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Gender inequalities

Breaking the bias: a woman's perspective of cancer research


Olivia Rossanese


Alexandra Gilbert


Pamela Kearns


Serena Nik-Zainal


Bethany Rothwell

In an online event to mark International Women's Day, the National Cancer Research Institute (NCRI) assembled a panel of five women at various stages of their careers to discuss the hurdles they had to overcome – often because of their gender – and their determination to succeed. Issues raised include the level of opportunities, promotion, pay gaps, taking time off to have a family, stereotyping, and unwelcome remarks and comments from their male counterparts.

Dr Gillian Murphy, a member of the NCRI consumer forum, chaired the session to celebrate achievements of all women in cancer research.

A system that fails women

The first speaker was Dr **Olivia Rossanese**, Head of Division and Team Leader at the Institute of Cancer Research. She pointed out that, while progress has been made in advancing women in the field, the numbers of women present at the PhD/post-doc level and beyond are still nowhere near their male colleagues. 'If we don't change the system to support women, when we know about the problems in post-PhD to professorship, then we are pushing women into a system where it is going to fail them,' she said.

The widening pay gap was another serious issue keeping women from pursuing scientific careers, said Dr Rossanese, who leads the Target Evaluation and Molecular Therapeutics Team developing assays and strategies to support the drug discovery process and investigating the underlying biology of cancer targets and the response to targeted therapeutics. To counteract this, she challenged leaders at all levels to find more creative ways to structure careers and the overall system.

The importance of mentorship and self-kindness

Dr **Alexandra Gilbert** is an Honorary Consultant and Senior Clinical Trials Fellow at the University of Leeds, where her research interests include the use of patient-reported outcomes (PROs) in radiation toxicity measurement in clinical trials and routine practice. She explained that she had children during her PhD as she felt it was a time where there was 'more flexibility.' Dr Gilbert emphasised the importance of mentorship and the support she receives in her current role in ways to 'manage challenging situations', have pastoral support, and learn different skills from her mentors such as managing people and grant applications. But she also underlined the value of self-care and self-kindness, adding: 'Nurture not only your working relationships but also make sure you look after yourself and your family along the way.'

Calling out poor behaviour against women

Following up, Professor **Pamela Kearns** shared her experience over a career spanning more than 30 years. She said: 'When I started working, the environment for women was very different. Women were subject to comments about their appearance and behaviour, but it has changed massively for the good.' However, she remains concerned about 'high attrition' further up the academic ranks. 'The number of young researchers that are women outweighs men but by the time you get to the professorial level it has flipped the other way,' said Kearns, a Professor of Clinical Paediatric Oncology at the University of Birmingham and Director of the Cancer Research UK clinical trials unit, as well as an honorary consultant at Birmingham Women and Children's hospital. She said women, as well as men, should call out poor behaviour against women and added that women should believe in themselves and have courage to take opportunities.

Setting priorities in a male-dominated field

Professor **Serena Nik-Zainal**, NHS honorary consultant in clinical genetics and NIHR Professor of Genomic Medicine and Bioinformatics at the University of Cambridge, reflected on her career path, which she described as being not straightforward. Arriving in the UK at age 17 with the aim of becoming an NHS consultant, she trained in medicine and specialised in clinical genetics but took a year off for each of her two children. 'Some people were concerned about this impacting my career, but it was an easy decision – babies are babies just once,' she said.

Prof Nik-Zainal has focused on NGS (next-generation sequencing) technology with research looking at the physiology of mutagenesis, combining computational approaches with experimental and cancer data. This area, she acknowledged, is still male-dominated and ultra-competitive, and remarked that 'sometimes unfortunate things happen' concerning gender, ethnicity, and dress. However, she added: 'It is perfectly ok for us to be ourselves, we do not have to be apologetic for who we are.'

Female mentors in a 'man's world'

The final contribution to the panel came from **Bethany Rothwell**, who is currently working on a PhD in a proton therapy research group based at the Christie Hospital in Manchester and at the University of Manchester, where her work involves the use of mathematical modelling techniques to investigate FLASH radiotherapy and cellular oxygen depletion. 'My background is in physics and I became interested in how tools and concepts in physics can be applied medically and biologically, particularly in cancer research. I became particularly interested in proton therapy, working at the interface of physics and biology,' she said. 'Physics can feel like a man's world, so having female role models and mentors can be a really important part of your academic life to keep you inspired and give you that sense of belonging here. It can be challenging to find these mentors and you have to make an active effort to seek role models out, but it can make a huge difference to your career.'

Report: Mark Nicholls


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Clinical computational tools

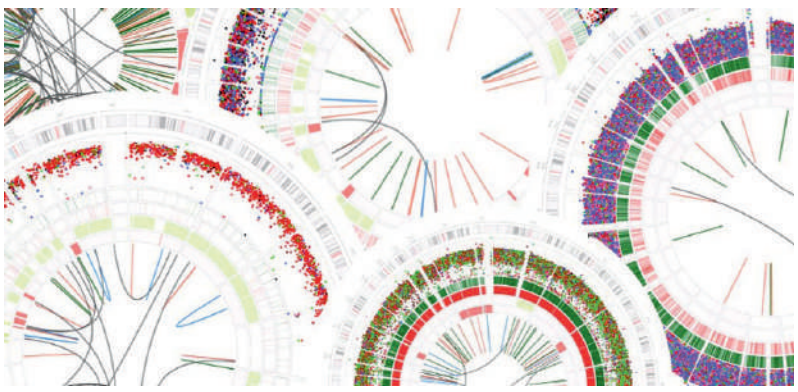
Managing cancer more effectively

Computational approaches are being applied on enormous amounts of data from sequencing technologies to develop tools to help clinicians manage cancer more effectively. Professor Serena Nik-Zainal explained that her team in Cambridge, UK, is working to further understand the physiology of mutagenesis to advance cancer diagnosis and care.

Advances in the ability to read the human genome have made it possible to sequence the entire 3000 million base pairs of the human genome in a single experiment. 'My team at Cambridge uses this accelerated whole genome sequencing technology to read all the mutations that are present in human cancers,' explained Professor Nik-Zainal, who is NIHR Research Professor of Genomic Medicine and Bioinformatics and Honorary Consultant in Clinical Genetics at the University of Cambridge. She explained that human cancers are full of mutations that serve as an historic report of anything that has gone wrong in the cells as they turned into cancer cells. 'If we can truly understand what those mutations signify, then we come closer to understanding the causes of each person's cancer, and how to inform clinical decision-making for individual patients,' she added. With computational methods critical in studying the large mutation datasets, she explained that the two main groups of mutations to try to understand are:

- the small handful of "driver" or causally-implicated mutations, which tend to happen in the body of genes, because these driver mutations can become targets for therapeutic intervention; and
- the large swathe of mutations that form patterns across the genome, which are called mutational signatures.

'Both of these types of mutations, drivers and mutational signatures, are important, because they help us to understand cancer development,' the expert said.



Montage of whole cancer genome visualisations: Professor Nik-Zainal's team creates these graphical representations to enable clinicians to "read" them.

Her team is particularly interested in mutational signatures and performs laboratory experiments to understand how and why those mutational signatures arise. 'Some of these signatures are like a signal, a biomarker, of a biological pathway that is awry, and sometimes those can be targetable,' she continued. 'For example, we can discern patterns of mutations that are due to DNA repair defects and drugs like immunotherapies can be used to target tumours with specific DNA repair defects.'

Tools to manage the "data deluge"

In order to derive maximum understanding of mutagenesis, her team combines experimental work with computational approaches. 'Ultimately, we want to use the new knowledge from the experimental data and big cancer datasets to develop clinical computational tools that can help us to manage cancer more effectively.'

From there, the team applies statistical methods – such as machine-learning models – to create algorithmic tools. 'The purpose of these tools is to enable clinicians to quickly identify patients that may have sensitivities to particular drugs or to help inform management in some way,' added Professor Nik-Zainal. 'We hope that our tools will facilitate clinicians in a future where cancer genomics is a routine part of cancer care.'

Given the current "deluge of data", there are few easy ways to analyse and interpret it, so her team is looking to create apps to support clinicians in cancer genome interpretation. One example for this is an algorithm developed through machine-learning called HRDetect to identify tumours that have an abnormality in the BRCA1/BRCA2-dependent DNA repair pathway based on their mutational signatures.

Creating the algorithm, however, was simply the first step, and subsequently the team had to demonstrate that HRDetect could distinguish breast cancers with good from bad clinical outcomes. This saw collaboration with colleagues in Sweden, and later with those in London and with pharmaceutical company Clovis to show that HRDetect was predictive of sensitivity to a drug. 'We collaborated to show that our algorithm did have early predictive capabilities and that breast cancers with high HRDetect scores showed activity to treatment with a PARP-inhibitor drug,' said Professor Nik-Zainal.

Preparing for a data-driven future

The next step is a Phase III trial with Genomics England – the national whole genome sequencing endeavour – to see whether their clinical algorithmic tools can be implemented into the NHS bioinformatics pipeline. 'The next stage of our work is to get our clinical algorithms to patients as soon as possible and get to a Phase III randomised controlled trial to show that our algorithms really help inform patient care,' she said. 'Ultimately, genomics will become another tool in the everyday management of cancer. Beyond creating individual algorithms for genomic interpretation, there is a large piece of work involved in creating holistic clinical decision support tools and educating the next generation on how to use these tools so that they are equipped for a data-driven future.' ■

Report: Mark Nicholls

Serena Nik-Zainal

Professor Serena Nik-Zainal is Professor of Genomic Medicine and Bioinformatics and an NIHR Research Professor at the University of Cambridge, UK. She is also an Honorary Consultant in Clinical Genetics at Cambridge University Hospitals NHS Foundation Trust. Having been heavily involved in the development of the whole genome sequencing (WGS) using next-generation sequencing (NGS) technology, she now leads the Genomic Medicine theme at the NIHR Cambridge Biomedical Research Campus.

Patient Reported Outcomes

Going PRO to advance cancer treatment

Involving cancer patients more closely in the treatment pathway can modify care and deliver better outcomes. Carefully designed questionnaires to gain a better insight into symptoms and the way patients respond to treatment are helping clinicians take therapies to a new level through a Patient Reported Outcomes (PROs) approach.

Clinical oncologist Dr Alexandra Gilbert from the Leeds Cancer Centre in the UK is using PROs to improve measurement of patient symptoms, with a particular interest in developing predictive biomarkers of radiotherapy effects and PRO methodology in clinical trials.

While doctors traditionally respond to what patients tell them during clinics about side effects or adverse events, she explained that using a questionnaire for PROs can provide extra information about side effects from the patients' perspective, including toxicity of treatment and the 'quality of life impact of cancer treatment.' With radiotherapy, the challenge clinical oncologists face is in achieving the balance between giving a dose to cure a patient of cancer, while keeping side effects to a minimum. 'This is the real impetus for my research – to better identify radiotherapy side effects so that we could then try and improve our radiotherapy treatments,' she explained.

Patient participation improves insights

Based on the findings so far, questionnaires designed to measure changes over time have been developed with patient input. 'It is also important that they are standardised to allow you to statistically and robustly look for differences,' she said. 'With a good questionnaire, you can measure change over time and differences between different treatments; you get much better granularity and detail about what patients are experiencing if you ask them directly.' There are a range of validated questionnaires available for clinical practice or clinical trials; for example, the EORTC (European Organisation for the Research and Treatment of Cancer) Quality of Life group has 66 questionnaires covering different cancer areas in multiple languages. Gilbert, who is also Cancer Research UK (CRUK) Senior Clinical Trial fellow at the University of Leeds, said PROs are supporting better communication, improving the patient journey, recognising the patient voice, and improving outcomes. 'There is good evidence that patients filling out a questionnaire about side effects can improve the way they are able to communicate with doctors.

'More recently, randomised controlled trials have shown benefits in overall survival through using PROs in routine care because by regularly measuring side effects from the patient perspective, doctors are able to intervene and better support patients with their side effects, enabling them to carry on their treatment for longer.'

When using PROs in clinical practice, Gilbert, who specialises in pelvic cancers, said the questionnaires often prompt patients to talk about aspects they may not normally discuss, such as concerns about sexual dysfunction.

Standardisation is key to consistency

At cohort level, data collected can show patterns in patient symptoms, enabling teams to better support and identify interventions or develop preventive mechanisms for side effects. 'That is really important, particularly in radiotherapy, where some side effects may not occur until years later,' said Gilbert. Additionally, as patients may see different doctors during their follow up care, the accounts in the questionnaires allow for a consistency of story.

