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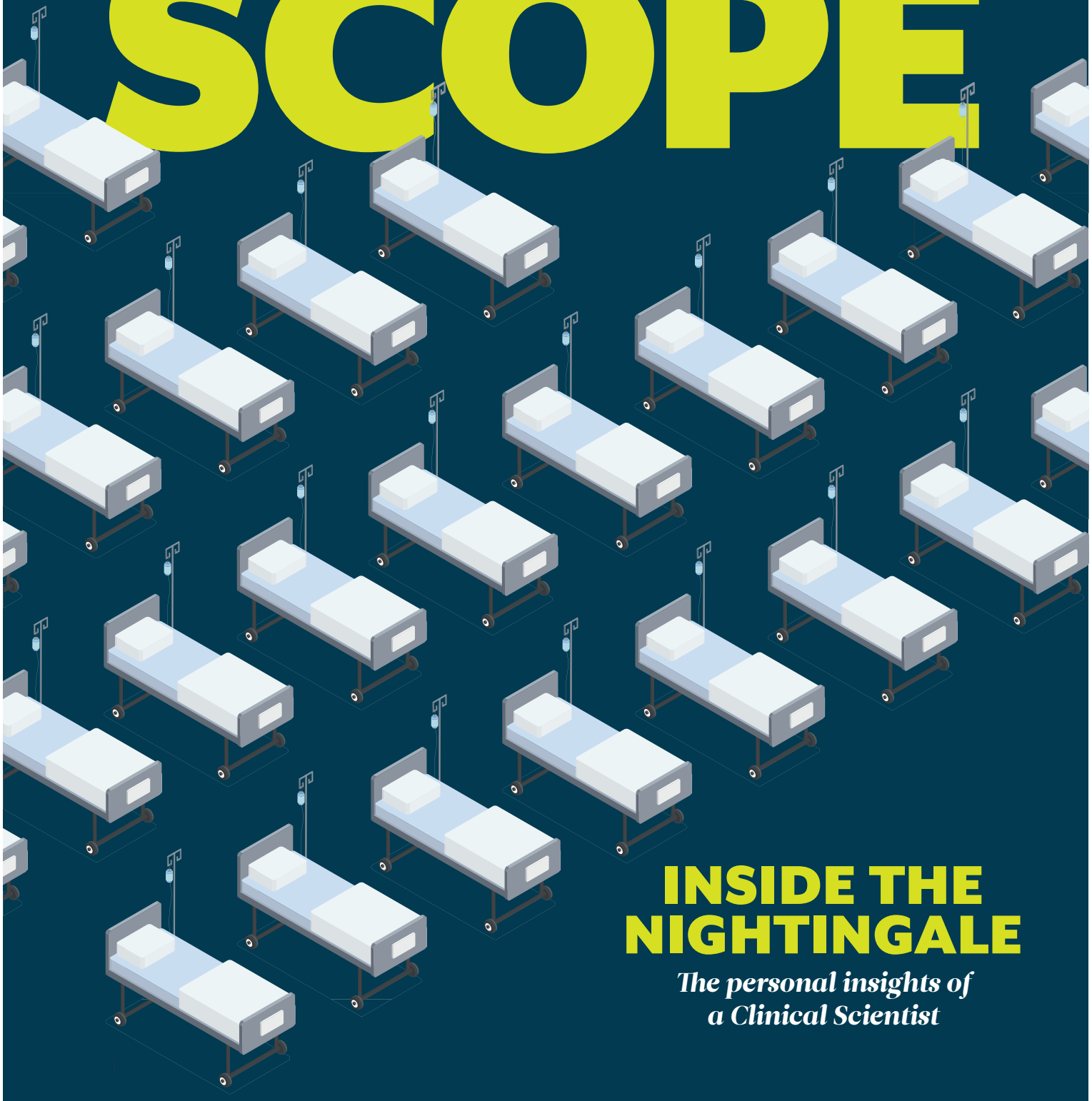
Volume 29 | Issue 3 | Autumn 2020

IPEM Institute of Physics and Engineering in Medicine

SCOPE



INSIDE THE NIGHTINGALE

The personal insights of a Clinical Scientist

THE BIG DEBATE

A discussion on medical device and software classification

HISTORY

The world's first radiobiological institute

PHYSIOLOGY

Breath-holding for medical imaging and radiotherapy

SPECIAL REPORT

The science of seating – research and equipment advances

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Shaping content

Usman Lula on the content in the latest issue of *Scope* and the evolutions of magazine's design and structure.

We bring to you a series of exciting features that we hope will be of interest and will also spur further discussions

Whilst we are now adjusting to the "new normal" with COVID-19, we bring to you a series of exciting features that we hope will be of interest and will also spur further discussions.

Professor Azzam Taktak has kindly shared with us his own personal insight into volunteering at the Nightingale Hospital (London). This is a fantastic piece detailing both the breadth and depth of work undertaken during the time and the added value we bring to the NHS. Turn to page 18 to learn more!

Balancing and shaping the content of *Scope* is challenging as it relies on voluntary submissions from all disciplines as represented under IPEM. Calls for submissions via mailing lists or the IPEM communication platform may not always meet our intended aims of providing this balance.

In the past, we introduced themes as a way to improve the balance and though it worked to some extent, it also meant that we heavily relied on specific submissions related to the theme in any one issue. One way to resolve this issue is to perhaps set a theme (e.g. cutting edge technology or techniques) and approach potential authors for an invited feature. I guess there may be lots of other approaches, so, on this note, we would like to engage with you the readers to provide us with ideas that could help us meet our aims!

Our original aim with *Scope* was to ensure we maintained quality of content whilst improving the design. With the new recent redesign of *Scope*, we are planning to send out a survey to find out what members felt about the changes - something we haven't yet undertaken formally. Please keep an eye out for this, as it will really help us understand your needs.

If you would rather join the Scope Editorial Advisory Board and take the lead on making changes to a specific section, we have exciting vacancies for an Applied Academic Editor and a Clinical & Biomedical Engineering Editor. Both of these positions are available to fill immediately and will mean you would act as a Commissioning Editor in that area. If you are interested, please drop me an email.

Have a great read and stay safe!

Usman Lula

Usman Lula
Chair of IPEM *Scope* EAB

FEEDBACK

The big debate

We couldn't have a *Scope* issue without our new "Big Debate" feature, only this time we are trying to answer a question that resurfaces every now and then.

In fact, one of the triggers for this question was a policy we were developing locally in our department around when an in-house "script" itself becomes a medical device.

If you would like to join in the debate, or would like to suggest a debate to be covered in a future issue, then a great way to join the conversation is by voicing your opinions on the Communities of Interest section of the website.

We look forward to seeing you there and furthering the debate.

IPEM Institute of Physics and Engineering in Medicine

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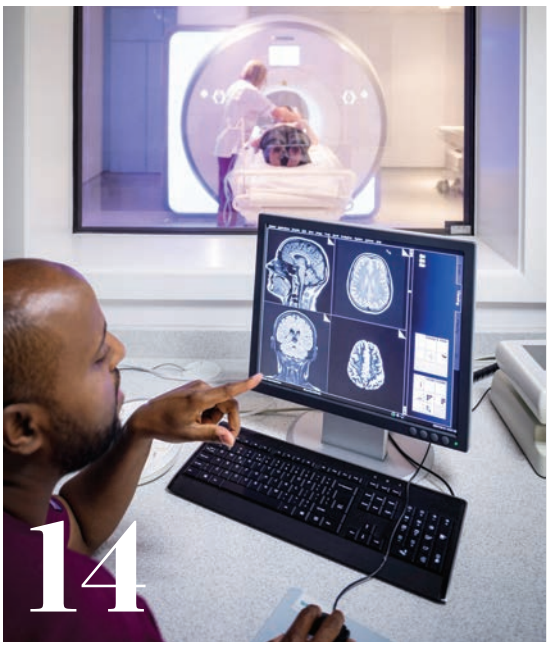


> The value of clinical engineering as a profession has been recognised in the response to the COVID-19 pandemic.
>
> – *Scott Brown and Andrew Frost* page 42

UPFRONT

Cover illustration by
ISTOCK

UPFRONT

14 / THE BIG DEBATE: DEFINING MEDICAL DEVICES
We asked four experts: "In a clinical workflow, how do you define whether/when scripts or custom functionality developed in a framework provided by a medical device software manufacturer need to be considered as medical devices in their own right?"

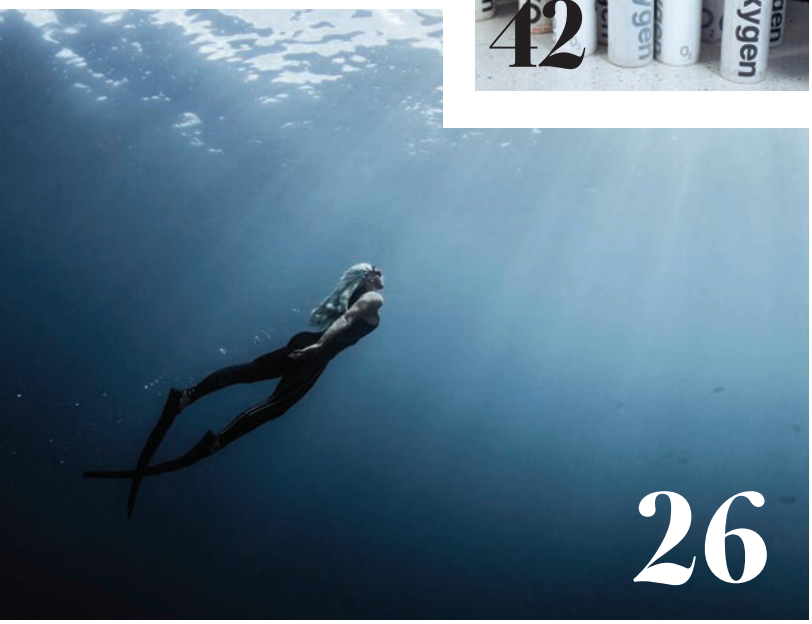
COVER FEATURE

18 / INSIDE THE NIGHTINGALE
From the shift patterns and unexpected tasks, to the tragedy of death and humbling experiences, Consultant Clinical Scientist Professor Azzam Taktak takes us inside the Nightingale Hospital London.

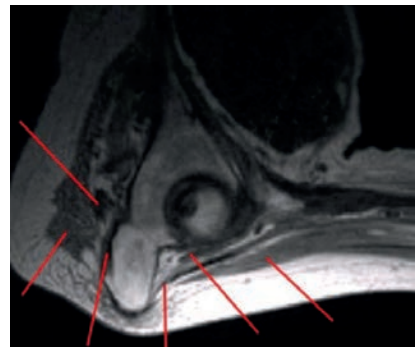
Volume 29 | Issue 3 | Autumn 2020

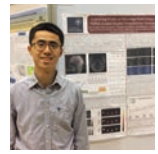
NTENTS

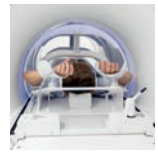
GENERAL FEATURES



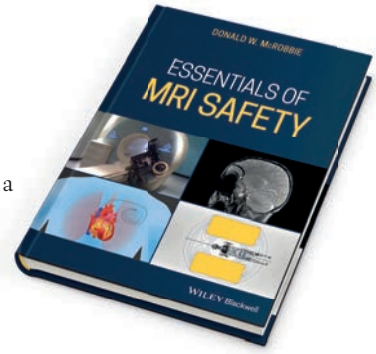
SPECIAL REPORTS







ENDNOTES



UPFRONT

PROSTATE CANCER

Computer-assisted ultrasound imaging

A computer algorithm that helps radiographers interpret ultrasound images could improve radiotherapy treatment for patients with prostate cancer.

The new algorithm helps radiographers to quickly locate the prostate in ultrasound scans, which can be time consuming to interpret on their own.

The algorithm, described in a new study led by scientists at The Institute of Cancer Research and our partner hospital The Royal Marsden, could help radiographers less familiar with ultrasound use the technology to deliver more accurate radiotherapy for prostate cancer.

The study, which was funded by Cancer Research UK, used the algorithm retrospectively on ultrasound scans for 32 patients with prostate cancer who were treated at The Royal Marsden.

Three technicians then used the scans to select the regions around the prostate to target with radiotherapy.

The algorithm reduced differences in the regions selected by the different technicians and increased the accuracy of radiotherapy targeting, and reduced the time required.

In the future, the team hopes to develop machine learning techniques to help radiographers who are unfamiliar with ultrasound, enabling them to more easily acquire high-quality images and interpret them in real-time.

This could make ultrasound a safe, easy and reliable way to guide radiotherapy treatment for the prostate cancer.

IMAGE: JAN CHLEBIK

Ultrasound is an affordable and readily available technology for monitoring patient health

Study leader Dr Emma Harris said: "Ultrasound is an affordable and readily available technology for monitoring patient health, but in the radiotherapy setting it's still relatively uncommon.

"Radiotherapy practitioners are more familiar with using CT scans to guide treatment and ultrasound produces images of the body that look quite different, so helping users identify tissues accurately and consistently is key to advancing its use.

"Our new algorithm helps radiographers match ultrasound scans, and because ultrasound doesn't use radiation, you could regularly monitor prostate motion during treatment to update radiotherapy, unlike with currently used CT. Our study could pave the way for more widespread ultrasound use to guide radiotherapy for prostate cancer and other diseases."

bit.ly/2XeniGU

PROSTATE CANCER FACTS

1 MOST COMMON cancer diagnosis in the UK

47,500 MEN are diagnosed every year

45 EVERY 45 MINUTES one man dies from prostate cancer

COVID-19 TESTING

RT-PCR-based detection of SARS-CoV-2

A cheaper, rapid, and accurate pooling strategy for the RT-PCR-based detection of SARS-CoV-2 in clinical samples has been described in a new paper.

This assay has a significant impact on large-scale population screening in the wake of the current pandemic.

The COVID-19 pandemic has caused a massive strain on global healthcare systems, governance, and economies. Testing for SARS-CoV-2 has lagged behind in many countries due to various bottlenecks, including but not limited to the failure of the reagent supply chain, lack of adequate test kits, and hindrances in the analytical and regulatory processes.

Lead author Ravindra Kolhe, from Augusta University, said: "We have proposed a mass population screening approach based on sample pooling strategy for rapid and wide-scale population screening that may be adopted by laboratories currently using RT-PCR-based methods to test for SARS-CoV-2."

According to Dr. Kolhe, this strategy would lead to an approximately five- to 10-fold reduction in the cost of testing of SARS-CoV-2.

The investigators analysed approximately 1,000 samples using this pooled sampling approach and achieved 91.6% PPA (positive percent agreement) and 100% NPA (negative percent agreement) when results were compared to the routine screening approach.

bit.ly/2PaLuWn

PHYSICS IN MEDICINE

COVID-19: RESPIRATORY DROPLETS STUDY

A mathematical model, proceeding from first principles, has been developed for the early phases of a COVID-19-like pandemic using the aerodynamics and evaporation characteristics of respiratory droplets.

Researchers modelled the pandemic dynamics with a reaction mechanism, where each reaction has a rate constant obtained by calculating the frequency of collisions between the infectious droplet cloud ejected by an infected person and a healthy person.

Swetaprovo Chaudhuri, one of the authors, said: "The size of the droplet cloud, the distance it travels, and the droplet lifetimes are all important factors that we calculated using conservation of mass, momentum, energy and species."

There study shows that without wind, depending on the ambient condition, droplets travel between eight and 13 feet before they evaporate or escape. This implies that social distancing at perhaps greater than six feet is essential.

bit.ly/3hQiWh5

NEWS IN BRIEF

Telemedicine

Singapore researchers have published a paper discussing the use of telemedicine in Singapore to bridge the gap among physicians with necessary medical expertise and ensure continuity of service. "This outbreak may spark a wider adoption of tele-nuclear medicine in the post-COVID-19 era – not just in diagnosis and therapy but also in education for developing nations with limited access to formal training," the authors said.

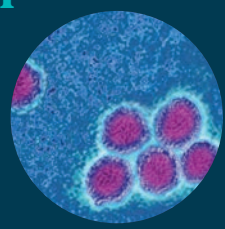
bit.ly/2PfkXqA

Africa radiotherapy

A new project supported by the Science and Technology Facilities Council (STFC) aims to design and develop new radiotherapy technologies to give more cancer patients in Sub-Saharan Africa access to treatment and to save lives. The project, "Innovative Technologies towards building Affordable and equitable global Radiotherapy capacity", will contribute to the development of novel radiotherapy machines, specifically designed to meet the needs of African hospitals.

bit.ly/2BM7UKr

Yellow fever



An international team of researchers, led by the Massachusetts Institute of Technology, has now developed a potential treatment for yellow fever. Their drug, an engineered monoclonal antibody that targets the virus, has shown success in early-stage clinical trials.

bit.ly/3ggcBuN

RADIATION THERAPY

"Real-time tumour tracking five times faster"

A faster way of tracking the movement of tumours in the body during radiation therapy has been developed by a team of scientists.

The team's work builds on the Linac-MR project, a radiation beam and magnetic resonance imaging (MRI) hybrid machine developed by researchers at the Cross Cancer Institute in 2013.

As patients lie in the machine, the MRI provides constant imaging of the tumour, allowing the system to track its movement and keep the radiation focused only on that area.

However, real-time tracking requires significant processing power and the current approach is too slow for day-to-day use, said the study's lead researcher, Kumaradevan Punithakumar.

He continued: "The original version of the tracking algorithm runs through the computer's central processing unit, but it can only handle eight or 12 processes at a time. That's too slow for real-time tracking. So we adapted the algorithm to use the graphics processing unit (GPU), which can handle thousands of processes at once."

GPU processing increased the speed by five times.

bit.ly/3hNknwC

UP CLOSE

ARTIFICIAL INTELLIGENCE

WHAT IS THE LATEST WITH AI AND HEALTHCARE?

A group of doctors and data scientists is calling on hospitals to create clinical departments devoted to artificial intelligence (AI) to harness the power of the technology to transform care.

WHAT IS THEIR ARGUMENT?

While there have been many predictions of AI's potential to benefit healthcare delivery the technology's benefits so far have been blunted by inconsistent implementation, the researchers say. They outline a plan to make hospitals "AI ready,"to enhance patient care and medical research.

WHAT DO THEY THINK OF CURRENT AI INTEGRATION?

"The reality of the available evidence increasingly leaves little room for optimism," they write. "There is a stark contrast between the lack of concrete penetration of AI in medical practice and the expectations set by the presence of AI in our daily life."

HOW WOULD THESE AI CLINICAL DEPARTMENTS HELP?

They would bring together diverse expertise, cut through red tape and address educational, financial and regulatory issues, say the authors. They also would help drive research efforts and focus AI implementations in the directions most useful to each hospital's patient population. In addition, they could map out and monitor performance and safety.

WHERE CAN I READ MORE?

Their paper is published in *BMJ health and care informatics* – **bit.ly/312cs7W**

IMAGES: SCENEPHOTO / ISTOCK / GETTY

GENOMICS

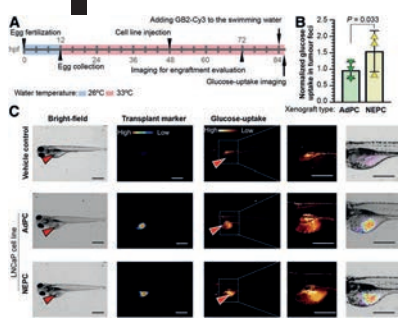
FDG-AVIDITY OF PSMA-SUPPRESSED PROSTATE TUMOURS

The genomic signature has been uncovered to explain why 18F-FDG imaging performs better than PSMA-targeted imaging for prostate cancer patients with low or no expression of the prostate-specific membrane antigen (PSMA).

The researchers determined that a neuroendocrine gene signature associates with a distinct differential expression of glucose transporters and hexokinase proteins, which allows for a more favourable uptake of 18F-FDG than PSMA-targeted radioligands.

