Vol 32 ISSUE 03-04/23 • October 2023

EUROPEAN HOSPITAL

THE EUROPEAN FORUM FOR THOSE IN THE BUSINESS OF MAKING HEALTHCARE WORK

Not always fair

AI in healthcare: diverse and balanced training datasets of high quality needed

Machine learning and artificial intelligence (AI) are playing an increasingly important role in medicine and healthcare, and not just since ChatGPT. This is especially true in data-intensive specialties such as radiology, pathology or intensive care. The quality of diagnostics and decision-making via AI, however, does not only depend on a sophisticated algorithm but – crucially – on the quality of the training data.


© metamorworks - stock.adobe.com

Artificial intelligence is a buzzword. Underneath the buzz, AI consists of algorithms based on certain machine learning methods. One of these methods, which has received a lot of attention in recent years, is the artificial neural network. The layers of nerve cells that are involved in learning processes in the human brain are algorithmically reproduced (albeit idealized). Highly complex learning tasks require many layers of artificial neurons – this is deep learning, another AI term that has become popular.

Learning from training data

A neural network and other forms of AI learn how to perform their task – such as making a specific diagnosis – based on training data. Imagine, the task is to distinguish malignant from benign findings on chest x-rays. In order for the system to be able to make a decision, many thousands or millions of x-rays of benign and malignant tissue changes are needed as training data. The algorithm classifies each of these training images and compares the result with the human-made diagnosis. If the algorithm's diagnosis was incorrect, the weights assigned to individual connections between the virtual neurons are reweighted to improve accuracy next time. Once all training data has been processed, a new, smaller data set is used to check the accuracy of the fully trained algorithm. This step is called validation.

Quality of the training data

No doubt: The accuracy of the AI algorithm can only be as good as the quality of the training data. If, for example, the training data contains many x-rays, in which a malignant tissue change was mistakenly considered benign by the human expert or vice versa, the AI will learn from false examples – which will affect its accuracy later on.

Slowly digitalized healthcare system

Obtaining high-quality training data for algorithms, however, often turns out to be difficult since our healthcare system is only slowly being digitalized. Data that has been carefully and manually validated is rare but the algorithm does require a huge amount of training data. When a high volume of digital data can be obtained, it is often from sources of inconsistent quality. This quantity and quality problem is further complicated by privacy issues in healthcare.

Garbage in, garbage out

Most IT users know the phrase "garbage in, garbage out": if the input data is garbage, the output will be garbage as well. This also holds true in AT where the accuracy of a classification algorithm always depends on the quality of the training data. But not all types of low-quality output are immediately recognizable as such. There can be subtle biases in the classifications of an algorithm caused by an unbalanced composition of the training data. The accuracy of diagnostic algorithms, for example, is worse in populations whose data was underrepresented in the original training data.

Well-known examples are algorithms to classify malignant skin tumors which were trained with data from predominantly fair-skinned (Caucasian) individuals. These algorithms show lower diagnostic accuracy when they are supposed to make a correct diagnosis in a dark-skinned person? The source of the bias is not always obvious: In the US, an AI algorithm was used to estimate which inpatients would need additional care. The training data used the costs patients had previously incurred as a marker for disease severity? This led to the fact that for African-American patients additional care was less likely to be recommended because these patients had in the past incurred lower costs. This was not due to their lower disease severity but to their lower access to health care, i.e. a pre-existing systemic disadvantage.

The unbalanced composition of training data is often described with the acronym WEIRD: "white, educated, industrialized, rich and democratic countries" are overrepresented.

Women and the elderly are also disadvantaged

And it's not just the ethnic and economic background that creates bias. Women are not fairly represented in AI either. For example, researchers suspect that women are overrepresented in the diagnosis of depression because, among other things, diagnostic algorithms query behaviors that are more common in women – regardless of clinical depression?. In contrast, the Institute of Health Informatics at University College London showed that an AI algorithm for diagnosing liver disease in women had a significantly lower hit rate: it was wrong in 44% of women, but only in 23% of men.

Age as a factor for the development of bias

And another factor that can play a role in the development of bias: age. Facial recognition algorithms, for example, are less accurate in an elderly population?. This is particularly disconcerting in view of the fact that robotics is increasingly being used in geriatric care, for example to inform and entertain elderly people and dementia patients. Particularly in this field there is substantial research being conducted to improve machine recognition of emotions based on facial expressions.

In order to address these biases and ensure equal treatment in a digitalized healthcare system diverse, balanced and high-quality training data sets are imperative. This also requires legal certainty with regard to the use of patient data for research and development. This issue will be addressed in Germany by the Federal Ministry of Health's? proposed laws in the context of the digitalization strategy and in the EU with the European Health Data Space? ■

Report: Dr. Christina Czeschik

CONTENTS

www.healthcare-in-europe.com

Huge gap between science and business

Predicting health indicators with AI? A long and rocky road

Today, artificial intelligence (AI) is everywhere. We unlock our smartphone with face recognition and watch movies recommended by AI. While AI is deeply integrated into our lives, we are still waiting for it to bring us that special smoothie in the morning or discuss the book with us that's sitting on our bedside table. Sure, AI still has a long way go. But maybe one day in the not-so-distant future, AI will provide us with information about our current state of health, such as the number of red blood cells, cholesterol levels and how many seconds last night's beer will shorten our life expectancy.

Unfortunately (or fortunately, depending on your point of view), the human body is such a complex organism that predicting health indicators is much more complicated than retrieving a song or a weather report. I might be happy with Spotify, but most of the diagnostic tools currently available are very disappointing. This is a global phenomenon: in healthcare, AI-based solutions are hitting serious obstacles. There is a huge gap between science and business, there are legal restrictions and a lack of labeled and publicly available data. And we haven't even talked about user distrust yet.

The world urgently needs intelligent solutions to the problems of modern medicine. Covid-19 has shown that the adoption of machine learning (ML) needs to be accelerated. With the help of AI, many amazing things can be done or created in the near future – medicines, vaccines, and improved clinical services. AI can be used to develop diagnostic tools, expand telemedicine, improve the accuracy of diagnoses, and even overcome logistical challenges. However, these valuable solutions are not yet available to a wider audience.

Here are some ways AI can bring benefits:

* It can accelerate processes such as drug development, assign patients to trials, process documents, make appointments, automate planning, and optimize schedules. ML models can be trained to recognize mentions of drugs and diseases, find optimal strategies, and identify specific patterns or images.

* AI can improve the decision quality to help with diagnoses and treatments, patient monitoring, and predictions. One of the goals of AI is to provide clinical guidelines and analyze patient outcomes and apply the knowledge learned by producing accurate results.

* AI can alleviate resource scarcity by using symptom checkers and telemedicine.

* AI can reduce human error by detecting unusual medication dosages, prescriptions, or suspicious analysis results.

* AI can help us respond quickly to changing situations by detecting adverse reactions via social media posts and opinion polls. It's crucial to be up to date. The use of social media and various data sources allows healthcare companies to adapt to a new reality easily and quickly.

* AI can trigger innovations and discoveries that might offer more precise diagnoses, gene editing, and even longer life expectancy. By leveraging real-world data sources (RWD), AI can provide new insights, dependencies, and relationships.

How can it be that a powerful tool like AI is not already being used in clinical settings? Why don't robots diagnose diseases and suggest treatments? The answer in a nutshell: while there are improvements, there are still obstacles on the way to clinical use.

These challenges are not always of a technical nature:

* Cultural and political restrictions: Although its benefits have been proven, AI is still unregulated and no ethical standards have been developed for its use. Many questions about privacy and accountability for AI decisions remain open, thus there are many concerns that are holding back its use in healthcare.

* A huge gap between business and science: Scientists and developers can't simply decide which problems the healthcare industry needs to solve; at the same time, medical staff and management typically don't fully understand ML capabilities. Therefore, any successful team needs to bring together the worlds of science and business.

* Distrust of users: Since most AI models are considered "black boxes", unlike other software, their internal logic is difficult to understand. Therefore, users consider the results unreliable. Customers need to understand how a model makes decisions, but high-precision models are usually difficult to interpret. To overcome this problem, the General Data Protection Regulation requires the algorithms that manipulate patient data to be explainable. But what exactly does "explainable" mean?

* Lack of publicly available data: The development of AI is driven by data, and the role of data is critical to training models. The industry keeps its data in silos and guards it like treasures. But it's hard, if not impossible, to imagine a productive interaction between data science and business without data sharing.

* Lack of experience in management: While data plays an important role in the development of AI, without competent management and well-established workflows its potential cannot be fully realized.

* Lack of standards: Collecting data from various sources and processing it takes time. A lot of time. With specifications missing, a wide range of tailor-made solutions are created, which makes optimal use of the data difficult. In order to normalize and standardize data and facilitate data exchange, various ontologies have been developed. They cover almost all areas of medicine and science, including SNOMED, NCIT, and AniML.

The way forward

The future of AI/ML is complex and requires effort and support from all stakeholders: scientists, developers, companies and government agencies. Unfortunately, these parties do not always cooperate effectively. It is not possible to transfer the ideas and models developed by scientists/data scientists to the world of users without bias. There is a barrier between scientists and users and they each speak their languages that can be incomprehensible to the other. What is needed is a kind of interpreter who transforms developed models and ideas into sustainable solutions that bring benefits to a company. This is a complex process that involves many experts – developers, designers, business analysts, and others. While science and business have already been brought together by software development specialists, regulation is still in the making. Who should be held liable for AI decisions and errors? How do we protect personal data used by smart applications? Are there ways to eliminate discrimination and prejudice? Only when these and many other questions have been answered can companies develop solutions that meet legal, ethical and social requirements.

By 2030, the artificial intelligence market in healthcare is expected to reach a value of $208.2 billion. The prediction and prevention of pandemics, the in-depth analysis of patients and constant monitoring to control and prevent possible health problems will be within reach, as will the use of VR in the training of medical staff, especially surgeons. But at the same time, problems are also inevitable.

Take home message

No matter how slow and rocky the path to AI adoption in healthcare is, AI still offers a way to integrate science into business. We see the future approaching, step by step. With steady and constant efforts from teams around the globe, AI will make its way into every area of healthcare. There are still many challenges ahead, but the future of AI in healthcare is promising. ■

Report: Valentina Endovitskaya and Anton Dolgikh

mgo fachverlage

Publisher
mgo fachverlage GmbH & Co. KG
E.-C.-Baumann-Str. 5
95326 Kulmbach/Germany
Phone +49 (0) 9221 949-311
Fax +49 (0) 9221 949-377

Managing Directors:
Walter Schweinsberg, Eva-Maria Bauch, Bernd Müller

Editor and Production Manager:
Sonja Buske (SB)
Phone: +49 201 17755092
E-Mail: s.buske@mgo-fachverlage.de

Editor: Wolfgang Behrends (WB)

Founded by Heinz-Jürgen Witzke
ISSN 0942-9085

Correspondents
Austria: Michael Krassnitzer (MK)
Belgium: Bernard Banga (BB)
Germany:
Cornelia Wels-Maug (CWM)
Dr Christina Czeschik (CC)
Great Britain:
Mark Nicholls (MN)
Spain:
Mélisande Rouger (MR)
USA: Cynthia E. Keen (CEK)

Subscriptions
Lena Krauß
kundenservice@mgo-fachverlage.de
Subscription rate
4 issues: 32 Euro, Single copy: 8 Euro.
Printed by: mgo360 GmbH & Co. KG, Bamberg, Germany
Publication frequency: quarterly

Representatives
Germany, Austria, Switzerland:
Julia Lutz
Phone: +49 9221 949-407
E-Mail: j.lutz@mgo-fachverlage.de

France, Italy, Spain: Eric Jund
Phone: +33 493 58 77 43
E-Mail: jund@european-hospital.com
GB, Scandinavia, BeNeLux:
Simon Kramer
Phone: +31 180 6200 20
E-Mail: kramer@european-hospital.com
Taiwan: Charles Yang
Phone: +886 4 232 236 33
E-Mail: medianet@ms13.hinet.net
USA & Canada:
Hanna Politis, Media International
Phone: +1 301 869 66 10
E-Mail: hanna@media-intl.com

Impact of technology

AI in radiology: helper or bane of society and the environment?

The climate crisis and AI – arguably two of the most hotly-debated and relevant topics of our time – share an intricate relationship: While computation of complex AI routines commands an immense carbon footprint, it is these algorithms that might be the very key to mitigate the effects of global warming. In a dedicated session at ECR 2023, radiologists explored the societal and environmental impact of the technology in healthcare.

Angel Alberich-Bayarri, CEO of Valencia-based AI company Quibim, looked at the technology's carbon footprint and the strategies to make AI sustainable in the opening talk. 'AI is the new electricity, and it will continue to change the world,' he told the audience. 'The power for positive change that AI brings holds the possibility for negative impacts on society.'

This impact is felt, among others, in the massive amount of CO_2 that is being generated when developing a new algorithm. 'Training a single deep learning, natural language processing algorithm can take approximately 600,000 pounds of carbon emissions,' the expert explained. 'It's the same amount of CO_2 produced by five cars over their lifetimes.' For example, training Google AlphaGo Zero, a tool developed to solve the Go game, generated 96 tons of CO_2 over 40 days – the same amount as 1,000 hours of air travel.