As well as her research in PROs in radiation toxicity measurement in routine practice and clinical trials, she is involved in international projects to improve standardisation of how PROs are measured, analysed, and reported and works with organisations such as the PROTEUS Consortium, which promotes tools and resources to optimise the use of PROs in clinical trials and practice.

Stressing the need for consistency in PROs, she emphasised how studies are showing that this improved level of communication with the patient has an 'obvious benefit in terms of overall survival that is hard to ignore.' ■

Report: Mark Nicholls

Alexandra Gilbert

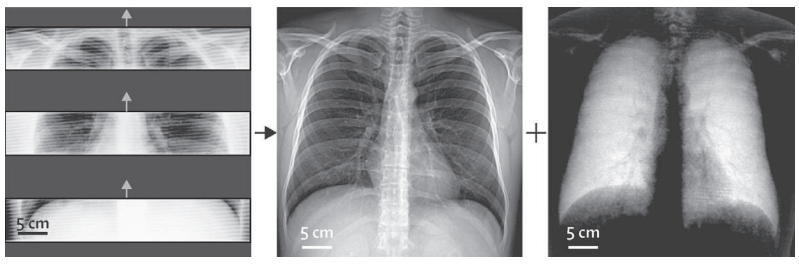
Dr Alexandra Gilbert is an Honorary Consultant in clinical oncology at Leeds Cancer Centre, and CRUK Senior Clinical Trial fellow at the University of Leeds, UK. Her research interests are in PROs in clinical trials and routine practice, and interventional radiotherapy trials. She is chair of the NCRI (National Cancer Research Institute) Methodology workstream and is an active member of the EORTC Quality of Life group.

EUROPEAN HOSPITAL @ ECR 2022

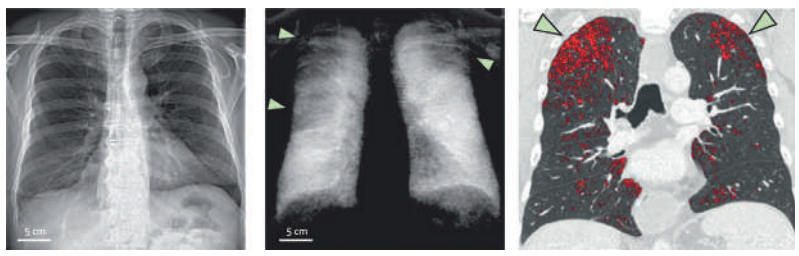
Modified radiography technique

Dark-field X-ray casts new light on lungs

It looks like a negative of a normal X-ray image but gives new insights into pathologies of the lungs and other organs: dark-field radiography uses a part of X-rays that has hardly been considered so far to expand the spectrum of diagnostic imaging. At the ECR congress, Theresa Urban from the Technical University of Munich (TUM) presented the new method and explained its advantages in the diagnosis of emphysema.



Dark-field radiography uses a previously unused part of the X-ray radiation to generate additional information (right) from the small-angle scattering from the raw data (left) in addition to conventional X-ray images (centre).



Left: Chest X-rays of male patient, aged 58: In the dark-field image (centre), regions affected areas affected by localised emphysema appear dark, indicating reduced small-angle scattering due to fewer air-tissue interfaces. By contrast, the attenuation image (left) is very limited in visualising the emphysematous changes. Right: A CT image provides similarly good results, but is associated with higher radiation exposure.

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'Unlike conventional radiography, which produces images by penetrating anatomical structures to varying degrees, dark-field imaging is based on the small-angle scattering of X-rays,' the expert explained. 'This effect occurs at transitions between materials with different densities, for example between tissue and adjacent air or fluids. The principle is similar to light refraction in water, only on a much smaller scale.' The evaluation of this small-angle scattering provides information on microstructures that cannot be seen in normal X-rays.

To generate the dark-field images, an interferometer is coupled to the X-ray device to record the scattering and translate it into image information. 'A major advantage is that the image information from conventional and dark-field X-rays is recorded in parallel,' Urban explained. This way, both modalities are available in a complementary way for diagnostics without the need for multiple radiation exposure.

Insight into microstructures improves early detection

So far, the lung has been the primary field of application for the new imaging technique. The organ offers good conditions for dark-field radiography because its alveolar structure contains numerous transitions between air and tissue. 'In a healthy lung, these structures are intact, thus producing a strong dark-field signal. On the images, these areas show up brightly. In contrast, emphysema creates dark patches; it destroys the alveolar structure so that large air bubbles appear with only few transitions.'

Normal X-ray imaging can also detect such pathologies in the lungs, but at a much later stage, Urban pointed out. 'With dark-field radiography, there is no superimposition of bones and surrounding tissue, so that we get a clearer view of the microstructure and pathological changes can be detected earlier.' Thus, pulmonary emphysema can already be seen in the early stages, while conventional X-ray imaging only registers anything upward of moderate manifestations. 'Up to now, CT imaging has been the method of choice for early detection, but dark-field imaging offers much lower radiation exposure while maintaining comparable sensitivity.'

Research is currently being conducted to find out whether the new method can also provide added diagnostic value for other lung diseases – with Covid-19 being an obvious focus; so far, the results of the studies are very promising, the expert said.

The use of dark-field X-rays is by no means limited to the lungs, explained Urban: 'In principle, the modality is suitable for all areas with a microstructure that is changed or arises as a result of a disease.' This applies, for example, to the formation of kidney stones, microcalcifications in mammography or musculoskeletal diseases such as osteoporosis, all of which can be seen in the dark-field. It is also conceivable to use it to visualise uric acid crystals that form in gout disease.

Three-dimensional advances

Several important milestones have already been mastered on the way to clinical application: In October 2018, the first clinical trial for the early detection of COPD started, with results recently published in the journal Radiology. 'We have already proven the added value of dark-field imaging in emphysema and are confident that we will also succeed in other clinical applications.'

Ongoing dark-field research also includes the combination with other imaging modalities such as CT. Using cross-sectional slices, the information gathered from the dark-field can be translated into three-dimensional images. However, using CT poses additional technical challenges for the scientists. For example, the rotation of the scanner's gantry causes vibrations that must be subsequently calculated out to obtain a viable dark-field image. First measurements on thorax phantoms were successful, so that dark-field CT will soon be used on patients.

A major benefit of dark-field imaging is that the method is compatible with commercially available X-ray systems, only an interferometer needs to be added. The company that manufactures the microgrids used in these devices is already working on bringing conversion kits to market, Urban reported. 'We hope that dark-field technology will become widely accepted and that many patients will be able to benefit from it.' ■

Report: Wolfgang Behrends

Theresa Urban

Theresa Urban, MSc, is a PhD student at the Department of Biomedical Physics at the Technical University of Munich (TUM) and the Munich Institute for Biomedical Engineering. She is part of Prof. Dr. Franz Pfeiffer's Biomedical Physics group, which focuses on the translation of modern X-ray concepts into clinical applications.

Ovarian cancer and endometriosis detection

Women's health imaging: PET/CT and T2*w MR show promise

Diagnostic imaging in women's health advances: Positron emission tomography–computed tomography (PET/CT) might provide a more accurate imaging alternative to CT in ovarian cancer. T2*-weighted MR imaging in deep endometriosis detection also shows promise, but ultimately falls flat. In a dedicated session at the ECR 2022 Overture in March, experts presented their latest research projects.

Dr Elaine Yuen Phin Lee from the Department of Diagnostic Radiology at the University of Hong Kong talked about monitoring treatment response in epithelial ovarian carcinoma (EOC) with PET/CT following neo-adjuvant chemotherapy (NACT). 'EOC presents late as advanced-stage disease because early-stage disease tends not to present symptoms,' she said. 'Cytoreduction remains the most effective treatment and the ability to achieve complete cytoreduction is prognostic for survival.'

To achieve cytoreduction, the patient can either undergo upfront cytoreduction or NACT, followed by interval debulking surgery. Treatment response to NACT is currently assessed by CT, but this may not be accurate all the time, Lee explained. 'The diagnostic accuracy of CT has quite a wide range, in between 57 to 94% depending on the study you look at. Mostly, this is limited by subcentimetre lesions and immeasurable disease, which is common in advanced stage carcinoma,' she said.

By comparison, PET/CT offers accuracy rates that are consistently high, with reported figures of 90-95% in primary evaluation of EOC. The reason for this is that PET/CT picks up on the metabolic changes in the patients, which occurs earlier than the anatomical changes that are detected via CT, Dr Lee said. 'Unfortunately, there's a lack of data on the diagnostic accuracy of PET/CT in the setting of NACT in EOC.' The expert and her team thus hypothesised that metabolic activity in these tumour deposits on PET/CT could increase the visual conspicuity of the tumours and diagnostic accuracy after NACT in EOC.

Evaluating the accuracy of PET/CT in monitoring treatment response

The objective of the study Dr Lee presented at ECR was to evaluate the accuracy of PET/CT in monitoring treatment response in EOC after NACT. 'We recruited 15 patients with stage III to IV of EOC who were scheduled for NACT and PET/CT after 3 cycles of NACT before interval debulking surgery,' she explained.

For PET/CT evaluation, the researchers divided the abdominopelvic cavity into 19 regions and used a 5-point Likert scale to score the evaluation, with 1 signifying the absence of disease and 5 being malignant. Region-based analysis was performed subsequently.

Lee and her team also used histopathological correlation as gold standard, and in the instances in which biopsy resection could not be performed, they took the surgical evaluation as standard.

They evaluated 285 regions with an accuracy of 88%, but low sensitivity at 38% and high specificity at 96%. Positive predictive value (PPV) was low at 56% while negative predictive value (NPV) was high at 91%.

This preliminary study showed that PET/CT achieves low sensitivity in all regions, but high specificity and NPV. Exceptions were found in two regions in the omentum, because of the presence of microscopic disease that could not be picked up on PET/CT, and also in the central pelvis because of low spatial resolution on both CT and PET examinations.

'PET/CT is highly specific with high NPV in treatment response assessment after NACT in EOC,' Lee concluded. Taking into account the relatively small sample size, she proposed that PET/CT might be useful in surgery planning, allowing for disease stratification to assess the viability of less aggressive and debulking surgery.

Endometriosis: A closer look at blood degradation products

In the following talk, Dr Paolo Niccolò Franco from the Department of Diagnostic Radiology at Papa Giovanni XXIII Hospital in Bergamo, Italy, shared the results of a study comparing T2*-weighted vs. standard MR imaging performance in detection of deep endometriosis. 'Endometriosis is a chronic gynaecological disorder characterised by the presence of ectopic functional endometrial tissue outside the uterine cavity,' he said. 'This condition affects approximately 10% of women of reproductive age. Deep infiltrative endometriosis is defined as the presence of implants extending 5 mm or deeper under the peritoneal surface.'

MRI has been shown to be an effective tool for both diagnosis and treatment planning of deep pelvic endometriosis. T2*-weighted sequences are susceptible to chronic blood degradation products – such as hemosiderin – which are visualised as signal voids. To take advantage of this, it has recently been proposed that these sequences can provide added value to detect ectopic endometrium by identifying hemosiderin deposited during cyclic bleeding.

The aim of Dr Franco's study was to evaluate the diagnostic performance of T2*-weighted sequences, compared to conventional pelvic MRI protocol, in the detection of deep pelvic endometriosis. The researchers enrolled 44 patients who underwent a pelvic MRI on a 3T scanner for clinical and/or ultrasound suspicion of deep endometriosis.

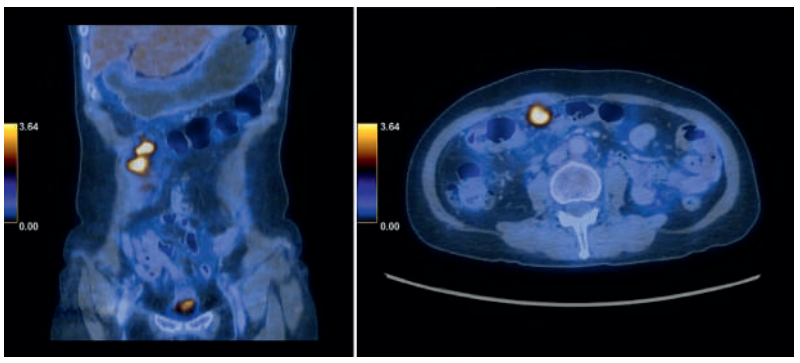
T2*w MRI prone to diagnostic overestimation

Three readers independently evaluated MR images. The first reader was a staff radiologist with ten years' experience, who analysed images taken with both conventional MRI protocol and T2*w sequences. The second reader, a resident with 2 years' experience, analysed conventional sequences. The third reader had limited experience and analysed images taken with both conventional MRI protocol and T2*w sequences.