The study also demonstrated that zebrafish xenograft tumour models are an accurate and efficient preclinical method for monitoring nonradioactive glucose.

bit.ly/2BJOUfq



NHSX

MEDICAL IMAGING PLATFORM SELECTED

A platform that allows doctors to view and discuss medical grade images on smartphones, tablets and desktops has been selected by the NHSX. This is a new unit responsibility for setting national policy and developing best practice for NHS technology, digital and data, including data sharing and transparency.

The platform, which is named Bleepa in a nod to the pager technology, offers digital imaging that can be used for diagnosis alongside secure messaging.

It has recently been awarded a place on the NHSX National Clinical Communication Tool Framework.

This framework will provide a vehicle for NHS trusts to buy Bleepa by drawing down from a £3m centralised fund over two years.

It will run for an initial period between August 2020 and August 2022, with a possible further extension for 12 months.

bit.ly/33dG0lC

ENGINEERING

Nano-focussed laser

Researchers from Japan have reduced the beam diameter in an X-ray free-electron laser to six nanometers in width.

This considerably improves the utility of these lasers for imaging structures closer to the atomic level than possible in prior work.

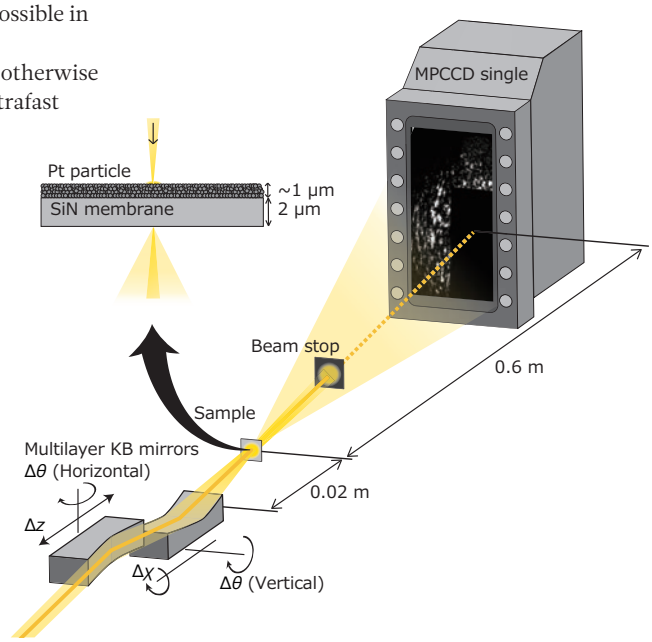
To "see" extremely small and otherwise invisible objects, and observe ultrafast chemical processes, researchers commonly use synchrotron X-ray facilities.

X-ray free-electron lasers are an alternative that can (in principle) image atomic-scale detail of, for example, a virus particle, on the timescale of an electron transition, without damaging the particle.

To do this, you need an incredibly bright X-ray laser that focuses extremely fast laser pulses on the nanometer scale.

"Using multilayer focusing mirrors, we narrowed the width of our laser beam down to a diameter of six nanometers," says lead author of the study Takato Inoue. "This is not quite the diameter of a typical atom, but we're making good progress."

bit.ly/2ECXQ7z



BIOTECHNOLOGY

PORTABLE COVID-19 DIAGNOSTIC SYSTEM

A team of researchers from the National University of Singapore (NUS) has developed a portable COVID-19 micro-PCR diagnostic system, called Epidax. It enables rapid and accurate on-site screening of infectious diseases and significantly reduces the time required to analyse patient samples.

Polymerase chain reaction (PCR) tests that are currently being used for COVID-19 diagnosis have to be carried out in specialised testing facilities, and it takes a few hours, or a few days, for results to be made known.

A 10-member team from the NUS Institute for Health Innovation and Technology, led by the institute's Director Professor Lim Chwee Teck, has developed a novel diagnostic system from scratch in a record time of two months.

A project of this scale

Epidax, which is a microfluidics-based PCR diagnostic system, is about the size of a toaster and very portable

NON-INVASIVE VENTILATOR

Open-source DIY ventilator

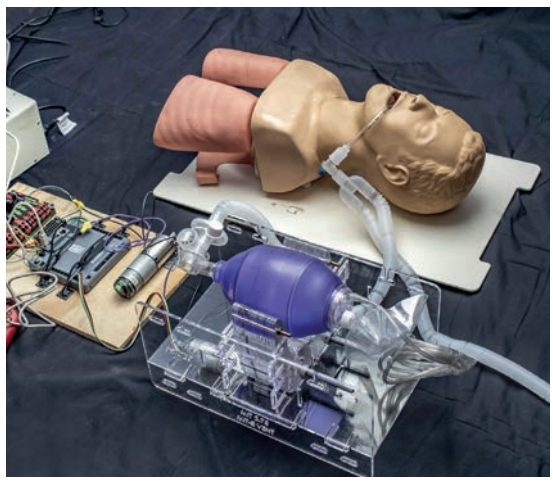
A low-cost, easy-to-build non-invasive ventilator aimed at supporting the breathing of patients with respiratory failure performs similarly to conventional commercial devices, according to a new publication.

The research paper provides a free to replicate, open-source description for how to build the ventilator. The researchers say the prototype ventilator could support treatment of coronavirus and other severe respiratory diseases in low-income regions, or where ventilator supplies are limited.

The research team was led by Ramon Farré, Professor of Physiology in the Unit of Biophysics and Bioengineering at the School of Medicine of the University of Barcelona, Spain.

They designed, built and tested the low-cost non-invasive ventilator with a small high-pressure blower, two pressure transducers and a controller with a digital display, which are available at a retail cost of less than £60 GBP.

bit.ly/2XaSeYn



would typically take at least one to two years to complete.

Epidax, which is a microfluidics-based PCR diagnostic system, is about the size of a toaster and very portable.

The system uses a specially designed microfluidic chip that comprises micro-channels where samples are processed. By employing microfluidic technology, the system is able to process a smaller amount of sample for quicker detection of COVID-19 infection.

Using a reagent that enables both RNA extraction and amplification on the chip, the PCR test can be performed right after a nasal swab sample is collected, thus bypassing the intermediate step of RNA extraction.

These features significantly minimise sample handling and shorten the test and waiting time, so patients can get their test results in about an hour.

nus.edu/2Do5O3A

TOTAL-BODY DYNAMIC PET

uEXPLORER first patient results

Results from the first study using uEXPLORER to conduct total-body dynamic positron emission tomography (PET) scans in cancer patients show that it can be used to generate high-quality images of metastatic cancer.

The research was presented at the Society of Nuclear Medicine and Molecular Imaging 2020 Virtual Annual Meeting in July.

While static PET provides a simple snapshot of radiopharmaceutical concentration, dynamic PET with tracer kinetic modelling can provide parametric images that show how tissue is actually behaving.

Parametric images have the potential to better detect lesions and assess cancer response to therapy.

A patient with metastatic renal cell carcinoma was injected with the radiotracer 18F-FDG and scanned on the uEXPLORER total-body PET/CT scanner. The static PET standardised uptake value (SUV) was calculated and kinetic modelling was performed for regional quantification in 16 regions of interest, including major organs and multiple metastases. The glucose influx rate was calculated and additional kinetic modelling was implemented to generate parametric images of the kinetic parameters. The kinetic data were then used to explore tumour detection and tumour characterisation.

Multiple metastases were identified on the dynamic PET/CT scan, confirming that it is feasible to perform total-body kinetic modelling and parametric imaging of metastatic cancer.

bit.ly/2Pcr3rT

EXTERNAL RELATIONS MANAGER

Evidence and collaboration

As the pandemic response moved into a second phase and the world began to settle down to a "new normal", IPEM members continued to play a vital role, writes **Sean Edmunds**.

Together with the Royal College of Radiologists and the Society and College of Radiographers, IPEM responded to a call for evidence from the House of Commons Select Health and Social Care Committee inquiry into "Delivering Core NHS and Care Services during the pandemic and beyond".

The evidence from IPEM, the RCR and SCoR focused on a response to comments made by the National Cancer Director to the inquiry about medical imaging services, who stated "we have the available workforce and now have the available kit", contrary to the data and experience of the three professional bodies. The response laid bare the continuing shortages of staff and equipment that could threaten patient safety. You can read the full response on the IPEM website.

Further collaboration with the RCR, SCoR, Cancer Research UK and Macmillan Cancer Support saw the production of

The response laid bare the continuing shortages of staff and equipment

NON-COVID UPDATES

The latest news on consultations, publications and presentations.

Away from COVID-19, Dr Jemimah Eve, IPEM's Head of Workforce Intelligence and Training, provided a detailed response to the latest consultation by the Migration Advisory Committee on the National Shortage Occupation List (NSOL).

The response outlined some of the main reasons why there is a chronic shortage of Clinical Scientists and Clinical Technologists. It pointed out that IPEM has carried out a variety of measures, including workforce surveys, to highlight the shortfalls to Health Education England, the Chief Scientific Officer, and NHS Education Scotland.

Dr Eve also pointed out the Office for National Statistics has updated the Standard Occupational Classification codes for these occupations, and recognition of this within the NSOL would be of great value.

Members of the Nuclear Medicine Special Interest Group responded to two separate, but linked, consultations from the Welsh Health Specialised Services Committee on PET-CT commissioning policy and service specification.

Several IPEM members were involved in helping to produce two new publications about the Ionising Radiation (Medical Exposure) Regulations.

The guidance, *IR(ME):R Implications for clinical practice in diagnostic imaging, interventional radiology and diagnostic nuclear medicine,* seeks to explain how the requirements of the regulations should be interpreted and used in practice. It was produced by a working party, which included representatives from IPEM, the British Institute of Radiology, the RCR, SCoR, the British Society of Paediatric Radiology, and the Medical Exposures Group of Public Health England.

The Radiotherapy Board also published *Ionising radiation (medical exposure) regulations: Implications for clinical practice in radiotherapy*.

Finally, Dr Geoffrey Charles-Edwards, Consultant Clinical Scientist at Guy's and St Thomas' NHS Foundation Trust, represented IPEM at a Westminster Health Forum. The online policy conference was on "Next steps for the regulation of medicines, medical devices and clinical trials".

IMAGE: GETTY

tailored coronavirus information for radiotherapy patients. The *Protecting people with cancer from coronavirus when going for radiotherapy* leaflet was created to reassure radiotherapy patients about what precautions were being taken by cancer centres to ensure patients and hospital staff were as protected as possible.

It stressed the importance of continuing to attend for treatment and explained some of the various safety precautions being taken by hospitals.

The Radiotherapy Board, made up of IPEM, the RCR and SCoR, issued new guidance for testing non-surgical oncology healthcare workers and asymptomatic patients attending oncology departments for elective treatment.

The guidance was written by two oncology specialists and approved by the board, which provides guidance, oversight and support for the continuing development of high-quality radiotherapy services for cancer patients in the UK.

At the same time, a new paper was published, summarising how engineers can transform ideas into advice and action to help minimise the risk and impact of COVID-19 beyond the immediate crisis.

COVID-19: Engineering a resilient future draws upon evidence and insights from the National Engineering Policy Centre, of which IPEM is a member, and the Royal Academy of Engineering. It contains a number of case studies illustrating how the engineering community has already provided rapid support and advice on the COVID-19 pandemic and how the response needs to continue to be agile to respond beyond the immediate crisis.

> **"THE RESPONSE NEEDS TO CONTINUE TO BE AGILE BEYOND THE IMMEDIATE CRISIS**

The COVID-19 IPEM website page was kept up-to-date with the latest information, advice, guidance and webinars being published from members and other organisations and bodies.

The Communities of Interest continued to be a valuable resource for members to share best practice, and a new COVID-19 Cross Speciality CoI was created.

MPEC 2020: Horizon Scanning - Beyond COVID 19

21 SEPTEMBER – 2 OCTOBER

This year IPEM has gone digital and moved both MPEC and the Biennial Radiotherapy Meeting online.

There is still time to book for the conference and meeting, which opens on Monday 21 September.

Tickets have been going fast but there are plenty of opportunites to access this exciting event. Kicking off with an opening talk by renowned theoretical physicist, author and broadcaster *Professor Jim Al-Khalili OBE*, over the course of the next two weeks there is a wealth of content on offer. You will be able to access a range of key note speakers, scientific sessions and workshops covering all aspects of physics and engineering in medicine.

Clinical engineering sessions will give you the opportunity to hear from *Professor Dan Clark* and *Professor Paul White* amongst others. There will be sessions on Artificial Intelligence, and MR in RT as well as Particle Therapy. You will be able to find out what the Centre for Sustainable Healthcare is doing as well as find out about new regulations.

You can join in a debate about how life could change when the Covid-19 pandemic is over as well as hear presentations from IPEM prize winners and senior members within the Institute. Finally the event will close with a talk from *Dr Phil Hammond*, the renowned broadcaster and comedian.

There are a number of options still available to access this fantastic event and you can find out more on our website **ipem.ac.uk**

SPEAKERS INCLUDE:

Professor Jim Al-Khalili OBE
Author and broacaster

Dr Phil Hammond
Broadcaster and comedian

THE BIG DEBATE

Defining medical devices

We asked four experts a topical question about medical device and software classification. Here's what they said.

Q ***In a clinical workflow, how do you define whether/when scripts or custom functionality developed in a framework provided by a medical device software manufacturer need to be considered as medical devices in their own right?***

IAN STRONACH

The situation differs depending whether we are considering the existing Medical Devices Directive (MDD), or the yet to be implemented Medical Device Regulations (MDR), for which formal guidance from the MHRA does not yet exist.

The MDD is clear that to be a medical device not only must the product "have the potential to affect an individual patient's treatment" but "these regulations don't apply if your device is only being used for patients within the institute it was made..." Thus if the scripts we develop are used only for our own patients, such scripts are not considered to be medical devices.

The situation under the terms of the MDR is less clear cut. These regulations define devices created by manufacture or modification of a device by a health institution as medical devices. This may include script development, as the MHRA states that manufacturing or modifying a device by a health institution includes "device software development... where this action is not explicit in a manufacturer's intended purpose or instructions for use".

In the case of scripts developed in a framework provided by the medical device software manufacturer, it is clear that this scripting can be part of the manufacturer's intended purpose. It may be the case that the scripting framework is incorporated into the main application as provided by the manufacturer, and the scripts cannot be run outside of that application. In addition instructions for development and use of scripts may be provided by the manufacturer in the main user guide or in additional official documentation explicitly providing guidelines for scripting.

In such circumstances, if we stay within the scope of

IMAGE: ISTOCK

documentation and training then we are using the scripting interface within normal use of the device. This might include recording macros, automating set functions or using internal tools and decision trees. For example, if the manufacturer's documentation describes a process where a script is made by recording a macro and then generalising the recorded code, that script would not constitute a new medical device. It is normal use of an existing medical device, as defined by the manufacturer, and we are, therefore, not manufacturing or modifying a device under the terms of the MHRA guidance.

We would consider a script to be a new medical device under the MDR if it goes beyond the manufacturer's normal intended use of the product. Our definition should, therefore, focus on whether a script falls outside the scope of manufacturer's intended purpose, as defined by their training, documentation and examples. If the script requires functionality that is not part of the scripting interface; extends the functionality beyond that possible in the original application; contains considerable amounts of logic that wasn't derived from macros; or relies on functions in external libraries that are not documented by the manufacturer, then it should be considered to be a new medical device.

GREGORY JAMES

Software development and bespoke programming is a contentious issue in medical physics. If performed properly, bespoke programming can offer the department unique tools to manage and analyse patient data. The most common applications of bespoke programming in medical physics are probably to troubleshoot DICOM issues, or to analyse data for diagnosis or quality control.

In nuclear medicine, patients are administered with radiopharmaceuticals. The uptake and/or clearance of the radio tracer is then studied either by imaging the patient with a gamma camera or by measuring radioactive physiological samples, such as blood or urine. Every patient is different and sometimes the "one-size-fits-all" approach offered by some commercial software platforms is not sufficient. Analysis software needs to be flexible to protocol changes as techniques develop and new evidence comes to light in the literature. It is irritating when often expensive, commercial software becomes outdated after the publication of a new scientific paper. Bespoke programming offers the opportunity to tailor software to the changing needs of the reporting clinician in the fast-paced and quickly changing field of nuclear medicine.

"SOFTWARE DEVELOPMENT AND BESPOKE PROGRAMMING IS A CONTENTIOUS ISSUE"

I am a strong advocate of bespoke programming, as I don't want to settle for what

MEET THE EXPERTS

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Consultant Clinical Scientist
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the commercial vendors provide. Whilst I acknowledge that many available commercial solutions are safe and of a high quality, there are many examples of poor-quality commercial software. After all, such software is developed by fallible humans, who although are skilled programmers, are often lacking in front-line clinical experience. Having said all that, the "do-it-yourself" option carries risk, as a seemingly small mistake in the code can have a serious consequence on patient care. Some managers may deem the risk of bespoke programming too great and opt to purchase commercial software (if indeed it exists).
The advantage of commercial software is that it will be CE marked and, therefore, considered safe. However, CE marking does not guarantee quality. Ultimately, a service provider strives for both quality and safety in clinical software. Where a good quality commercial solution exists, it will always be the favoured option. However, bespoke programming can play a vital role in filling in the gaps where either a commercial solution does not exist, or it is of poor quality.

In response to the question posed, I believe that bespoke programming should be considered a medical device as this holds in-house written software to the same safety standards as commercial vendors, but hopefully with improved quality. Perhaps the next question for the community should be: "What exactly does this mean [to consider something a medical device]?"

"A SERVICE PROVIDER STRIVES FOR BOTH QUALITY AND SAFETY

STE LAKE

A software item is defined as any identifiable part of a computer program – i.e. source code, object code, control code, control data, or a collection of these items.

A computer program is defined as a syntactic unit that conforms to the rules of a particular programming language and that is composed of declarations and statements or instructions needed to solve a certain function, task, or problem.

Stand-alone software is defined as software that is not incorporated in a medical device at the time of its placing on the market or its being made available.

An interesting extension to this is the concept of functional documents defined as "software that requires separate software to perform its function. Often this will be a general purpose application". The MHRA stated in 2020 that examples include):

- A PDF that reproduces a treatment decision flow chart with logical links
- Spreadsheets -particularly if they provide complex functionality that is beyond that of existing paper charts e.g. an Excel spreadsheet that calculates glomerular filtration rate
- Documents with macro or script-enabled functions -complex medical applications can be written with languages such as Visual Basic for Applications
- Interactive web pages -these can utilise programming languages such as JavaScript to produce medical applications
- Scripts written in mathematics-oriented interpreted languages, like R and MATLAB.

Scripts, custom functionality and possibly configuration itself could all be considered to be software items. Highly configurable items could provide logic that interprets medical inputs to create different medical outputs.

The following questions are from an MHRA device determination flow chart.

- Computer program or functional document?
- Is the software performing actions on data different from storage, archival, communication or simple search?
- Is the action for the benefit of individual patients?
- Is the action for a specific medical purpose as assigned to the software item by the manufacturer?

IMAGES: SCIENCEPHOTOLIBRARY / ISTOCK

"THE REQUIREMENT TO DEVELOP THE SCRIPT IN A SAFE MANNER IS STILL MANDATORY

If the answer is "yes" to all of the above, then the software item itself is likely to be a medical device.

Manufacturing or modifying a medical device could include using an existing device for a different purpose to that intended by the manufacturer, or modifying a device for a new purpose, function or performance, and where this action is not explicit in a manufacturer's intended purpose or instructions for use.

The intended purpose is defined as the use for which a product, process or service is intended according to the specifications, instructions and information provided by the manufacturer. Does the added or changed software item:

- Provide additional functionality not covered by the manufacturers statement of intended purpose?
- Change the devices ability to achieve its intended purpose?
- Make changes to the intended purpose of the medical device as stated by the manufacturer?