Sustainability must come into the limelight

To date, sustainability has barely been explored in AI ethics, a field that studies ethical and societal issues facing developers, producers, consumers, citizens, policy makers and civil society organizations. Alberich-Bayarri expressed his conviction that times are calling for a change and sustainability must now come into the limelight. 'Sustainable AI is in its infancy: it's underdeveloped, under researched and underfunded, but we're starting to explore it. It's time to analyse the environmental impact of AI. We can't neglect the carbon footprint that we are creating when training a model.' Efforts to direct AI uses towards good purposes are increasing, but there are no real business tools available to measure AI's carbon footprint yet. 'We're starting to get concerned about the impact of AI on our environment,' the Quibim CEO explained the inherent contradiction. While AI is being proposed to power up society, its development and use make society unsustainable at the same time. Deep learning models are posing both financial and environmental costs – from hardware, electricity and cloud computing time to the carbon footprint generated when fuelling modern tensor processing hardware. 'The energy required to do so is considerable,' he said.

Tracking, shrinking, specializing: Strategies to reduce AI's carbon footprint

There are already a few tools that AI developers can use to calculate their carbon emissions – for example the Machine Learning Emissions Calculator, to estimate the carbon footprint of GPU computing, and the Carbontracker, an experiment impact tool for real time assessment of energy consumption and carbon emissions. 'This carbon tracking is being increasingly asked in grant applications or proposals in hospitals to measure impact on the environment. I encourage all of us to track our CO_2 emissions.'

There are three main aspects to consider to foster sustainable AI. The first consists in designing smaller models when implementing AI. Several research initiatives are exploring how to train models faster and more efficiently, relying on techniques like pruning, compression, distillation and quantization. 'The goal is to shrink down the size of the models and use fewer computing cycles to decrease financial and environmental costs of building and deploying AI,' Alberich-Bayarri said.

The second aspect is to alternate deployment strategies, including the use of specialized hardware like application-specific integrated circuits (ASICs); prevention of idle consumption and sub-optimal computational processing distribution; and optimizing the use of existing hardware like general-purpose CPUs. Last but not least, the AI community must work to improve carbon awareness, the expert appealed. 'We have to partner with cloud providers who are aware about the issue. Some data processing centres are using immersion-based cooling for different devices, grid interactive UPS batteries or hydrogen batteries instead of diesel generators as a backup for main data processing centres.'

Not in a rush? Keep your data cool

AI developers must also consider where they store the files depending on how quickly they need to be retrieved, he urged. 'Amazon, for instance, offers different portfolios: we can have a very warm storage with immediate access to data, but if we don't need to use the data right away, we can store it in an iceberg instead and have the data in hours instead of seconds. That's another way to reduce our environmental impact.'

Ana Jimenez-Pastor, Vice President of AI at Quibim, then focused on how AI can help mitigate the lack of radiologists in low- to middle-income countries. In these regions, she argued, the global shortage of radiologists is felt more acutely. For example, in Tanzania, roughly 60 radiologists have to tend to a 25 million population, or Kenya, where here are only three fellowship-trained breast radiologists to scan over four million women who need annual mammography. 'AI could have a great impact in these countries with few to no radiologists available, by automating image interpretation and potentially enabling a few radiologists to manage the workload of hundreds,' she suggested. ■

Report: Mélisande Rouger


© Starmarpro - stock.adobe.com

Ángel Alberich-Bayarri

Ángel Alberich-Bayarri is a Telecommunications Engineer with specialisation in electronics by the Technical University of Valencia and PhD in Biomedical Engineering for his research on the application of advanced image processing techniques to magnetic resonance imaging.
Founder and CEO of Quibim (Quantitative Imaging Biomarkers in Medicine), company dedicated to the advanced analysis of medical images using artificial intelligence. He is the author of more than 90 scientific articles in prestigious international journals and inventor of 5+ patents. He is also the author of more than 100 communications to international congresses, editor of international books and author of 20+ book chapters.
He has participated in a high number of international research projects and clinical trials. He is an active member of several scientific societies, among which stands out his participation as a member of the Board of Directors of the European Society of Medical Imaging Informatics (EUSOMII).

Ana Jimenez-Pastor

Ana Jimenez-Pastor is a Telecommunications and Biomedical Engineer from the Polytechnic University of Valencia (Spain). She currently works as VP of AI at Quibim, leading the coordination and development of new and innovative AI solutions applied to the field of radiomics together with MLOPs pipelines to ensure data governance and AI models reproducibility. Ana has dedicated the last seven years to the research, development and integration in clinical practice of solutions that combine image analysis, quantification and AI.
Ana has participated and coordinated different European H2020 projects focused on the development of European infrastructures for the study of cancer using AI and image analysis. Author of more than ten publications and book chapters, she has presented her research in different national and international congresses.

Impact of ICM packaging and delivery systems

Contrast media bottles: benefits of switching to multi-dose

Iodinated contrast media (ICM) enhance CT imaging, but its single-dose packaging is increasingly proving at odds with modern, more sustainable imaging practices.

New award-winning research by a radiology resident and faculty members at Vanderbilt University Medical Center in Nashville, Tennessee, proposes a promising alternative: A switch from using single-dose injectable contrast media kits to regulatory agency-approved multi-dose bottles and syringeless injection systems could conserve ICM supplies, mitigate the impact of future shortages of contrast media, minimise waste of residual contrast media remaining in bottles after use by over 70%, reduce plastic polymer waste from syringes and ICM bottles by 93%, and slash costs by up to 35% on medical and pharmaceutical supply spending related to contrast-enhanced CT examinations.

This simple protocol modification, producing dramatic positive cost-cutting and environmentally sound changes that any radiology department could implement, is analyzed in detail in Academic Radiology

Multi-dose syringeless injector systems use two individually exchangeable 500 ml ICM bottles as reservoirs but have similar workflow to standard syringe administration of ICMs.

The global shortage of contrast media caused by Covid-19 production shutdowns in 2022 has stimulated mitigation strategies by hospitals worldwide. And with escalating concerns about the detrimental effects of plastics production, use, and disposal in the environment, healthcare practitioners are beginning to think about ways to develop better, smarter practices.

Led by Jennifer S. Lindsey, MD, the researchers conducted a comparative analysis of ICM waste, plastic waste, and the associated financial costs for both the single- and multi-dose ICM delivery systems. They estimated 24-hour contrast usage based on two weekdays and a day on the weekend at their hospital, and then extrapolated this data to estimate 365-day usage and average monthly usage.

Contrast media injection system used for CT scans. © Angelov - stock.adobe.com

One fifth of ICM going to waste

The development of advanced CT hardware technology and software allows for protocols that require lesser amounts, leading to increased quantities of unused contrast agent in 100 ml sized packaging. At Vanderbilt, on average 20% quantity of a 100 ml bottle is not used and requires disposal. The radiology department performs an average of 4,078 contrast-enhanced scans per month, or 48,938 scans per year generated by six CT scanners deployed for inpatients, outpatients, and emergency department patients. This equates to an estimated 964,039 ml (964 litres) wasted per year, at a cost of more than US $103,000 annually.

Switching to a multi-dose delivery system has the potential to reduce ICM waste by 704.7 litres annually, or approximately 73%, according to the authors. They estimate that the capital cost of purchasing multi-dose delivery systems for its six CT scanners would be recouped in six months, and that the monthly savings for the Vanderbilt radiology department would be an estimated US $41,205.

After calculating the weight of the two sizes of empty bottles with rubber stoppers, the weight of the plastic packaging for each, and the weight of syringes/packaging used for single-dose ICM injection, the researchers determined that single-use plastic polymer waste was approximately 6,019.1 kg per year compared to only 444.3 kg for multi-dose ICM delivery systems, a reduction of 93% of plastic polymer requiring disposal.

The team then compared the cost of purchasing single-use syringes, as well as auxiliary supplies including tubing, transfer sets, and saline. They estimated total cost savings to be US $587,256 per year, less the capital costs to purchase multi-dose syringeless injector systems as needed.

Positive impact on finances and the carbon footprint

Other benefits include reduction in packing and shipping costs to a manufacturer's recycling facility. GE Healthcare, which built the first recycling facility for ICM iodine in Norway in 2006, has added more to serve its global clientele, but shipping costs can still be substantial and may be prohibitive for hospitals that are not located close to them.

'500 ml plastic ICM bottles have the lowest environmental impact compared to glass bottles and smaller plastic bottle sizes for greenhouse gas emissions, resource consumption, and cumulative energy demand,' the researchers write.

'The Vanderbilt radiology department has been very supportive of this research,' Lindsey tells European Hospital. 'In fact, our preliminary analyses showed such a positive financial and environmental impact that our radiology department decided to purchase the multi-dose contrast injectors for a subset of our CT scanners, and we are currently conducting a follow-up study to prospectively measure their impact on waste.' The Association of University Radiologists (AUR) awarded the authors its 2023 Memorial Award, honoring the most original and outstanding research article written by medical students, 1st year Fellows and radiology residents. Lindsey presented the findings at the 2023 AUR annual meeting and has received numerous inquiries about them. 'This research shows it is possible for new technologies, in this case, syringeless multi-use injector systems, to overcome the upfront capital investment and have a significant impact, both financially and on our carbon footprint,' she said. ■

Syringeless multi-dose injector system
© Ulrich Medical/GE Healthcare

Report: Cynthia E. Keen

Prostate cancer treatment

MR-guided radiotherapy: a game changer?

MRg-A-SBRT can significantly enhance the safety of radiotherapy for prostate cancer patients.
© Netherlands Cancer Institute (NKI)

Prostate radiotherapy techniques have been transformed over the past two decades. One promisting technique in this context is magnetic resonance-guided radiotherapy. The latest clinical results show a dramatic reduction in side effects, improving patient outcomes and quality of life.

Prostate cancer is the fourth most common cancer worldwide. According to the International Agency for Research on Cancer (IARC), there were over 1.4 million new cases worldwide in 2020, and by 2040 this is set to rise to 29.5 million new cases and 16.3 million deaths annually. Radiotherapy remains a fundamental component of effective treatment, with 50% of all cancer patients receiving it as part of their care. In external beam radiotherapy, radiation is delivered to the prostate five days a week from a machine outside the body.

Prostate radiation therapy: 90% success but short-term side effects

'This standard treatment option for prostate cancer can lead to short- and long-term side effects, however, including urinary problems, bowel problems, fatigue, erectile dysfunction and damage to surrounding tissue,' said US radiation oncologist Dr Jonathan E. Leeman. Oncologists and radiotherapist teams use several main strategies to minimize the risk of these side effects, including careful treatment planning and close patient monitoring during and after radiation therapy.

In a risk-adapted strategy, contemporary radiotherapy treatment algorithms use pretreatment prognostic factors to stratify patients into low-, intermediate-, and high-risk groups. Then, precision radiation delivery techniques, such as intensity-modulated radiation therapy and image-guided radiation therapy, are used to help avoid exposure to normal tissues.

Magnetic resonance-guided radiotherapy (MRgRT) uses offline MR imaging to help plan radiation volumes in order to ensure accurate tumour targeting while sparing critical normal tissues. MRg-A-SBRT is the product of advances in MR-guided radiotherapy and stereotactic body radiation therapy (SBRT) and emerged at the beginning of the decade from a collaboration between US and European researchers and clinicians.

These include the Department of Radiation Oncology at Stanford University, Memorial Sloan Kettering Cancer Center (MSKCC), New-York the Belgian University Medical Center Utrecht (UMC Utrecht) and the German Research Center for Oncology (DKFZ) in Heidelberg. SBRT uses MRI 'to deliver high doses of radiation to precise targets in the body', said Leeman. Real-time monitoring enables treatment to be adapted on a daily basis, tailoring radiation delivery to prostate changes and thus reducing side effects.

Prospective study analyses data from 29 clinical trials

This technology has already been used successfully to treat breast, prostate, pancreatic, liver, lung and limited metastatic cancers, in addition to non-cancer indications such as cardiac ablation. MRg-A-SBRT enables clinicians to accurately target the prostate while sparing bladder, urethra, and rectal tissue. However, its impact on clinical outcomes and side effects compared to standard computed tomography-guided SBRT (CT-SBRT) was unclear.

A team of researchers from the Dana-Farber Cancer Institute has just published a large study of MR-guided daily adaptive SBRT in Cancer, which directly assesses its benefits compared to standard techniques for the first time.

60% reduction in short-term bowel side effects

The study combined data from 29 clinical trials including a total of 2,547 patients to compare the side effects of MRg-A-SBRT to more conventional treatment methods with CT guidance but without daily adjustments. 'We found that the risk of short-term urinary side effects was reduced by 44% [a 1.79-fold reduction] and the risk of short-term bowel side effects was reduced by 60% [a 2.5-fold reduction]', said Leeman.