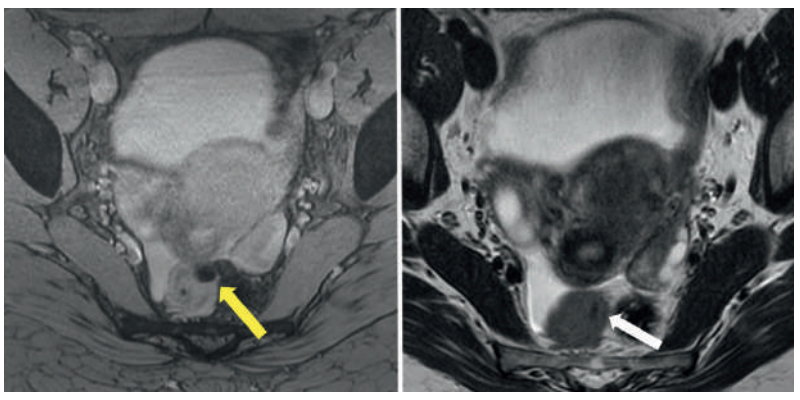
The first reader diagnosed endometriosis lesions mainly in the ovaries, the torus uterinus, retrocervical space and the utero sacral ligament. The first two readers agreed on endometriosis sites on both conventional protocols and T2*w sequences. 'The number of lesions detected by the third reader on T2*w sequences was significantly higher, mainly because the reader mistook some findings for endometriosis lesions, for example gas in the vaginal fornix and rectal lumen or artifacts caused by caesarean scars,' the expert said.

T2*w sequences do not seem to bring added value to expert readers in their assessment of endometriotic lesions, Dr Franco concluded. 'Artifacts caused by undesirable sources of magnetic signal voids may lead to diagnostic overestimation, especially for readers with limited experience.'

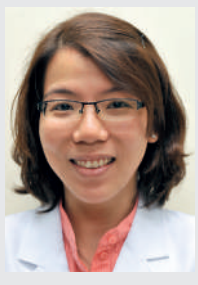
Report: Mélisande Rouger



A true positive lesion in the greater omentum involving the transverse mesocolon, confirmed at interval debulking surgery and subsequently on histopathological specimen.



An ovoidal signal void (yellow arrow) on T2*-weighted imaging (left image) corresponding to artifacts caused by gas within the rectal lumen (white arrow), showed in a sagittal T2*w image (right).



Elaine Lee

Following her radiology training in the UK, **Elaine Lee** joined the Department of Diagnostic Radiology, Li Ka Shing Faculty of Medicine, University of Hong Kong in 2010 and is now a Clinical Associate Professor. She has subspecialty interest in gynae-oncology, specifically in the application of functional and molecular imaging techniques. She is the primary investigator and recipient of competitive national grants in advancing the research in gynae-oncology imaging. She enjoys post-graduate mentoring and undergraduate teaching.

Paolo Niccolò Franco

Dr Paolo Niccolò Franco was born in Cosenza, Italy, and obtained his medical degree at the University of Florence. He is a fourth-year resident at the Post-Graduate School of Diagnostic Radiology of the University of Milano-Bicocca and his residency was at San Gerardo Hospital in Monza and Papa Giovanni XXIII Hospital in Bergamo. He has a special interest in pelvic, genitourinary, and gynaecological imaging. Dr Franco is a member of the European Society of Radiology and the Italian Society of Medical and Interventional Radiology.

New tool: Be accepted

Support for female cancer patients

The new tool, called "Be accepted", was presented in a round table discussion organized by the European Society of Radiology Patient Advisory Group (ESR PAG) at the ECR Overture in March. The product, which has received the full support of the ESR, is an information campaign, with resources in printed and online form.

It is designed as a comprehensive source of relevant information for patients who have been diagnosed with cancer, Caroline Justich, the project founder, explained. '"Be accepted" contains information that is filtered, scientifically proven and summarised in one medium, to enhance the life of both patients and radiologists,' she explained.

Supporting the healing process

Justich, a long-time member and now chair of the ESR PAG, was diagnosed with stage 4 breast cancer in 2016, when she was 39. She explained how knowing the needs of both cancer patients and radiologists inspired her to develop the project to support other women in that situation. Recalling the time when she received the cancer diagnosis, she acknowledged the support she got from her radiologist, Professor Michael Fuchsjäger. The Professor of Radiology and Chairman of the Department of Radiology at the Medical University of Graz, Austria, and Chairman of the ESR Board of Directors not only caught his patient in her first shock, but also prepared her for the next steps and equipped me with the right mindset. 'He told me this would be a rollercoaster ride and my job was to put my focus on the end of the ride, and believe my journey through it will be ok,' she said. 'It took ten seconds of his time – for me, it changed the game.' Thanks to her radiologist's support, Justich was able to accept her diagnosis and put her focus on where her energy should flow to: recovery.

However, not all patients who are in "free fall" after the life-changing diagnosis can rely on such support. "Be accepted" was designed for female patients to withstand the initial shock and support patients' physical and mental wellbeing by providing access to basic information, answers to the most important questions, and the latest peer-reviewed studies in the field. Using "Be accepted" right from the start after receiving a cancer diagnosis will help women come to terms with their disease, visualise their goals and act to achieve them, Justich explained. 'When they are given their diagnosis, patients are often not able to take in the information,' she said. 'That's why we launched the project, to build resilience from the very first moment and support the healing process. For radiologists, it delimits the time for and optimises communication and helps them put the patient on the right track.'

'"Be accepted" is mainly for our patients, but also for us radiologists,' added Prof Fuchsjäger. Every cancer diagnosis puts patients on a roller coaster ride, he explained, so it is of great importance to have them focus on the exit, rather than the arduous journey. 'As radiologists, we're here right from the start, beginning with screening where we detect cancer until the end where we just do follow-up.'

"Be accepted" is aligned with the ESR's position on value-based radiology, an approach that looks at the benefits for patients and society by providing radiology services. 'One way to measure value-based radiology for the ESR is the relationship between patients and radiology personnel,' Fuchsjäger said. 'We need to offer patients instructions for different examinations, distribute customer satisfaction questionnaires and audit, and be available to talk to patients whenever requested.' A patient friendly environment is important, he added. 'We must be able to provide low-cost reading programs where patients can get in and be screened for major cancers.' Radiologists can deliver value everywhere in the radiology chain, from selecting which imaging and other diagnostic tests to perform to the appropriate communication of the results. Having a tool that empowers patients and enhances communication right from the start can help make all the difference, he explained. 'We want to have perfectly informed patients because this gives them perfect safety. We as radiologists are medical gatekeepers, we have to appreciate it and we can make all the difference at the beginning of the patient's therapeutic journey,' he concluded. ■

Report: Mélisande Rouger

Round table discussion

Specialists build bridges in interventional oncology

Delivering a drug directly inside a lesion using minimally invasive procedures opens up new perspectives for patients and medical teams. At the ECR Ouverture in March, speakers looked at how to best join forces to advance the promising field of interventional oncology during a round table discussion.

Injecting a chemotherapeutic agent into a tumour locally has gained ground in clinical practice, but there is still some way to go before immunotherapy or other target agents are used in this setting, according to Prof Dr Thomas Helmberger. The Chairman of the Department of Radiology, Neuroradiology, and Minimally Invasive Therapy at Munich Klinik Bogenhausen, Germany, made a case for more interdisciplinarity as he opened the session: 'I've been lucky to work closely with oncologists and surgeons for many years,' he said. 'Traditionally, specialists dealing with oncological patients tend to stick to their specific therapies for a long time before they even consider trying something else. Nevertheless, joining efforts for our patients will be worthwhile.'

Stepping out of the comfort zone

While he sympathised with oncologists being cautious about interventional oncological treatment options, or even feeling "threatened" by interventional radiology, Helmberger advocated that they should not hesitate to seek radiologists' support to provide collaborative therapy concepts. 'Interventional oncology has proved its efficiency and safety in hundreds of thousands of patients worldwide. When the first procedures were introduced 30 years ago, other specialties were sceptical too. Now, tumour embolisation for hepatocellular cancer, radioembolisation and thermal ablation – to name a few – are standard,' he said.

Today, peripheral and cerebral vascular procedures remain at the core of interventional radiology's scope. One of the main obstacles to further deployment in oncology is the reluctance of many radiologists to work in this setting since it might be more demanding. 'Interventional oncology is much more interactive and challenging for radiologists because they have to think like an oncologist and learn about new terminology,' Prof Helmberger said. 'They have to deal with patients who are often much sicker, facing complex therapies, and they also have to advise their families, just like a surgeon or an oncologist would.'

An aging population and increasing cost pressure on healthcare systems accelerate the trend for hospitals to deliver smart multimodality treatment options, the expert predicted. In this setting, radiologists can provide more than just reading scans. 'You'll have to learn to leave your comfort zone and step into the treatment field,' he said, addressing his radiologist colleagues. 'Interventional oncology is a very smart career choice for the new generation.'

Andrés Cervantes

Andrés Cervantes is Head of the Medical Oncology Department at the University Hospital of Valencia and Professor of Medicine at the University of Valencia, Spain. He is the General and Scientific Director of the Institute of Health Research - INCLIVA. His main areas of interest and research are gastrointestinal and gynaecological cancer, as well as Phase I trials and new drugs development.

Thomas Helmberger

Thomas Helmberger is Professor of Radiology and Chairman of the Department of Radiology, Neuroradiology, and Minimally Invasive Therapy at Munich clinic Bogenhausen, Germany. His medical specialties include diagnostic imaging of the abdominal and thoracic organs, including functional and tissue-specific imaging (liver, pancreas, small and large intestine), the spectrum of diagnostic and interventional vascular medicine, and interventional oncology.

Clear benefits for the patient

The expert went into detail on the benefits of interventional oncology, which can help oncologists manage systemic treatments' side effects in patients. For instance, local application of low dose chemo or immunotherapeutic agents can also allow disease control, while

Mammography

Breast cancer screening: AI shows promise

A major new study shows that artificial intelligence (AI) is a promising tool for breast cancer detection in screening mammography programs.

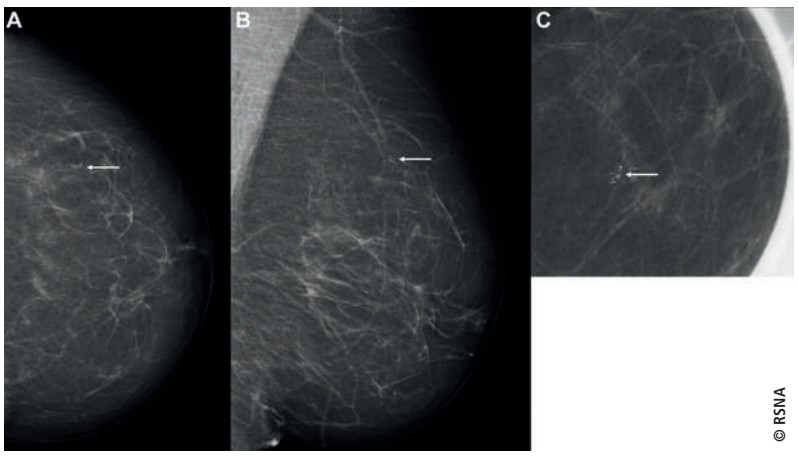
Mammograms acquired through population-based breast cancer screening programs produce a significant workload for radiologists. AI has been proposed as an automated second reader for mammograms that could help reduce this workload. The technology has shown encouraging results for cancer detection, but evidence related to its use in real screening settings is limited.

123,000 examinations performed on more than 47,000 women

In the new study — the largest of its kind to date — Norwegian researchers led by Solveig Hofvind, PhD, from the Section for Breast Cancer Screening, Cancer Registry of Norway in Oslo, compared the performance of a commercially available AI system with routine independent double reading as performed in a population-based screening program.

The study drew from almost 123,000 examinations performed on more than 47,000 women at four facilities in BreastScreen Norway, the nation's population-based screening program.