If the answer is "yes" to any of the above questions then manufacturer's responsibilities under the MDR (2017) need to be addressed and a decision needs to be made on who is the manufacturer.

Finally, when is a manufacturer not a manufacturer? The manufacturer is defined as a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trademark.

The manufacturer of the medical device being added to or changed may adopt the software item as an isolated medical device or may incorporate it into a new version of their medical device and, therefore, take on manufacturer's responsibilities. If the manufacturer of the medical device being added to or changed does not accept manufacturer responsibilities for the software item, even if it has been developed under their governance framework, then the developer will need to accept manufacturer responsibilities if the software item is to be "put into use", possibly adopting the Health Institution Exemption, or even "placed on the market" and, therefore, CE marking the item. This response was written in collaboration with Taktak AFG, Eleuteri A, Payne TG and McDonald I. The arguments made are evidence-based. If you'd like the references, please email splake@nhs.net.

PAUL S GANNEY

There are two schools of thought on this one (naturally, otherwise there'd not be any debate). One view is that scripts are covered by the device's CE mark as the device is intended to host scripts and therefore is operating as intended.

If the device doesn't have a CE mark, for example being covered by Article 5.5 (the Health Institution Exemption – see *Scope* **27:3** for a description) then the question as to whether the device requires a CE mark should be addressed first, taking into account the functionality of the script in question.

This view (that the CE mark covers the script) does not make the manufacturer liable for any errors in programming, however, as the author/owner is still responsible for the safe application of the device (and, therefore, the safe execution of the script). In this view, the question as to whether the script is a medical device in its own right does not arise as it is part of the functionality of the main device.

The alternative view is that scripts form software modules and, therefore, are independent. The MDD (and, therefore, the MDR) defined software as being able to be broken down into modules where each one correlates with an application of the software, some having a medical purpose and some not. (The MDD actually goes down to algorithm level, but that is only really applicable when an entire software system is being considered).

In this view, the question as to whether the script is a medical device (or even an accessory to one) does have to be considered. In order to determine this, helpful flowcharts exist on the MHRA website.

While the first view is probably the most accurate (certainly in the majority of cases where scripts mainly aggregate data), a risk analysis may reveal a requirement to treat the script as independent, thus leading to the second view.

In either view, the requirement to develop the script in a safe manner (including testing, lifecycle considerations, testing, risk analysis, proper documentation, testing and the probable use of a QMS or similar – plus some more testing) is still mandatory. There is, of course, an entirely new can of worms when a script running on a non-medical device may bring that device into the scope of the Medical Device Regulations (e.g. by providing prognosis or diagnosis).

INSIDE THE

The personal insights of a Clinical Scientist

From the shift patterns and unexpected tasks, to the tragedy of death and humbling experiences, Consultant Clinical Scientist **Professor Azzam Taktak** takes us inside the Nightingale Hospital London.

In early April, there was a call asking for volunteer clinical scientists to help provide scientific and technical support to the Nightingale Hospital in London. I had previously worked as a Critical Care Engineer for eight years at the North Midlands Hospital, so offered to help.

After obtaining the necessary approvals from my head of department and the divisional manager, I travelled to London to start a three-day training course on ventilators, infusion devices, patient monitors and medical gases, among other things.

This was followed by a two-day induction at the ExCel Centre, which included mask fitting and training in donning and doffing PPE. We then returned home and were told to await the call while the roster system was being sorted.

NIGHTINGALE

IMAGE: GETTY

FAST FACTS

500

The temporary hospital had the initial capacity for 500 patients

4000

However, it had the potential to house up to 4000 patients

150

It was designed with the capacity to receive and discharge up to 150 patients per day

700

The hospital was due to be run by NHS staff and volunteers, with 700 military personnel providing logistic assistance

16,000

The number of staff when the hospital reached full capacity was initially reported as 16,000

1555

In April, existing London hospitals increased their combined intensive care capacity from 770 beds to 1555

Return to London

After spending five days at home, I travelled back to London on 15 April to start my first shift the following morning. We were divided into four teams of five to six scientists based on the wards. There was also a clinical engineering team and a biochemistry team from Barts Health NHS Trust based outside the wards, which we were able to call upon for support. The work pattern was two morning shifts, two night shifts followed by four days off. Each shift was 12.5 hours long from 8–8:30, with a half-hour period for hand-over. We were offered accommodation at hotels nearby.

Roles and expectations

It was an extremely daunting experience when I first walked into the ward to see all the staff rushing around in full PPE and alarms going off everywhere. Our role was to provide first-line maintenance and troubleshooting equipment on the ward. On a typical shift, we started by doing a round checking all breathing circuits and ventilator settings replacing any items that needed replacing, such as filters, water traps and flow sensors. We carried out daily checks and quality control on point-of-care testing equipment for measuring blood gasses, electrolytes and metabolites. We were also expected to help clinical staff in duties, such as proning and turning patients and changing linen. We were also helping staff in transferring patients to and from renal dialysis bays and the CT scanner. This was quite a challenging task, considering the sheer size and number of equipment, tubes and leads connected to the patient. It required meticulous planning and co-ordination from a multidisciplinary team of anaesthetists, doctors, nurses, operating department practitioners, porters and Clinical Scientists. We were also expected to help the crash team by making available the right equipment to the bedside in case of a life-threatening event. Such events included cardiac arrests or a breathing tube getting dislodged. I witnessed four such events during my shifts, which were very emotional.

Unexpected tasks

During our secondment to the Nightingale, we picked up other unexpected tasks. We setup an electronic logbook to record as much detail as possible on technical failures and other issues related to equipment. This helped a great deal in improving communication between the different teams and in reporting any technical issues to the clinical engineering team and the manufacturers. We were tasked, with help from the clinical team, to investigate minor adaptations to breathing circuits for optimum methods of adding oxygen and monitoring expired gasses. We also got involved with analysing patients' vital signs before and after proning to investigate the effects of proning and who is most likely to benefit from such intervention.

TIMELINE

NIGHTINGALE LONDON

22-23 MARCH
Military planners and NHS England staff visited ExCeL London to determine if the armed forces could support the NHS response to the outbreak

24 MARCH
Plans to create the hospital were announced in a press briefing by Health Secretary Matt Hancock

3 APRIL
The facility was formally opened by the Prince of Wales (via video link)

7 APRIL
The first patients were admitted

11-12 APRIL
Over the Easter weekend the hospital had 19 patients

4 MAY
It was announced the hospital would be put on standby, as no new COVID-19 patients were expected to be admitted.

IMAGES: GETTY / PA / SHUTTERSTOCK / REUTERS

❶ The "Green Team" at the end of a gruelling 12.5 hour night shift. It was a very nice surprise to see Clinical Scientists contribution to the crisis being valued

❷ NHS Nightingale Excel - vertical view of fully equipped ward of beds

❸ The "Yellow Team" in full PPE in the donning area. Visors were kept inside the ward. We were all issued with our own visors every four days.

With heavy heart

I spent 16 days at the Nightingale Hospital London before returning home with a heavy heart. It was such an incredible humbling experience that I will remember for the rest of my life. I formed some great friendships with Clinical Scientists and other medical and non-medical staff, who all demonstrated great enthusiasm and pride in helping out with the COVID-19 crisis. Everyone played a vital role from medics to porters to cleaners to nurses. I could not have worked with a better bunch of people. It confirmed to me how lucky we are to have this fantastic NHS system with such dedicated, caring staff, which I witnessed first hand.

Challenges faced

In my view there were some challenges in the setup of the Nightingale project, which is not unexpected given the short time scale in which it had to be implemented. The main challenge was shortage of critical care nursing staff. This fact, coupled with strict admission criteria, meant that numbers did not rise anywhere near those predicted when the hospital first opened. There were also some issues regarding lack of standardisation of equipment or familiarity of clinical staff with the equipment, especially the types of ventilators used; most of which were ventilators for theatre use adapted quickly to be used in an ITU setting.

These challenges could be remedied in the future (should there be a need) by clear plans to upskill and train staff on the job as some of the volunteer staff including some medics were not trained in critical care. There was also a need in my view for some clear role definitions and task assignments to groups of staff to ensure everyone is working in a coherent manner.

On standby

The hospital has now discharged all remaining patients, but remains on standby to re-admit patients, if needed. Overall, Nightingale Hospital London treated 54 patients all requiring assisted mechanical ventilation; 34 recovered and were subsequently discharged; 20 sadly died.

Azzam Taktak *is a Consultant Clinical Scientist at Royal Liverpool University Hospital. He is also an Honorary Professor at the University of Liverpool and the University of Manchester.*

1 The exterior of Mount Vernon Hospital at Northwood in 1930.

THE GRAY LABORATORY

A brief history pt.1

Edwin GA Aird delves into the history of the world's first radiobiological institute and its connections with Mount Vernon Hospital.

My main reason for writing this series of articles is my great surprise at finding how little is written on Wikipedia about the Gray Laboratory. Although it is possible to find good sources of information about some of the leading scientists in the first 30 years – particularly Harold Gray, Oliver Scott and Jack Fowler (especially their obituaries) – there is nothing that puts the whole story together. The recent *BJR* supplement (2019) for a meeting commemorating both J Fowler and O Scott goes some way towards a better understanding of the history of the Gray Laboratory, but there is still a lack of accessible information in the public domain.

Scientists who worked in the Gray Lab produced some remarkable, groundbreaking work over a period of nearly 50 years, which has helped our understanding of radiation on living organisms. This provided us with a much-needed understanding of how best to deliver radiotherapy to minimise side effects and maximise the tumour damage. In particular, the work on normal tissue damage and the modelling of cell kill using the α/β ratio translated into the design has defined new fractionation schedules; particularly: a) many breast cancers can be treated safely with shorter regimes; b) some lung cancers benefit from an accelerated regime (see CHART by Saunders, published in 1999 for more information); prostate cancer radiotherapy can be given safely and beneficially with larger dose fractions.

There is also the legacy of Gray's work with oxygen (some of it together with Thomlinson) and a better understanding of the value of improving the tumour cell kill by reducing the areas of hypoxia. A *BJR* commentary "Hypoxia in biology and medicine: the legacy of LH Gray" (2006) gives the detail of Gray's intense work on oxygen in tissues. Then, very recently and a reminder that this is still a very live subject, a paper by Tharmalingham and Hoskin was published in the *BJR* supplement in 2019: "The strong evidence in head and

IMAGES: SHUTTERSTOCK

neck cancer in particular suggest that hypoxic radiosensitizers should be used more frequently than is currently the case".

The origins of the Gray Laboratory

In this first article, I will describe the birth of the Gray at Mount Vernon Hospital (MVH) and some of the people involved with Gray that determined the direction he would take with his work. I will also begin to put together some of the relevant facts that will give the reader a feel for the vital position that the Gray Lab achieved in the subject of radiobiology and its links to modern radiotherapy. In the subsequent articles in this series, I will look at the lives of those that led the lab over these years: Hal Gray, Oliver Scott, Jack Fowler, Julie Denecamp and Ged Adams, all of whom at some point during that 50 years were directors of the lab.

The early days

In a sense, the story starts well before Gray founded the laboratory, and tells us why he chose Mount Vernon Hospital site to build his laboratory. This hospital, together with The Radium Institute in London, was already well

known for its use of radium to treat cancer. In 1930 it had been set up as a national post-graduate school of radiotherapy, with the aim to "increase the number of effective workers in radiotherapy and to educate these workers in the latest and most efficient development of both radium and X-ray therapy", and it was already known as "The Empire Centre for the Treatment of Patients Suffering from Cancer"– receiving patients from all parts of the Empire for radium therapy. Radium was obtained from The National Radium Commission. Four grams were made available; three of these to be used for patient treatment, the other for research (at about £15,000 per g). Mount Vernon Hospital was also chosen as one of the main stores for radium during the emergency arrangements in place during the war. A 50 ft bore-hole was made, surrounded by concrete. It would seem that many millions of pounds worth of radium was stored there.

In these early days of the introduction of radiation to treat cancer, it became evident that this would be where physicists would be needed in order to understand and measure the radiation from radium

❸ Hal Gray at his desk at the Gray Lab

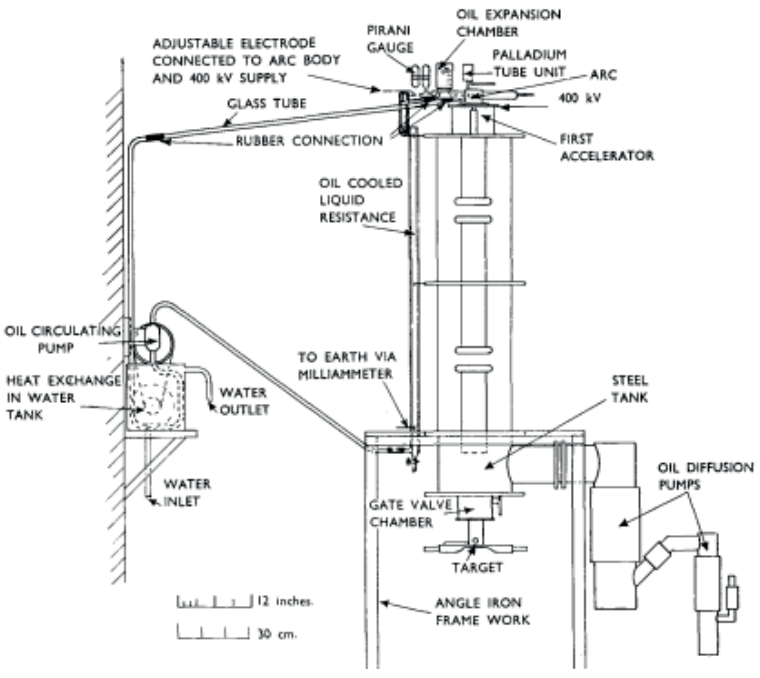
and X-ray sources and to measure the dose received by the patients. Before we look at Gray's work it is important to acknowledge the work of JC Mottram, the pathologist at Mount Vernon Hospital. He had worked at the Cancer Research Laboratories with Professor Sidney Russ (see the summer 2020 issue of *Scope* for an article on Russ by Francis Duck). Russ wrote in his obituary: "...he was for years the outstanding pathologist in this country, to whom radiologists looked for authoritative opinion and with whom they collaborated actively on a large variety of subjects" (note: the title "radiologist" at that time referred both to a physician working in the X-ray imaging department or the clinician in the treatment of cancer with X-rays and radium). This is evident from Mottram's extraordinary body of work in 1908-1940.

Mottram became Director of Research Department at the Radium Institute and with the change in status of MVH became Director of Pathology Research at MVH in 1931 until his death in 1945. He realised that he was in need of a physicist and asked Ernest Rutherford to recommend a bright young post-doc to investigate the radiobiology of neutrons. At the time (1928-1933), Gray was working at the Cavendish Lab, (❻ Cavendish team photo), gaining an understanding of ionisation by photons and developing a theory of the relationship between ionisation and absorbed energy. Some of his colleagues included Rutherford, JJ Thomson, Harold A Wilson, Patrick MS Blackett, CD Ellis and James Chadwick.

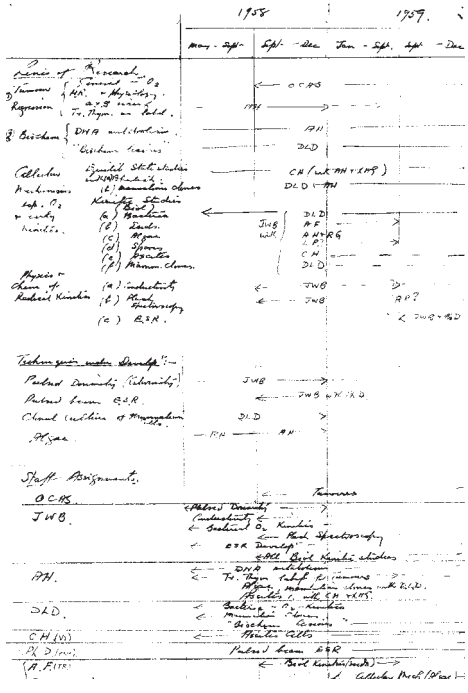
Change of pathway

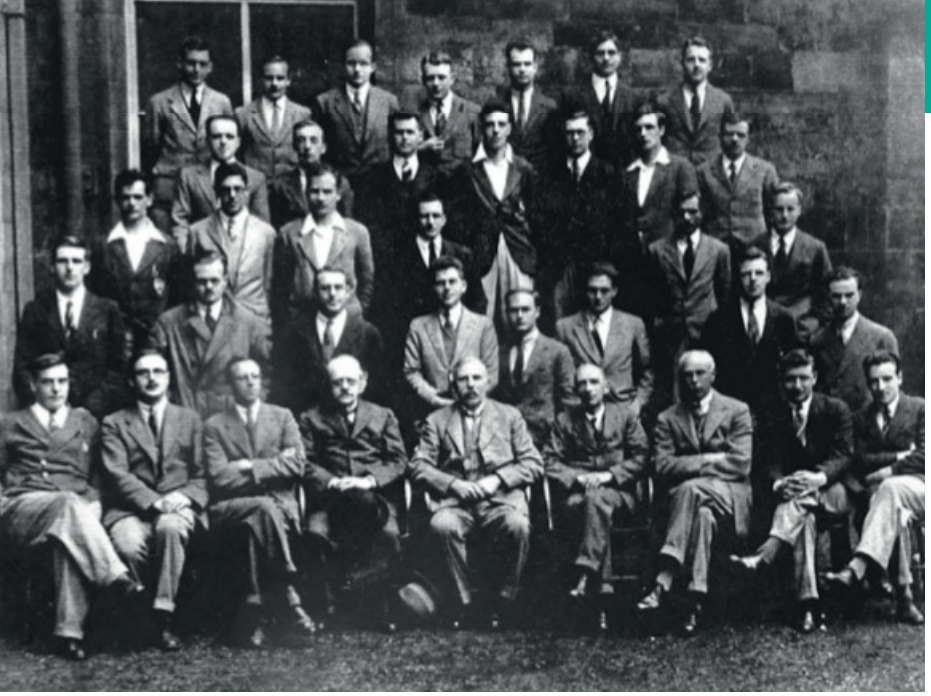
The Director of the hospital, Sir Cuthbert Wallace, encouraged Gray to study some of the medical aspects of cancer, so he went on ward rounds with him and the other clinicians. Mottram was already studying the effects of radiation on broad bean roots. Gray helped him with his studies

❹ Neutron generator schematic



❺ Gray's Research Plan for 1958/59





⓺ (left) Research students and staff of the Cavendish Laboratory in 1930. Front row: P Kapitza, CD Ellis, J Chadwick, Prof Sir JJ Thomson, Prof Sir E Rutherford, Prof CTR Wilson, FW Aston, JD Cockcroft, WH Watson

⓻ (below) The original wooden hut for the neutron generator, used by Hal Gray in 1955-56 while the main lab was being built

of the radiation dose received by using aspects of his understanding of "energy absorbed from a fixed amount of ionisation". Gray and John Read, a physicist appointed to assist him in 1938, began studies on the effect of oxygen to modify radiation response – a subject, which would later indirectly change the pathway of his career and ultimately lead to the founding of the Gray Laboratory.

Chadwick had discovered the neutron at the Cavendish, and Gray must have understood immediately the possibilities for neutrons as alternative radiations for tumour cell killing.

He decided to augment his bean root studies using X-rays and alpha particles with neutrons, but needed a suitable source of high energy neutrons.

Read and Gray built their own neutron generator over a period of two years. They built this from scratch, even winding their own focusing coils. The accelerating tube had a 400kV source (it all cost £600 and the wooden hut ⓻ that housed it cost £150). They used this experimentally with bean shoots to study the differential RBEs of neutrons, alpha particles and gamma rays. In the 1983 book *History of HPA* edited by John Haggith, it says Read "regards those five years collaboration with Gray as the happiest and most stimulating of his life".

