This has a negative impact in terms of scientific communication and is important in meta-analysis, potentially leading to false positive outcomes that misinform researchers, doctors, policymakers and elements of the scientific community. It is extremely important to report cases where circumstances were not effective.

While the biggest problem is created by us as researchers – because we still see a "negative result" as a failure, a point of weakness that can affect our career, reputation, and even economic status – sometimes, in order to avoid the loss of credibility by the public and the market, even companies avoid the publication of negative information. It was companies that support research who started the competition for findings and citations, which can lead to a distortion of science.

Try asking a PhD student how they feel when they have negative results. Immediately, they start looking for alternative reasons. I understand that you should check all your methods and techniques. The job of a researcher is to look for answers. But, remember, before starting any kind of research, you set up a question where the answer might be "yes" or "no". The human race will still benefit from that information, even if it is "no".

Reproducibility

Another problem is the reproducibility of published results. According to a survey published in 2016, 70% of researchers were not able to reproduce the experiments published by other scientists. Another recent study indicated that a large number of major cancer research results could not be replicated; and among those that could be replicated, the results were 85% lower than originally reported in the 2016 survey.

This can happen for a number of reasons.

First, and most serious, is the pressure for publishing positive results, which can lead to fraud and data manipulations, particularly if there is pressure from supervisors.

The second corresponds to the limitation of words in scientific journals. When you have a certain number of words available, you must save it for when it is needed. This tends to happen in the results and its discussion. A part of scientific reports where people tend to save words in the famous "Materials and Methods". But those are the most important parts of the study – the results are only valid according with the conditions set up in there.

Table ❶ Causes of negative results.

Causes of negative results
The original hypothesis was false
Technical errors
Unable to replicate findings from published experiments

Third, there are data available that indicate that publications with negative results are less frequently cited by other researchers. And who does not want their work to be cited?

Open-source science

Unfortunately, most of the experiments with negative results are still very difficult to publish and end up being printed in journals with low impact factors. However, there are some journals – such as the *Journal of Negative Results* and the *Journal of Negative Results in BioMedicine* – that exclusively publish negative results. And journals like the *Journal of Cerebral Blood Flow and Metabolism* have a special section for negative and unexpected results.

One of the solutions that can help solve these problems is open-source science. It is important to review the existing publishing system and allow different people to comment and challenge the freely available work.

With more than 10 years of publishing experience, I am definitely not young, but I am still innocent enough to believe that negative results should be published and that all scientists are amazing for how much effort, energy, time and money they put into their research.

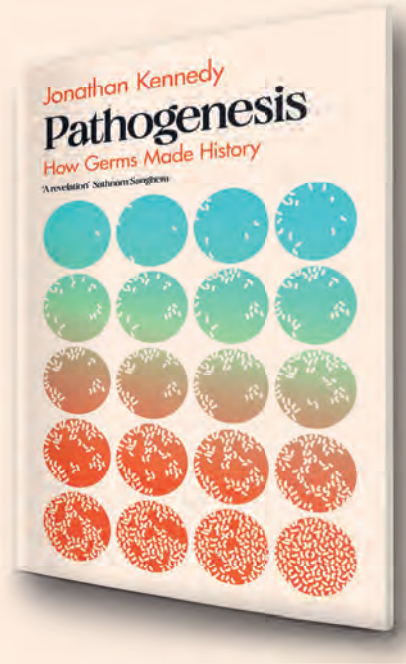
Negative results only mean that the answer to the research question is "no". It can still help to improve patient health and enhance the healthcare system, serving the well-being of humanity. All scientists should work by the motto "the truth, the whole truth, and nothing but the truth" by publishing projects with negative results with the same emphasis that we give to positive outcomes.

The following sentence has been with me for more than 10 years but maybe it is a good time to re-write it: "Real science publishes negative results." ○

BOOK PITCH

Pathogenesis:
How Infectious Diseases Shaped Human History

Dr Jonathan Kennedy outlines the ideas behind and the content within his new book.



In medicine, pathogenesis refers to the origins and development of a disease, with a particular focus on the way that pathogens infect our cells and the effect this has on our bodies. *Pathogenesis* brings together insights from classics, genomics, and economics, archaeology, anthropology and microbiology to retell the history of the world from the perspective of microbes. It explores how viruses, bacteria and other microbes impact aggregations of bodies – that is, the body politic, body economic and body social.

Galileo was the first person to see the microscopic world in the early-17th century, when he realised that reversing the order of the lenses in his telescope made it possible to see things that were invisible to the naked eye. But Galileo preferred to look up at the sky and it was a haberdasher from Delft in the Netherlands who pioneered the use of microscopes a few decades later. Antonie van Leeuwenhoek initially used his lenses to inspect the quality of textiles but after a while he turned his gaze upon the natural world. His letters to the Royal Society in London describe his astonishment at discovering that everything from a drop of water to the plaque on our teeth is teeming with what he called "animalcules".

> **"OVER MILLIONS OF YEARS, BACTERIA EVOLVED THE ABILITY TO INFLUENCE OUR MOODS**

We now know that bacteria and viruses perform a wide range of roles that are vital to the healthy functioning of our bodies and even our minds. The microbiome is crucial for gut health, but recent research demonstrates that more than 90% bacteria strains in our gut produce neurotransmitters like dopamine and serotonin. Over millions of years, they evolved the capacity to communicate with and influence our moods. We can't be sure why but one hypothesis is that, with more dopamine and serotonin coursing around our brains, we're more likely to socialise and provide bacteria opportunities to jump from one body to another.

Viruses also have a huge impact on the human body and mind. Retroviruses reproduce by inserting a copy of their DNA into the genome of the host cell. When a retrovirus infects a sperm or egg cell, its DNA is then passed on to every cell in every subsequent generation. Amazingly, 8% of the human genome is retrovirus DNA. Some of these genes allowed our ancestors to acquire the ability to form memories and give birth to live young rather than lay eggs.

Pathogenesis weaves together the latest scientific and historical research to show that bacteria and viruses have been the protagonists in many of the most important social, political and economic developments in history: the extinction of Neanderthals; the spread of farming; the demise of the great empires of antiquity; the growth of world religions; the shift from feudalism to capitalism; the devastation wrought by European colonialism; the agricultural and industrial revolutions; and the creation of the modern welfare state.

In *Pathogenesis*, I hope to change the way you think about history and our species' role in it – to convince you that the modern world has been shaped by microbes as much as by women and men.

***Dr Jonathan Kennedy** is a Reader in Politics and Global Health in the Centre for Public Health and Policy at Queen Mary, University of London.*

myQA® PROactive

The only commercial prospective risk management solution for radiation oncology.

- Create flowcharts to clearly detail your workflows. Flowcharts can be annotated and colour coded without adding complexity.
- View risk status with the library dashboard and use version control to track development of your risk analysis.
- Automated analysis of risks, based on measurable quantities like “event rate” (affected patients per year).
- Automated cost benefit analysis of all safety measures to support change for your department.

Maximise your departmental safety.

Contact OSL to arrange a demo!

Ask us about:
DOSE-X
Next-generation reference class electrometer.

osl

+44(0) 1743 462694
enquiry@osl.uk.com
www.osl.uk.com

RETURN ADDRESS:
IPEM
Fairmount House
230 Tadcaster Road
York
YO24 1ES
UK