The dataset included 752 cancers detected at screening and 205 interval cancers, or cancers detected between screening rounds. The AI system predicted the risk of cancer on a scale from 1 to 10, with 1 representing the lowest risk and 10 the highest risk. A total of 87.6% (653 of 752) of screen-detected and 44.9% (92 of 205) of interval cancers had the highest AI score of 10. The researchers created three thresholds to assess the performance of the AI system as a decision-making tool. Using a threshold that mirrors the average individual radiologist rate of positive interpretation, the proportion of screen-detected cancers not selected by the AI system was less than 20%.



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Images in a 60-year-old woman with an invasive screen-detected cancer with an artificial intelligence (AI) score of 1 on the screening mammograms. (A) Mammogram of left breast from craniocaudal view. (B) Mammogram of left breast from mediolateral oblique view. (C) Craniocaudal cone view mammogram with magnification. AI score is defined as the overall examination-level score from the AI system, and a score of 1 is indicative of low probability of breast cancer and 10 of high probability. The arrows indicate the malignancy.

AI will be of great value in interpretation of screening mammograms

While the AI system performed well, the study's reliance on retrospective data means that more research is needed. 'In our study, we assumed that all cancer cases selected by the AI system were detected,' Hofvind said. 'This might not be true in a real screening setting. However, given that assumption, AI will probably be of great value in interpretation of screening mammograms in the future.' The results showed favorable histopathologic characteristics associated with a better prognosis for screening-detected cancers with low versus high AI scores. Opposite results were observed for interval cancers.

This may indicate that interval cancers with low AI scores are true interval cancers not visible on the screening mammograms. The

Solveig Hofvind

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mgo fachverlage

Publisher
Mediengruppe Oberfranken – Fachverlage GmbH & Co. KG
E.-C.-Baumann-Str. 5
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Phone +49 (0) 9221 949-311
Fax +49 (0) 9221 949-377

Editor-in-Chief:
Mareike Scholze (MaS)

Production Manager:
Sonja Buske (SB)

Editorial team:
Wolfgang Behrends (WB)
Sonja Buske (SB)
Sascha Keutel (SKE)

Senior Writer:
Mark Nicholls (MN), Great Britain
Mélisande Rouger (MR), Spain

Publishing Director:
Mareike Scholze (MaS)

Managing Directors:
Walter Schweinsberg, Bernd Müller

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Correspondents
Austria: Michael Krassnitzer (MK)
France: Jane MacDougall (JMD)
Germany:
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Katrin Schreiter (KS)
Dr Christina Czeschik (CC)
The Netherlands:
Madeleine van de Wouw (MvW)
USA: Cynthia E. Keen (CEK)

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Simone Sesselmann
kundenservice@mgo-fachverlage.de
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Representatives
China & Hongkong: Gavin Hua, Sun China Media Co, Ltd.
Phone: +86-0755-81 324 036
E-Mail: 627416876@qq.com
Germany, Austria, Switzerland:
Ralf Mateblowski
Phone: +49 6735 912 993
E-Mail:
r.mateblowski@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
Maria Kaiser
Phone: +1 250 726 4007
E-Mail: mkads@mac.com

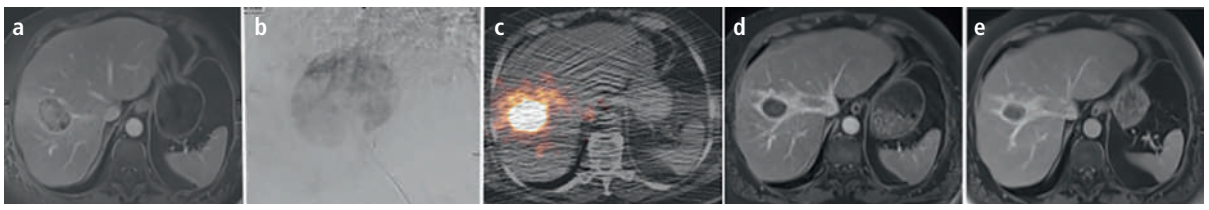
significantly reducing side effects in patients with localised tumours in the lung or kidney.

Prof Helmberger reported on how he often carries out liver focused therapy such as chemoembolisation not just in hepatocellular cancer, but also metastatic disease of colorectal cancer, to help patients recuperate between chemo or immunotherapy cycles. 'Offering patients a pause helps them to recover. During this break, oncologists may also decide whether further treatment is necessary or not, if they see that their patients are getting better,' he said.

Triggering a chain reaction

Directly delivering treatment inside a tumour (intratumoral therapy) may have an impact not only in the lesion itself, but also on other tumour locations in the body, Prof Dr Andrés Cervantes, Head of the Medical Oncology Department at the University Hospital of Valencia, Spain, explained in the following talk. 'For example, if you inject a drug in a 2cm nodule of a given compound in the liver, you may also get a response in a cervical node. This reaction also applies to other parts of the body.' Thus, the goal is to use this treatment effect in a specific accessible lesion to combat additional cancers. 'The only requirement is that the tumour is at least 2cm in size and can be injected without the risk of a toxic event,' he said.

Intratumoral immunotherapy is a strong area of development now; researchers are looking into what agents or drugs may stimulate the immune response more effectively when injected into a given tumour. Some of the trials are exploring the efficiency of existing anti-cancer drugs that have not been FDA-approved in that context yet. 'We have huge preclinical evidence that this could be a very important finding, but it's still very early and we have to consider safety and toxicity issues,' said Cervantes.



Radioembolisation of a intrahepatic cholangiocarcinoma (ICC)

Together with his multidisciplinary team at INCLIVA Institute of Health Research, the expert is working on advancing this approach. 'Radiologists need us because we have patients and we need them because they have the techniques and tools that may improve patients' outcomes and help surgery develop further,' he concluded.

In another talk, Dr Guido Torzilli, Head of the Liver Surgery Department at the Humanitas Research Hospital in Milan, Italy, explained how surgical oncology is moving towards minimally invasive treatments for the patient's benefit. ■

Report: Mélisande Rouger

high percentage of true negative examinations classified with a low AI score has the potential of substantially reducing the interpretive volume, while allowing only a small proportion of cancers to go undetected. By using AI as one of the two readers in a double reading setting, the radiologist could still identify these cancers, the researchers said.

'Based on our results, we expect AI to be of great value in the interpretation of screening mammograms in the future,' Dr. Hofvind said. 'We expect the greatest potential to be in reducing the reading volume by selecting negative examinations.'

Results help to establish a basis for future research

Although more study is needed before clinical implementation of AI in breast cancer screening, the results of the study help establish a basis for future research, including prospective studies, Hofvind said. 'We are looking forward to testing out different scenarios for AI using retrospective data and then running a prospective trial,' she said.

Source: RSNA ■

Patient-focused radiography

Dementia and autism patients in the MRI: not aggressive, just lost

Patients with neurological conditions such as dementia or autism can prove especially challenging for radiographers. A session at the ECR Overture in March gave insights to a patient-focused approach, with experts sharing the results of research projects as well as touching insights from their own experience.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Professor Mark McEntee, a radiographer at University College Cork, Ireland, opened the early morning session by presenting the work of one of his students on the attitude of radiographers towards management and care of patients with dementia. In a moving presentation, the expert shared his experience both as a radiographer and the parent of a patient with dementia, a range of symptoms often misunderstood as a disease. 'Dementia is an umbrella term used to describe a range of symptoms rather than a disease itself,' he said. 'Dementia is associated with cognitive impairment and multiple diseases such as Alzheimer's.'

While there are about 400 diseases that can cause dementia, a common factor is the gradual shift in behaviour, McEntee explained. In early stages, family members might start to notice subtle changes in the execution of simple tasks like making tea, managing schedules or medication. As dementia advances, communication becomes more difficult. 'Caregivers may be needed for daily tasks such as feeding, dressing and personal hygiene. That can be troubling for family members, as the person with dementia begins to forget people's names,' the expert said. In late stages, full time care is often needed, with many patients having problems eating and swallowing, and become susceptible to infections.

Conflicting concerns for radiographers

As his own mother suffers from dementia, McEntee had to switch perspectives to visit the x-ray department as a patient relative. He wrote down some of the experience in a personal reflection that was published in the Journal of Medical Imaging and Radiation Sciences in 2021. This personal view of dementia tells the story of an x-ray examination and was the basis for a study he carried out with student Caitlin Devereux and radiographers in Ireland. In the study, they asked participants to detail their experience and attitudes towards patients with dementia. The radiographers expressed concern about their practice and worried about patient care and imaging quality, but also about distressing patients. 'They worried about patients' fear and safety, but also about physical violence, consent and justification for the examination,' McEntee said.

Some of those concerns are based on a lack of training, knowledge, and education, he explained. 'Radiographers said they would have liked to have more experience with those types of patients experience and didn't feel empowered to do things differently,' he summarised. 'They didn't know what to expect but were aware that there was a stigma around the symptom. They were nervous that they were going to annoy patients or get them worked up.'

Those fears show common misunderstandings and highlight the necessity to change practice, the expert stressed. 'We need to improve radiographers' practice and knowledge about dementia patients and dementia care. Radiographers must remember that a patient is not an aggressive person, but someone who's confused and scared. We should all involve the carer in the examination and bring them in the examination room. That will make the biggest difference,' he concluded.

In another talk, Nikolaos Stogiannos from City University of London, UK, shared the results of a study that looked at the patient's perspective in autism friendly MRI. 'Autistic individuals may experience communication challenges, heightened anxiety and increased response to sensory stimuli,' Stogiannos said. 'They also face different challenges when accessing healthcare services, such as poor staff awareness, stigma and suboptimal communication. These differences may result in great challenges and a poor patient experience when coming to an MRI environment.' The isolated and noisy MRI unit in combination with long scan times and the need for patient immobilisation often cause significant challenges to autistic individuals, he added.

Two online surveys were conducted in autistic adults and children to explore efficient ways to improve both radiographers' practice and patient experience. The surveys were distributed through the UK National Autistic Society, the London Autism Group, and the researchers' networks on social media. From the 128 valid responses that were received, poor communication was identified as the main obstacle to successful MRI scans.

Non-disclosure of autistic identity was noted in more than half of the respondents, which resulted in MRI departments unable to provide customised examinations.

Patient empowerment

Poor patient experience was mainly attributed to the acoustic noise, lack of physical comfort inside the scanner and lack of integrated aftercare. 'To improve examinations, MRI departments should receive adequate and timely information about a patient's autistic condition and have the capacity to reduce acoustic noise during the examination,' Stogiannos said. 'Radiographers must ensure physical comfort inside the scanner and offer other scan options, for example open-bore scanners.'

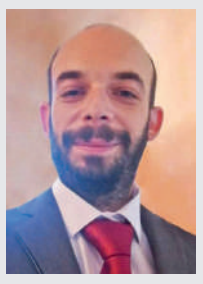
Autistic service users should also be encouraged and empowered to disclose their autistic identity as well as their needs and preferences prior to the examination. 'Customised communication should be employed to achieve autism friendly MRI examinations. Radiographers should always adapt their communication style to their patients' needs,' he concluded.

Other talks in the session featured Dr Francis Zarv from Msida, Malta, who spoke of the effect of music during mammography breast screening; Elin Kjelle from Gjøvik, Norway, who detailed the implementation of a telemedicine and stroke evaluation service; and Anselm Chukwuani from Birmingham, UK, who focused on the imaging service demand of an increasingly ageing population with cancer care needs. ■

Report: Mélisande Rouger

Mark McEntee

Prof Mark McEntee is the Chair of Diagnostic Radiography at University College Cork and the Deputy Editor of the Journal of Medical Imaging and Radiation Sciences (JMIRS). When his mother was diagnosed with dementia in 2010, he realised how little work had been done on caring for patients with dementia during imaging. He has subsequently carried out focus group surveys with patients and radiographers in Australia and Ireland and has written and presented on the subject, with the aim of translating research into practical guidance.



Nikolaos Stogiannos

Nikolaos Stogiannos is Honorary Research Fellow at City University of London. He is also a research assistant at the University College Cork, Ireland, and the Lead MRI Radiographer in the Medical Imaging Department at Corfu General Hospital, Greece.

Energy conservation & waste reduction

Reducing the eco-footprint of radiology

Contrast agents in the wastewater and huge, power-hungry imaging systems: The eco-footprint of healthcare is significant, and radiology departments are often regarded among the main culprits. An expert panel at the ECR explored ways to make the field "greener", with the help of upcoming technologies as well as tools that are available today.