Gray wrote many exceptional papers in this period, in particular a lengthy paper on using ionisation to determine gamma ray energy absorbed (1936). But then an extraordinary set of papers

"IT ALL COST £600 AND THE WOODEN HUT THAT HOUSED IT COST £150

with Read (and others) in the *BJR* in 1942 to 1950 on the effects of ionising radiation on the broad bean root. They also established the increase in RBE with ionising density and that the radio-sensitising effect of oxygen was lower with neutrons than with X-rays.

Gray's work with radium

Gray also worked on the dosimetry of radium (following on from his achievements with a small ion chamber in kV X-ray beams: BJR Radiation Dosimetry Part 1). Gray established the "ouput" from a standard radium source as 8.4R/h at 1cm. This value was later used by Paterson Parker for their standard manual of methods and tables for treating tumours with radium. (Those familiar with brachytherapy radium sources will know the old "output" used for radium as 8.25R/H; this is for the more commonly used radium sources which had 0.65mm platinum as a wall thickness instead of the older 0.5mm thickness).

Gray received the Roentgen award from BIR in 1938. The HPA was formed in September 1943 under the chairmanship of Professor Sidney Russ, Middlesex Hospital. Gray was president of the HPA from 1946 to 1947.

In 1946 he moved to Hammersmith Hospital as Senior Physicist initially, then Deputy Director of the MRC Radiotherapy Research Unit. With access to the new cyclotron at Hammersmith he was able to continue his work on the role of oxygen in cell/tissue response. He wrote one of his definitive papers in 1953: "Gray, Conger Ebert, Hornsey and Scott" in *BJR*. This demonstrated his belief in the importance of oxygen tension within the tumour as a major.

The founding moves

A fundamental disagreement with the Medical Director of the unit led to Gray resigning his post at Hammersmith.

The MRC wanted to help him with his work but could find no funds for buildings. This is when Oliver Scott enters the story as the benefactor of the first buildings at MVH that would eventually become the Gray Lab. In 1953 Gray was formally appointed "Nuffield Fellow and Director of the BECC Research unit in Radiobiology at Mount Vernon Hospital" In that year he also gave the Sylvanus Thompson Memorial Lecture at the BIR.

Scott was also one of the first members of Gray's staff together with R R Ransley – a technician. J Boag eventually joined them when the lab was completed in 1958 after working with Rotblat at Barts.

The BECC Research Unit in Radiobiology formally opened in 1957. After the untimely death of Gray in 1965, the unit was renamed the "Gray Laboratory" in 1971.

TAKE A DEEP BREATH

Physiologist **Michael Parkes** looks at prolonged breath-holding for radiotherapy and medical imaging.

> IT IS PRACTICALLY IMPOSSIBLE FOR A PERSON AT SEA LEVEL TO VOLUNTARILY HOLD THEIR BREATH UNTIL THEY BECOME UNCONSCIOUS

Spontaneous breathing causes respiratory movement of all structures within the chest and abdomen. This remains a major problem for radiotherapy delivery and medical imaging. This is not just because of the size of each breath, but also because breathing is naturally irregular in frequency, depth and drive (how fast each inflation is achieved). This irregularity has multiple causes. Firstly, conscious and awake humans will override their automatic breathing control system every time they just think about their breathing. Secondly, the automatic control system is constantly adjusting breathing to match metabolic rate (oxygen [O_2] consumption rate), arousal, posture and multiple other factors (including swallowing, speech, airway sensations and emotion).

One strategy increasingly used in radiotherapy and imaging to mitigate respiratory movements is to ask patients to breath-hold. In particular, what are now popularly known as "multiple (10+?) short (20 seconds?) breath-holds". Their exact details are not usually published. Indeed, we now propose standardising the terminology to refer to all breath-holds achieved with air as "short" and those with preoxygenation and hypocapnia as "prolonged".

For breast cancer treatment, multiple short breath-holds have produced measurable improvements in reducing treatment margins and in heart sparing and are presently undergoing widespread clinical adoption.

Until now, breath-holding had no medical application. So the physiology of breath-holding is not taught in medical schools, nor as part of radiotherapy training or medical physics courses. Yet breath-holding could be far better applied clinically if what has already been discovered (much since the 1950s) was more widely known.

The safety of breath-holding

When breathing air at rest (typically ~10 breaths per minute –br.p.m.- of ~ 0.5 litres –L- air) , the partial pressure of O_2 in arterial blood (PaO_2) remains at ~ 100 mmHg and blood haemoglobin is ~ 98% saturated (SpO_2). The normal arterial partial pressure of carbon dioxide ($PaCO_2$) remains at ~ 40 mmHg.

Breathing is so irregular because our automatic breathing control system is adjusting it breath by breath to match metabolic rate and maintain these

blood gas levels constant. The control system is so good that they remain constant all the way from rest to maximum exercise! How this is brought about still baffles scientists. We consume about 250 ml O_2 min.$^{-1}$ to burn food (fuel) to release energy. We then produce waste (water and CO_2, also at about 250 ml min.$^{-1}$). A maximum lung inflation inhales ~5 L of room air (21% O_2) to provide 1 LO_2. So this inhaled volume could sustain resting metabolic rate for ~4 minutes. Blood contains another ~4 minutes worth of O_2 bound to haemoglobin. So when breath-holding we shouldn't run out of O_2 for ~8 minutes.

Apparently, all mammals can breath-hold, (but nobody yet has tried to train mammals other than humans to do it!). When breath-holding, humans continue to consume O_2, first from alveolar air in the lungs and then from blood haemoglobin. This will start causing Sp $O_2$to fall. Tissues continue to produce CO_2, so $PaCO_2$ rises. But most of this CO_2 remains dissolved in the blood. This is because the absence of breathing means there is no longer the partial pressure gradient necessary to drive this $CO_2$from the blood into the gas phase in alveolar air. Ultimately, all humans must pass out if they breath-hold for too long. Unconsciousness is caused by PaO_2falling below ~ 27 mmHg (SpO_2 < ~55%) and or $PaCO_2$rising above ~ 90 mmHg.

A maximum inhalation of room air enables a breath-hold for a mean, surprisingly, of only about one minute. Why is this nowhere near 8 minutes? Humans have evolved a breakpoint mechanism so safe that "it is practically impossible for a person at sea level to voluntarily hold their breath until they become unconscious". Normally this prevents us from breath-holding for anywhere near long enough for blood gases to reach the levels at which we pass out. Additionally, there is a further and simple safety precaution, described below, that can be taken to ensure this doesn't happen. Following a maximum inhalation of air, mean SpO_2at breakpoint has barely fallen (reaching only ~96-98%) and mean $PaCO_2$ rises only slightly, reaching ~44-50 mmHg.

Safety monitoring equipment

We have deliberately devised very cautious clinical safety limits for breath-holding. Clinically it is so easy to monitor SpO_2 with a non-invasive pulse oximeter clipped onto a finger or toe. We also recommend connecting the patient to a non-invasive blood pressure monitor and an electrocardiogram (ECG) machine.

We advise breaking a breath-hold if SpO_2 falls <94% and or systolic blood pressure is consistently (> 10 beats in a row) above 180 mmHg. Surprisingly, breath-holding has no effect on heart rate. Having devised these safety limits, it is actually very difficult when breath-holding with air for most healthy volunteers or patients ever to reach them. Indeed, in our laboratory nobody has ever reached them consistently from day one and only one person has ever managed to force them self to learn to reach them every

"THE CONTROL SYSTEM IS SO GOOD THAT THEY REMAIN CONSTANT ALL THE WAY FROM REST TO MAXIMUM EXERCISE! HOW THIS IS BROUGHT ABOUT STILL BAFFLES SCIENTISTS

MICHAEL PARKES

Michael, pictured above, is a physiologist at the School of Sport, Exercise and Rehabilitation Sciences, Wellcome Trust Clinical Research Facility and Depart of Radiotherapy, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, United Kingdom. He has a Marie Sklodowska-Curie Individual Fellowship from the European Commission at the Radiation Oncology Department,Academic Medical Centre, University of Amsterdam in the Netherlands, starting in October 2020.

time. The main purpose of this monitoring equipment is to reassure clinical staff and patients that proper safety monitoring is a being undertaken.

The breakpoint mechanism

For at least 400 years we have always used the words "breath-holding," because the chest naturally recoils (deflates) at maximum inflation. So we have to use inspiratory muscles to actively hold the chest inflated and these can only be the diaphragm, some external intercostal and scalene muscles. We know that the breakpoint mechanism is nothing directly to do with the fall in PaO_2 nor rise in $PaCO_2$, because arterial blood gas levels can be normal at breakpoint (see below). Nor is it anything to do with sensations from within the chest. We know this because you cannot prolong breath-holding by preventing these sensations reaching the brain; neither those sensations from the lungs (by anaesthetizing the vagus nerves) nor from the chest (by anaesthetizing the spinal cord).

The mechanism appears to originate within the diaphragm itself, because breath-hold duration can be greatly prolonged by preventing the information from the diaphragm (in the phrenic nerves) from reaching the brain. Since we spend our lives rhythmically contracting and relaxing the diaphragm (~ 10 times per minute), a one-minute breath-hold is an abnormally long and continuous diaphragm contraction. This may impede its own blood supply. The lack of O_2 delivery may cause a local build up of hypoxic metabolites (protons and CO_2, among others) that in turn stimulates muscle chemo-(metabolo-) receptors within the diaphragm. This information then goes back up the phrenic nerves, stimulates the brain and provides the almost irresistible urge to restart breathing.

The importance of understanding this is to reassure patients that when asked to breath-hold as long as they can, their increasingly irresistible urge to breathe is a sensation coming from a muscle and not of asphyxia! It is, therefore, quite safe to briefly resist this urge.

How to prolong

Because breath-holding physiology was never taught at medical school, the clinical practice has evolved of only asking patients to breath-hold for about 20 seconds. We have already established that on their first day in the laboratory (day one), the first ever duration (without any instruction, practice or training) of breath-holds from air in breast cancer patients is 42 ±2 seconds (with none < 29 seconds). So in a situation where minimal training is provided to patients, and the clinical requirement is for multiple breath-holds with minimal gaps, the 20 seconds guess was not unreasonable.

Everyone can improve their breath-hold duration from air by~ 30% just by instruction in good technique and by practising. The good inhalation technique is:-

1) Maximum inhalation, by keeping the shoulders down, ensuring the diaphragm descends (the belly button rises) and that the chest rises,

2) Completely refreshing the alveolar air, by always inhaling maximally, exhaling maximally and only then inhaling maximally to breath-hold.

Practise also is crucial, for the patient to familiarise and learn to tolerate the sensations preceding their breakpoint; to recognise that nothing dramatic or embarrassing happens if they try to hold for a bit longer and to bond with their radiotherapy team. Humour and jesting at this stage are a great bonus (and fun) for everyone and help enormously in building patient's confidence.

We have established that after such instruction, practice (and humour), healthy subjects, even on day one, can then hold with air for a mean of 1.4 ±0.2 min and breast cancer patients for 1.0 ± 0.1 min.

Many radiotherapy treatment rooms will have access to a piped, medical O_2 supply and everyone so far can ~ double their breath-hold duration simply by inhaling 60% O_2, (rather than room air). Thus with 60% O_2 on day one, our normal subjects held for 2.8 ±0.4 min and breast cancer patients for 1.6 ±0.1 min. Despite holding for longer, their SpO_2 at breakpoint is now 100% i.e., better than normal. The explanation for this is simply that replacing alveolar

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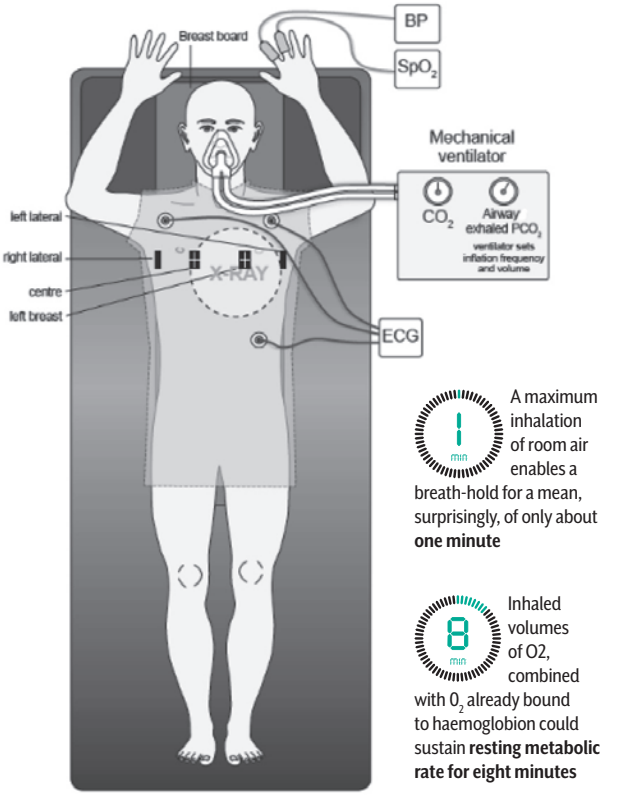
air (21% O_2) with 60% O_2 increases the total O_2 available to sustain resting metabolic rate, now for ~16 minutes. Inhaling 60% O_2 has barely any effect on SpO_2. There is just more O_2 in the alveolar air. Similarly, more available O_2 means that hypoxic metabolite levels in the diaphragm will take longer to build up, so they can breath-hold for longer. However, 100% O_2 should not be used, because there is a theoretical danger of atelectasis (regional lung collapse) occurring during breath-holding, once all alveolar O_2 is consumed. Whereas by inhaling 60% O_2, alveolar gas still contains enough nitrogen (40%) to prevent atelectasis.

It should be obvious that patients could now be routinely breath-holding for longer, just by inhaling 60% O_2, rather than air. Also, that this is the simple means of preventing SpO_2 ever falling during breath-holding (and hence preventing passing out).

Regularisation of breathing

Twenty years ago, we devised the technique of connecting conscious, unmedicated subjects to a non-invasive mechanical ventilator ❶ via a facemask and training them to allow the ventilator to take over their breathing completely. This usually takes about 20 seconds.

❶ Equipment on the patient during mechanical ventilation in the simulator room.



This offers two features to revolutionise radiotherapy delivery. Firstly, by completely taking over the patients breathing, the ventilator can impose on the patient a breathing pattern of completely regularised frequency, volume and drive. Others in Europe too are now evaluating this. It should make tumour tracking far easier and offers the treatment planner the possibility of personalised radiotherapy delivery anywhere between:

Slow deep ventilation (e.g. 3 br.p.m @ 1.8L), where the target is predictably stationary between breaths, but when it moves, the movement is big

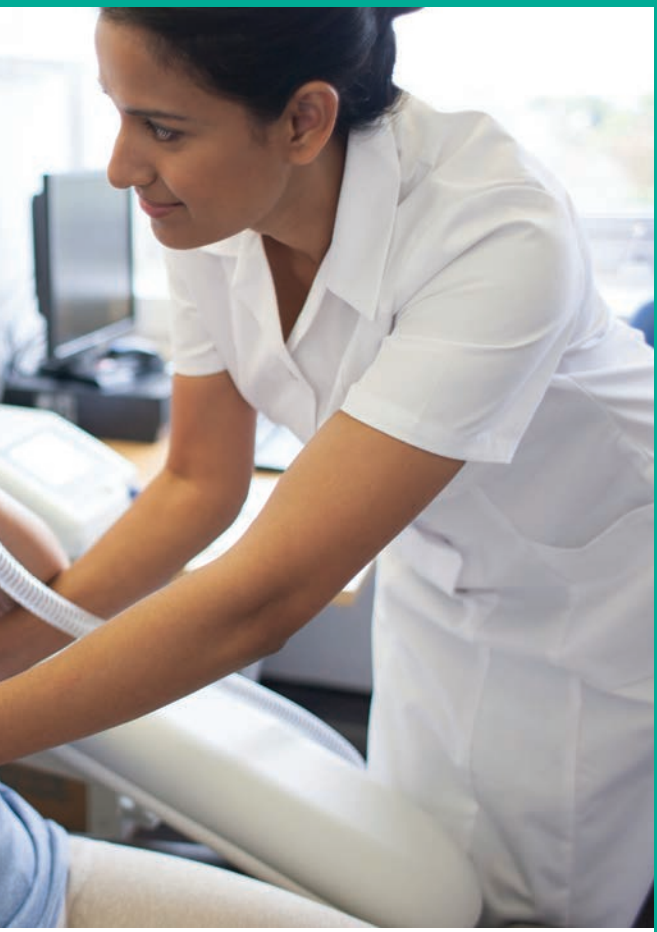
Rapid shallow breathing (e.g., 25 br.p.m @0.2L), where the target is always moving predictably, but by such a small amount, i.e. <1 mm chest surface movement per breath.

Prolonging with preoxygenation and hypocapnia

Secondly, It has been known since at least the 1950s, that breath-hold duration can be safely and dramatically prolonged by at least five fold by combining preoxygenation with hypocapnia. Not only is more oxygen available to sustain metabolic rate. But also halving the blood content of CO_2 means double the amount of CO_2 can be absorbed during breath-holding before CO_2 levels rise back to normal, resting levels. Breath-hold duration is prolonged because both processes will delay the build up of hypoxic metabolites in the diaphragm. The two most important physiological consequences of stopping breathing are thus temporarily mitigated.

There are only two means of lowering $PaCO_2$. Early breath-holding studies used voluntary hyperventilation (voluntarily over-breathing by more than in proportion to metabolic rate). But this is just too difficult for patients to undertake routinely. The effort in over-breathing itself produces more $CO_2$and the level of hypocapnia is too difficult to control safely.

Instead, we use mechanical hyperventilation. Once the patient has let the ventilator take over their breathing, we can increase the ventilator frequency slightly (to 16 b.p.m.) and the inflation volume (now with 60% O_2) such that $PaCO_2$ falls to 20 ±0 mmHg. This is the lowest $PaCO_2$ level that can be



FAST FACTS

A maximum lung inflation inhales five litres of room air

21%

Of this air his O_2

This provides a total on 1 litre of O_2

accurately and safely maintained (for over an hour, if necessary).

Our study in 2016 showed that using mechanical hyperventilation with preoxygenation, 15 breast cancer patients undergoing radiotherapy (and some also chemotherapy) could now hold on day one for 2.9 ±0.3 min. SpO_2 at breakpoint was still 100 ± 0%. Remarkably, with just three further practises with this mechanical ventilation, our breast cancer patients (even the eldest, at 74 years old) could consistently deliver breath-holds of over five minutes, (a mean 5.3 ± 0.2 min), while lying supine on a breast board in a treatment room.

Such prolonged breath-holds are perfectly safe, with mean breakpoint SpO_2 levels of 98 ± 1% and $PaCO_2$ of 37 ±1 mmHg i.e. the same as those during normal breathing! (This elegantly shows too that arterial blood gas levels don't cause the breakpoint). There is also a huge morale boost for patients. Both in realising that here is something they can do towards their own treatment and a skill that even their partners can't do! It also works as well for breath-holding in the prone position.

We have now shown that healthy subjects can perform multiple prolonged breath-holds (nine in a row). This offers the possibility of 41 minutes of treatment time (breath-holding) in a one-hour treatment session, or two breath-holds of four minutes each, within the duration of a typical treatment session.

Benefits for cardiac patients

Such mechanically induced hypocapnia is so simple and so safe that it can be done even by patients with angina awaiting coronary artery bypass surgery. This hypocapnia has no clinically significant effect on even their hearts or ECG. This also shows that the main purpose of routine the ECG monitoring during prolonged breath-holds is actually in reassuring clinicians that their cancer patients are being properly monitored.