While these results strongly support the use of MRg-A-SBRT as an effective treatment option in prostate cancer, Leeman noted that longer follow-up is required to see whether the short-term benefits will lead to more impactful long-term benefits for benefits. ■

Report: Bernard Banga

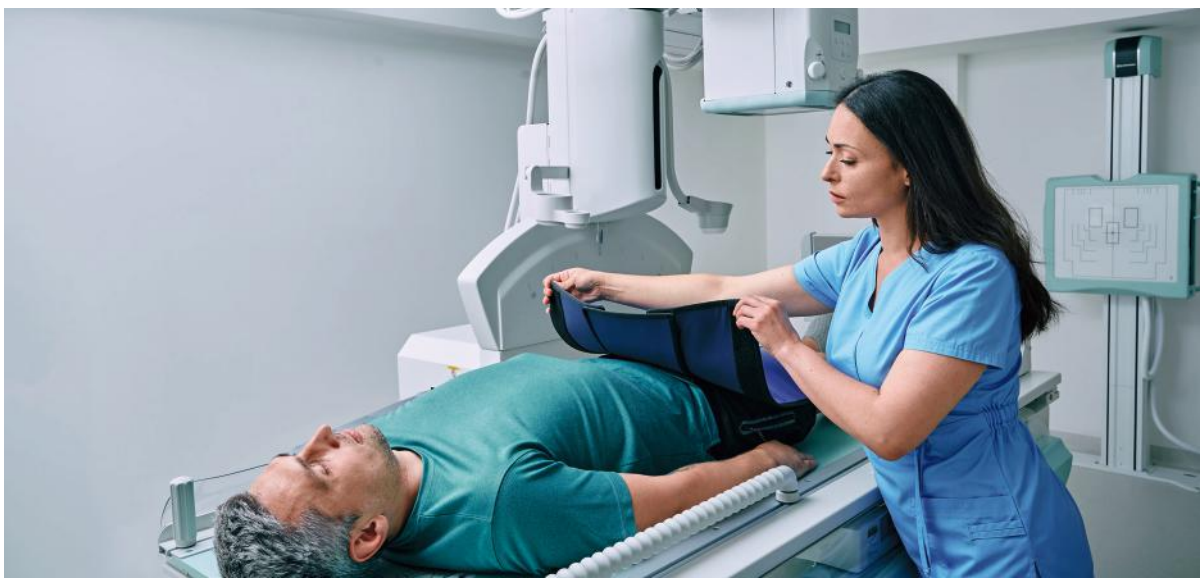
Jonathan E. Leeman

Dr Jonathan E. Leeman is a radiation oncologist at Dana-Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School, USA. He specializes in the treatment of prostate cancer and MRI-guided radiation treatment for multiple cancer types. Dr Leeman's clinical expertise lies in the areas of MRI-guided radiotherapy, adaptive radiotherapy, and prostate cancer. He serves as the physician lead of the MRI-guided radiation program at Dana-Farber Cancer Institute. His research focuses on the treatment of prostate cancer and the development of MRI-guided radiation therapy. He is also an instructor and has specialties in cancer research, radiation oncology, prostate cancer, and head and neck cancer.

Radiation protection debate

Patient shielding: a relic from the past?

Against a backdrop of changing technology and reduced patient dose, a new momentum is emerging within radiology to eradicate patient shielding. The subject has been extensively debated and researched in recent years but there is now a growing consensus to end the practice, apart from with a few exceptions. The topic was the focus of a session at ECR 2023 in Vienna where different perspectives were discussed by a medical physicist, radiographer, and radiologist about discontinuing patient shielding.



The need for radiation protection during an x-ray examination is currently being re-discussed © Peakstock – stock.adobe.com

The session, "Discontinuing patient shielding in radiology: the wind of change," was chaired by Associate Professor Paddy Gilligan, President of the European Federation of Organisations for Medical Physics (EFOMP) and Mater Misericordiae University hospital and University College Dublin, Ireland.

With the latest technologies and lower doses, he emphasised the importance of the European consensus statement on the issue to provide clear guidance for healthcare professionals and patients. This, he added, led to professional European radiology bodies coming together on the issues, which produced the European Consensus statement published in December 2021, though a straw poll of session delegates indicated that the majority were still using shielding in their practice.

Times have changed – and so should shielding practices

Medical physicist Dr Marta Sans Merce from the Department of Radiology at University Hospital Geneva, Switzerland, said the patient protection garments introduced in the 1970s to reduce the dose to organs were influenced by 'knowledge of radiosensitivity, prevailing dose level and risk estimates' at the time. However, she said: 'Dose levels, and thus estimate risk, have changed over the years with the help of technical improvements such as digital detectors in x-ray imaging and the introduction of automatic exposure control systems. While we have changed quite a lot in the entrance dose, nothing much has changed with respect to shielding.'

Epidemiological studies have also increased knowledge of radiosensitivity of tissue and organs, she continued, with research findings about the effectiveness of contact shielding leading to inconsistency in application. In some cases, that has even led to 'friction between patients requiring radiation protection equipment and professionals who consider it unnecessary or even potentially dangerous.'

With several countries and medical physics societies having decided to abandon routine use of contact shielding for radiology patients, Dr Merce pointed to the drawbacks of continued shielding. These include negatively affecting the automatic exposure control system, obscuring anatomy, compromising diagnostic information, discomfort for patients, hygiene issues when used in surgery, and the potential need for repetition of image acquisition.

Delegates heard that shielding does not prevent internal scatter – which is not reduced by shielding – and can also degrade image quality. The expert said the optimization principle can be fulfilled even more efficiently, with higher dose reductions to those obtained with shielding, when minimizing the number of acquisitions/projections/images, adjusting the field of view size, positioning the patient correctly, and implementing modern dose reduction technologies. Offering the radiographer perspective, Professor Graciano Paulo underlined the need to communicate the benefits of performing an examination without shielding to adult patients and parents of paediatric patients. Latest guidance should also be conveyed to practitioners, added Paulo, who is President of Coimbra Health School of the Polytechnic University of Coimbra, Portugal, and Head of the WHO Collaborative Centre for Radiation Protection and Health. He said: 'A better understanding of how to effectively translate research results into clinical practice is important, as habits of patient shielding are difficult to change.' But that, he continued, required 'overcoming more than six decades of use,' and the fact that patients/parents may not understand, especially as some radiographers have different approaches for the same procedure in the same department.

Regulatory factors: appeal for European consensus

Radiologist Claudio Granata from the IRCCS Ospedale Infantile Burlo Garofolo in Trieste, Italy, said there is 'negligible or no benefit' from shielding and that it may in fact introduce risks by interfering with AEC and dose in non-shielded areas and obscure important findings. Making the point that dissemination and education of professionals is pivotal in the implementation of no-shielding policies, he said European and national professional bodies are fundamental in this, with the need for radiation protection authorities to also be involved.

Dr Karla Petrov, Director of the Radiation Protection Section within the State Office for Nuclear Safety in the Czech Republic, pointed out that regulatory legal requirements vary in some countries. She underlined the importance of consensus being reached and a harmonised approach being implemented, whilst emphasizing the need to be pro-active in communicating the subject of not shielding. ■

Report: Mark Nicholls

Marta Sans Merce

Dr Marta Sans Merce is a medical physicist from the Department of Radiology at University Hospital, Geneva, and President of the Swiss Society of Radiobiology and Medical Physics (SSRMP). She is also a member of EURADOS (EUropean RAdiation DOSimetry Group) and the GAPS group that produced the European Consensus statement.

Graciano Paulo

Professor Graciano Paulo is President of Coimbra Health School of the Polytechnic University of Coimbra; Head of the WHO Collaborative Centre for Radiation Protection and Health (IPC-ESTESC Coimbra Health School); a Euramed Board member; a member of the EUROSAFE Steering Committee; and Past President of the European Federation of Radiographer Societies.

Paddy Gilligan

Associate Professor Paddy Gilligan is the President of the European Federation of Organisations for Medical Physics (EFOMP); Chief Physicist, Mater Misericordiae University hospital/ University College Dublin; Euramed Board member and the former Chair of the Gonad and Patient Shielding (GAPS) group that produced the European Consensus statement.

First non-invasive diagnostics

PCCT: Hope for high-risk cardiac patients

Ultra-high-resolution all-digital photon counting computed tomography is enabling precise noninvasive screening for heart disease in high-risk patients for the first time, according to a study in the journal Radiology.

Researchers at Freiburg University Hospital show in that study that the new generation of computed tomography scanners, known as photon-counting CTs, significantly improve the diagnosis and image quality of coronary heart disease in high-risk patients. This could be a significant benefit for individuals who have previously required rapid, invasive cardiac catheterization. 'Our results show that with the new CT technology, significantly more patients benefit from a non-invasive CT scan of the heart than before,' said Prof. Fabian Bamberg, MD. 'This is excellent news for these patients and will further improve clinical care.'

Coronary CT angiography is particularly useful for ruling out coronary artery disease in patients at low or intermediate risk for coronary artery changes. However, this has been difficult in high-risk individuals because of common coronary calcifications and stents. Muhammad Taha Hagar, first author of the study, explains, 'in classic CT images, coronary artery calcifications often appear larger than they actually are. This effect is stronger the larger the calcification is.' Until now, this could lead to an overestimation of constrictions and plaques and, as a result, to overtreatment. That's why, until now, these individuals were quickly referred for minimally invasive cardiac catheterization or examined with magnetic resonance imaging. In the study, 68 subjects were evaluated using photon counting CT and invasive coronary angiography as the reference standard. The patients all suffered from severe aortic valve stenosis. Photon counting CT scanning was shown to be very accurate in detecting or ruling out coronary artery disease. Also, image quality was rated good or excellent in nearly 80 percent. Photon counting CT is significantly more sensitive than traditional CT scanners and actually requires less radiation for comparable images. However, to obtain the image quality achieved in the study, a somewhat higher radiation exposure was necessary than with classical CT methods. For this reason, the method is initially suitable primarily for high-risk patients, who benefit particularly from the high-resolution images.

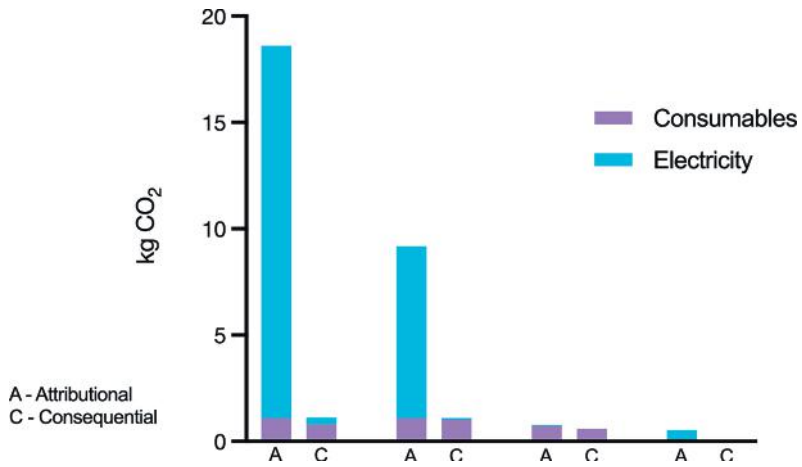
Photon-counting CT scanners like the one at Freiburg University Hospital are still relatively rare worldwide, but experts expect this technology to become increasingly widespread over the next ten years and to significantly change CT diagnostics. ■

Source: Freiburg University Hospital

Plenary discussion

Sustainable radiology: why it takes more than "greener" imaging systems

Despite the strong Irish presence at this year's ECR, it's clear that radiology is lacking in the "green" department: healthcare still causes a large share of global greenhouse gas (GHG) emissions, not least due to diagnostic imaging. But while it might be easy to pin the blame on power-hungry CT and MRI systems, things might not be quite as clear-cut after all: Dr Sarah Sheard, Consultant radiologist at Imperial College Healthcare, UK, invited her ECR audience to take a closer look at radiology's climate footprint.



Carbon emissions from electricity and consumables (in kg CO_2e) of imaging modalities, as estimated by attributional (ALCA) and consequential (CLCA) life cycle analyses.

While carbon dioxide (CO_2) has become a synonym for gases that accelerate global warming, other compounds used in healthcare have a far greater impact – such as the anaesthetic gas desflurane ($C_3H_2F_6O$), or sulphur hexafluoride (SF_6), which is used as a contrast agent in ultrasound imaging and has a global warming potential (GWP) 22,900 times greater than CO_2. 'For this reason, the NHS has announced that it will completely phase out the use of desflurane by the beginning of next year and replace it with lower-GWP anaesthetic gases,' Dr Sheard reported.

The huge impact of HVAC

Radiology may be largely built around the use of huge, power-hungry scanners, but the actual share of these systems on the energy consumption of a typical radiology ward is comparably small, the expert continued. Recent investigations have shown that the journey of a patient through a interventional radiology unit generates substantial GHG volumes, a majority of which come not from the imaging itself, but from energy used to maintain climate control, followed by emissions related to single-use surgical supplies. According to this paper, HVAC – heating, ventilation and air conditioning – contributes to almost half of the total emissions (49.2%), while the energy expenditure (plug load) for imaging only makes up 2.78%. 'A huge challenge is seeing the impact from heating and cooling our departments, especially in old, inefficient buildings,' Dr Sheard said, pointing out the need for more energy-efficient construction and renovation.

In imaging, however, the devil is often in the details. For one, a recent study found significant variations in the carbon footprint of the most common modalities: the average carbon emissions per scan were highest for MRI (17.5 kg CO_2 equivalents), followed by CT (9.2 CO_2e). By contrast, chest X-ray and ultrasound imaging generated much smaller footprints per scan, using only 0.76 and 0.53 CO_2e, respectively. Strikingly, the amount of energy used for a single scan on a previously inactive system was far greater than that for any additional scans performed on a system that was already running. This, the radiologist said, makes a strong case for operating imaging systems at full capacity whenever possible.

Sustainability can be further improved by reducing overdiagnosis, unnecessary tests and interventions, the expert suggested: 'The greenest scan is the one you don't need to do.' This mindset reduces emissions from the energy required by the scanner itself but may also avoid additional patient travel – another major source of healthcare-related GHG emission.