While CT and MRI scanners need a lot of power to operate, the greatest potential to save energy lies elsewhere, said Joachim Hohmann, Professor for Radiology at the University Hospital Basel, Switzerland. For example, radiological reporting systems use a significant portion of their power in an idle state. This is because, by default, many systems only enter stand-by mode after four hours of inactivity, Hohmann reported. 'Reducing this timespan to one hour would have a huge impact, with energy savings of up to 45%,' he said. Introducing more energy-efficient stand-by configurations would reinforce this effect. These observations were based on the "Green Fingerprint" project, in which Hohmann and colleagues measured the energy consumption of 36 reporting stations.

The energy used by these stations in the University Hospital's radiology department would suffice to power 12 family households. 'The most important aspect, however, is to be aware of these systems' power consumption,' Hohmann said, pointing out that for the reduction of energy waste to be effective, active staff participation is required.

Keeping contrast agents from entering the water cycle

Radiology departments also pollute the environment through contrast agents in wastewater, explained Francesco Sardanelli, Professor of Radiology at Milan University, Italy. 'The number of CT and MRI examinations are ever increasing, with millions of scans performed every day all over the world,' he said. In many cases, imaging is enhanced by using iodinated (ICAs) or Gadolinium-based contrast agents (GBCAs) – compounds that are not metabolised, but excreted by the patient and thus end up in the hospital or home wastewater. The ecotoxological effects of these contrast agents remain unclear, but it has been established that the compounds persist for a long time after having served their medical purpose.

To stop this aquatic pollution, Sardanelli offered two complementary approaches: Reducing the injected contrast dose before scans and recovering the agent afterwards. The former strategy seems particularly promising, with newer studies pointing out that dose reduction of up to 90% could be achieved through deep learning techniques. In the upcoming "Greenwater" study, Sardanelli's team explore the potential of post-imaging recovery of contrast media. Since participants have to extend their stay to leave their urine at the hospital after their scan, the study also measures the "green sensitivity" of patients, Sardanelli added.

Environmental impact as a performance metric

One of the main challenges for future "green" radiology departments will be to reduce the carbon footprint without sacrificing quality of patient care, predicted Prof Andrea Rockall, Clinical Chair of Radiology at Imperial College London, UK. 'Currently, we prioritise safety, cost savings and convenience, rather than sustainability,' she stated, pointing out that this balance needs to shift. 'Departments need to start measuring and evaluating their performance against environmental impact,' she argued, similar to today's assessments of diagnostic accuracy or patient turnaround time.

The imaging industry has heard the call for greater sustainability 'loud and clear', confirmed Kees Wesdorp, leader of the Precision Diagnosis business cluster at Philips. If manufacturers and healthcare systems worked together, significant progress could be made, he said, referencing his company's "Closing the loop" program, which aims to establish trade-ins on all professional medical equipment by 2025. In addition to recycling and refurbishment, hospital IT structures should move from maintaining on-site servers in favour of cloud-based solutions, which operate more energy efficient. Additionally, the biggest cloud solution providers have established programs to source the required energy in an eco-friendly way.

Further improvement could be made by establishing energy performance certificates (EPCs) for medical imaging systems, akin to those used for household devices like fridges and washing machines, ventured Prof Lorenzo Derchi, Head of the Department of Radiology at the University of Genoa, Italy. Healthcare in general, and radiology in particular, are governed by a mindset of consumerism, he remarked. 'This is a problem that will erode the resources of the planet.' To reduce this, hospitals should avoid non-indicated imaging wherever possible. This notion was seconded by the panel's co-chair Boris Brkljačić; the Professor of Radiology at the University of Zagreb School of Medicine, Croatia, referenced a recent Luxembourg study that found 39% of CT and 21% of MRI scans to be inappropriate.

The pandemic impact: one step forward, one step back?

The session's Co-chair Prof Adrian Brady pointed out the effects of the coronavirus pandemic on sustainability efforts. Covid-19 proves to be a double-edged sword in this regard, the consultant radiologist at the Mercy University Hospital in Cork, Ireland, found; while corona-related advances in digitisation and virtual meetings have reduced CO_2 emissions from transport, the pandemic also brought greater reliance on single-use equipment, such as face masks and disposable plastic cups. He expressed his hope that in the aftermath of the pandemic, previous sustainability improvements that were temporarily put on hold might be re-established for the benefit of the environment.

The environmental impact of their work is not something many radiologists consider today, Prof Brkljačić concluded. As a result, a lot of energy is wasted needlessly; this is something that ought to change. ■

Report: Wolfgang Behrends

The expert panel discussing "green" radiology solutions (from left): Prof Lorenzo Derchi, Prof Luis Martí-Bonmatí, Prof Boris Brkljačić, Prof Adrian Brady, Prof Andrea Rockall, Prof Joachim Hohmann Prof Francesco Sardanelli; on screen above: Kees Wesdorp

Advances in cancer risk assessment and prevention

French oncologists pick up the pace after pandemic time-out

The pandemic-imposed pause for oncology care is coming to an end: Real-life data and personalised screening techniques are set to improve cancer prevention and patients' quality of life. In a dedicated press conference in Paris, French oncologists presented promising research that might bring hope for many cancer patients.

French cancer centres are catching up after the coronavirus pandemic put oncology interventions on hold in 2020, and the spirit of a fresh start was prevalent at an event organised by Unicancer, a federation regrouping 19 leading institutions specialising in oncology. 'We're getting out of it, after experiencing delays that have been detrimental to patients' recovery,' Unicancer President Jean-Yves Blay, a professor of medical oncology at Claude Bernard University in Lyon, said.

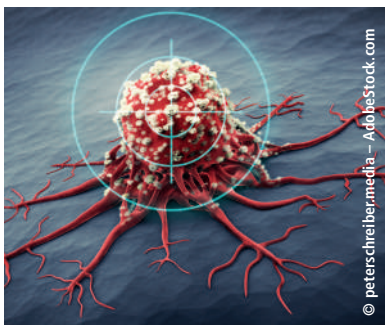
After all, the pandemic left a considerable dent in cancer care: French facilities registered a 7% diagnostic delay for oncology patients in the aftermath of the Covid-19 outbreak in 2020. One year later, Unicancer centres, which treat about 20% of patients with cancer in France, reported a 6% increase in activity. Unicancer presented a series of proposals to better fight cancer, which remains the leading cause of death in France, with nearly 400,000 new cases and more than 157,000 deaths each year. Proposals target healthcare professions' attractiveness and remuneration and offer strategies on how to boost follow-up and prevention. The experts agreed that 40% of cancers could be avoided if current knowledge about risk factors was translated into effective public health strategies. 'We want to develop highly connected research points to improve prevention from risk factor identification to screening,' Blay said. 'Treatment follow-up of cancers in children and rare cancers, which remain difficult to treat, is also one of our priorities.'

With over 100 studies enrolling 8,000 patients in 2021, Unicancer touches on several aspects of research beyond the clinical spectrum, focusing on issues such as patients' quality of life and how to make use of data which is already available.

A few months ago, the organisation launched a pilot project with Health Data Hub, a platform dedicated to facilitating the sharing of health data from a wide variety of sources, to help accelerate research. The program, called UNIBASE, aims to harness data from electronic patient records and create a collection of cancer reference databases within three years. 'Having this huge amount of real-life health data will help us better predict or evaluate treatment,' Blay said.

Personalising screening and patient involvement

Underlining the historical weakness of France's public health culture, the latest report of the French National Audit Office on prevention policies mentioned 'mediocre results', despite significant financial efforts similar to those of European neighbours. For example, screening remains problematic in France. National programmes are organised for breast cancer, colorectal cancer and cervical cancer, but participation remains insufficient. To improve screening efforts, researchers are looking to more personalised approaches, for example in breast cancer screening programmes. To this end, Unicancer is taking part in MyPeBS, an EU-funded randomised controlled trial that aims to assess the value of personalised breast cancer screening for women aged 40 to 70 in Europe. The study plans to determine whether risk-based cancer screening in these women is non-inferior to the standard screening programme currently offered in Belgium, France, Israel, Italy, and the United Kingdom. The project will follow 85,000 women over four years and could mean a great advance, Blay explained. 'This study is a revolution in screening management. If completed, it will transform the routine,' he said.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Patient empowerment is another promise of personalised cancer medicine. The aim is to involve the patient in clinical decision-making, another speaker highlighted in the conference. 'We're witnessing a cultural change and a reconstruction of clinical decision-making,' Ariane Weinman, a representative at EURORDIS, a non-governmental alliance of rare disease patient organisations, said. 'Patients and their families are increasingly involved and informed, sometimes even receive dedicated training to prepare for the experience.'

Patient organisations also increasingly take part in clinical trials, which benefits everyone, according to Weinman. 'The more involved the patients are, the better they will be able to follow their treatment and support research near the authorities,' she concluded. ■

Report: Mélisande Rouger

Artificial intelligence and Deep learning to drive precision medicine

Diving into medical big data

Big data is transforming diagnosis and medical care, but the critical challenge remains over how to equally apply the benefits it delivers across real-world clinical settings. Industry expert Benoît Macq recognises that high quality data can be harvested from major university hospitals and academic centres but is convinced that the true value will emerge when it is accessible in a relevant way to clinicians and patients in smaller hospitals too.

Prof Macq, who leads the PiLAB research team from the Institute of Information and Communication Technologies, Electronics and Applied Mathematics (ICTEAM) at the Université Catholique de Louvain in Belgium, explained that large-scale data sets can create predictors for diagnosis, treatment planning, and drug use, by harnessing Artificial Intelligence (AI) and Deep Learning (DL) technologies to acquire and analyse data to realise these goals. However, what is key is that there is no centralised point of the data, but a system of "federated learning" where the DL model accesses a range of data silos in different hospitals. This brings data together to create a distributed big data set, but with each institution retaining control of its data from a regulatory, cybersecurity and patient privacy perspective.


An example of a prototype of Cone Beam CT that Prof Macqs team jointly developed with the IBA company for image-guided proton therapy. In the photograph is (from left): Eric de Lamotte (IBA), Benoît Macq, Merence Sibomana (PiLAB) and Rudi Labarbe (IBA).

From this concept of federated learning, which groups organisations together, the drive is to move to the next step of coalitional learning between different institutions 'to feed the new predictors, the new diagnosis and the new biomarkers'. With a challenge lying in the varying data quality, annotation, clinical decision making and diagnosis, the move from federated learning to coalitional learning will help provide cross control of data quality, he said. That will remove the variability in data and 'align human judgement across a coalition' in sharing data, procedural approaches, and joint strategy on the use of the data.

A shift to coalitional learning increases the quality of the data, ensures validated expertise, and increases accuracy, said Professor Macq, who already applied this together with his team in areas such as proton therapy treatment planning and early detection of breast cancer. As an engineer, rather than a clinician, he emphasised the importance of 'diving into the data' from different places and making sense of it and being relevant to the patient. 'We want to have a convergence with a coalitional learning system where the data acquisition and the predictive model is increasing thanks to the contribution of the different institutions,' said Macq. He further underlined the importance of different types and sizes of institutions working together, as well as engineers collaborating with clinicians and data scientists, in constructing a DL model that is applicable and relevant to all clinical institutions and their patients.

Precision medicine

The benefit is to create precision medicine to deliver better diagnosis and patient care, but also facilitate improved natural medicine. 'The idea is to better understand diseases by trying to find causal relationships between DNA, RNA proteins and metabolics, and between different levels in the biology continuum to augment medicine,' he said.

He believes precision medicine will lower the costs as screening will be more efficient and treatment more precise and personalised. 'Accessibility is our goal,' he said, 'and to increase the quality of treatment because it will be more personalised and delivered earlier with better diagnosis and better screening.' This, he hopes, will create a new democracy to the use of the data so patients – whether at a university hospital or local hospital – will benefit equally. ■

Report: Mark Nicholls


Benoît Macq

Professor Benoît Macq leads PiLAB, a research team from the Institute of Information and Communication Technologies, Electronics and Applied Mathematics (ICTEAM) at the Université Catholique de Louvain in Belgium, where around 30 researchers focus on three main research topics of: Signal & Pixels, Medical Imaging, and Interaction. The co-founder of 11 spin-off companies, he is a Fellow Member of the IEEE (The Institute of Electrical and Electronics Engineers) and a Member of the Royal Academy of Science of Belgium.