One further exciting development in radiotherapy physics is the use of radiotherapy for cardiac ablation, instead of lesioning the ventricle wall using radiofrequency or freezing for patients with cardiac arrhythmias. Currently such radiotherapy is being considered only when treatments with all other ablation and pharmacological techniques have failed. Instead, patients may soon undergo stereotactic ablative body radiotherapy (SABR), precisely targeted to destroy the aberrant ventricle tissue causing the incorrect electrical signals that induce an abnormal heart rhythm. The advantage of SABR over radiofrequency or freezing is its complete non-invasiveness. Whereas the other techniques require a vascular catheter, threaded via a vein in the groin, or an artery in the neck, into the cardiac ventricle and then placed next to the aberrant part of the ventricle wall to apply electro-coagulation or freezing. But the patient's breathing remains a problem because each inhalation pushes the heart downwards (caudally). Stopping breathing with a safe breath-hold of over five minutes, using preoxygenation and mechanically induced hypocapnia, could allow the medical physicist to target the radiotherapy for cardiac ablation much more precisely.

Conclusions

There are now a number of very simple means available to reduce respiratory movement in radiotherapy and medical imaging. The simple combination of training, practice and inhaling 60% O_2 will double patient's breath-hold duration. Since no specialist equipment is required and medical O_2 is always available, these could be introduced easily into radiotherapy practice and soon make multiple short breath-holds redundant. A non-invasive mechanical ventilator will completely regularize patient's breathing and enable treatment planners to deliver personalised radiotherapy anywhere between slow deep and rapid shallow breathing. If prolonged breath-holds (>5 minutes) are required, preoxygenation and mechanical hyperventilation can deliver these too.

I am always very happy to visit radiotherapy departments to discuss these developments and their implementation with anyone who might be interested.

CareMin650™

Groundbreaking phototherapy system aimed at revolutionising the treatment of **oral mucositis** and **radiation dermatitis**

- Safe, simple + accurate
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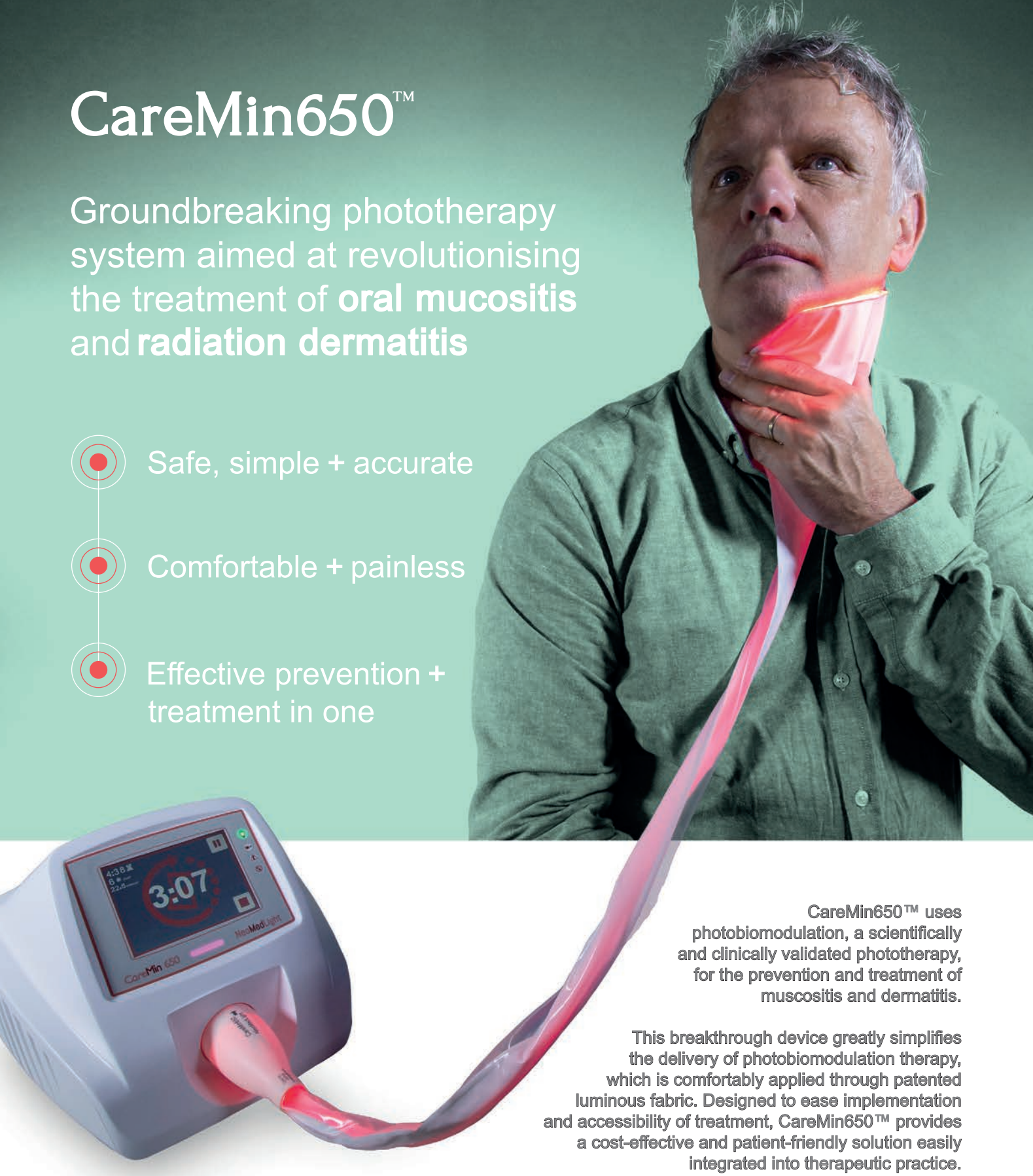
- Effective prevention + treatment in one



CareMin650™ uses photobiomodulation, a scientifically and clinically validated phototherapy, for the prevention and treatment of muscositis and dermatitis.

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CareMin650:

A new device for the management of radiotherapy/chemotherapy-related oral mucositis or radiation dermatitis

CareMin650 is a new photobiomodulation device that has been developed to improve prevention and treatment of oral mucositis and radiation dermatitis in cancer patients.

A. Visbecq, MD[1], P. Saint-Girons[1]

1. NeoMedLight. Corresponding author: Pierre Saint Girons, NeoMedLight

Oral mucositis (OM) and radiation dermatitis (RD) are among the most frequent and disabling adverse effects experienced by patients who receive chemotherapy (CT) and/or radiation therapy (RT) to treat cancer. The management of these conditions represents a major unmet medical need.

PREVALENCE OF OM AND RD

● **Oral mucositis** The incidence of OM depends on the therapeutic protocol used, therefore depends on the underlying disease. It varies from 20–40% in patients who receive CT alone to 80% in those who receive myeloablative conditioning before hematopoietic stem cell transplantation (HSCT), and affects nearly all patients treated with RT ± CT for head and neck cancer [1]. In the latter, a literature review showed that incidence of OM all grades was 97% for patients receiving conventional RT, and 100% for those who received altered fractionation RT (RT-AF) [2]. The incidence of grade 3–4 OM was 34% and 57% respectively. The mean duration of mucositis was 39.7 days (range 7–98).

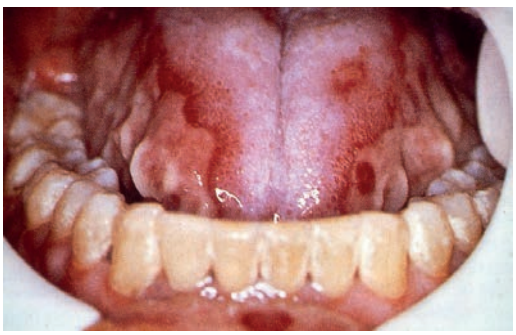
OM has multiple and serious consequences, the severity of which increases with OM grade *(Table 1 and Figure 1)*.

OM provokes dysphagia (56%), and pain (70%), which impair the patient's ability to talk, swallow and eat [2,3]. Pain-related OM requires opioid use in more than half of the patients [2]. Severe OM is associated with increased weight loss [4] and insertion of feeding tubes may be necessary when OM prevents food intake. OM increases the risk of bacterial or fungal infections due to mucosal injury, with potentially life-threatening

Table 1: WHO classification of OM[29]

Grade	Description
0 (none)	None
I (mild)	Oral soreness, erythema
II (moderate)	Oral erythema, ulcers, solid diet tolerated
III (severe)	Oral ulcers, liquid diet only
IV (life-threatening)	Oral alimentation impossible

Figure 1: oral mucositis grade 3



sepsis [2,3]. OM may provoke interruption or modification of anticancer treatment plans, potentially leading to decreased efficacy [2]. Finally, OM may require hospitalization of otherwise ambulatory patients [2]. Taken together, all these OM-related consequences significantly increase the cost of patients' management [4], and significantly impair the patients' quality of life (QoL), even in case of low OM grade [5].

● **Radiation dermatitis** RD is a very frequent side effect of RT since it affects approximately 95% of patients [6]. It usually occurs within 4 weeks after the start of RT (acute RD) and varies in severity from mild erythema to dry or moist desquamation and ulceration [7]. Late toxicity is less frequent, but it usually persists and severely impairs QoL. Some tumour sites are more frequently associated with RD, such as brain, breast, head and neck, perineum and anal canal [7]. Nearly all women treated with RT for breast cancer experience some degree of RD [8]. Intensity modulated radiation therapy may reduce the severity of RD compared to standard radiation; however, moist desquamation still occurs in approximately one third of patients [9]. Several classifications have been established to grade RD, the most frequently used being RTOG/EORTC and CTCAE [7] *(Table 2 and Figure 2)*.

Although RD usually resolves spontaneously after the end of RT, it can be very painful and disabling during the acute phase, causing discomfort, irritation, itching, and burning. Therefore, it can severely impair the patients' quality of life during treatment and in some cases, it requires treatment interruptions [6].

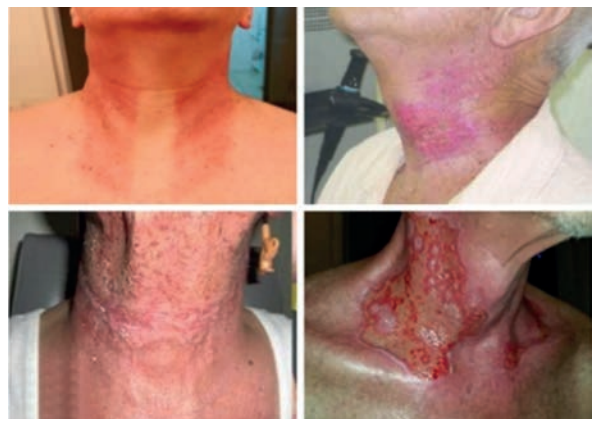
MANAGEMENT OF OM AND RD: EVIDENCE SUPPORTS THE ROLE OF PHOTOBIOMODULATION (PBM)

PBM is a non-invasive treatment that has been used for more than 40 years in a number of different settings, to stimulate healing, reduce inflammation, oedema and pain [10]. PBM has a wide range of effects at the molecular, cellular, and tissue levels [11], the basic biological mechanism being absorption of red and near infrared light by mitochondrial chromophores, with a

Table 2: RD severity, CTCAE v5

Grade	Description
0 (none)	None
I (mild)	Faint erythema or dry desquamation
II (moderate)	Moderate to brisk erythema; patchy moist desquamation mostly confined to skin folds and creases; moderate edema
III (severe)	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion
IV (life-threatening)	Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated

Figure 2: Grade 1 to 4 radiation dermatitis



cascade of events leading to biostimulation of various processes. PBM alters the cellular redox state and alters the affinity of transcription factors concerned with cell proliferation, survival, tissue repair and regeneration.

Very few options demonstrated efficacy for prophylaxis and/or treatment of OM, although a huge variety of treatments have been experimented (growth factors, cryotherapy, mouthwash using various compounds, honey, aloe vera, sucralfate...). The same applies to RD with still less options available. Only PBM could demonstrate significant benefits in several randomized clinical trials of OM, in patients with head and neck cancer [12-16] or in those undergoing HSCT [17-22]. In a meta-analysis that included 18 randomized clinical trials (1,144 patients), prophylactic PBM reduced the overall risk of severe mucositis (RR: 0.37, 95%CI 0.20; 0.67, p=0.001) [23]. In a Cochrane review that included 32 trials involving 1,505 patients, only PBM showed a reduction in severe OM when compared with the sham procedure (RR 5.28, 95%CI 2.30; 12.13) [24]. According to guidelines issued by the Multinational Association of Supportive Care in Cancer (MASCC), PBM is recommended to prevent OM in patients receiving high dose CT with or without TBI as a conditioning regimen for HSCT and in patients undergoing RT ± CT for head and neck cancer25. The National Institute for Health and Care Excellence (NICE) determined that PBM for OM shows no major safety concerns and that evidence on efficacy is adequate in quality and quantity26.

In dermatology, PBM can be used in a wide range of pathologies, such as psoriasis, vitiligo, burns, hypertrophic scars and keloids, herpes virus lesions [11]. In cancer patients, evidence for RD is lower than in OM as the experience is more recent. However, in the DERMIS trial that compared 2 successive groups of patients undergoing identical RT regimens, skin lesions at the end of RT had worsened in the control group but not in the PBM group (RTOG grade 2: 29% vs. 3%, p<0.005). The RISRAS subjective score decreased in the PBM group only 27. More recently, the TRANSDERMIS trial randomized to PBM or placebo 120 patients with breast cancer scheduled for RT 28. At the end of RT, more patients experienced grade 2 or higher skin reactions in the placebo group (30%) than in the PBM group (6,7%, p=0,004). In the PBM group, no patient developed grade 3 dermatitis, the objective RISRAS score increased less than in the placebo group, showing less severe skin reactions, and QoL (Skindex-16) improved while it remained stable in the placebo group.

Unfortunately, PBM is not standardized since medical teams use various equipment, set with various parameters: wavelength, irradiance or power density, pulse structure, coherence, polarization, energy, fluence, irradiation time, contact vs. non-contact application, and repetition regimen. In addition,the procedure is not fully reproducible even in a single institution and is operator dependent. The distance from the skin is difficult to assess and to control accurately. Thus, the amount of energy delivered at each session cannot be exactly known. Finally, the procedure requires cumbersome and expensive equipment.

CAREMIN650

CareMin650 has been developed to overcome these issues. It will allow a reproducible delivery of light, regardless of the operator. As light will be emitted in a homogeneous fashion by a flexible textile surface in contact with the skin/mucosa, the dose delivered will be clearly controlled and operator independent.

The CareMin650™ system is made of 3 components:

- **The lightbox** *(Figure 3)* emits red light at a frequency of 650 nm. Its touch screen makes it possible to select the desired light dose (between 1J/cm² and 9J/cm²). The system automatically calculates the duration of the treatment (2 to 5 minutes).

Figure 3: CareMin650 lightbox

Figure 4: CareMin650 oral pads and dermal pads

Figure 5: sleeves used to cover CareMin650 applicators

- **The Light Pads.** It is possible to choose between the Oral Pad for the treatment of oral mucositis or the Dermal Pad for radiation-induced dermatitis *(Figure 4)*.

Thanks to an easy plug and play system, the lightbow automatically identifies which pad is plugged. The Oral Pad consists of two pads with double-sided light emission for a total treatment area of 50 cm^2. The Dermal Pad, emits light from only one side for a total treatment area of 75cm^2.

- **Special protection sleeves** must be used for the pads. These sleeves cover the light pads so that they can be applied to the skin or mucous membranes *(Figure 5)*.

Pads covered with the sleeves are placed into the mouth (oral pads) or on the skin (dermal pad) to illuminate the target area *(Figure 6)*.

EVALUATION OF CAREMIN650 IN THE SAFE PBM STUDY

The feasibility, safety and preliminary efficacy of CareMin650 are being evaluated in a clinical study (Safe PBM) that includes patients with 2 different conditions (head and neck cancer or breast cancer) in 2 different settings (prevention or cure) *(Figure 7)*. An interim analysis was performed in March 2020.

Nineteen patients (351 sessions of CareMin650) were analysed including 7 in cohort A1 (36.8%), 3 in cohort A2 (15.8%), 7 in cohort B1 (36.8%) and 2 in cohort B2 (10.5%). No treatment emergent adverse event was considered related to CareMin650 and no adverse event led to CareMin650 discontinuation.

Among 7 patients included in cohort A1, only one grade 3 OM was reported. In this patient, PBM had been initiated 6 days after the start of RT instead of starting at day 1 of RT as planned per protocol. This patient received concomitant chemotherapy with cisplatin and had 2 radiation areas (oropharynx and bilateral cervical nodes). Among 7 patients included in cohort B1, only one grade 3 RD was reported. It occurred 51 days after the start of RT: the patient had no lesion during the whole RT course, RD was diagnosed at the follow-up visit 13 days after the last RT session, and was grade 3 upfront.

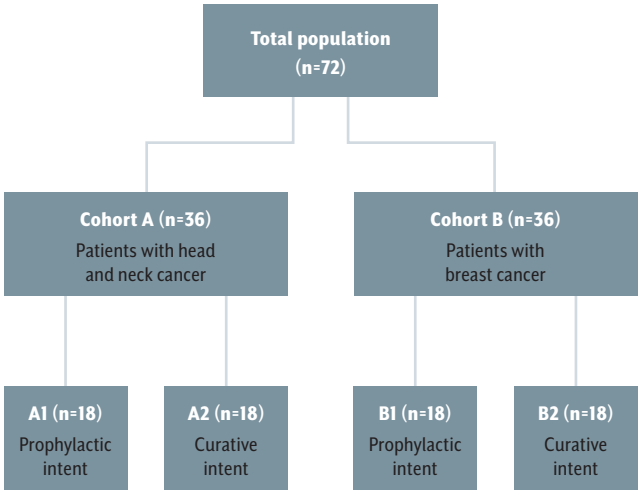
Although preliminary, these results strongly suggest a very good tolerance profile of CareMin650 and provides encouraging data on efficacy in the preventive setting.

CONCLUSION

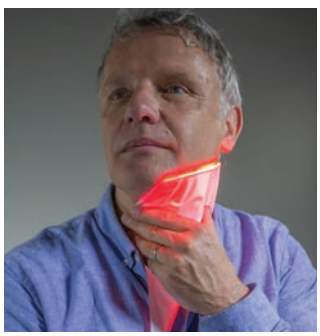
Oral mucositis and radiation dermatitis are very frequent and disabling complications of radiotherapy

Figure 6: utilisation of CareMin650

Figure 7: Safe PBM study design



and / or chemotherapy in cancer patients. There are very few options to prevent and treat these deleterious side effects. Photobiomodulation (PBM) showed the highest level of evidence for efficacy and safety, with several randomized clinical trials and meta-analyses. However, current devices used for PBM are cumbersome, difficult to use and do not allow reproducible effects. CareMin650 is a new PBM device that has been developed to overcome these issues: it uses flexible surfaces in contact with the skin/mucosa, the dose delivered is accurately controlled, and the device is user and patient friendly. Preliminary results of an ongoing clinical study suggest a very good safety and efficacy in the prevention of OM and RD.



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Sue Powell and colleagues look at anatomy changes during radiotherapy treatment using volumetric modulated arc therapy and ask when we need to consider re-planning.

WEIGHT LOSS IN RADIO-THERAPY

Weight change is a common side effect of radiotherapy. This usually occurs due to loss of appetite following nausea, diarrhoea or vomiting. Radiotherapy can also disrupt normal physiological functions, particularly in the gut, resulting in anatomical changes.

These changes are easily identifiable due to the routine use of cone beam computed tomography (CBCT) throughout radiotherapy treatment. Anatomical changes are a common cause of concern for treatment radiographers, particularly when critical structures – organs at risk (OARs) – are in close proximity to the planning target volume (PTV).