Waste management

Another area with huge potential for improvement is waste management, Dr Sheard said, pointing out how incorrect disposal of consumables can greatly enlarge any procedure's carbon footprint. For example, contrast bottles, tubing sets and residual contrast are often indiscriminately thrown into the bin for sharps and infectious waste, she reported. This type of waste is incinerated – a highly carbon-intensive procedure that generates 1.85 tonnes of CO2 for every tonne of waste. 'Often, only a very small part of the equipment – for example, the spike used for injection – needs to go into the sharps bin. All of the plastic tubing can be thrown into the non-infectious/offensive waste stream.'

Leftover contrast agent can be collected in a special tub and sent to the supplier for proper disposal, while the rinsed contrast bottles are perfectly fine to go into regular municipal recycling.

The expert urged that staff must be educated on this topic: 'Often, people just lack confidence to separate things, and are worried about risking contaminating waste streams. Therefore, they take the safest street, which is to put everything into the highest clinical hazard category. Much more clear instruction is needed here.' In a radiology ward with two CT scanners, where this approach was put into practice, Dr Sheard reported that the amount of waste disposed in the sharps/infectious bin was reduced by 98%, saving € 11,300 and over 20,000 kg of CO_2 equivalents per year.

In conclusion, Dr Sheard pointed out that there are many more ways to reduce the carbon footprint of radiology – for example, by using renewable energy sources, or buying imaging systems according to their environmental impact. However, the most important factor as well as arguably the biggest challenge is behavioural change, she appealed to her colleagues: 'Anything you can do to normalise sustainable healthcare, to start the discussion in your department and empower the people around you, is going to be very valuable. Finally, get a team together, network, and use your position as clinician to bother the chief executives, to put this issue on their agenda.' ■

Report: Wolfgang Behrends

Sarah Sheard

Dr Sarah Sheard is a consultant cardiothoracic radiologist and Head of Thoracic Imaging at Imperial College Healthcare NHS Trust (ICHNT) in London, UK. At ICNHT, Dr Sheard chairs a cross-disciplinary Imaging Environmental Sustainability Group and sits on the hospital trust Green Advisory Committee.

The ESR's Green Meeting Concept – a mission statement

Acknowledging the impact of climate change, the European Society of Radiology (ESR) has included sustainability into its guiding principles. As an umbrella organisation for European radiologists with over 130,000 members, it has a considerable voice in promoting eco-friendly practices for radiology. This is reflected in the society's "Green Meeting Concept":

'The European Society of Radiology (ESR) is a progressive organisation, committed to supporting sustainable development and the right to live in a healthy, ecologically diverse environment. We encourage our employees, partners and customers to adopt practices that promote awareness of environmental conservation and sustainable use, and we endeavour to adhere to these principles throughout our entire enterprise. In our continuous quest for innovation, we will always pay close attention to good economic practice, ecological concerns and social responsibility, in order to achieve several aims: innovative events, conservation of natural resources, and human well-being.

Our organisation observes these principles of sustainability according to the following guidelines:

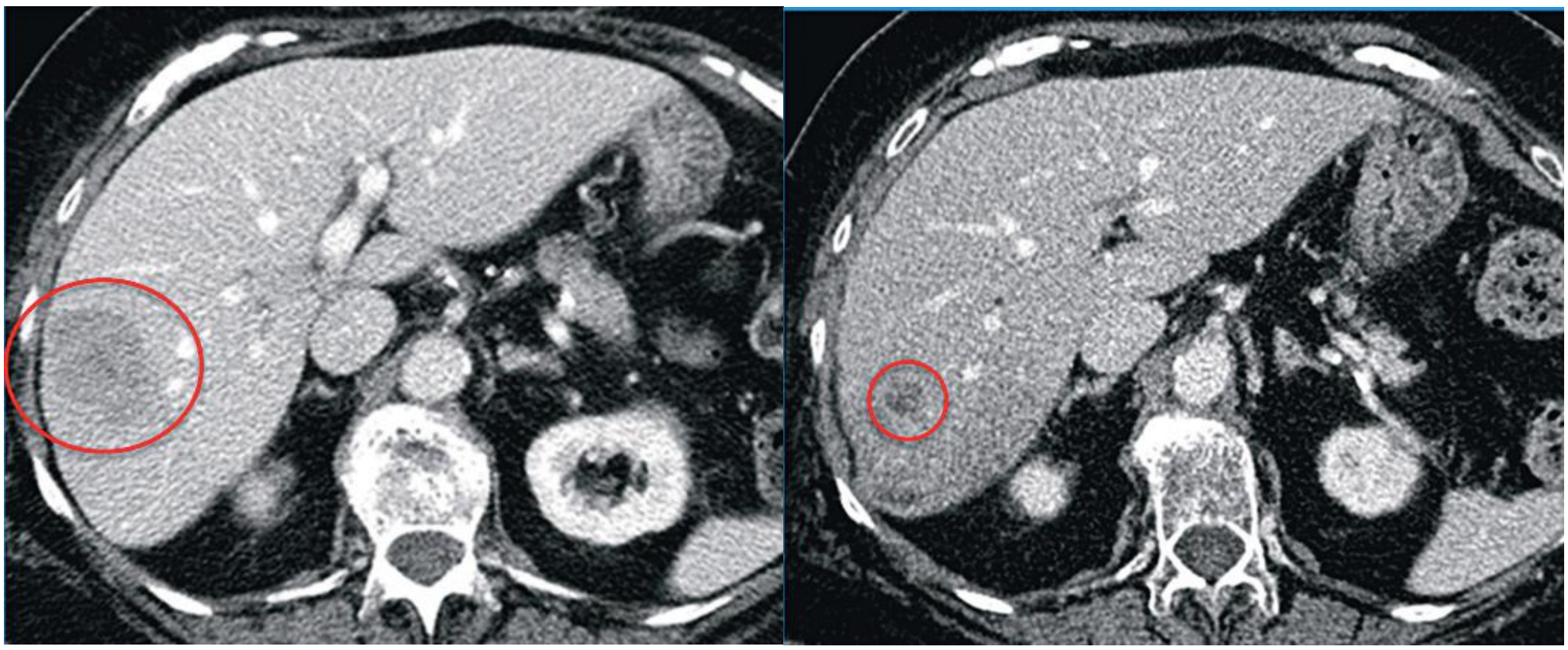
- The environmental impact and sustainability of any new activity or project will be assessed in advance.
- All necessary measures will be taken to prevent contamination of the environment and to promote social sustainability.
- Our employees, partners and customers will be informed of the environmental and social aspects of our activities in an appropriate manner.
- We will strive to ensure our partners meet the appropriate environmental standards.
- We will strive to continually increase environmentally and socially responsible behaviour within the organisation in every way possible.

This philosophy consists of:

- An understanding of the importance of environmental protection and the provision of comprehensive information to our partners and employees.
- Active encouragement of the responsible use of resources such as electricity, water and paper.
- A commitment to buying, as far as possible, only local, eco-friendly and Fairtrade products.
- The promotion of environmental awareness as a major objective of the company.
- The involvement of all partners in this important task.

Radioembolization

Breast cancer metastasis: benefits and limitations of trans-arterial therapy



Left: 82-year-old woman with solitary 4.5 cm metastatic breast cancer in the right lobe of the liver; right: CT scan 5 months after Y90 shows tumour size reduction to 1.3 cm. The patient was also on Xeloda.

Evidence that radioembolization, a trans-arterial therapy, is safe and stops disease progression in metastatic breast cancer is increasing, a prominent American interventional radiologist showed at the Spectrum conference in Miami.

It is common for patients with breast cancer to develop metastasis, according to Robert Lewandowski, MD, a professor of vascular and interventional radiology, medicine and surgery at Northwestern University in Chicago, US. 'Over 50% of patients develop liver metastasis, which worsens prognosis,' he said. 'While 6 to 7% of patients have liver-only disease, less than 1% are candidates for surgical resection.' The development of additional metastases, such as in the brain, is the cause of mortality in many patients who have metastatic breast cancer, he added.

Impact on liver function

Minimally invasive procedures are increasingly offered as an alternative or complementary to chemotherapy or hormonal therapy, but they may come at a cost. 'Image-guided cancer therapies are impactful and expanding in application for patients with metastatic breast cancer,' Lewandowski said. 'However, these therapies can impact liver function, so this has to be considered when deciding which patients are best candidates for local therapies.' Image-guided intra-arterial cancer therapies have been traditionally employed in the salvage setting, in patients with liver-only disease and limited to no systemic treatment options. These treatments are also an option in patients with stable limited extra hepatic disease and progression of hepatic tumours. 'The goal is to control hepatic disease burden while preserving liver function,' he said. 'The other objective is tumour debulking and pain palliation from large hepatic masses.'

It is still unclear the impact image-guided cancer therapies, such as radioembolization, have on overall survival. 'We still haven't been able to show whether tumour control correlates with overall survival improvement,' the expert said. 'It's complicated to evaluate what kind of a clinical impact we have on overall survival.'

A recent systemic review showed that radioembolization conferred control of tumour growth rate in most patients. However, its effect on patient survival needed to be elucidated further, the authors concluded.

A safe and efficient procedure

Lewandowski and colleagues conducted a study in 2014 that showed that radioembolization stopped progression of breast cancer liver metastases after failed chemotherapy. Glass microsphere radioembolization proved safe in a heavily pre-treated population with multi-focal liver metastases. 'In our study, we treated 75 patients with metastatic breast cancer. 85% had multiple liver tumours and 77% had extra hepatic disease at the time of radioembolization, including 13% who had brain disease,' he said, highlighting the collaborative approach required to care for these patients.

Most patients in the trial had been treated with chemotherapy or hormonal therapy before they underwent radioembolization. 'There was an objective decrease in tumour size in 82% of patients after the procedure,' said Lewandowski, who shared the images of a 54-year-old patient treated concomitantly with an oral chemotherapy agent and radioembolization. 'The tumour reduced by over 50% on the next first follow-up scan one month after treatment onset,' he said.

Finding the right patient groups

Another study conducted on 81 patients injected with resin microspheres reported on the safety, efficacy, and prognostic factors after radioembolization of hepatic metastases from breast cancer. 'Results showed a 30% decrease in maximum standardized uptake value on FDG-PET for up to five treated lesions in 52% of patients,' he said. 'Radioembolization had the biggest impact in patients with baseline normal liver function and limited liver disease burden.

Most recently, several studies have evaluated factors to consider when selecting best patients for radioembolization. These include estrogen-receptor positive patients, bone-only extra-hepatic metastases, and radioembolization performed earlier in the disease course (within six months after initial breast cancer metastases diagnosis).

'Emerging data on local intra-arterial therapy for metastatic breast cancer demonstrates that radioembolization is safe, preserves quality of life and stops disease progression,' Lewandowski said. 'It also allows reinitiating of chemotherapy in 67% of the patients if that option remains.' A few small cases series have shown the potential benefit of combining local and systemic therapy in this patient population.

An interesting concept is combining immune therapy with radioembolization. Recent work published in the Journal of Vascular and Interventional Radiology has studied genetic profiling, finding a potential benefit of combining radioembolization with immune checkpoint inhibitors to improve outcomes.

Future evaluation will have to focus on optimizing patient selection and considering that application of radioembolization earlier in the course of disease, Lewandowski suggested. 'We should further assess the efficacy of radioembolization in combination with systemic therapies,' he concluded. ■

Report: Mélisande Rouger

Fluorescence-guided surgery

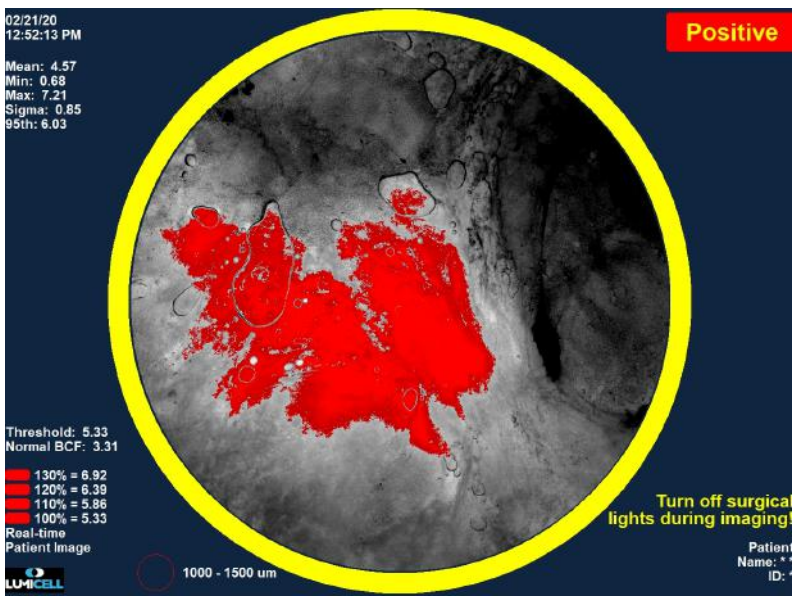
Identifying breast cancer in margins

Breast surgery is a traumatic experience for a woman, no matter whether breast-conservation surgery (BCS) or a mastectomy. Trauma levels are greatly enhanced, if pathological evaluation findings of an excised breast tumour following a lumpectomy suggest that additional cancer may still be in the margins, and a second surgical procedure is required. A new system with the ability to accurately identify residual tumour in the operating room could reduce re-excision rates, and potentially allow surgeons to excise the tumour with narrower margins.