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Preanalytical challenges and their clinical impact in POCT

The European Society for Emergency Medicine (EUSEM) held their annual congress on October 27th to 31st, 2021 in the Portuguese city of Lisbon, to promote education, training and research in European acute care. The event's hybrid format allowed for more than 2000 in-person and virtual delegates from over 70 countries.

On October 30th, BD Life Sciences, Integrated Diagnostic Solutions (IDS), hosted a lunch-time educational workshop entitled, 'The impact of non-reported point-of-care testing (POCT) errors on patient care and hospital resources.'

The event was moderated by Anthony Malpass, Clinical Project Manager, BD IDS and presented by a team of expert guest speakers:

Kevin Rooney

Antonio Buño Soto

Ulf Martin Schilling

- **Professor Kevin Rooney**, Consultant Anaesthetist and Intensivist, United Kingdom
- **Dr Antonio Buño Soto**, Point of Care Director and Head of Laboratory Medicine, Spain
- **Dr Ulf Martin Schilling**, Consultant in Emergency and Internal Medicine, Sweden

Throughout the presentation, attendees were interactively polled for their clinical opinions on a number of patient case studies to demonstrate the impact of POCT errors and their clinical consequences, even among experienced professionals.

POCT and the imperative of test quality

Professor Kevin Rooney explained that in a busy emergency department (ED), 'POCT can reduce turnaround time 'from vein to brain' by bringing diagnostic testing to the patient's bedside'.

The ideal POCT kit meets the standards established by the Institute of Medicine's Six Domains of Health Care Quality: it is safe, efficient, and effective to use, and generates timely results which assist in providing equitable and person-centred care.

So, POCT in the ED has the potential to decrease delays to treatment, increase ED efficiency, positively influence patient care and negate the effects of overcrowding. The key word in that statement is 'potential.' For to meet this potential, the testing has to be of high quality. And therein lies the problem – the reliability of POCT results.

Clearly if the sample is compromised, so too is the result. In a Stat laboratory setting, up to 61.9% of errors occur at the preanalytical phase due to the manual nature of sample collection. Similarly, POCT is susceptible to preanalytical error from poor sample quality and improper handling.

Anyone, even an experienced clinician working in a busy ED, may miss a potentially erroneous POCT result, one that causes the development of a faulty clinical management plan. To prove the point, the audience was polled on the real-life clinical cases outlined below.

Case Study:
30 weeks pregnant: emergency caesarean section or not?

Rooney asked: 'Would an incorrect POCT haemoglobin (Hb) force you down an incorrect management plan?' A pregnant patient presented to the ED with 72-hour back pain radiating to the front, along with dizziness, shortness of breath, malaise and reduced foetal movement. She experienced increased urinary frequency from 20 weeks gestation. She also has a childhood history of vesico-ureteric reflux.

On examination, the patient looked unwell: diaphoretic, anxious and writhing around the bed.

- Glasgow Coma Scale (GCS) 14 with Verbal 4 (confused)
- Temperature 37.5°C
- Heart rate 138 BPM, blood pressure 82/63, capillary refill time 3 seconds
- Respiratory rate 30, oxygen saturation 92% on air, reduced air entry at bases
- Bloody show on her sanitary towel

A POCT arterial blood gas analysis showed a partially compensated metabolic acidosis, with a carbon dioxide partial pressure of 3kPA, a lactate of 2.6 mmol/l and an Hb of 80 g/l.

Was the patient experiencing a concealed antepartum haemorrhage, requiring emergency caesarean section? 33% of the audience thought so.

One hour later, the patient's formal laboratory results arrived: white blood count 2.3 x109/l, Hb 106g/l, Haematocrit 0.3 l/l, C-reactive protein 100 mg/l. A diagnosis of urosepsis/pyelonephritis was confirmed. Would the low Hb results guide you down an erroneous patient management plan? They did for one third of the audience.

Urea and Electrolytes (U and E) and hidden haemolysis

To further illustrate the impact of preanalytical errors, Dr Ulf Martin Schilling outlined the cases of three young women, each who presented with very similar complaints: severe abdominal pain and general malaise over the previous 24 hours, with vomiting, diarrhoea, nausea and vertigo. Their clinical observations were also similar and generally unconcerning.

Then the Urea and Electrolyte results arrived:
How can it be that while the women presented similarly, according to the blood results, one had a simple gastroenteritis while the other was undergoing a potentially life-threatening Addisonian crisis?
Haemolysed samples can give an abnormally high K+ level or mask a true hypokalaemia. In central laboratory processes, haemolysis is flagged for a visual inspection of the centrifuged sample and subsequent analysis of the Haemolysis Index. However, with POCT these tools are not available, meaning haemolysed samples are not identified.

Result	Case Study 2	Case Study 3	Case Study 4
Potassium (K^+) mmol/l	3.2	4.2	5.2
Sodium (Na^+) mmol/l	128	135	122
Creatinine mmol/l	65	95	110
Chloride (Cl^-) mmol/l	90	98	90
Clinical interpretation	Spurious result	Hyperchloraemic hypokalaemic alkalosis + pseudohyperkalaemia	Addisonian crisis

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The hidden cost of preanalytical errors

Following the case presentations, Dr Antonio Buño Soto presented the causes and costs of these preanalytical errors. He demonstrated that most errors in laboratory medicine occur in the preanalytical stage during patient preparation, blood collection and sample handling/transport.

He noted that the impact of erroneous results can reach from patient management and safety to even the institute economy.

But what about the impact of POCT preanalytical errors within the ED? According to Schilling, 'Emergency departments have quite a high level of pre-analytical error'. As illustrated by the clinical cases, POCT errors in the ED can produce misleading readouts, with similar implications for patient care and resource use.

What is the solution? Schilling advised the audience to 'be sure that whatever is done, is of high quality'. The aim is to produce POCT results that are equivalent to those generated by a central laboratory. But what does this mean in practice? A multidisciplinary approach involving laboratory professionals is the best way to mitigate POCT errors and to improve patient care. The central laboratory should lead and control every aspect of POCT: from the outpatient clinic to the hospital ward, from the intensive care unit to the physician's office.

Multidisciplinary involvement is supported by professional healthcare organisations. ISO22870:2016, which is intended to be used in conjunction with ISO15189, gives specific requirements applicable to point-of-care testing, such as the creation of a POCT network and committee, whose members include representation from the central laboratory and who oversee all aspects of POCT management.

When interpreting POCT results, stop and think

POCT is vulnerable to similar preanalytical errors as central laboratory testing but lacks the mitigating technology inherent to those systems. Even if the POCT is impeccably managed and operated, clinical discretion is required when actioning results. As Malpass said, 'An analyser even if well maintained, well quality checked, well controlled and well managed, is still capable of giving you a wrong result. It is based on the sample put into it. If the sample is no longer representative of the patient, you are making judgements which could have significant consequences.'

Every caregiver's primary aim is to provide the best possible care to all patients. Every clinical sample represents a human life, a person whose wellbeing relies on the accuracy of that sample. A good clinical decision is only supported by sound clinical results, and sound results can only come from a quality sample. If we depend on POCT to inform our clinical management, we must ensure that the sample remains representative of the patient's true clinical picture.

Though complex and multi-faceted, mitigating preanalytical errors in POCT can be supported by the integration of a dedicated, diverse POCT team that gives the ED central laboratory support. Training, device maintenance and safety measures can then be rolled out, with evidence-based practice at the forefront.

However, even if the ED has an exemplar POCT system in place, Rooney cautioned the audience: 'If you get a POCT result think, is that blood result consistent with the patient?' ■

For references, please contact BD Life Sciences.

Mass spectrometry and chromatography techniques

Predicting Covid-19 infection severity

Using mass spectrometry and chromatography techniques, UK researchers have developed an approach to predict infection severity among Covid-19 patients, as well as potential outcomes.

Diagnosis of Covid-19 is normally based on the qualitative detection of viral nucleic acid sequences. Although metabolic profiles are well suited to capture host state, many of the early metabolomics studies suffered from methodical weaknesses, stated doctoral researcher Ivayla Roberts from the Institute of Systems, Molecular and Integrative Biology in the Centre for Metabolomics Research at the University of Liverpool.

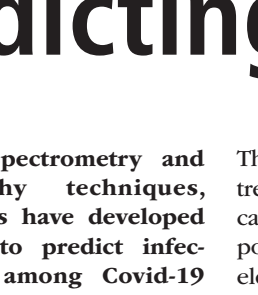
She said that many of the early metabolomics studies were either underpowered, measured only a restricted subset of metabolites, compared infected individuals against uninfected control cohorts that are not suitably matched, or did not provide a compact predictive model. Roberts outlined how the study team had created a well-powered study focused on 'untargeted metabolomics of Covid-19 patient serum' and validated their findings in a separate blind study on an additional 90 patients.
High resolution untargeted LC-MS (liquid chromatography-mass spectrometry) analysis was performed on patient serum using both positive and negative ionisation modes. A subset of 20 intermediary metabolites predictive of severity and outcome were selected based on univariate statistical significance and a multiple predictor Bayesian logistic regression model.

The predictors were selected for their relevant biological function and include deoxycytidine and ureidopropionate (indirectly reflecting viral load), kynurenine (reflecting host inflammatory response), and multiple short chain acylcarnitines (energy metabolism) among others.

The study was launched in 2020 in the earlier stages of the coronavirus pandemic. Roberts said: 'Our aim was to explore how metabolomic profiles can predict disease severity and outcome in infection. The demographic reflects known trends in Covid-19 infection with cases predominant in males and poor outcomes more likely in the elderly.' Delegates heard that 74% of patients involved in the trial were eventually discharged. The expert explained that the trial started with 9,000 compounds and looked at ways of reducing the number of predictors, initially down to 900, and then down to 20 compounds, with a known biological function.

Inflammatory process

Roberts reported that some of these markers were found to be predictive of the inflammatory process in patients. She said pyrimidine metabolism changes in severe cases and poor outcome was likely to be an indicator of higher viral replication activity, while fatty acid beta oxidation indicates energy metabolism differences and are in higher levels in more severe cases of Covid-19 in patients and those with poor outcome. Another finding of the study was that the tryptophan/kynurenine degradation was a sign of host immune response. With untargeted metabolomics of Covid-19 patient serum revealing potential prognostic markers of both severity and outcome, the researchers believe that following the findings of the study that prognostic tests based on the markers could help lead to improvement in the planning of Covid-19 patient treatment. (MN)



Ivayla Roberts

Ivayla Roberts is doctoral researcher at the Institute of Systems, Molecular and Integrative Biology in the Centre for Metabolomics Research at the University of Liverpool. Originally with a computer science background, she transitioned to molecular biology research. Her research interests are metabolomics, mass spectrometry and the application of statistical and machine learning computational approaches to metabolomics. Her PhD is focused on metabolomics in Covid-19.

Diagnostic test regulation

IVDR: Stop complaining, start contributing

The in vitro diagnostic regulation (IVDR) aims to make IVD products safer, more reliable, and sustainable. Unfortunately, it is also widely regarded a bureaucratic nightmare which will render many tried-and-true lab tests obsolete, slow down diagnostics and generate horrendous additional costs. At the ECCMID day on diagnostics, experts discussed the possible impact of the new IVDR on commercially available and in-house testing and why laboratories would do better to leave mere defiance behind.

With large portions of the IVDR coming into effect in May 2022, the time for complaining about the new regulation is over, said Professor Elizabeth Macintyre, and instead appealed for a more constructive approach.

After all, the idea behind the new IVDR is sound, the expert attested: 'The basic principle is that we do maximum patient benefit for the money spent.' But while in principle, the bureaucrats devising the new rules act in the interest of the taxpayers and patients, they do not know about how laboratories work, she cautioned. 'We have to be at the table when the implementing acts are happening. The devil is in the details, so we have to be involved.'

Speaking as a board member of the Biomedical Alliance in Europe, Prof Macintyre advocated the role of the organisation, which represents 36 medical societies, in this process. 'It is very difficult for the European Commission to reach out to all medical specialties since there are so many. So, one of the main interests of the Biomed Alliance is to speak as a common voice for our members.' This gives the laboratories a chance to contribute to shape new legislation, rather than silently suffer its consequences.