The planning team were often (an average of four per week) asked by the treatment radiographers to complete "dose assessments" on volumetric modulated arc therapy (VMAT) treatments to assess the impact of anatomical changes on dose distribution and dose to organs at risk. This had continued for some years, and had not been formally reviewed. Anecdotal evidence suggested that very few rescans due to weight change had been needed for VMAT treatments. This revealed the need to provide guidance to radiographers on acceptable levels of anatomical change and develop some tolerances to demonstrate when rescanning patients treated with VMAT plans would be appropriate.

An audit was conducted. Information from dose assessment requests for VMAT treatments over a three-month period were collated and assessed. The VMAT dose assessment requests were categorised into treatment regions and the changes assessed varied from weight gain or loss, to internal changes such as bladder fill, tumour shrinkage and lung consolidation. The following discussion summarises the findings of this audit.

Dose assessment methodology

CBCT images were imported into the Treatment Planning System TPS (Pinnacle V16.2.1, Philips Healthcare, Nederland B.V.), and the CBCT images were fused to the original planning scan.

Three treatment regions were the focus of this audit as they formed the majority of dose assessment requests. The total number of dose assessments for each site are indicated in Table 1.

For external contour changes, a region of interest (ROI) was created to mimic the change in body contour. If weight

gain was observed then tissue density of 1gm/cm^3 was applied to the region of contour change. Similarly, if weight loss was observed then tissue density of 0.01gm/cm^3 was applied to this ROI. The dose was then recalculated on the original scan, using these new density values, with the treatment monitor units applied. The new treatment plan dose distribution was then compared to the original dose distribution.

For internal changes, each instance must be assessed on an individual basis. OARs visualised on the CBCT were contoured. Then the dose to that OAR was assessed, along with at which fraction the change was identified. If the dose to the OAR had increased and was out of tolerance then action could be taken, either to rectify the internal change or to make the clinician aware of the increase in dose for consideration of replan. All VMAT plans are produced and reported using ICRU Report 83 guidelines.

Discussion

Head and neck

For head and neck treatments, anatomy change most often occurs in multi dose level (MDL), bilateral patients. Fast growing tumours react quickly to treatment and the irradiation of a larger area of tissue results in increased side effects when compared to unilateral treatments.

When considering the most extreme example taken from our sample, weight loss around the neck was noted and the tissue thickness change quantified as 1cm on one side and 0.7cm on the other. The isolines wrapped around the spinal cord, and at planning the cord dose maximum was 37.9Gy. The plan was recalculated using the amended body contour with the relevant mass density override applied. The cord dose maximum increased to 38.2Gy i.e. an increase of 0.3Gy (0.8%) over the whole treatment. A further observation for this patient was that the isolines moved deeper in this patient only by around 1mm. Therefore PTV minimum coverage was not compromised.

All MDL head and neck treatment are planned using dual full arcs (two, 360 degree arcs). Therefore, any change in effective path length, i.e. weight loss/gain, is minimised by the sweep of at least one full arc.

A dose assessment was carried out for all head and neck patients investigated in this audit. In all patients the cord maximum dose either did not change, or the dose increased by a maximum of 1%. It appears that as VMAT plans are optimised to shield the spinal cord as much as possible, the dose to the spinal cord is largely unaffected by weight

Table 1. Summary of dose assessment requests over a three month period.

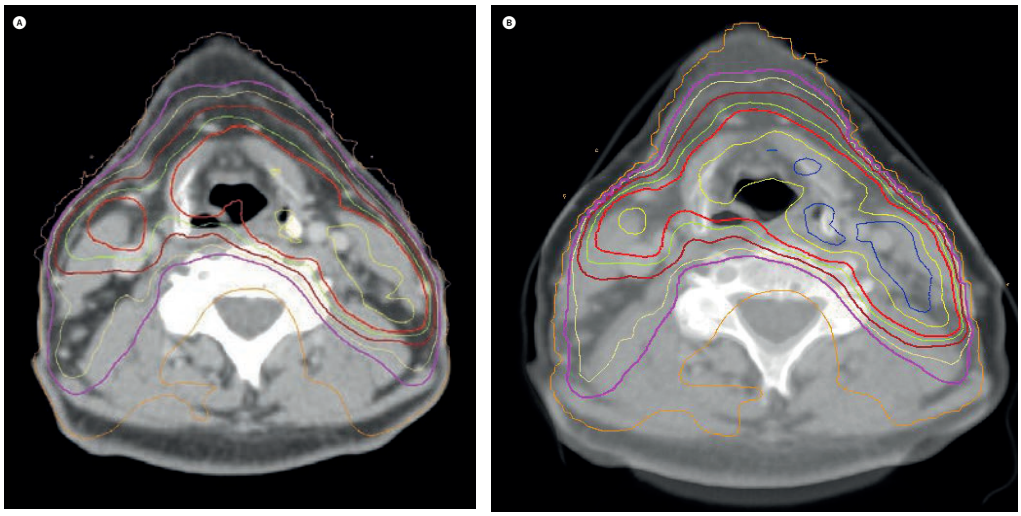
	Total	External Contour Changes	Internal Anatomy Changes
Head and Neck	34	34	none
Pelvis	17	5	12
Chest	3	1	2

❶ Fraction 24 of 30 fractions, total 65Gy. Two full arcs

Ⓐ Distribution approved by clinician.

Ⓑ Distribution after recalculation with density override applied to regions of weight loss (images overlaid) 1cm weight loss observed laterally. Yellow isoline is 100% dose, blue isoline 102%, purple line 80%, orange line 50%. Note the overall increase in dose across the high dose region by around 2%, the 80% isoline moved slightly, the 50% isoline no significant movement.

S canal PRV max dose was 44.9Gy at planning, 45.5Gy after dose assessment (1% increase).



loss. Therefore, we can say that for a dual arc head and neck radiotherapy treatment, 1cm of weight loss (tissue thickness circumferentially) will result in a maximum increased dose to the cord of about 1.5% total dose. An example of how the dose distribution changes with weight loss is shown in Figure ❶.

"A CHANGE IN BODY CONTOUR UP TO 1.5CM WILL NOT AFFECT THE DOSE DEPOSITED WITHIN THE PTV

Pelvis

Anatomical changes in pelvic patients commonly take the form of either external contour changes, internal anatomy changes, or both. A dose assessment was carried out for all the pelvis patients investigated in this audit. The dose was then recalculated using the method outlined above and the new treatment plan dose distribution compared to the original.

For example, one patient lost a lot of weight – around 1.5cm anteriorly. Two full arcs were used and the PTV was very central within the pelvis. A region of interest (ROI) was created to mimic the weight loss and tissue density of 0.01gm/cm3 was applied to the new body ROI. The dose was then recalculated with the relevant mass density override applied. The new isodose distribution was inspected and compared with the original distribution. They appeared to be very similar, and the ICRU reporting values remained the same, however, the PTV minimum point dose was 38.6Gy at planning, and increased to 39.1Gy after recalculation, ie a 1.3% increase. No notable changes to the OAR doses were observed.

A further example of how the dose distribution changes with weight loss is shown in Figure ❷.

Another factor affecting dose when external contour changes are observed is that, generally, a VMAT plan may not be equally weighted from all directions. For example, for a prostate patient, dose deposition into the rectum and bladder (OARs) are limited from the posterior and the anterior direction by the optimiser. Therefore, there will be more dose deposited laterally. Any external contour change laterally may have a larger impact on the dose distribution than a contour change anteriorly. In contrast when considering a bladder patient, there is no OAR between the anterior surface and the PTV and so more dose will be deposited anteriorly. Hence, large changes in contour anteriorly will have a larger impact on the dose distribution for a bladder treatment when compared to a rectal or prostate treatment.

Internal contour changes: if internal anatomy is not maintained, then the position of the target and other OARS can shift unpredictably. For example if the bladder is not filled as at the planning scan, then loops of bowel may drop into the space previously occupied by the bladder. The gross tumour volume (GTV), e.g. uterus or prostate, may then move anterior and superior as it is not pressed down by the full bladder. Therefore the GTV may potentially move outside the irradiated volume.

Depending on the direction of dose deposition, for pelvic treatments, a change in body contour up to 1.5cm will not affect the dose deposited within the PTV and is acceptable. But internal anatomy must be maintained or a geographic miss may result, or unacceptable dose to OAR may be incurred.

Chest

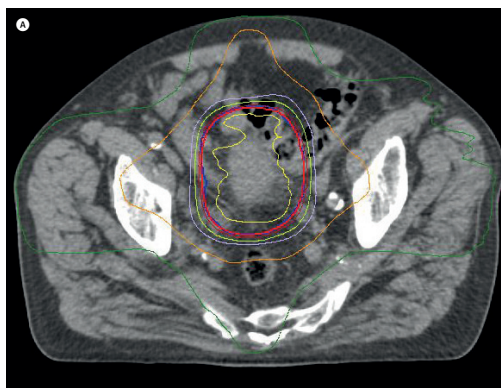
External contour change is uncommon in this site. However, if there is internal change then these internal changes may result in a change in dose deposition either across the PTV, or to OAR.

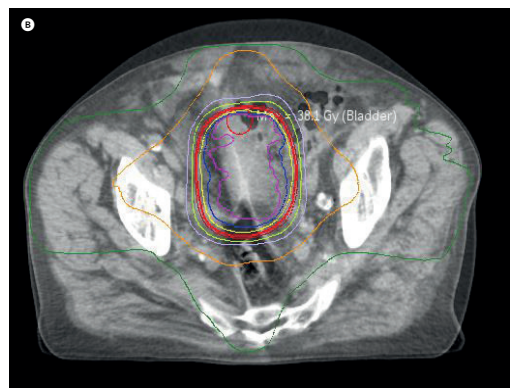
For example, if the GTV reduces in size, prior to, or during treatment, then there may be more lung tissue around the PTV and therefore less photon interactions at that point. Therefore the dose may be deposited deeper in the patient than calculated at the planning stage. This may increase the dose to OAR. In one patient, the cord maximum dose

❷ Fraction 4 of 6 fractions, total 36Gy. One full arc

Ⓐ Distribution approved by clinician.

Ⓑ Distribution after recalculation with density override applied to regions of weight loss (images overlaid) 1.5cm weight loss observed anteriorly. Dose assessment carried out. Yellow isoline is 100% dose, blue isoline 102%, lavender line 80%, orange line 50%. Note the overall increase in dose across the high dose region by around 2%, note the 80% isoline moved slightly, 50% isoline no movement.
No change to OAR doses.





increased from 38Gy to 39.1Gy (~3%), when the GTV shrunk by 1cm radially. If there is lung consolidation, i.e. the lung tissue has been replaced by tissue with a higher density, dose deposited in the PTV may be reduced. This is due to a relatively large increase in the effective path length. Therefore, it was felt that there were too many variables at play to confidently issue guidelines for chest treatments. An example of how the dose distribution changes with internal changes is shown in Figure ❸.

Conclusion

These results show that for VMAT plans with single or dual full arcs, any external contour change of below 1.5cm is unlikely to result in either changes to PTV coverage that fall outside of ICRU 83 constraints, or significant increase to OAR dose and therefore no rescan is required. However, if positional changes are observed on CBCT images then action should be taken:

- Head and neck positional change should be corrected by using departmental methods i.e. change of shims.
- Internal pelvic anatomy positional change should be corrected by following bladder or rectal filling protocols.
- Internal anatomy change in chest patients should be corrected for, or sent for dose assessment.

Advice given to treatment radiographers as a result of this audit:

Head and Neck VMAT plan produced using either one full arc or multiple full arcs:

- Confirm that contour change is below 1.5cm tissue thickness circumferentially
- Confirm that the plan exceeds the ICRU reporting guidelines.
- Confirm that any OARs are at least 3% below maximum tolerance.

If all parameters above are met, then treatment can continue, with no rescan required.

Pelvis VMAT plan produced using either one full arc or multiple full arcs:

- Confirm that contour change is below 1.5cm tissue thickness circumferentially
- Confirm that the plan exceeds the ICRU reporting guidelines.
- Confirm that no internal anatomy positional change has occurred.

If all parameters above are met, then treatment can continue, with no rescan required.

VMAT plans that are produced using partial arcs, and where a change in patient shape is observed, should be reviewed by a member of the treatment planning team.

Training was given to all treatment radiographers in the form of an audio/visual presentation, followed by a question and answer session. All of the findings above were discussed in detail and radiographers encouraged to consider all factors prior to requesting dose assessments.

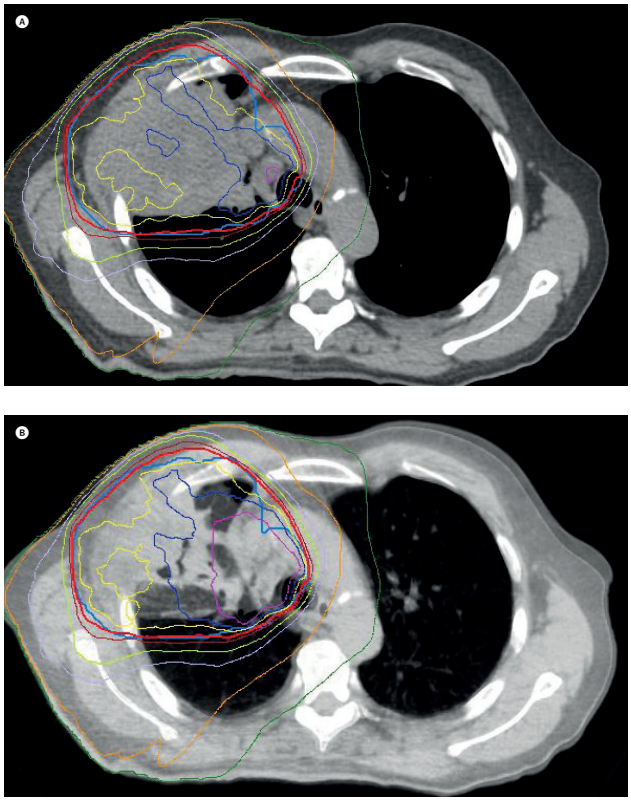
❸ Fraction 23 of 33 fractions, total 66Gy. Two half arcs

Ⓐ Distribution approved by clinician.

Ⓑ Distribution after recalculation with density override applied to regions where GTV has shrunk (images overlaid).

Dose assessment carried out. Yellow isoline is 100% dose, blue isoline 102%, purple line 105%, lavender line 80%, green line 30%. Note the overall increase in dose across the high dose region by around 4%, the 80% isoline moved slightly, and the 30% isoline moved towards the spinal cord.

Both lungs V20Gy was 19% at planning, amended lung volume V20Gy was 27% after dose assessment (tolerance: 30%).



Since the guidelines and training were delivered, the number of requests for assistance has reduced from about four times per week, to around four times per month. This has resulted in a significant reduction in workload within the planning department (estimated to be around seven hours per week of planning time). Further, the radiographers have reported a significant increase in confidence when making decisions in the time-pressured environment that is treatment and associated imaging.

***Sue Powell**, Senior Dosimetrist, **Elaine Buck**, Head of Radiotherapy Treatment Planning and **Andrew Morgan**, Locum Clinical Scientist, are all based at the Royal Cornwall Hospitals NHS Trust.*

LESSONS LEARNED FROM THE FIRST WAVE

From woefully inadequate pandemic stores to flimsy drip stands, **Scott Brown** and **Andrew Frost** cast a critical eye over clinical engineering in the pandemic.

Now that the first wave of SARS-CoV-2 virus has abated, clinical engineering and estates departments have an opportunity to take stock of the past few months and review what lessons can be learnt. We do not know what the future holds; is there going to be a second wave or even further waves? Will this occur again in subsequent years?

Medical gas supplies

One of the challenges faced by hospitals was the predicted unprecedented demand for oxygen. Hospital medical gas pipeline systems (MGPS) are designed using diversified flow design calculations set out in HTM 0-01. However, many hospital critical care units have dramatically increased their ventilatory capacity four- or five-fold by expanding into other areas that would far exceed the design flow of the original MGPS. Clinical engineering departments have provided calculations on flow rates required by different medical devices and hence total system demand.

We have seen examples across the UK where pipeline systems and vacuum insulated evaporators (VIEs) storing liquid oxygen, have been installed very rapidly to increase capacity, however, this is not feasible in all hospital sites.

Guidance from BOC/air products on suggested adjusting the primary regulator pressure to 4.5barg maximum at the VIE, so that the increased demand for oxygen will ensure pressure from the terminal unit (TU) at the bed head remains within normal limits. That said, where large quantities of high-flow devices, such as CPAP, are deployed, the system still may not be able to deliver the desired total flow rate, and there are still limitations due to pipe sizing.

The HTM was written in 2006 and we have seen rapid changes in medical equipment that use medical gases. The requirement for nitrous oxide (N_2O) has dramatically reduced in the hospital setting, many patient ventilators now only require a high-pressure oxygen supply as air is entrained from the atmosphere. Whilst the HTM is an excellent source of guidance on MGPS design, is there now an opportunity to revise the document to align

IMAGES: SCIENCEPHOTO / SHUTTERSTOCK

with current practice/technology and the experience of COVID?

Many community hospitals are not equipped with piped oxygen, so we have seen an increase in the asset base of portable oxygen concentrators to provide oxygen to patients.

New ventilator designs

The predicted shortage of patient ventilators across the United Kingdom prompted the Ventilator Challenge UK initiative. Manufacturers were challenged with designing new ventilators and engineering companies switched production from their normal work to building ventilators. The MHRA published the Rapidly Manufactured Ventilator System (RMVS), which set out the specification of a minimally clinically acceptable ventilator for UK hospitals to use during the pandemic. The design was for life support and intended for short-term ventilation; a few hours, up to one day. The devices would not be CE marked, but approved through the MHRA through the "Exceptional use of non-CE marked medical devices" route.

The challenge now is what happens to this equipment post-COVID.

As it is not CE marked, it cannot be used clinically.

- Do we retain the RMVS for possible future pandemics?
- Do we need to regularly service the equipment, so it is ready for use?
- Will manufacturers seek CE approval for these ventilators?
- Availability of service parts and consumables for equipment coming from non expected sources

Adapting medical equipment

With the challenges around ventilatory capacity, clinical engineering has also been tasked with adapting equipment.

Typically, anaesthetic machines provide short-term ventilation when a patient is undergoing a surgical procedure; normally a few hours at most. Modifying anaesthetic machines to provide long-term ventilation:

- Converting the anaesthetic machine to use medical air as the ventilator drive gas rather than oxygen, where applicable
- Removing the N2O hose, cylinder and regulator
- Changing the configuration so the self-test does not look for an N2O supply
- Soda lime absorber had differing opinions for use: Empty the soda lime in the absorber to keep the circuit moist. Or used in closed-circuit mode with soda lime due to the lack of availability of ET tube adaptors with Luer ports to support side stream CO2 monitoring lead to issues with using HME filters (they have a Luer port) at the ET tube in a humidified circuit causing rainout.

By switching to a closed circuit with an HME filter at the ET tube then solved the problem.

> "MANUFACTURERS OF MEDICAL EQUIPMENT HAVE BEEN CHALLENGED WITH UNPRECEDENTED DEMAND

Pandemic store

Most hospitals will have some form of major incident or pandemic store. We have seen that these have been woefully inadequate to meet the requirements for COVID-19.

There was a lot of equipment purchased to meet the clinical pressures for COVID-19, including ventilators, infusion pumps and CPAP devices.

Space is at a premium in hospitals, so having an on-site store, whilst ideal, may not be feasible. This raises a number of questions:

- We could look at expanding an existing medical equipment library, or should we look for an off-site facility?
- Where should it be located?
- What transport is available to move equipment quickly if needed?
- Where does the cost sit?
- Do we service and maintain as with our normal hospital equipment or wait until it is needed?
- Do we need to set up a replacement programme to ensure this equipment is current?