An intracavity visualisation system using fluorescence imaging to identify residual cancer in a tumour bed during a surgical procedure has been successfully tested for performance and safety in a prospective randomized clinical trial involving more than 400 patients undergoing BCS at 14 US cancer treatment centres. Results from the Investigation of Novel Surgical Imaging for Tumor Excision (INSITE) trial revealed that the investigational Lumicell Direct Visualization System identified cancer remaining after a lumpectomy procedure in 7.6% of the participants it imaged. The system, developed by biotechnology company Lumicell, made 22 of 27 findings from sites deemed negative by standard histopathology assessment. In addition, 14.5% of patients with positive margins had all margins cleared and were spared a second surgery.

The study also evaluated the safety of Lumicell's investigational optical imaging agent Lumisight (pegulicianine), which becomes fluorescent at residual tumour sites. Pegulicianine had an excellent safety profile, consistent with other imaging agents used in breast conservation surgery, reported INSITE's lead investigator Barbara Smith, MD, PhD. Complete tumour excision during BCS remains a huge challenge because preoperative imaging and current intraoperative examination methods do not accurately identify the microscopic extent of tumours. An estimated 20% to 40% of lumpectomies have positive margins, requiring a second surgery several days later following histopathology analysis. A system with the ability to accurately identify residual tumour in surgical margins in the operating room not only could reduce re-excision rates, but also potentially allow surgeons to excise the tumour with narrower margins.

The pegulicianine fluorescence-guided system (pFGS) includes the injectable activatable fluorescent imaging agent, a handheld probe, and a patient-specific tumour detection algorithm. Images are viewed on a computer screen in the operating room. All patients were administered 1 mg/kg of the pegulicianine dye two to six hours before surgery. After receiving standard-of-care lumpectomy, 35 patients were randomised to the control arm, and the remaining were assigned to the treatment arm. For the latter group, imaging with the system following tumour excision added approximately 10 minutes to surgical suite time.



Real-time images from inside the breast cavity, based on a patient-calibrated cancer detection software, guide the surgeon in the removal of residual cancerous tissue. © Lumicell

When intraoperative images demonstrated a red signal indicating pFGS uptake, the surgeons excised additional shave margins in the interior and inferior lateral orientations, until the signal was eliminated from the image displayed on a monitor. The researchers assessed the diagnostic accuracy of pFGS by comparing each positive or negative image to the histopathological margin assessment at that site. They reported that pFGS detected tumour tissue that had been left behind by standard lumpectomy in 27 patients. In the 17% who had positive margins after standard surgery, nine of 62 patients had all the margins cleared by pFGS, potentially avoiding a second surgical procedure.

This technology is still in an investigational phase, and additional clinical trials are needed. In addition to breast cancer, its use is being explored for excision of prostate cancer, brain cancers, gastrointestinal cancers, sarcoma, and peritoneal metastases. To date, over 800 patients have been clinically evaluated in seven different cancer types at 18 US medical centres. ■

Report: Cynthia E. Keen

MRI controversial

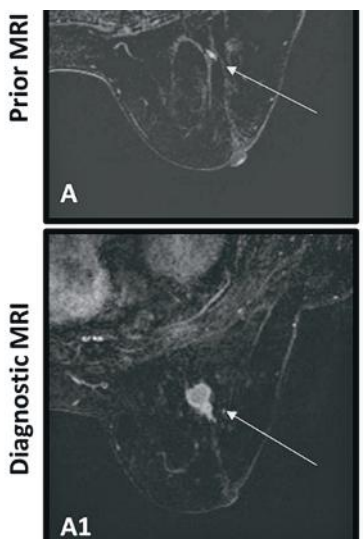
Breast cancer screening of high-risk women

Breast MRI is increasingly being used as a primary screening breast cancer screening exam for young women. The technique is also being ordered as a supplemental screening exam following mammography or breast ultrasound for women of all ages at high risk. But use of breast MRI as a screening tool is controversial.

It takes longer for patient set-up and to perform than mammography, may be a scarce imaging resource for radiology departments, and is very expensive compared to the cost of mammography and breast ultrasound exams. However, several recent studies strengthen the argument for breast MRI use as an essential breast cancer screening exam for high-risk women.

Women who have extremely dense breasts are four to six times more likely to develop breast cancer than women with mostly fatty breasts. BRCA1 and/or BRCA2 gene mutations are an additional risk factor, putting those affected at an estimated 60% risk of developing breast cancer, compared with 12.5% of women worldwide who have normal BRCA1/2 genes. Malignant breast tumours of BRCA carriers double in volume very rapidly, increasing their size up to four to five times over twelve months. This rapid tumour size growth, combined with the fact that BRCA1 carriers tend to develop aggressive triple-negative cancers, makes early detection crucial.

The sensitivity rate of MRI in detecting early breast cancer in BRCA carriers is as great as 96%, but cancers that look like subcentimetre lesions with benign appearing features may be overlooked. Researchers at Sheba Medical Center in Ramat Gan, Israel, have developed and clinically tested an artificial intelligence (AI) tool designed to accurately classify enhancing foci seen on breast MR images to help prevent them from being misinterpreted as benign. In its first evaluation test, the AI tool accurately identified more than half of the foci which were initially considered benign but identified as malignant twelve months later. The researchers had identified 53 BRCA carriers who were diagnosed with breast cancer between 2012 and 2021, and who had had two consecutive breast MRI exams within an 18-month period. They were matched with cancer-free BRCA carrier controls who had been seen at the same clinic with breast MRIs performed in the same time frame.



Cancer case of a successful classification of the AI network.
© Anaby et al., Cancers 2023 (CC BY 4.0)

Prior MRIs of both groups were used for analysis, with subsequent diagnostic MRIs serving to identify the tumour area and its delineation. Radiologists manually marked the central slice of the tumour on the sub-dynamic contrast enhanced (DCE) image and used anatomical landmarks to mark the corresponding region in the prior scan. They marked lesions or abnormalities reported in the prior MRI of cancer-free women, or if there were none, marked a prominent enhancing focus. The corresponding region of the subsequent MRI was also marked.

Lead author Debbie Anaby, PhD, and colleagues report that the AI tool successfully classified 65.6% of cancer cases as cancerous and 88.7% of cancer-free cases as non-cancerous. Triple-negative tumours were more frequently successfully classified as cancerous compared with other histological tumour types. Interestingly, in the cancer-free cohort, almost 40% of enhancements detected in the prior scans did not appear in the follow-up MRI. The researchers are planning a large prospective test and broadening the AI network to an automatic detection of suspicious abnormalities. 'The ability to detect triple-negative breast cancer at such an early stage, while abnormalities are mostly foci with no rim-enhancement, may reduce the clinical burden of the disease,' they write.

Who specifically benefits from breast MRI screening?

The Breast Imaging Clinic at the University of California San Francisco (UCSF) uses both mammography and breast MRI as screening exams for high-risk women. These patients have an annual mammogram, followed by a breast MRI six months later. 'Does breast MRI cancer screening in high-risk women detect early-stage breast cancer?' Lauren Ton, a third-year medical student, asked rhetorically during a scientific session of the Society of Breast Imaging's (SBI) annual meeting. 'Yes! Our breast MRI screening detects 99% of cancers before tumour stage 2.' UCSF recommends that high-risk patients start having mammograms (or breast ultrasound if very young) in their late 20's or early 30's. If a family member has had breast cancer, they recommend screening start ten years before the age the family member was diagnosed. Ton and colleagues conducted a retrospective study to review the clinicopathologic and imaging outcomes in dynamic-enhanced breast MRIs of patients diagnosed with breast cancer, investigating who specifically benefits from breast MRI screening. The study included all high-risk patients with diagnosed breast cancer who had breast MRI screening between 2012 through 2022, a total of 79 women. They ranged in age from 27 to 71 years. Forty-six percent were pre-menopausal. Most (63%) had heterogenous fibroglandular tissue; only 14% had extremely dense breasts. BRCA carriers represented 42%, 32% had a personal history of breast cancer, and 11% had a family history. The most commonly detected cancer on breast MRI was invasive ductal carcinoma (55%), with or without ductal carcinoma in situ. Invasive lobular carcinoma represented 6%. The median lesion size was 1.2 cm, with the majority being mass. Fifty-nine percent were detected at tumour stage 1, and 40% at tumour stage *in situ*. Only 4% of these early-stage breast cancers had axillary lymph node involvement.

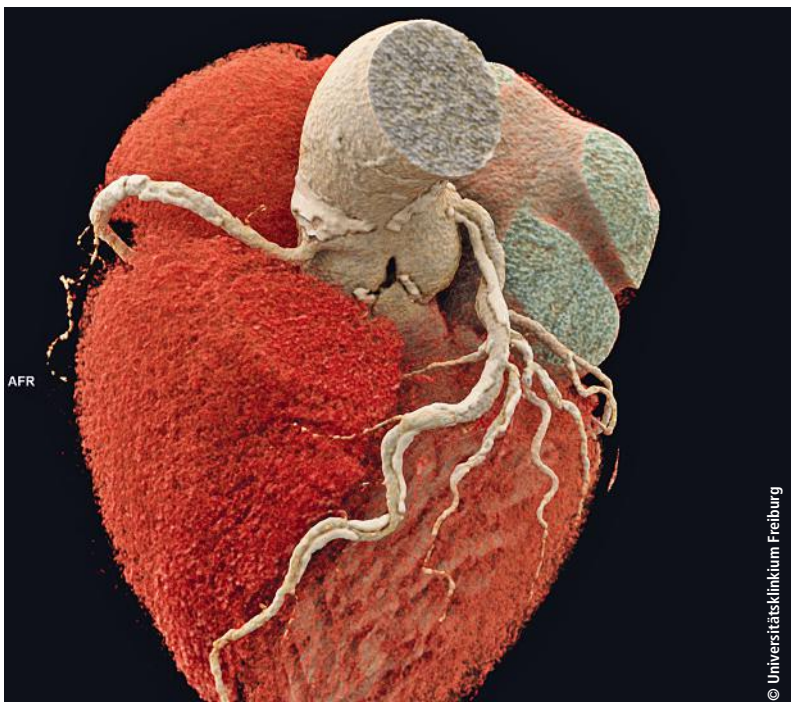
Ton: 'These results support the growing role of screening breast MRI as it enables early breast cancer detection.' ■

Report: Cynthia E. Keen

Men are from Mars, women are from Venus

Sex differences in imaging cardiovascular disease

An interplanetary title for a quite down-to-earth topic: The symposium „Men are from Mars, women are from Venus“ at this year's EACVI congress (European Association of Cardiovascular imaging) launched into the differences between the hearts of men and women. While the speakers could firmly establish that both sexes share the same home world, variations in their cardiac anatomy warrant a more gender-specific approach to imaging. To this end, Patricia Ann Pellikka, MD, Professor of Cardiovascular Disease Clinical Research at Mayo Clinic in Rochester, Minnesota, went into detail on how aortic valve disease presents differently in male and female patients, and why current guidelines put women at a clear disadvantage.



The session title references John Gray's relationship guide, but for Dr Pellikka, the distinctions between men and women run deeper than the psychological level: 'There are anatomic, physiologic and pathophysiologic differences between the sexes that have implications for aortic valve disease, and for our role as imagers.'

For one, stenotic valve leaflets in women tend to have less calcification, but a higher degree of fibrosis than men. Their aortic annulus is smaller, and their coronary height is lower. 'Of course, this has implications for aortic valve prosthetic sizing,' the expert pointed out. 'And, in the way of left ventricular remodeling, women are more apt to have hypertrophy that results in a narrowing of their left ventricular cavity, as opposed to eccentric hypertrophy, which is more prevalent in men in aortic stenosis. Women also have more extracellular matrix and more myocytes will be found in men.'

But how do these changes affect disease progression? 'Many studies have suggested that progression of aortic stenosis is similar in men and women, but a couple of recent CT studies suggest that once calcification is present, it may actually progress more rapidly in women.' In higher age groups, the imbalance becomes even more pronounced: while for patients over 65, the ratio of men to women with aortic stenosis is already at 1 : 1,25, in the 85+ age group, it rises to 1 : 1,78. This imbalance can also work the other way around, for example with biscuspid aortic valve (BAV), a disease that affects men more than twice as often than women.

In addition to differences in prevalence of such conditions, symptoms may also differ between the sexes, the expert stated. As BAV patients, men typically present with aortic regurgitation, aortopathy, aortic dissection or endocarditis, while women are more often affected by aortic stenosis. 'There is something about women that prevents their aorta from dilating, presumably due to differences in the aortic wall.' This is also reflected in altered hemodynamics, where women with severe aortic stenosis tend to have lower stroke volume, peak velocity, and aortic valve area, but higher left ventricular filling pressure and E/e' ratio.

Guidelines geared towards male hearts

However, current guidelines for valvular heart disease largely fail to factor in these differences, resulting in women falling through the diagnostic cracks, Dr Pellikka warned: 'These guidelines emphasize the importance of peak velocity and mean systolic gradient in characterizing severe aortic stenosis. I think the valve area is something we need to particularly pay attention to in women. Because of their lower stroke volume, they may not achieve the same gradient and peak velocity as men, even for severe aortic stenosis.'

Timing of intervention in chronic aortic stenosis currently depends on when a patient becomes symptomatic or presents with a high left ventricular end-systolic dimension (LVESD) – both parameters work against female cardiac characteristics: 'When we wait for the patient to be symptomatic, we may be waiting too long,' the expert said. 'In asymptomatic patients, if we fail to index for body surface area, women will tend to not qualify for surgery.'

This puts female patients at a serious disadvantage, as aortic valve surgical intervention (AVS) significantly improves survival in patients with chronic aortic regurgitation (AR). 'Women have a survival disadvantage in chronic AR – but if they do make it to surgery, they do just as well as men.'