Six years to work out LDT implementation

The impact of the new IVDR on everyday laboratory practice will likely be significant, the expert pointed out. 'A main difference between the previous directive on IVD and the new IVDR is that the former was open to member state interpretation – and the latter is not: It is to be applied as it is, to improve harmonisation and standardisation.' Unlike its predecessor, the IVDR now also covers diagnostic tests developed in-house (laboratory-developed tests; LDTs). 'This was born of good intention, to make sure that the tests are of optimal benefit to patients.'

This was a matter of concern, as in-house tests tend to be more complex than commercially available solutions. A recent survey from the Biomed Alliance to assess IVDR readiness among its members revealed that LDTs make up roughly 26% of tests used in laboratories, with some fields relying on in-house solutions for more than half of their diagnostics. Due to its high requirements for documentation, many critics see the new IVDR as a death knell for LDTs. However, there is a reprieve: Until May 2028, in-house tests may still be used under the condition that there is no equivalent solution on the market, or that the LDT is proven to be superior to the commercial alternative.

While this is a much-debated issue, Prof Macintyre believes that, if the remaining six years are put to good use, viable solutions will be found, with the key element being continued constructive communication. 'The IVDR is there to dictate what we have to do, but it is up to us as diagnostic specialists to define and accompany how we do it.'

Who will go the extra mile for better tests?

Judging from the results of the IVDR survey, the Biomedical Alliance so far mainly seems to be preaching to the converted: countries with well-established pan-diagnostic federative structures, such as Belgium or the Netherlands, were overrepresented, while other countries, which are more likely to run into problems with IVDR implementation, tended to respond less often, the expert noted. 'My take-home message is that we need pan-diagnostic interaction between our societies, from pathologists and geneticists to laboratory medicine, if we want to face up to these regulations in an appropriate fashion.' She cautioned that countries which lack such umbrella bodies will have a hard time preparing their laboratories for the new requirements, and thus be more susceptible for diagnostics companies peddling their IVDR-compliant solutions, instead of developing tests on their own.

Prof Macintyre made it clear that the new regulation will make a temporary, but significant dent in diagnostic test availability: 'There is no grandfather clause, so current tests will not automatically be accepted.' In other words, everything has to be retested – a tall order for the notified bodies in charge, with an estimated 30.000 to 40.000 tests to be approved. As a result, the diagnostic sector should prepare for vital tests simply disappearing, with no option of running in-house tests as a workaround.

In the subsequent Q&A session, the expert voiced her concern of the increased regulatory requirements stifling motivation to create new or improved LDTs across the fields: 'I'm worried that many people just won't bother anymore.' She predicted that, as soon as one diagnostic test is on the market, most experts would be content with the status quo, as finding ways to improve the test would simply be too much hassle. While the development would roughly take the same amount of work, the paperwork is another story, Prof Macintyre cautioned: 'Bear in mind that you have to document every step, and clearly show to the health authority and national competence authority that everything is done according to good medical practice.'

'Working towards IVDR compliance will be a major effort in terms of time and budget,' the expert summarised. 'The cost of diagnostics is going to increase – we don't know yet whether this will be offset by other benefits.' To be prepared for the new IVDR, member societies of the Biomed Alliance declared a general need for guidance – information, templates and workshops on existing and upcoming standards, availability of commercial diagnostic tests, and the sufficiency of both IVDR and ISO 15189 accreditation. Additionally, many felt that requirements for in-house tests should be more flexible. To meet the demand for IVDR-related guidance, the expert appealed to the diagnostic specialties to establish overarching communication structures to provide and share information. While these structures should work on both national and European levels, possible synergies should be explored while redundancies should be avoided. ■

Report: Wolfgang Behrends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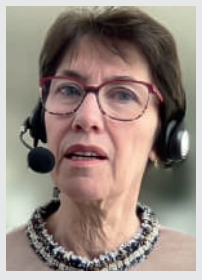
Elizabeth Macintyre

Professor Elizabeth Macintyre, MD PhD FRCP FRCPath, is a diagnostic haematologist at the Necker-Enfants Malades Hospital in Paris, France, and President of the European Hematology Association (EHA). She is also board member of the Biomedical Alliance in Europe, an initiative of 36 European medical societies, and chairs the organisation's IVDR task force.

Sponsored • Safety blood collection set

The gentle touch: Vacuette Evoprotect

Evoprotect is the next stage in blood collection. The semi-automatic click mechanism protects the user from the risk of needlestick injuries and makes the daily task of blood collection easier.

Vacuette Evoprotect provides for gentle collection and safety from injury because we believe that every needlestick is one too many. The safety blood collection set meets current safety recommendations and requirements and provides substantial support for safe blood collection and infusion with the same set.

User-friendly with optimised design

The Vacuette Evoprotect is ergonomically designed and intuitive to use. It has a winged needle, specially developed for one-handed use. The potential for needlestick injuries is minimized by the activation of the safety mechanism while the needle is still in the vein. The Vacuette Evoprotect is suitable for a blood collection and a following infusion with the same set.

The Vacuette Evoprotect Safety Blood Collection Set has a semi-automatic safety mechanism. The triggers are located on the side of the product, facilitating one-handed activation. The needle is then automatically retracted and, at the same time, safely and irreversibly enclosed in the safety shield. A clearly audible click confirms that the safety mechanism is successfully activated. The safety mechanism is activated while still in the patient's vein, offering the user an even higher level of safety. The design of the safety mechanism promotes a straight removal of the needle from the vein, therefore offering more patient comfort.


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Designed with patient comfort in mind

The ultra sharp, triple bevel needle tip ensures optimal patient comfort. A view window between the needle and the tubing gives an immediate visual indication that vein entry was successful. The tubing is designed to ensure that the needle stays as still as possible in the vein. The location of the safety mechanism triggers on the side of the device minimises the risk of the needle moving in the patient's vein during activation.

The same device can be used for taking blood and for a subsequent infusion immediately following afterwards. Using the same set for blood collection and infusion means a second puncture is not needed.

More information: www.gbo.com or www.power4safety.com. ■

Patient-based real-time approach

PBRTQC: improving quality control in the lab

Implementing patient-based real-time quality control (PBRTQC) protocols within the laboratory testing setting can offer benefits in terms of patient safety and reducing risks. While the concept has been around since the 1960s as a quality control (QC) strategy, it is still not being widely used as a frontline process, according to one of the leading experts in the field, Professor Tony Badrick. He outlined the latest developments in PBRTQC at a symposium at the EuroMedLab congress in Munich in April, examining advances in internal quality control (IQC) tools and techniques in the laboratory.

Introducing the concept and developments in the field, he said there are a number of reasons for using patient results for quality control. While IQC has evolved over time to become an essential part of laboratory process control, PBRTQC models have more recently been investigated as alternatives in the lab. 'Sometimes other results are unavailable or impractical, or patient results might detect an issue that other forms of quality control cannot,' said Prof Badrick, who is the CEO of the Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP).

In addition, the state of the testing processes can be assessed between the times of routine control-based QC. The expert explained that QC is a retrospective process and there is little cost, and the sample is commutable.

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Understanding patient population characteristics

Prof Badrick offered some general considerations for implementing patient-based quality control. For example, it can bring insights into the biological and analytical characteristics of certain tests, such as reference intervals, pathological values, and biological and analytical variation. PBRTQC also helps to understand the patient population characteristics served by the laboratory and the capability of the laboratory information system, such as which data can be extracted and analysed. He said: 'Currently, most laboratories' QC systems perform a QC sample run once a shift or once a day. There may be hundreds of patient samples between these QC samples, so if there is a problem, a lot of samples must be rerun, and results retracted.'

The expert explained how PBRTQC implementation has become more manageable due to recent technological advances. 'Now we have the IT capabilities and the patient numbers to make it viable,' he said. 'The challenges are getting the software to make it work in real-time. This needs to be in middleware or on the analysers.'

The development of better techniques and middleware to allow the practical application of PBRTQC has subsequently led to a rethinking of conventional QC, and the relationship between internal and external quality assessment (EQA), as a process designed to independently assess the performance of methods across laboratories and platforms. With manufacturers now working to adapt software solutions accordingly, the symposium considered the prospects with PBRTQC and how it could be used in conjunction with IQC, or instead of it.

Increased error detection, decreased patient risk

Organisations such as the International Federation of Clinical Chemistry (IFCC) are working to raise the profile of the potential of PBRTQC. The IFCC has produced a series of papers focusing on this area, describing all the steps that are needed to develop, implement, and validate PBRTQC, Prof Badrick added. He said: 'Labs and manufacturers are being made aware that PBRTQC is now a possibility, and there is an interest from these parties into what is needed to progress this.' Looking ahead, the expert said: 'I believe PBRTQC will become the main form of quality control integrated with some conventional QC on most high-volume clinical chemistry analysers.' Envisioning clear benefits for clinicians, hospitals and health systems, as well as patients, he continued: 'PBRTQC provides better QC and hence less likelihood of errors not being detected. This should reduce the risk for patients. In addition, there would be reduced cost for labs with QC, leading to better comparability between labs.' The Munich symposium also included presentations on how conventional QC is practised and how can it be improved; the importance of demonstrating the commutability of reference materials with IQC; and implementing PBRTQC into routine practice. ■

Report: Mark Nicholls

Tony Badrick

Professor Tony Badrick has been the CEO of the RCPAQAP (Royal College of Pathologists of Australasia Quality Assurance Programs) since 2015. Before that he was Associate Professor, Faculty of Health Sciences and Medicine, at Bond University, Gold Coast, Australia. He is currently the Chief Examiner of the Faculty of Science of the Royal College of Pathologists of Australasia and has published over 180 papers in the field.

Sponsored • Chromatogram analysis

Peak detection: AI raises reliability

Chromatograms from mass spectrometry (MS) feature characteristic peaks to signify the response of a target molecule. Artificial intelligence (AI) can help in the challenging task of identifying these peaks. We spoke with Atsuhiko Toyama, International Product Manager (LCMS) at Shimadzu, about the company's Peakintelligence software and its benefits for result interpretation and variations in parameters.

A peak's height and area hold information on the presence and amount of a compound, but as Toyama explained: 'If we do not see a peak, or recognise a peak, then we have no data. This is why peak detection is so important.' However, interpretation is also a matter of weighting the parameters: 'Area is more reproduceable because we are recording at certain intervals and is more representative of the abundance than the height,' the expert added.

More accessibility, less variability

Current computational analysis models rely on slope detection to recognise peaks. However, variability in settings carries over to variability in results, which can make it difficult to interpret them, especially for non-MS expert personnel, Toyama said: 'Someone who has only little experience in evaluating MS data might find it difficult to estimate the impact of a given parameter and can therefore not judge whether the detected peak is adequate.'

Several different algorithms for detecting peaks exist, but each comes with its own drawbacks, Toyama continued: 'For example, an approach which sets a threshold for peak detection will yield different results depending on which value is chosen as the threshold.' To offer a more consistent approach and solution, Shimadzu has developed its Peakintelligence Version 2 software for liquid chromatography with tandem mass spectrometry (LC-MS/MS). Equipped with algorithms developed using AI, it quickly, reliably, and automatically detects peaks appearing in chromatograms. The detection is performed without adjusting parameters, which substantially reduces the need to visually confirm and correct data. The Peakintelligence solution is trained to recognise peaks, parameter free. 'It is one single algorithm that detects all sorts of peaks in all contexts,' Toyama explained. 'This eliminates a big issue – the trade-off between detection sensitivity and precision. Before, parameters had to be adjusted depending on the target compound – blood, saliva, or other fluids require different parameters to avoid mismatch between the baseline value and the threshold.'

The AI used for Shimadzu's parameter-free algorithm was trained on 70,000 pieces of data from chromatograms, allowing it to automatically define baseline and threshold values for every application. 'The training data has been reviewed and processed manually for ideal peak detection by a MS expert,' said Toyama. 'On this foundation, the algorithm delivers adequate peak detection even with difficult samples.'

The Peakintelligence software aims to narrow down the variability of traditional, parameter-based algorithms. 'Because this AI technology is parameter-free, it helps standardise the process to get the same result every time,' the expert said – in short: without the need for parameter adjustment, peak detection also works at a reliable and constant level.

A huge time-saver

Version 2 of the software has been developed in collaboration with Fujitsu Limited, and is five times faster than in its previous iteration, Toyama reported. This means it can process approximately 600 chromatograms in 15 seconds – a task that previously required 75 seconds. In automatic peak detection and visual correction, Peakintelligence completes the process in 10 minutes, roughly a third of the timespan necessary for other software.