Nightingale hospitals

Manufacturers of medical equipment have been challenged with unprecedented demand for stocks of both equipment and consumables and they have ramped up production in an attempt to satisfy this demand. However, this could not happen overnight and resulted in extended delivery

times. With the building and equipping of the nightingale hospitals, time was at a premium; tasks that would normally take weeks or even months were completed in a matter of days. In order to achieve this, an abridged acceptance test routine needed to be implemented but not at the expense of safety. Health Tech Solutions were pleased to provide some guidance on this for the equipping of the London Excel Nightingale hospital.

Unfortunately, not all the equipment provided was fit for purpose, predominantly for three reasons:

1. Inappropriate for use in a Critical Care environment

2. Poor technical design including poor ergonomics

3. Build quality issues potentially compromising safety.

Clinical engineers have identified several examples during the acceptance and commissioning tests, which reinforces the value of the inspection process. At the London Nightingale, Andrew Frost, Technical Director at MTS Health Ltd, oversaw the equipping process and the Barts Health team highlighted several problems:

- Equipment inappropriate for use in a critical care environment.
- Beds supplied for patients were rejected due to the absence of a CPR handle in the event of a cardiac arrest and were of a specification appropriate to a care or nursing home, rather than a critical care environment.

Furthermore, due to the absence of a battery backup or manual method of adjusting, patient profiling any interruption in power could be considered to be an operational risk. The headboard could only be removed with the use of a spanner; not a good scenario when an anaesthetist is trying to get airway access in an emergency. The headboard also appeared to be made of wood and so would not be acceptable from an infection prevention and control perspective.

Poor technical design

A syringe pump had extremely poor design with an unprotected ribbon cable between the two halves of the casing visible from outside and there was no seal between the upper- and lower-case, permitting fluid ingress. The earthing arrangement inside the syringe pump was also questionable, even though it was clearly with CE approval!

Software on the syringe pump was also questionable and did not appear to operate smoothly. This, together with difficulty in incorporating an appropriate drug library, forced their quarantining. For patients suffering from Acute Respiratory Distress Syndrome (ARDS), including COVID, it is often found beneficial to warm and humidify the oxygen-air gas supplied to the patient from a ventilator.

The humidifier is fitted in series with the inspiratory limb of the ventilator. Modern humidifiers will have a digital readout display for the temperature, or even controlled and displayed at the ventilator via a data cable. One design of humidifier supplied to the London Nightingale hospital had no digital display and relied on the user eye-balling a small alcohol thermometer inserted into the patient port to give an indication of the temperature. Not only was the thermometer very small, but the graduated scale was only "calibrated" in whole degrees centigrade, so it was difficult to determine the temperature.

Build quality

Drip stands that were too flimsy so bent when even only a few infusion pumps or syringe pumps were attached. Others did not have a wide enough base and so were unstable and subsequently toppled over. Although this may seem trivial it could result in injury to the patient and/or the clinical staff attending to the patient.

Training

One especially useful initiative came out from the UK government's Ventilator Challenge UK in addition to the manufacture of more ventilators. The Ventilator Training Alliance (VTA) App was supported by many manufacturers who gave access to training and product manuals for medical professionals. This has been useful for clinical staff who may be called to use equipment that they were unfamiliar with and for engineering staff.

Many manufacturers have provided remote training to clinical staff on their products through a video conferencing medium. Will we see more of this way of learning in the future and development of e-learning training? We believe this has shown the importance of underpinning knowledge that is not device specific. i.e. principles and clinical applications and this applies again to both clinical and engineering staff.

Conclusion

The value of clinical engineering as a profession has been recognised in the response to the COVID-19 pandemic which will hopefully attract more people to join the profession.

With the massive drive to equip our hospitals to meet the predicted demand for COVID patients, we are now in a much better position to meet potential future waves of this virus.

The importance of Clinical Engineering being involved with helping to steer or act as a gatekeeper with the equipping of these emergency facilities should not be underestimated.

Otherwise we could see ourselves back in the 1970s where anything is bought from anyone, irrespective of safety and usability, as there seemed to be quite a few procurement traps the NHS management teams fell into, mainly because they did not appreciate the consequences of what was being bought. As a result, you end up spending money on inappropriate equipment.

Dr Scott Brown *is Lead Consultant at Health Tech Solutions and* **Andrew Frost** *is Technical Director at MTS Health.*

The science of seating

Mark Bowtell and **Jacob Redwood-Thomas** reflect on the 36 International Seating Symposium.

I hope you are sitting comfortably, as yes – there are international conferences all about seating (and wheeled mobility). So, what is the healthcare field of seating, and why is it important? We work in the Special Seating and Pressure Ulcer Prevention and Intervention Service teams as part Rehabilitation Engineering at Swansea Bay University Health Board. We went to present, share knowledge and experience, and to learn from the latest research and equipment advances.

The three-and-half-day conference in Vancouver saw over 1100 therapists, engineers and equipment representatives from 26 countries attend. The programme was busy and varied, with themes of ageing, obesity, early age mobility, biomechanics, powered assist, posture and function, pressure ulcers and anatomy, and dynamic seating.

Adventure in powered mobility

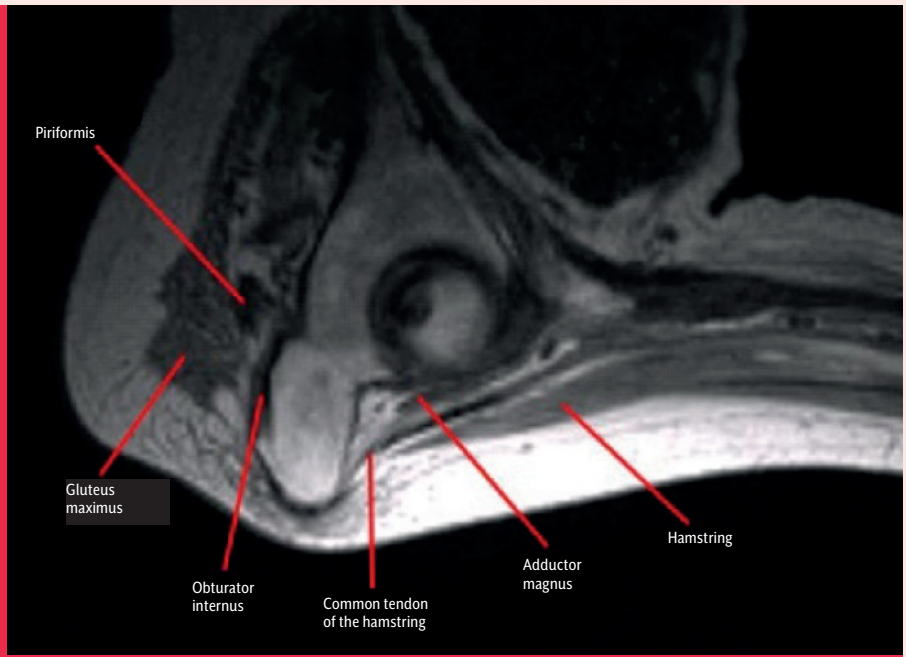
One highlight was a conversational plenary session with Dr Lisbeth Nilsson, an occupational therapist from Sweden, and Dr Tim Adlam, an engineer and educator from the UK. They discussed why powered mobility is enabling for children and adults with cognitive disabilities. When asked what mobility mean to you, Lisbeth commented: "Mobility is a key to developmental learning... to explore the world, without limitation." She went on to say we often get it wrong in assessment, as we have a culture of being "directing" when we should be prioritising a "safe, secure environment to best discover a child's needs, desires and limitations". Lisbeth spent years campaigning through her research and practice to provide powered mobility for children below the age of 12. She saw the importance in understanding cause and effect, in being trusted to let go. "I don't call it learning, I call it growing consciousness of the world around us," she said. "Crashing is really important." Tim agreed, saying that we should allow our children to fall over because we learn by repetition and failure, and it is the same for those with disabilities. "Appropriate boundaries are still important as you wouldn't let a child fall in a lake, but safety in healthcare can too easily be the antithesis of adventure."

Anatomy and pressure ulcers

Dr Sharon Sonenblum presented explorations of ischial and coccyx anatomy from seated MRI tests. She compared able-bodies to those with spinal cord injury, for example, commenting on a lack of gluteal maximus coverage underneath the ischial tuberosities for both groups. She also compared the thickness of soft tissue under the ischial tuberosities for different cushions, showing as little as 16mm of compressed soft tissue when sitting on a flat foam cushion, compared to 40mm on a research cushion with ¼ of the surface cutout to intentionally offload the pelvic loading areas. It was also interesting to see how the coccyx differs between people, and how these four vertebra at the base of the spine adopt different postures dependent on sitting position.

Dynamic seating

One session introduced the draft Rehabilitation Engineering and Assistive Technology Society of North America (RESNA) position paper on dynamic

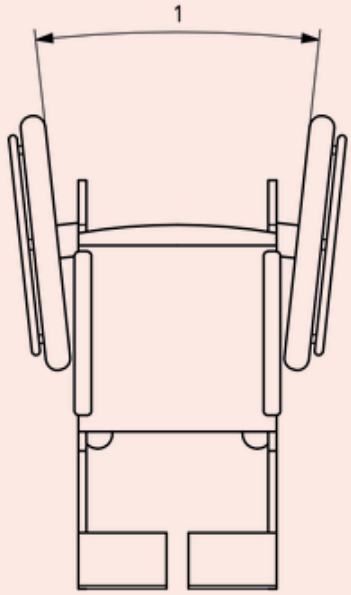


SEATED MRI OF THE PELVIS FOR A PERSON WITH A SPINAL CORD INJURY © REARLAB AT GEORGIA TECH

seating, opening it up for consultation. The paper defines dynamic seating as: "Movement which occurs within the seating system and/or wheelchair frame in response to intentional or unintentional force generated by the client. Dynamic components absorb force, which in turn assists the client back to a starting position."

The paper continues to state possible clinical applications of dynamic seating. Clinically, it appears beneficial for patients to be able to express their extensor pattern and return to their original position whilst minimising risk of injury. Mechanically, the ability of components to absorb forces generated by clients will prolong the components' lifetime compared to static components. In addition, dynamic seating could be prescribed with the aim of providing sensory input. Finally, such components can improve postural control, stability and function. See the column opposite for applications that are potential benefits of dynamic seating components.

Overall, the talk provided a valuable insight into the progress surrounding a RESNA positioning paper and its contents. The purpose of such papers are to provide advice to healthcare professionals when seating a person, but also to manufacturers and to funding bodies. An area that was not discussed was the possible contraindications of using dynamic seating. This was raised during the discussion, with the presenters stating that contraindications will be added in the ensuing stages.



❶ Example of toe-in wheel alignment, reproduced from International Standards Organisation (ISO) 7176-26 (2007)

Rolling resistance losses

One interesting study focused on the effect of toe in/out ❶ on rolling resistance in manual wheelchair propulsion. Rolling resistance is the force that acts against a user as they manually propel themselves forward. Many shoulder injuries result from self-propelling, and rolling resistance is a major factor. An increase in rolling resistance effectively means that the force required to manually propel is increased. Rolling resistance is the result of energy loss when the tire deforms and reforms, making the material of the tyre a very important consideration during the prescription process.

The study measured the average change in rolling resistance between six different tyres. A test rig showed an average change of 72% of rolling resistance between the best and worst performing tyre – a difference equivalent to carrying an extra 46kg load. An environmental factor of medium pile carpet was also tested across the six tyres. The next part of study performed a field study looking at toe in/out (malalignment) and slop (play) in wheelchairs being used by the public. Across the 200 participants, the average toe in/out was 0.92° and the average slop was 0.54°, which equates to adding 11kg and 2kg, respectively, to the user's lap when propelling. Tyre pressure was also analysed. The average tyre pressure was 35% of the maximum, which equates to adding 9kg to the user's lap. The field study highlighted the importance of issuing the appropriate type of tyre; checking for slop or toe angle at review appointments; and educating patients on inflating their tyres and checking for slop.

Why is appropriate seating important?

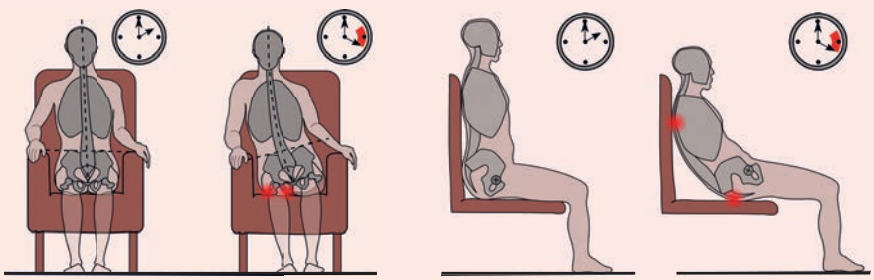
Seating is important in terms of size, set-up, surface and shape, for anyone who sits for a period of time without good ability to move or recognise the need to move. Appropriate seating should allow a person to remain supported, safe, stable and comfortable.

The alignment and orientation of the pelvis is paramount, as this will also affect the positioning of the lower limbs and the trunk. At the seating interface, an estimated 75% of a person's body weight will pass through the pelvis, with the ischial tuberosities being the main structures of the pelvis in contact with the seat. Two common forms of poor sitting posture ❷ are "sacral sitting" and "lateral asymmetry". Many develop pressure ulcers over the vulnerable coccyx and/or sacrum, if sat in a slumped position with their pelvis tilted backwards. Secondly, many develop pressure ulcers under one or other ischial tuberosity due to spinal curvature, pelvic obliquity and/or leaning to one side. Uneven loading of the body can often be avoided by providing appropriate support.

When sitting for any period of time, our body looks for positions of least energy expenditure. Where there is insufficient support, this often results in adopting postures that are damaging to the body, whether that be through pressure ulcers

POOR SITTING POSTURE

❷ Typical changes in seating posture over time, sacral sitting and asymmetry (Illustrations © Helen Frost & PUPIS)



developed over hours, or postural asymmetries and limitations developed over weeks and months. To reduce the likelihood of pressure ulcers developing, the aim is to spread their weight evenly over a larger surface area.

SITTING IN A CHAIR

Why is it important to sit out in a chair, rather than remain in bed?

- Quality of life – social interaction
- Mental health – goals, routine
- Circulation
- Respiration
- Eating and digestion
- Prevent infection – pneumonia, urinary
- Prevent muscle atrophy & contractures
- Pressure distribution.

Take home messages

Thank you to IPEM for travel grant funding, as well as partial bursary from ISS, and support from our local department. The experience did not disappoint, and it confirmed the importance of widening our horizons as professionals. We were able to feed back to the Swansea Rehabilitation Engineering department, with new products and novel processes. We have also gained insight for our clinical practice, whether considerations of how we consider cushions for those with prominent pelvic anatomy, when we consider dynamic seating, or how to promote optimal wheelchair set-up.

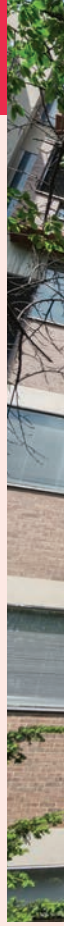
Dr Mark Bowtell *is Principal Clinical Scientist, Rehabilitation Engineering, MPCE, Swansea Bay UHB and* ***Jacob Redwood-Thomas*** *is Pre-registrant Clinical Scientist, Rehabilitation Engineering, MPCE, Swansea Bay UHB*

Dynamic seating benefits

The following are potential benefits of dynamic seating components:

- To protect the wheelchair user from injury
- To protect wheelchair and seating hardware from breakage
- To increase sitting tolerance and compliance
- To enhance vestibular input
- To facilitate active range of motion
- To increase alertness
- To decrease agitation
- To decrease fatigue
- To increase function
- To increase strength and postural control
- To reduce active extension
- To reduce energy consumption.

Combining disparate disciplines



Engineering Lecturer **Ankush Aggarwal** looks at combining image processing and mechanics in biomedical imaging at the Penn Image Computing and Science Lab.

Patient-specific diagnosis and treatment planning is an important area of biomedical engineering, which starts with using one of the imaging modalities, such as MRI, CT, or ultrasound. The Penn Image Computing and Science Lab (PICSL) at the University of Pennsylvania in Philadelphia is a world-leading group in segmenting these images and extracting geometrical aspects of our anatomical state. These segmented images are then subsequently used to perform patient-specific biomechanical analysis in order to calculate information about the functional state.

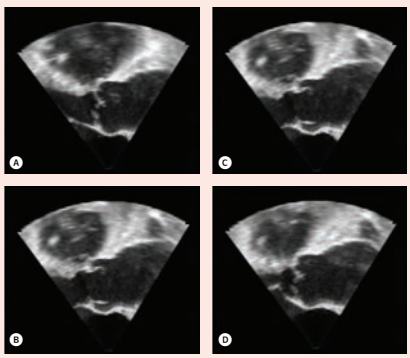
Usually, the image processing/segmenting and biomechanical analysis have been seen as two disjointed research areas, where the former is carried out in computer science and radiology community and the latter is associated with the engineering and mechanics community. I have long been interested in combining these two areas, rather than treating them as discrete steps in a pipeline. Therefore, one of my research aims is to leverage the advantages of both areas to simultaneously and automatically produce both anatomical and functional information about patients. PICSL is a world-leading group in the area of biomedical image processing and segmentation, which is why I spent two weeks with them, with Dr Alison Pouch kindly agreeing to host me in their lab.

Learning the ropes

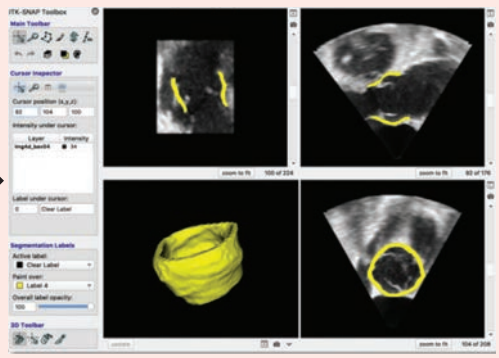
I spent the first week learning various tools developed by PICSL researchers and started "getting my hands dirty" by manually segmenting an aortic root image. I started with the intuitive and graphical open-source software ITK-Snap. I also started learning the command-line tools, such as c3d to automate steps in the image processing. I learned about the various automatic segmentation algorithms

BOX HEAD

❶ Series of echocardiographic images of the aortic valve



❷ Segmentation of the aortic root in a single 3D frame using ITK-SNAP



❸ Propagation of the aortic root segmentation to other images in the series with image registration

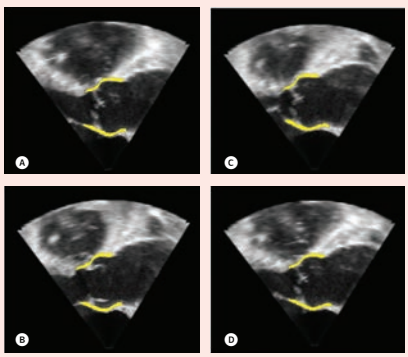


IMAGE: ALAMY

Exterior of the University of Pennsylvania Richards Medical Research Laboratories, Philadelphia

implemented in ITK-Snap and their respective pros and cons. In the process, I realised the challenges in accurately and objectively segmenting the thickness of aortic root, especially in the area where it is connected to mitral valve. I also learned about different techniques to "manually correct" the resulting segmentations.

Next, I started learning the image registration tool called "greedy", which propagates one segmented image to other time frames. This is an important tool that saves large amount of time, and I recognised the importance of rigid registration in the success of the overall registration. The last step in the image processing pipeline is to create a medial model for thin structures (such as aortic root), which is achieved using the "cm-rep" tool developed at PICSL. Interestingly, the cm-rep technique is similar to a spline-fitting technique that I developed a few years ago. However, it is performed more robustly and without considering the mechanical aspects of the problem.