Summarizing her presentation, Dr Pellikka urged her audience to be aware of the sex differences in heart anatomy and pathophysiology in women, which may impact progression of aortic valve disease and lead to undertreatment of female patients. 'As imagers, we need to remember to index the left ventricular size, using either volumes or linear dimensions in aortic regurgitation,' she added. 'In aortic stenosis, remember to look carefully at the aortic valve area, not just the peak velocity and mean gradient. Consider CT calcium scoring if the aortic stenosis severity is uncertain.' ■

Report: Wolfgang Behrends

Patricia Ann Pellikka

Patricia Ann Pellikka, MD, is Professor of Cardiovascular Disease Clinical Research at Mayo Clinic in Rochester, Minnesota, USA. Her professional interests include echocardiography, artificial intelligence, imaging, and stress testing, and their application to valvular heart disease, heart failure, carcinoid heart disease, and ischemic heart disease. She is Editor-in-Chief at the Journal of the American Society of Echocardiography and has contributed – often as first author – to numerous publications concerning the non-invasive detection of cardiovascular disease and timing of intervention.

Pilot project

Early detection of heart attacks in women

One of the most important AI health pilot projects for the early detection of heart attacks in women is launched. PwC Germany and Strategy& are collaborating on the project with the Peter Osypka Heart Center Munich and the Technical University of Munich under the patronage of Judith Gerlach, Bavarian State Minister for Digital Affairs. The goal is to develop a forward-looking gender-specific AI application to detect gender-specific symptoms earlier and further reduce mortality from heart disease, especially among women. Until now, AI applications have too often been fed with data that focus on male symptoms.

For medicine in Bavaria – and prospectively also nationwide – the project aims to create added value in the form of insights and concrete use cases that can be made available to research and science. This added value comes, for example, from best practices for the responsible use of AI, network building for future projects, development of new service offerings, scalability of applications – and, of course, the potential reduction of misdiagnosis of heart attacks.

'This is a good example of how many of the challenges ahead are best met when different disciplines work together and human expertise is combined with pioneering technologies. We are therefore very excited about this pioneering collaboration in an important field. AI can help to make it easier to collect, evaluate, objectify and specify health information – especially when it comes to gender-specific differences, which are very large in the prevention, diagnosis and treatment of cardiovascular diseases,' explains Petra Justenhoven, spokesperson for the Management Board at PwC Germany.

Gender Health Gap: Women at a disadvantage in heart health

Scientific studies show significant differences in women and men when it comes to the symptoms of heart disease and the corresponding treatment: for example, the symptoms for a heart attack are much less clear-cut in women than in men. Severe chest pain that can radiate to various parts of the body – a typical indication of a heart attack in men – is less evident in women. Rather, many women are more likely to report feelings of pressure or tightness in the chest. As a result, many of these complaints may not be interpreted correctly and quickly enough, and women may undergo adequate diagnosis later than men. Incorrect or delayed diagnosis and the resulting ineffective treatment massively increase the likelihood that cardiovascular diseases in women will take an unfavorable, in the worst case fatal, course. Women are also less likely to receive interventional treatments and rehabilitation measures than men. As a result, the mortality rate among men has fallen much more sharply than among women in recent decades.

'With cardiovascular disease being the leading cause of death in Germany, it is overdue to use ways of AI to identify those people who have so far fallen through the screening grid. Women in particular could benefit from the AI project now initiated, either to prevent them from suffering cardiovascular disease or so that an existing condition can be treated more quickly and in a more targeted manner,' said PD Dr. med. Clemens Jilek, Senior Physician for Cardiology and Electrophysiology at the Peter Osypka Heart Center Munich.

An interdisciplinary team from research, clinical medicine, artificial intelligence and trustworthiness as well as innovation and strategy consulting has been assembled for the project. Over the next two years, they will develop – together with other partners – a scalable AI model. ■

Source: PwC

Knowledge gaps

Covid-19: higher mortality of male patients

The Covid-19 pandemic has affected scientific research in numerous ways – for example by highlighting knowledge gaps in gender medicine. In many studies differences in morbidity and mortality between women and men surfaced incidentally. While the extent and causes of these differences remain largely unexplored, the preliminary insights confirm the need for further research.

As early as spring 2020, studies of Covid-19 patients in China indicated that mortality among men was higher than among women. Data from Italy corroborated these findings and at the same time suggested that more women than men were infected. The latter result however was not confirmed consistently: other studies reported either identical infection rates among men and women or even higher rates among men. Quickly, a causal relationship was established between the expression of the ACE2 receptor, which works differently in men and women. ACE2 is an enzyme whose membrane-bound form is SARS-CoV-2's entry point to cells.

In many tissues of the female body, ACE2 expression is higher than in tissues in the male body, among others due to the fact that the ACE2 gene is located on the X chromosome. The genes on the second X chromosome of women are largely "silenced", i.e. they are not expressed in the quantity, as one would assume, but are inactivated. This silencing however is incomplete: in the presence of two X chromosomes ACE2 is expressed 110% compared to the expression rate when only one X chromosome is present. This might explain the higher incidence of Covid-19 in women: women, the assumption goes, have more entry points for SARS-CoV-2 on their cell membranes.

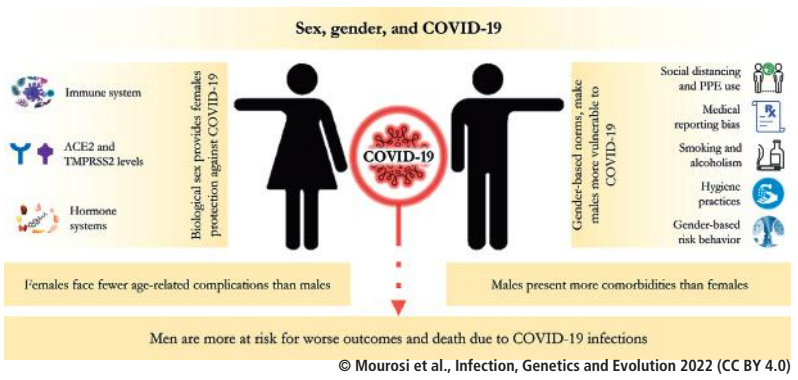
But how can the lower mortality of women be explained? Lower mortality in women remains statistically significant even when the data is adjusted for other factors such as age, life style, previous diseases, time of onset of therapy, etc.

The same holds true for the fact that men are at a higher risk to develop a severe Covid-19 infection. The stats: a meta-analysis of 90 studies has shown that men compared to women have a so-called odds' ratio (OR) of 2.84 for ICU admission due to Covid-19 and an OR of 1.39 for Covid-19-caused death.

One possible explanation is the fact that the genes of certain proteins that the immune system needs are located on the X chromosome and thus are slightly overexpressed in women compared to men. An example would be TLR7, which plays an important role in fighting viral infections.

The male immune system and the cytokine storm

In a system that is as complex as the human immune system it would be misleading in a given situation to talk about a "stronger" or "weaker" defence against a certain virus and consider the first one to be tied to a more favourable prognosis. Indeed, certain functional impairments or organ damages are caused by the activities of the immune systems rather than by the virus itself. Following a Covid-19 – or other – infection, men are more likely to develop a so-called cytokine storm, i.e. an excessive response to an inflammation which is caused among others by the cytokine IL-6, a protein that is expressed in men to a higher degree than in women. The damage caused by the cytokine response, which often leads to severe acute respiratory syndrome (SARS), explains for example the efficacy of glucocorticoids, which in fact are an immunosuppressant, in severe Covid-19 cases. Moreover, there are indications that reduced testosterone levels in male patients might improve their Covid-19 prognosis. The beneficial effect of oestrogen on Covid-19 mortality was shown in a Swedish study which included postmenopausal women. Patients who received an oestrogen replacement had lower Covid-19 mortality rates than patients without such hormone substitutes. Whether the opposite is also true, i.e. patients with an anti-oestrogen therapy after a breast cancer diagnosis have a higher Covid-19 mortality due to the lower oestrogen levels, has not been established conclusively.



© Mourosi et al., Infection, Genetics and Evolution 2022 (CC BY 4.0)

Again, the interaction is complex: some researchers assume that the less severe Covid-19 course in women can be attributed among others to the lower (rather than higher) expression of ACE2 particularly in the lung tissue of women.

Gender medicine: relevant for all, no matter which sex

This brief look into the research on Covid-19 and sex shows that the relationships and interactions between sex hormones, immune system and specific viruses are complex. A better understanding of these factors could improve therapies for given diseases for both sexes as it might pave the way for new approaches or confirm efficacy of known medicines. Some researchers point out that the role of sex was insufficiently taken into consideration during the pandemic. A review found that only about 18% of the clinical studies published during the first year of the pandemic contained gender-specific sub-group analyses. A recent survey conducted with the participation of the Institute for Social Medicine at the Charité and the German Medical Women's Association (Deutscher Ärztinnenbund) found that only nine of the 16 interviewed virologists were aware of the fact that there are sex differences in Covid-19 epidemiology; only three considered sex-specific differences in their discipline, virology, to be important. New approaches are required if infectiology and immunology are to progress towards truly individualised medicine. ■

Report: Dr. Christina Czeschik

Tackling gender inequality

Radiology – still a "man's world"?

A panel of experts assessed the challenges women have to face in radiology and explored strategies to help take gender inequalities at ECR 2023 in Vienna, Austria.

As populations become increasingly diverse, organizations need to adapt, Laura Oleaga, MD, PhD, told the audience. 'Gender equity is a key factor in achieving excellence in academic medicine,' the professor of radiology said. 'It contributes to excellence in all professions, allowing for a global vision of all situations from different perspectives and sensitivities.'

So far, however, this is only partly reflected in reality: While the proportion of women in academic medicine is similar to men, the proportion of female professors is significantly lower, the expert pointed out. 'In 2019, the proportion of women heads of institutions in higher education was 23.6%, and they made up 31.1% of the members of scientific boards,' she said. 'Women represented 33.8% of all researchers in the EU in 2018, and as we go up in the career pyramid, the number of women decreases.' Forty-eight percent of all doctoral students were women, while they represented 24% of the highest roles in academia. In Europe, women represent 54% of physicians and 40% of radiologists. Female representation in radiology decreases at increasing levels of leadership, she noted.

Women underrepresented in crucial future fields

Radiology is a technological field, an area where women remain a minority, Prof. Oleaga pointed out. 'There are less women in digital information technology, computing, physics, mathematics, engineering and AI. We have to pay attention to that, because these are the fields that are driving many of the future jobs.' The percentage of women with AI skills is much lower than men, and women are also leaving technological fields in greater numbers than men. 'This trend makes us think that progress towards gender balance could be compromised,' she said. 'We have to promote scholarships to attract women in technology and to incorporate and retain them in these fields.' To influence change, increasing the number of female role models and mentors is essential, the radiologist explained. 'A lack of mentorship and role mentoring may be deterring women from pursuing radiology,' she said. 'Mentorship and sponsorship of women programs directly impact female advancement and career satisfaction. Leadership and management programs represent effective ways to cultivate leadership skills to promote the professional career,' she concluded.


A rare picture: women are underrepresented in radiology. © amorn – stock.adobe.com

The next speaker, Dr Carolyn Horst from Kings College London, UK, shared her perspective as a radiology trainee with the delegates. She showed a picture of her two-year-old daughter as part of her disclosures. 'Having a child as a female physician can feel like something you have to disclose,' she said. 'I say this jokingly, but it can feel like something that hampers you professionally.'

To prove this point, she then talked about her non-linear training story, starting medical school when she was 28, and then working as a junior doctor for two years, as she was always told her career would go. Until she decided to embark on a PhD and have a baby. 'I took an eight-month break to have my child, and now I'm back in radiology training and still have a couple more years before I reach the golden field of consultants,' she said. 'The truth is it doesn't always happen the way you've been told it was going to happen, especially when you have a family.' In the UK, the expectation for trainees is that they are young, willing and able to move anywhere they might be needed, may have some independent financial means if they stay in London, and have no caring responsibilities, she explained. 'This approach diverts good trainees with any or all of the above pressures to GP and other specialties, which have short and less popular training schemes,' she said. In the UK, only 37% of consultant radiologists are female, even though there has been parity of men and women in medical schools for decades. 'We have an image problem,' Dr Horst said. In addition, there is a structural problem with regards to the way radiology is being taught. 'The apprenticeship model is often successful when the trainer is like the trainee. So, we need women training other women.'

Finally, women with caring responsibilities tend to be seen as 'uncommitted' because they leave after they have completed their work to pick up children – and don't have time to stay and talk with colleagues. ■

Report: Mélisande Rouger

MCED

Cancer: a simple test for early detection

Academic labs and biotech firms pioneer multi-cancer early detection with emerging technologies. Screening for multiple cancers with a simple blood or urinary draw could be a game-changer. Two research teams in particular have advanced the field.

Currently established screening tests are type-specific, meaning patients have to be tested for each cancer type individually. 'Existing single-cancer screening tools face several challenges, including lack of adherence to screening recommendations, low positive predictive value or high false positives and missed or interval cancer cases,' Montserrat Garcia Closas explains. This Spanish researcher and academic, who specialized in identifying cancer biomarkers and the genetic susceptibility of cancer, is the director of the Trans-Divisional Research Program, at the Division of Cancer Epidemiology and Genetics at the National Cancer Institute (NCI) in the US. Additionally, population-scale cancer screening is only recommended for a few cancers in the United States – such as breast, cervical, prostate and lung cancer in high-risk patients and on a per-patient basis. 'Eighty percent of cancer deaths involve a type of cancer for which no population screening is currently available in the UK,' said Peter Sasieni, professor at the Comprehensive Cancer Centre, King's College London.

Multi-cancer early detection (MCED) could address an unmet need. It detects a signal by a number of cancers, including cancers not routinely screened for today, to allow for earlier treatment. 'When cancers are diagnosed early before they have the chance to spread, the overall 5-year survival rate is four times higher that when diagnosed in later stages,' said Megan Hall, vice-president of Medical Affairs at Grail, a biotech company from California. The principle of MCED is that it searches for traces of a cancerous tumour in a sample of body fluid – for example, blood or urine – analysing it to trace the origin of the cancer. Most of the technologies under development are blood-based tests, also known as "liquid biopsies". They highlight either DNA or biomarkers.

Two teams are particularly advanced in this field: one at Chalmers University of Technology based in Gothenburg, Sweden, and another at Grail. The Swedish team opted to study biomarkers. Set up in 2017 by chemical engineer Francesco Gatto, along with Jens Nielsen, a professor of system biology. 'We are using free glycosaminoglycan profiles (GAGomes) – carbohydrate macro molecules that appear in blood and urine at the earliest stages of cancer,' said Nielsen.

'It appears that about a third of all cancers activate a metabolic programme very early on that severely affects the normal level of GAGomes – in both plasma and urine,' said Nielsen. His team first developed a kit which uses ultra-high performance liquid chromatography coupled with triple quadrupole tandem mass spectrometry (UHPLC-MS/MS) to identify 17 different free glycosaminoglycan disaccharides. The researchers then went on to develop a machine learning in vivo cancer progression model, which uses algorithms to detect changes in glycosaminoglycan carbohydrate macro molecules.


© Grail

14 different cancer types diagnosed

The Swedish team published a study, which looked at free glycosaminoglycan profiles in urine and plasma using 2,064 samples from 1,260 cancer patients and healthy subjects. 'We observed widespread cancer-specific changes in biofluid GAGomes replicated in an in vivo cancer progression model,' said Gatto. The technique has been shown to be suitable for detecting 14 types of cancer in plasma and urine samples with sensitivity ranging from 41.6 to 73% in detecting stage I cancer at 95% specificity. 'In contrast, other assays have reported 39–73% sensitivity to stage I cancer,' Gatto explained. GAGomes doubled the stage I sensitivity reported by state-of the-art genomics biomarkers compared with DNA-based MCED tests. Besides this, the technology has 'helped detect types of cancer not being screened for today and which cannot be detected using DNA-based MCED tests – such as brain and kidney cancers,' added Gatto.

This new assay under development uses a small volume of blood or urine, which makes it more practical and cheaper to use, with a 5-10 times lower cost factor, according to the team. The same blood specimen can be used to test for both glycosaminoglycans and genomic biomarkers. 'This strategy could detect even more cancers than with either method alone, and the resulting performance may well be sufficient as a one-stop-shop screening program,' said Gatto.

Test to predict origin of the cancer signal

For its part, the team from Grail boasts that Galleri is the first MCED test capable of detecting, through a routine blood draw, more than 50 types of cancer including adrenal cortical carcinoma, uterus, bladder, bone, breast, oesophagus, kidney and lung cancer or plasma cell myeloma. 'We use next-generation sequencing and machine learning. Artificial intelligence algorithms can isolate cell-free DNA and analyse methylation profiles to detect the presence of a cancer signal,' said Megan Hall, vice-president of medical affairs at Grail.

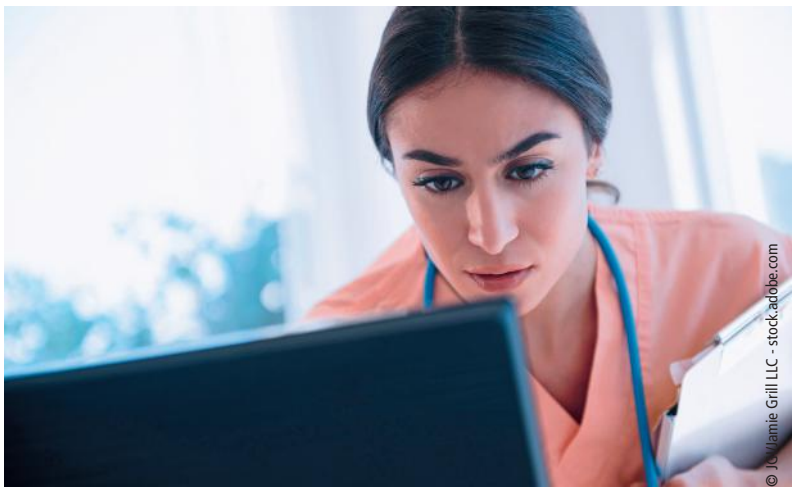
First results presented by Grail, including a large-scale prospective observational cohort study, a clinical evaluation, and a real-life early experience of a MCED, has shown promise in improving cancer diagnosis, treatment and patient care. However, before integrating MCED technology into clinical care, the benefits and risks must be assessed, as well as potential outcomes, costs and value. 'Modelling efforts as well as systematic clinical studies and data collection, along with public health and primary care efforts, need to be undertaken to determine whether MCED tests become an opportunity to decrease the heavy burden of cancer for all,' said Larry Kessler, Professor at the University of Washington School of Public Health in Seattle. Kessler is the deputy chair of the Multi-Cancer Early Detection Consortium, a public-private collaboration between organizations in the US and UK. In August 2022, the consortium released its first paper, establishing the current landscape and plans for future guidance on these technologies. A first step by the international scientific community 'to help establish standards and implementation guidance for MCED technologies' potential use in clinical care,' Kessler stresses. ■

Report: Bernard Banga

Sponsored · Protecting nurses

The importance of safe blood collection

In recent years, we've all witnessed the sustained pressure on frontline healthcare professionals. 'Before Covid healthcare professionals seldom had to worry that one day their work would put their health, maybe even their lives at risk,' says Constance Mak, a registered nurse and phlebotomy technician based in Hong Kong. But the effects of the pandemic will endure for many years to come. So how are healthcare providers protecting their nurses from infection; so that they can do their jobs, and aren't put off a career in nursing in the first place?


© JC Jamie Grill LLC - stock.adobe.com

Staff are acutely aware that they are exposed to the risk of infection in a hospital or clinic. There are often breakouts of multi-resistant bacteria, and for a phlebotomist, these risks are heightened. Hep B, Hep C and HIV can be contracted from a needlestick injury and blood potentially carries a risk of bloodborne infection if not collected, handled, and stored properly. 'Collecting blood and setting up an intravenous catheter – these are the two major high-risk and high-volume procedures our healthcare professionals perform in acute and emergency settings,' says Constance. 'And needlestick injuries usually happen during use and before disposal."

Nurse fatigue and patient safety

How do healthcare professionals stay safe during phlebotomy? Around the world, nurses are managing increasing caseloads, surges in the demand of clinical care, and interruptions to the availability of quality products. All this amid squeezed budgets and a crisis in nurse retention.

Constance is keen to emphasize the rigorous and mandatory training for accreditation in phlebotomy certification that all healthcare professionals must complete and maintain in order to perform blood collection, as well as the regular audits that hospitals and clinics are subject to. In the last twenty years, the methods for collecting blood have also evolved to protect both nurse and patient: 'Like a lot of the world, we've used the closed collection system for drawing blood samples; safer sharps devices keep the risk of exposure to a minimum during blood collection from a patient.'

The use of a non-contained, exposed syringe needle in blood collection [open collection] was the cause for the high incidence of infection from injury and was the standard when Constance began her career. Being able to rely on a quality, safety-engineered device for this method allows staff to perform their tasks with the minimum of fuss.

Go with the safety flow

We know that the small details of blood collection kit matter in the lab, just as much as they do on the ward. It is why every detail of our products and services are designed with that safety approach in mind. From the moment a blood sample is drawn, to the moment it becomes data. ■

Literature can be requested from GBO.

Read the full article and other interesting stories on the Safety Blog by scanning the QR-Code:

Tubular tissue biofabrication

Creating lab-grown blood vessels

New technology that creates ultra-thin layers of human cells in tube-like structures could spur development of lifelike blood vessels and intestines in the lab.

The technique, known as RIFLE – rotational internal flow layer engineering – enables the construction of separate layers as delicate as one cell thick. Such versatility is crucial to developing accurate human models of layered tubular tissue for use in research, offering an important alternative to animal models, experts say.

Scientists have been able to demonstrate the technology by manufacturing cells into super-thin layers that mirror those seen in a human blood vessel. Layered tubular tissue is found throughout the body – in blood vessels, the digestive tract and other organs. It can feature multiple cell types, generating layers with different properties and functions.

Crucially, this uses the same materials and cells we find in our own bodies. This level of accuracy is essential for researchers who want to develop new medicines and investigate diseases

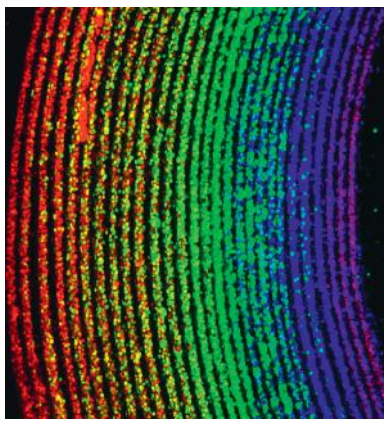
Current methods used to manufacture human tissue in the lab – known as biofabrication – can lack the detail needed to mimic these complex structures. Developed by experts at the University of Edinburgh, RIFLE is a low-cost and fast biofabrication method that can work to a very small scale. The technique involves injecting a small volume of liquid containing cells into a tube rotating at high-speed – up to 9000rpm. The speed of the rotation causes the cells to distribute evenly across the internal surface of the tube, with higher speeds resulting in thinner layers. When this process is repeated, it builds up cell layers to create a tubular structure made of different, distinct layers, with a high density of cells.

The ability to economically create layered tubular tissue in the lab could offer an important model for drug development, experts say. Accurate human models of intestinal tissue could allow companies to monitor how medicines taken orally are absorbed in the gut. 'With the RIFLE technology, we can create, in the laboratory, the high-resolutions that we observe in human layered tubular tissue, such as blood vessels. Crucially, this uses the same materials and cells we find in our own bodies. This level of accuracy is essential for researchers who want to develop new medicines and investigate diseases – ultimately reducing the need for experiments involving animals,' says project lead Dr Ian Holland from the University of Edinburgh.

Working with the University's commercialisation service, Edinburgh Innovations, the team has now patented the RIFLE technology and is working to develop further applications of this novel technique. Developers of RIFLE caution that further testing and clinical studies are needed before lab-grown tissue is available for use in human transplants.

The technology was developed by scientists from the Universities of Edinburgh and Strathclyde and has been supported by EU Horizon 2020, EPSRC, BBSRC and WT iTPA funding. ■

Source: University of Edinburgh



A microscopic rainbow created using ultra-thin layers of human cells and the new RIFLE biofabrication technology.
© Ian Holland/University of Edinburgh

Progress, limitations, and opportunities

Precision oncology: incredible potential, but not a miracle cure

A cancer educator has highlighted how unanswered questions are hampering clinicians in their efforts to get the best out of a precision medicine approach for their patients. Pointing to the "great example" of non-squamous small cell lung cancer as a positive, Dr Elaine Vickers said the benefits of being matched to an investigational drug remain questionable for most people with advanced cancer. Speaking at the Genomics and Precision Medicine Expo in London at the end of May, she outlined the "progress, limitations, and opportunities in precision cancer medicine," posing key questions and offering partial solutions.

AI-generated render of cancer cells © Sebastian - stock.adobe.com

While precision medicine aims to tailor treatment according to the underlying biology of an individual's disease, the experts told delegates: 'Matching one mutation to one treatment is unlikely to work if the patient's tumour is driven by multiple mutations. Testing for hundreds of mutations, looking at markers of checkpoint inhibitor sensitivity, and bringing together a panel of experts seems our best chance of success. But we can't get away from the fact that we lack effective and safe treatments for many of the most common mutations. Also, where immunotherapy fits into precision medicine is unclear.'

A focus was on six unanswered questions:

- How important is timing for precision therapies?
- Which mutations should be targeted?
- Is every mutation tumour agnostic?
- Which tumour clone should be targeted?
- How well should oncologists know their patients?
- When should immunotherapy be administered?

Vickers outlined how with aging, the mutations in cells gradually increase while the immune system becomes less vigilant and tissues become less hostile to cancer cells. She said: 'Targeting a single mutation, or a single process, will not be enough to destroy every cancer cell in a patient's body, particularly if they have metastatic disease.' As precision medicine moves away from set treatments for specific cancers towards targeting mutations, the expert said half of patients with non-squamous non-small cell lung cancer (NSCLC) have a mutation that can be matched with an approved treatment, and spoke about the K-Ras inhibitors as a specific example. However, that leaves half of patients without a matched treatment, she added.

Vickers also looked at Bcr-Abl inhibitors for chronic myeloid leukaemia (CML) but emphasised the importance of applying targeted therapy as early as possible. She also noted that the same applies with immunotherapy using checkpoint inhibitors, noting the positive results coming out of neoadjuvant trials. While there are targeted treatments for some cancers, and good progress is being made on others, some do not have options at present. 'Our first problem,' continued Vickers, 'is that we don't have treatments that match most of the common human mutations found in human cancers. Our second problem is that many of these mutations are commonly found in non-cancer cells and even if we find a powerful mutation in a person's cancer cells, we can't be sure that its worth matching with a treatment.'