New ideas

Once I had a better understanding of the image processing steps and tools, we decided to calculate strains from the segmented and registered aortic root images. Previously, I have developed tools to calculate strains from three-dimensional point clouds using reproducing kernel particle method (RKPM). I applied the same technique to the registered images, and the preliminary results were rather interesting. There was a large variation in the strains that indicates variations in the aortic biomechanical properties. However, there were points with negative Jacobian, which is not physiological. We hypothesise that the negative Jacobians are caused by errors in the registration, and these errors can be fixed by adding a regularization term that penalises the negative Jacobian points. Similarly, the strains can be calculated on the medial model fitted using cm-rep, however, that requires a two-dimensional manifold interpolation instead. It would be interesting to implement strain calculation on medial model and compare the calculated strains using two approaches. We envisage that such a comparison would allow us to combine the two steps together.

> "VARIATIONS IN STRAINS INDICATES VARIATIONS IN THE AORTIC BIOMECHANICAL PROPERTIES

The other potential collaborative project would be to automate the determination of tissue thickness from segmented images. Once a medial model has been obtained, it is possible to create a level-set of the image and apply a threshold for tissue thickness around the model. It is extremely important because the biomechanical analysis depends heavily on the tissue thickness. Hence, a more objective/consistent approach will result in improved analysis. Lastly, we wanted to combine different imaging modalities, such as CT and ultrasound since they contain complimentary information. Interestingly, PICSL had a CT and ultrasound image of the same patient's aortic root. However, the two images are usually obtained in different reference frames. Therefore, I attempted to use rigid registration to align the two images. Although the rigid registration was not successful, this presents another opportunity to advance the field.

Next steps

I had a highly informative and thought-provoking visit to PICSL, and I would like to thank Alison for hosting me. There are three concrete joint projects that we have identified and hope to work together on. In order to ensure that our collaboration continues, we plan to apply for joint research grants through appropriate mechanisms. I am enthralled by the possibilities that lie ahead, and this would not have been possible without the support from IPEM.

Ankush Aggarwal *is an Academic Engineer and Lecturer at Glasgow Computational Engineering Centre, University of Glasgow.*

Yan Tong reports from an international conference on the cutting-edge work being carried out in ultra-high magnetic resonance imaging.

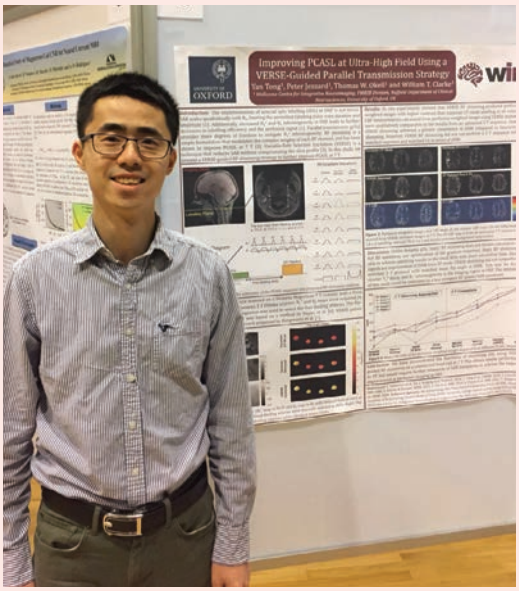
Ultrahigh field MRI

I received the IPEM Student and Trainee Grant to attend the workshop on ultrahigh field magnetic resonance organised by the International Society of Magnetic Resonance in Medicine (ISMRM) in Dubrovnik, Croatia. Over four days, students and researchers gathered to present cutting-edge breakthroughs in ultrahigh field (UHF) MRI.

I presented my work as a poster – "Improving PCASL at Ultra-High Field Using a VERSE-Guided Parallel Transmission Strategy" and received positive feedback and valuable suggestions, which will help me plan the next step of my project.

❶ Students and researchers at the International Society of Magnetic Resonance in Medicine (ISMRM) in Dubrovnik, Croatia

❷ (Below) Yan Tong



Labelling efficiency

The aim of the study was to improve the labelling efficiency of pseudo-continuous arterial spin labelling (PCASL) at 7 tesla using parallel transmission (pTx). Arterial spin labelling (ASL) is a non-invasive perfusion imaging technique which offers various clinical applications in areas such as stroke, dementia, and chronic vascular diseases. During an ASL scan, spins in blood vessels upstream of the imaging plane are inverted or saturated (labelled). After a post-labelling delay to allow the labelled blood water to reach the tissue, an image is acquired. A control image where the blood is not labelled is also acquired, and the subtraction of the labelled and control images produces a perfusion-weighted scan. ASL has intrinsically low signal-to-noise ratio (SNR) due to the relatively low amount of perturbed water magnetisation delivered via blood flow versus the signal from static tissue. Thus, ASL can benefit from ultrahigh field (>3 tesla, UHF) strengths due to the increase in overall SNR. Despite these theoretical advantages, the implementation of ASL at UHF is not trivial. An increase of B1+ (radio-frequency (RF) field) and B0 (main magnetic field) inhomogeneity is the main challenge of ASL at UHF. Parallel transmission (pTx) enables different RF waveforms to be played out in different transmit coils, and provides additional degrees of freedom that allow for constructive and destructive interference of different RF transmit channels to mitigate the B1+ inhomogeneity.

Clinicians

The workshop addressed the need to involve more clinicians in UHF MRI research. Although UHF MRI scanners

Ultrahigh field MRI

Some advantages

- Increased signal-to-noise ratio
- Increased spatial resolution
- Increased contrast resolution
- Decreased acquisition time
- Increased magnetic susceptibility.

Some disadvantages

- Increase in side effects
- Increased magnetic susceptibility
- Image degradation artifacts
- Increased specific absorption rate
- Smaller flip angles.

> "I IDENTIFIED COLLABORATION OPPORTUNITIES WITHIN THE "RESEARCH NEURO" GROUP

have recently been approved for diagnostic imaging, UHF scans for routine clinical exams or clinical research are rare. The additional calibrations required in the scanning session prevented UHF scanners from being adopted more widely in clinical research. Moreover, MRI analysis tools such as FSL (FMRIB Software Library) and SPM (Statistical Parametric Mapping) were tailored towards images acquired at lower field strength. Therefore, segmentation and registration of images acquired at UHF might fail due to artefacts and distortions that are particularly pronounced at higher field strength. The clinicians advocated that the vendors should adopt and implement more advanced and robust strategies to correct for the $B1^+$ and B0 inhomogeneities on the UHF scanners so that the workflow of scanning a clinical population could be simplified. The clinical community also urged research groups managing the MRI analysis tools to provide software updates that are more compatible with UHF data.

Interact

In addition, there was a session dedicated to collaboration within the UHF MRI community. The attendees were split up into six groups, "clinical neuro", "clinical body", "clinical musculoskeletal", "safety", "research neuro", and "research beyond neuro/ beyond proton". Group members then discussed and identified areas that were in urgent need for collaboration within each group. Through interactions with scientists across the world, I identified several possible collaboration opportunities within the "research neuro" group.

The ISMRM workshop was a wonderful opportunity not only for me to see the progress in magnetic resonance physics, it also provided a platform for basic scientists to interact with clinicians.

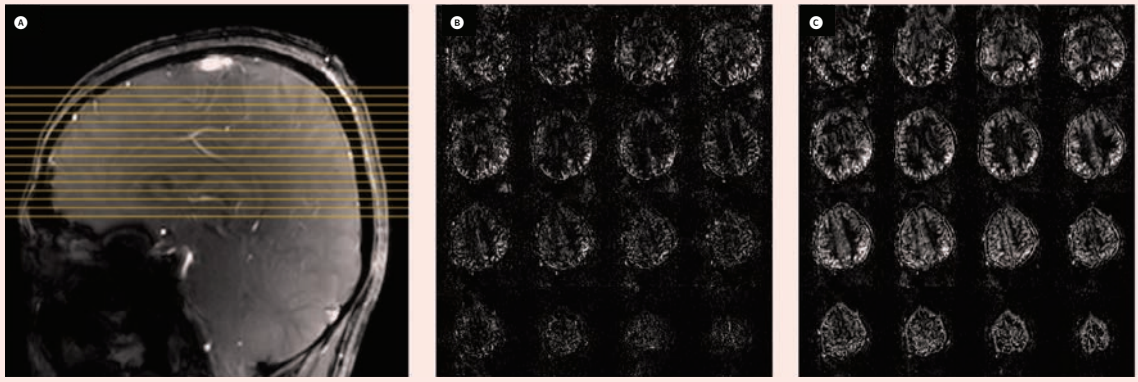
Yann *is a DPhil Student at University College Oxford.* *He would like to thank IPEM for providing the IPEM Student and Trainee Grant to attend the workshop.*

SLICE POSITIONS

Ⓐ A sagittal localizer of subject 5 showing the slice positions of parts b and c in yellow.

Ⓑ Perfusion-weighted images of Gaussian CP mode of subject 5.

Ⓒ Perfusion-weighted images of VERSE shimming of subject 5.



Clinical Scientist **David Carnegie** reports back on an imaging course run by the European Society for Radiotherapy and Oncology.

Imaging for Physicists

This course is primarily aimed at trainee physicists in radiotherapy but has content that is useful to experienced physicists and clinicians who are interested in advanced imaging techniques.

Consisting of 26 lectures (and coursework) over five days, attendees cannot argue that they are not getting their moneys' worth in terms of content.

The school was broadly divided into three archetypal imaging modalities, namely CT, PET and MRI. Experts on each topic from around the world provided an excellent refresher on the fundamental physics and the origin of contrast in each modality. Beyond the basics the faculty also presented and discussed cutting-edge research in the application of medical imaging to radiotherapy. There was a particularly strong focus on the progress of the various MR Linac and MR imaging for radiotherapy projects that are ongoing around the world.

PET for adaptive radiotherapy and response evaluation

A fascinating series of lectures from Professor Eirik Malinen (University of Oslo) on PET showed us how it can be used during radiotherapy treatment to evaluate the response of the disease to the treatment. Examples to estimate prognosis were presented, such as using 18F-labelled fluoromisonidazole to gauge the level of hypoxia in head and neck cancers part way through treatment and using this information to dose paint you can adapt the radiotherapy treatment to increase tumour control probability. Also discussed was the potential for PET to evaluate normal tissue complication. This was demonstrated in a paper using FDG to assess bone marrow function in the spine following irradiation of the thorax and also in a paper using PET to monitor parotid function following head and neck treatment. Research was also presented that analysed recurrences and showed that the majority of recurrences appear within GTVs defined by FDG-PET more than other GTVs or CTVs.

Update on the MR Linac

A highlight was the opportunity to visit the Elekta Unity MR Linac that has been installed at the Christie. They've recently finished their first cohort of prostate patients and the staff are very excited about the work they are doing. It was particularly interesting to learn about the workflow they've implemented and their solutions for patient setup. Currently, they are still CT planning patients but there is a desire to move towards MR only planning. It was impressive to learn that their average treatment times are continually improving and can be as low as 30 minutes. That's still longer than a traditional linac appointment but with the trend towards increased hypo-fractionation, it does not feel like they are far away from overtaking a traditional linac in terms of patient through-put. The online image quality is, of course, far superior to traditional kV imaging and the inevitable

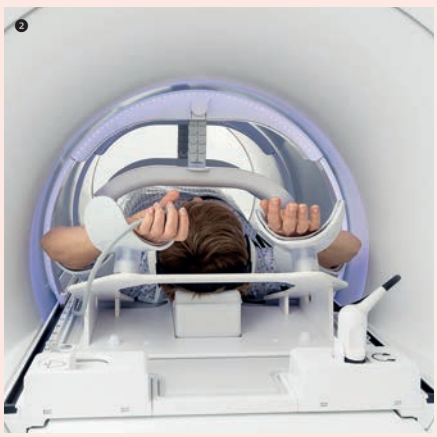


IMAGE: ELEKTA

❶❷ Elekta Unity is a state-of-the art MR-linac that is setting a new standard for personalised radiation therapy

Course details

This course includes 25 lectures (50 minutes each) and a total of six hours of discussions including case assignment presentations. The course consists of didactic lectures, interactive sessions and case assignments. For more information and to see when the course is next running, visit **estro.org**

move towards truly adaptive radiotherapy seems to be only a matter of computing power. Even the very concept of a planning scan may soon be obsolete. As someone from a "three linac" centre, the progress being made is astonishing and a bit of a wake up call.

Dr Rob Tijssen (University Medical Centre Utrecht) delivered a lecture detailing the various design solutions that exist for practical MR Linacs with a particular focus on the Elekta Unity design ❶❷. This lecture also focused on the practicalities of implementing an MR Linac all the way from the building requirements to the commissioning and quality assurance needed right and to eventually going clinical.

We also heard updates on the Australian MR Linac from Professor Gary Liney (Ingham Institute for Applied Medical Research, Liverpool, AU) which, due to its different design from the Elekta and ViewRay systems, has a potential application in proton beam therapy that the other designs are unsuitable for.

> "AS SOMEONE FROM A "THREE LINAC" CENTRE THE PROGRESS BEING MADE IS ASTONISHING

MR workflow and the end of CT planning

A big theme of the course was the advances in MR imaging and the progress in MR-assisted and MR-only planning for radiotherapy. A constant message from the faculty was that the weakest link in radiotherapy planning is tumour delineation and anything that improves this will correspondingly improve clinical outcomes. There was good discussion about the best ways to implement an MR planning workflow and the differences between using diagnostic MR machines, as opposed to dedicated MR simulators, were highlighted. The main drawback of using diagnostic machines is the lack of a flat couch top and difficulty in accommodating immobilisation devices. When planning on your CT images, registering the MR images is a source of uncertainty, especially if you need to use deformable image registration.

Another challenge moving towards MR-only planning is how to deal with the lack of electron density information. One of the purposes of a CT scan for radiotherapy planning is the generation of an electron density map that is required for the dose calculation algorithm, and so without a CT scan how do you obtain this? Several solutions and examples from the literature were discussed by Professor Liney, including the use of specialised MR sequences to separate out fat, water and bone and then assigning HU values to generate a synthetic (or pseudo) CT. There is some uncertainty in this method but the overall effect of the HU uncertainty on dosimetric uncertainty was addressed in some publications and was quoted as being 0.3-2.5% for pelvic sites.

There was also a lot of time for analysis of common (and some not so common) imaging artefacts, with a heavy focus on MR in particular. These were covered in an engaging series of lectures (and quizzes) from Professor Tufve Nyholm (Umeå University, Umeå). The real clinical impact of some of these artefacts was discussed by Dr Cynthia Ménard (Princess Margaret Cancer Centre, Toronto) during her lectures on the clinical impact of imaging in radiotherapy. Dr Ménard also presented a lecture on the different types of evidence used in medicine and discussed ways in which their quality can be ranked which, as a physicist, I found most insightful and I've certainly gained a new appreciation for the overwhelming amount of information that clinicians have to deal with.

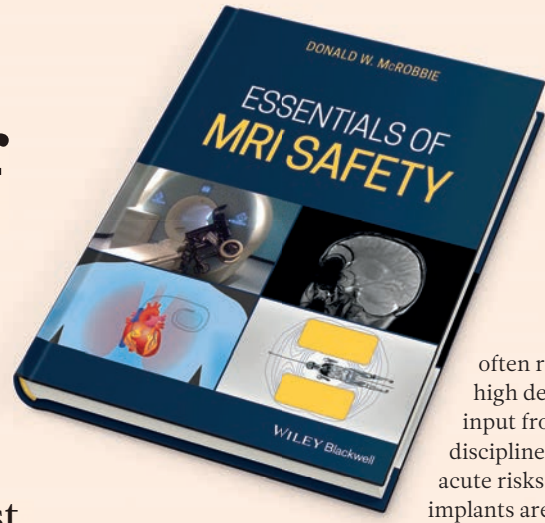
This was a very thorough course and covers almost all of the fundamental physics going on in each imaging modality but the focus and discussion of cutting-edge research is what really adds value to this course. I would very much recommend this course for trainee radiotherapy physics, as our reliance on knowledge of imaging physics is only going to increase with the implementation of MR simulation, MR guided radiotherapy and PET/MR adapted radiotherapy.

THANKS

David would like to thank IPEM for supporting his attendance at the European Society for Radiotherapy and Oncology (ESTRO) summer school, which was held at The Christie in Manchester.

BOOK REVIEW

Essentials of MRI Safety



Aaron McCann, a Clinical Scientist at the Belfast Health & Social Care Trust, gives an overview of this new publication.

Standards in MRI safety governance have been slow to mature. Within the UK, access to scientific safety expertise can vary significantly between sites and regions. The room housing an MRI scanner is often described as the most dangerous in the hospital. It is unsurprising then that sites with limited scientific support may have unduly conservative safety policies, in particular around patients with implants who may be denied access to beneficial imaging despite minimal risks.

Recent years have seen welcome initiatives to strengthen and standardise the safe management of MRI departments. An international consensus document was published in 2016 – *Recommended Responsibilities for Management of MR Safety*, the American Board of MR Safety was founded (with representation from IPEM) to provide education and certification for specific roles, and IPEM's MR SIG has brought plans for teaching and accreditation of the role of MR Safety Expert in the UK close to fruition (the inaugural course was recently postponed due to COVID-19).

To this convergence comes the timely addition of *Essentials of MRI Safety*, a comprehensive text that aims to arm all those with a role in MR safety management with "sufficient knowledge to practise safely for the benefit of their patients." Dr McRobbie is perhaps best known as the lead author of *MRI from Picture to Proton*, an unconventional guide to MR practice and theory that has become a staple of MRI departments.

The first five chapters build from the fundamental physical processes of MRI a clear, mathematical picture of the forces, heating and other effects on biological tissue and other objects in the MR environment. This section provides the basis for later chapters characterising the hazards of acoustic noise and scanning of passive and active implants. These are of greatest practical use, as screening for and scanning of implants occupies ever more of the average MR practitioner's time, and often requires a high degree of input from other disciplines. Specific acute risks of active implants are discussed in detail and it is noted that scanning of patients with implanted drug infusion pumps has in recent years led to more accidental deaths in MRI than any other single cause.

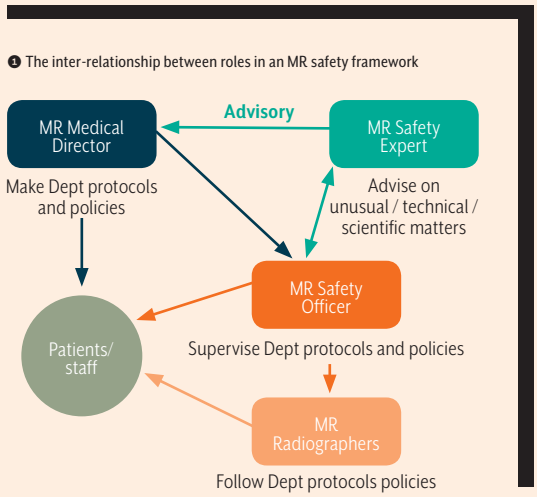
Largely self-contained chapters are included on pregnancy and contrast agents. The latter provides a sober analysis of gadolinium retention, noting that radiological evidence of deposits sparked huge controversy and revision of licensing, despite data on chemical instability of certain agents having been available for decades. In a chapter on suite design, the author laments the failure of many sites to adopt safe design principles and strongly advocates for the American College of Radiology's four-zone system.

Few other single-volume equivalents exist, and the flow and concision are greatly enhanced by being the work of a single author.

The text is peppered with "mythbusters" that seek to challenge common misapprehensions, and they certainly relieved this reader of a few. There is also an exceptional array of illustrative calculations.

The author suggests that for most MR workers and general readership, selective reading (omitting the mathematically dense portions of the initial chapters) is sufficient.

Aspiring MRSEs are advised that "every chapter, including the appendices, is essential." I agree.



1 The inter-relationship between roles in an MR safety framework

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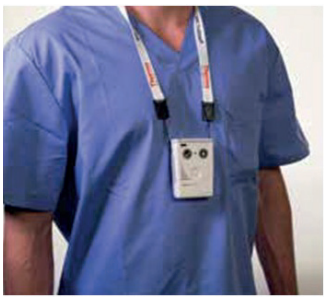

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