She said targeted treatments work best when the cancer's behaviour is dominated by one or two powerful mutations and there is a limited amount of variation between cells. Immunotherapy works best when the initiating cell had already accumulated many mutations before it became a cancer cell. This creates a pool of clonal mutations – mutations that are common to every cancer cell in the person's body.

Managing expectations in advanced cancer stages

The expert pointed out potential solutions, which lie in: new treatments for common mutations, pointing to the need for more Ras inhibitors; the importance of "matching scores"; and the ESMO scale for Clinical Actionability of Molecular Targets as an attempt to guide precision medicine and identify suitable patients. 'One of the big challenges with precision medicine is that there are so many mutations driving cancer cells for which we have no solution in terms of a matching treatment and precision medicine.' She said that most of our current treatments target proteins found on the surface of cancer cells or overactive kinase enzymes. But many common mutations affect tumour suppressor genes such as TP53, RB and CDKN2A, for which there are no solutions.

Vickers warned that if somebody has advanced cancer, a treatment matching just one mutation is not likely to cure them as there is too much variation amongst their cancer, so managing expectation is important. Immunotherapy can provoke the immune system into action. However, bringing immunotherapy and targeted therapy together, and getting the most out of both treatments remains a challenge, she pointed out.

Novel approaches warrant cautious optimism

She expressed her confidence that artificial intelligence and machine learning will have a role in finding the right combinations, and also looked to advances being made in the antibody drug conjugate group of treatments, which are less affected by how much variation there is within the tumour.

In summary, Vickers said: 'Precision medicine is the future of cancer treatment and there are reasons to be optimistic.' But with so many unanswered questions, she believes precision medicine is not going to cure every patient, though it can be 'incredibly beneficial' for some. 'We have to bring in immunotherapy, we have to bring in novel approaches like antibody drug conjugates,' she added. 'It is about marrying together different approaches to get the best out of them for each patient.' ■

Report: Mark Nicholls

Elaine Vickers

Dr Elaine Vickers, PhD, is founder of Science Communicated Ltd and has worked as a cancer educator for more than 20 years. Her goal is to unravel the complexities of cancer biology and new cancer treatments and to make these topics interesting and accessible to non-scientists. Her book, "A Beginner's Guide to Targeted Cancer Treatments", was highly commended by the British Medical Association medical book awards in 2019 and she is currently working on a second edition. A regular speaker at cancer conferences, she has a degree in Medical Science from the University of Birmingham and a PhD in Molecular Biology from the University of Manchester.

The role of arginine

Metabolite drives tumour development

Cancer cells are chameleons. They completely change their metabolism to grow continuously. University of Basel scientists have discovered that high levels of the amino acid arginine drive metabolic reprogramming to promote tumor growth.

This study suggests new avenues to improve liver cancer treatment. The liver metabolizes nutrients, stores energy, regulates the blood sugar level and plays a crucial role in detoxifying and removing harmful components and drugs. In the past decade, scientist have made much progress in understanding the multiple facets of cancer. There is growing evidence that cancer is a metabolic disease. In other words, cancer arises when cells rewire their metabolism to allow uncontrolled cell proliferation. How do cells change their metabolism and how does this change in turn lead to tumourigenicity? With their new study, researchers have discovered a key driver of metabolic rewiring in liver cancer cells.

Healthy liver cells gradually change their behavior when turning into cancer cells. They reprogram their metabolism to grow as fast as possible, for example, they consume much more glucose than normal cells and they enhance the uptake of nutrients. 'We investigated liver tumour samples from mice and patients and found elevated levels of arginine, although cancer cells produce less or none of this amino acid. The tumour cells accumulate high levels of arginine by increasing its uptake and suppressing its consumption,' says lead author Dr. Dirk Mossmann. 'Furthermore, we found that the high levels of arginine are necessary for tumour development, independently of the amino acid's role in protein synthesis. This then begged the question, how does arginine lead to tumourigenicity?'

At high concentrations arginine binds to a specific factor, which triggers metabolic reprogramming and promotes tumour growth by regulating the expression of metabolic genes. As a consequence, tumour cells revert back to an undifferentiated embryonic cell state, in which they can divide indefinitely. Interestingly, tumour cells also benefit in another way from increasing the uptake of arginine. 'Our immune cells depend on arginine to function properly,' says Mossmann. 'Therefore, depleting arginine in the tumour environment helps the tumour cells escape the immune system.' The scientists propose to target the specific arginine-binding factor rather than depleting arginine. 'When treating liver tumours with the anticancer drug indisulam, we induce the degradation of this factor and thus prevent metabolic reprogramming,' adds Mossmann. 'Via this route, one can avoid unwanted side effects of reducing overall arginine levels, like harming immune cells that need arginine to work properly.' ■

Source: University of Basel

Personalized therapies

Speeding up biomarker detection in pharmaceutical research

Digital pathology can be used to great effect in pharmaceutical research: it can accelerate analyses, give deeper insights into cellular mechanisms, and enable better understanding of their role into clinical development. This potentially offers clearer predictions on how patients may respond to treatment and lead to personalized therapies.

In a session titled "How Digital pathology can help to speed-up Biomarkers detection in Pharma Research," Dr Carole Chotard will outline the benefits of the new technology for the field at the forthcoming 10th Digital Pathology and AI Congress in London in December.

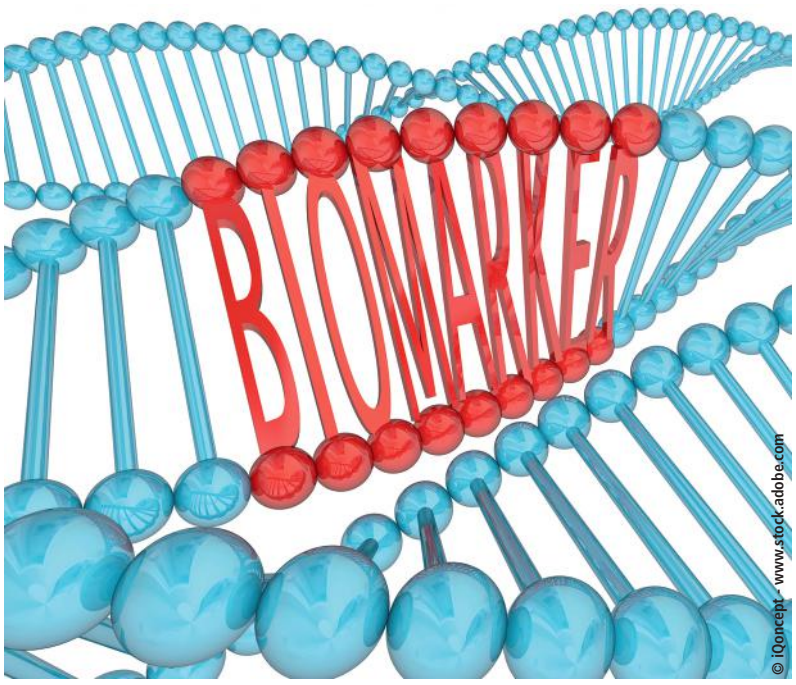
As Head of the Histopathology Department in the Servier Research Institute in Paris, France, she explained how expertise within the department covers various approaches to biomarker detection, using DNA (Fluorescent In Situ Hybridization – FISH technology), mRNA (RNAscope technology using RNA probes), and proteins (Immunohistochemistry/IHC technology using specific antibodies), which can be used to detect markers of interest on animal and human tissues. 'These biomarkers are measurable indicators of a biological state or condition, which will have a clinical role in guiding treatment decisions. They can be predictive, prognostic, or diagnostic,' she said.

Within this, digital pathology has been key, with digital image analysis implemented in the Histopathology department to speed up quantification of biomarkers and into daily routine.

Ten times the speed of a human pathologist

Dr Chotard's presentation will focus on the tumoral microenvironment in oncology and use of technology to detect several proteins of interest that could be used as biomarkers on the same tissue section (multiplex immunohistochemistry). She said there are several ways digital pathology can speed-up biomarker detection such as when performing an experiment to detect a protein on a tissue. Digitalizing the tissue slides and setting up algorithms with image analysis software can quantify the level of expression of these proteins. 'We can then ask the computer to quantify hundreds of tissue slides. This quantification will be exactly the same for all the images and, compared to a pathologist, we will get the results much faster,' she said.

Using Tissue Micro Arrays (TMAs) slides, which can contain several biopsies from one pathology of interest or from several pathologies, her team can perform IHC experiments and quickly screen the level of expression of a biomarker on these pathologies using automatic image analysis on digital slides. 'That allows us to evaluate as many pathologies as we want since the computer will be ten times quicker than a pathologist to quantify the biomarker.'



© iQoncept - www.stock.adobe.com

A closer look at the microenvironment

Immunofluorescence, used for multiplex immunohistochemistry, allows evaluation of co-expression of several markers in one cell, and calculation of distances between different cell types to understand the mechanism of action. 'This information will help us to more easily dissect the microenvironment,' she said. 'A pathologist will have some difficulty to quantify by eye co-expression more than two markers in one cell whereas image analysis software can quantify dozens of markers.' Digital pathology is being applied in various areas by Servier, including projects in oncology, immuno-oncology, immuno-inflammation and neurology but can be adapted for all types of pathologies. The aim, said Chotard, is to utilise new technologies to rapidly increase knowledge in the histopathology domain, and 'especially to detect more and more proteins and mRNAs on a single slide. This will allow us to better understand the interaction of biomarkers within their environment.' When working on serial sections, she said the heterogeneity of the tissues can prevent clear understanding of the interactions of proteins, especially in oncology. However, being able to observe all of them together 'narrows down' an understanding of the pathologies. While using the technology to characterize biomarkers and acceleration of their application into translational research and clinical development, the next step is to use AI on the histology slides to detect small abnormalities that a pathologist could not see by eye.

Paving the way for personalized treatment

For clinicians within pharma companies, improved knowledge of biomarkers expression and location will help to predict patient response to a treatment. 'For clinicians in hospitals,' continued Chotard, 'the increase of digital pathology should allow small hospitals to get access to new technologies, and more knowledge in some pathologies will allow for better diagnosis.' There are benefits for patients too. 'In oncology, where we are the most advanced with all these new technologies and digital pathology in Servier, this will increase personalized treatment for patients, target their subtype of cancer, and evaluate if they can benefit from immunotherapy for example instead of chemotherapy.' ■

Report: Mark Nicholls

Carole Chotard

Dr Carole Chotard is Head of the Histopathology Pole in the Servier Research Institute in Paris, working from early Research programs to clinical studies. A biologist by training, she holds a PhD in Neuropharmacology from the University René Descartes, Paris V working in the Neurosciences field using Histopathology approaches. After a postdoctoral position and a role as an Investigator Scientist in Neurosciences at the National Institute for Medical Research (NIMR) in London, she joined the Servier Pharmaceutical Company in 2009 in the Histopathology pole in Paris and took over the lead of the pole in April 2022.

**The 10th Digital Pathology and AI Congress: Europe takes place at the Intercontinental O2, London, on December 7 & 8.*

Important ideas for the entire health market

Medica Labmed Forum: four exciting topic days around hot issues and current trends

Cancer and coronary diseases, infections and new anti-bacterial active substances, digitalisation and artificial intelligence – these are some of the top issues discussed this year at the Medica Labmed Forum, which is part of the Medica 2023 trade fair in Düsseldorf, Germany.

Over the last years, the forum has developed into an especially noted part of the programme at the internationally leading trade fair for the health and medical technology industry, and will be held on all four days of the Medica event from November 13-16 in Hall 1.

Presentations and panel discussions

Though the topics are complex, it is a hallmark of the Medica Labmed Forum that all presentations are short, to the point and easy to understand, and can be addressed in further depth in panel discussions.

Like last year, the sophisticated programme was organised by Prof. Stefan Holdenrieder and Prof. Georg Hoffmann (German Heart Centre at the Technical University of Munich). During each lunch break, exhibiting companies at Medica 2023 are given the opportunity to introduce themselves with short presentations about their company.

Starting with two scandalous issues

On Monday, Medica starts with two "scandalous" issues which currently cause heated debates throughout the field of laboratory medicine: the potential threat to the existence of small IVD companies and specialised labs posed by the "In-Vitro Diagnostics Regulation" (IVDR) and the use of artificial intelligence (AI) with new possibilities and also risks.

On the second day, there will be a discussion of new developments in laboratory medicine within the fields of oncology and cardiology.

The third day of the Forum traditionally belongs to the next scientific generation within laboratory medicine. Young physicians are invited to report on their current research and thus give an outlook on the future of the scientific field.

An overview of diagnostic solutions

The last day of the event starts with an overview of diagnostic solutions that noticeably shorten the time it takes to identify a pathogen, thus allowing physicians to make the most effective therapeutic response at an early stage instead of turning in risky diagnostic circles and losing time. Special attention is given to managing septicaemia through quick identification of the pathogen and the targeted use of antibiotics.

More thorough research into scientific basics and possible applications yields a perspective for future options beyond classic antibiotic therapy, with the goal of countering the problematic development of resistances through innovative approaches. The spectrum of possible approaches under discussion ranges from the use of small molecules against bacterial toxins or specific transporters in the bacterial wall to phage therapy. A look inside the world of "Next Generation Sequencing" (NGS) and bioinformatics rounds out the event. The focus here is on characterising the microbiome of newborns, a very vulnerable patient group. ■

www.medica.de
Source: Medica