The Shimadzu software achieves about 98% concordance with data analysis by experienced users, but delivers results much quicker, accelerating workflows at research sites. This in turn allows technicians to be reallocated from labour-intensive roles to more creative tasks, increasing overall productivity. While there is still a manual verification for the remaining 2% of the results, the final review can be performed by the system administrator alone, Toyama added. 'The AI software is not going to take over the complete process, but it is going to standardise and liberate a large proportion of the workload.'

Peakintelligence

Image source: Shimadzu

Users can give AI "specialist training"

The aim of Shimadzu's AI package is to streamline the data processing in a flexible way to accommodate a wide range of settings. 'The next big challenge is giving users the tools to further train the AI for themselves,' Toyama said. 'We trust that the existing fixed algorithm is precise enough for general purpose. However, to be equipped for more specific applications, users may further customise the AI's training – this is our next development target.'

Current applications of the software are within the food safety sector, with Shimadzu aiming for greater range within a clinical laboratory and medical environment in Europe. To promote the solution in this setting, Shimadzu includes a one-year demo licence of Peakintelligence in every MS installation. The company is confident that this way, organisations can be convinced of the product's benefits and assess potential return on investment in the technology. ■

Technology advances

The importance of social sharing

During the first Chemnitz' Robotic-Symposium, two experts reported on the current state and the future of robot-assisted surgery and highlighted why it is a good time to be involved in this field of technology.

Once thought of as technique viable only in a far-off future, the use of robotics in surgery now is part of everyday life. The current systems are 'essentially master-and-slave-devices', said Henry Tilney, MBBS, MD, FRCS, Consultant Colorectal and Robotic Surgeon, UK-Frimley Health NHS Foundation Trust. These machines are not autonomous, they are under the control of the surgeon in the operating room at all times.

Robotic surgery can be used for many types of procedures, including cancer operations, colon surgery and prostate, gynaecologic and cardiothoracic cases. Despite the rising number of procedures and systems, there are several dissenting voices. 'The criticism we sometimes get labeled with is that we are big boys with big toys,' Tilney says.


© CMR

Yet there are real benefits to using robotics for patients. He pointed out that two known limitations of conventional laparoscopic surgery were the degrees of freedom and the mobility of instruments. The expert pointed out that robotics have a greater degree of movement within the abdomen and thus allowed the surgeons to essentially place mini versions of their hands in the abdominal cavity. That way, they would be able to manipulate and make small-scale movements with greater precision. 'We get greater confidence in the dissection we carry out and preserve the critical structures we're trying not to damage,' Tilney said. Additional benefits are that minimally invasive robotic interventions lessen the potential complications of larger wounds and shorten the patients' convalescent periods.

The state of robot-assisted surgery

The major player in the market of robotics is Intuitive Surgical. Founded in 1995, the company introduced its first da Vinci system in 1999. Since then, the platform has gone through several refinements to become the benchmark that other systems are measured by. 'The "Ferrari of robotics" is the Intuitive 4th Generation Xi,' said Joel Dunning, MD, MB.BCH, Ph.D., FRCS, Consultant Thoracic Surgeon, Department of Cardiothoracic Surgery, James Cook University Hospital. He added: 'Intuitive is really thinking about the best way to the actual mechanics of the robotic system itself.'

Another central player is CMR Surgical, which was established in 2014. Because they had some experience with robotics, Tilney's team got involved with CMR in the early days of the company to help validate their Versius system. 'We have always believed that the systems we have now are not the systems that we will use in the future,' Tilney said and added: 'We wanted to be involved in the development of other systems to be part of what we termed "the democratisation of robotics".'

One major difference in the systems is Versius' open console, which allows better interaction between the scrub team and the surgeon. The da Vinci system, however, allows for a more immersive experience when surgeons put their heads into the box console. Yet, for Tilney, the difference is a matter of personal preferences. 'We have two operating theatres with the Versius and da Vinci next to each other, and we can move comfortably between the two.'

Besides da Vinci and Versius, several other systems are coming to market, e.g., Johnson & Johnson who, in 2019, acquired the remaining stake in Verb Surgical Inc. from Verily Life Sciences, a unit of Google parent Alphabet Inc. The companies had collaborated on surgical robotics since 2015. In 2020, Johnson & Johnson unveiled their Ottava platform, which features six arms to provide more control and flexibility in surgery, while its arms are integrated into the operating table. The company plans to start first in-human studies in 2022.

The "new kid on the block" is Hugo by Medtronic. In 2021, the system was used in its first-ever patient procedure: a minimally invasive prostatectomy performed in Santiago, Chile. Each part of Hugo's system is housed on a separate rolling cart and the surgeon can control up to four independent robotic arms during the procedure from one console.
'I think more competition and more systems are only a good thing for robotics. It's an area that is exciting to be in at the moment because it is developing so rapidly,' Tilney said. 'Get away from the notion that the exciting thing about robotics is which system you are going to use – because they all are going to be good,' Dunning said. For him, the future lies in sharing and scoring surgeons' videos. He pointed out that all players are working on solutions that imbed the capacity to capture videos during surgeries.

One such surgical data management and learning platform already exists. Run by Johnson & Johnson, CSATS allows surgeons to track their performance, and refine their skills based on AI-driven clinical insights and analytics as well as assessment from board-certified surgical experts.

'If we have an ecosystem in which we can share our robotic surgery videos, we are going to see it. We are going to learn and want to do it in that fashion. And that will become a vast advance in any randomised studies," Dunning said.

'Let's innovate in robotics as well as in non-robotic surgery to decide what the best operation is. But the way we are going to innovate is by sharing our videos, by remote telementoring, and by patching into each other's theatre,' Dunning said. 'This is what's going to keep patients safe because we will be able to assess each other. This is why robotics is better than non-robotics, because of the ecosystem that is being built,' he concluded. ■

Report: Sascha Keutel

Sponsored • CMR Versius

Next-generation robotics

Recovering from the pandemic impact, hospitals face increasing pressures and must find ways to optimise cost efficiencies whilst improving treatment quality. To achieve this, many institutions are embracing technology which helps reduce the cost of healthcare and improve quality of care.

Approximately 16 million surgical interventions are performed in German hospitals every year. Minimal access surgery (MAS) has revolutionised surgery, bringing many benefits, including reductions in post-operative pain, complications and scarring, as well as a shorter length of inpatient stay and faster return to normal activities. However, despite the proven advantages, only around half of the suitable procedures are performed using MAS techniques.

Surgical robots enable surgeons to perform more minimal access surgeries, allowing more patients to benefit from this type of treatment. The robots provide a practical way for surgeons to perform more complex and strenuous surgeries.

CMR Surgical (CMR) is a global medical devices company dedicated to transforming surgery with Versius, a next-generation surgical robot. Versius was designed to give more power to surgeons, to make the benefits of minimal access surgery available to more patients.

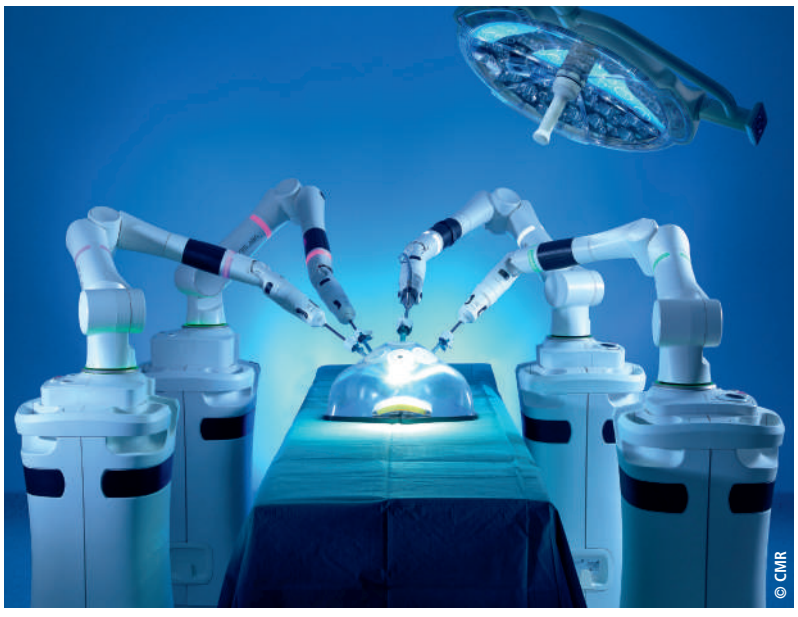
Every day, surgeons set out to achieve the best outcomes for their patients. Versius has been specifically designed with surgeons in busy operating rooms in mind to help meet high clinical standards in surgery, while also offering essential versatility that hospitals running busy ORs need.

More power to perform complex procedures: Versius enhances the surgeons' accuracy and dexterity with its fully-wristed instruments, direct hand-to-instrument mapping and 3D vision. This gives surgeons the power to perform more complex procedural steps and entire procedures in a minimally-invasive way — whether fully robotic or using a combination of manual and robotic techniques.

More power to operate with comfort: Research has found that the leading causes of surgeon discomfort during MAS are awkward positions or movements, and prolonged periods of standing. Versius has an open console which allows surgeons to sit or stand in an ergonomically beneficial position during surgery. This allows them to adapt their working environment to their ergonomic needs and helps to reduce the physical impact of surgery – with the potential to prevent early retirement of surgeons due to MAS-induced back, neck or shoulder pain.

More power over port placement: Versius has a modular design that gives surgeons freedom of port placement to best suit the needs of their patient; enabling them to think laparoscopically, and act robotically.

More power to maximise utilisation: With a footprint of just 38cm x 38cm per bedside unit, Versius can fit into virtually any operating room and can be set up in a matter of minutes. This gives hospitals the power to move Versius to where it needs to be, whenever it needs to be there.


© CMR

What's more, Versius provides a digital interface between the surgeon and patient, opening up a wealth of insights to help surgeons and hospitals deliver the best surgical care and improve hospital efficiency.

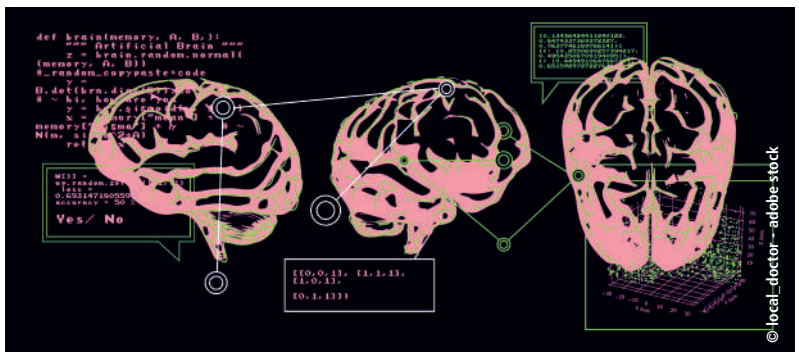
Versius is now an established surgical tool and is being used by public and private healthcare systems across Europe, Australia, India, and the Middle East in a wide spectrum of specialties including gynaecology, urology as well as colorectal, general, and thoracic surgery. ■

www2.cmrsurgical.com/more-power-to-you

Scanner manipulation prevention

Protecting medical imaging devices from cyberattack

Tom Mahler specialises in artificial intelligence (AI), anomaly detection, and cyberspace security. He has spent years analysing the vulnerabilities to external manipulation and sabotage of radiation-emitting medical imaging device systems as part of his doctoral research at. He believes that imaging modalities are quite vulnerable in clinical settings to the risk of cyberattack, and that CT scanners in particular face the greatest risk. In a recent publication in the Journal of Digital Imaging, he and his colleagues present a model for incorporating active participation by radiologists. To increase awareness, Mahler also speaks about digital threat at radiology events such as the RSNA congress.



EH: How did radiologists and radiology department managers react to your concerns?

Mahler: 'RSNA attendees were quite interested in learning about the vulnerability of their hospital "workhorses", CT scanners in particular. Radiologists whose work focuses primarily on healthcare find it hard to imagine anyone wanting to maliciously attack medical devices. Individuals with an IT technical background tell me that attacks are even easier than anticipated due to security concerns in the hospitals. I think that today there is a greater awareness of potential risk by cyberattack since 2017.'

How vulnerable are these systems today? Have improvements in security been made?

Mahler: 'Many hospitals have increased security in the digital network environment of the hospital network. Some PACS vendors have also made their products more secure. However, I am not aware of any significant improvements in the imaging modalities domain. These devices are still outdated and exposed to many vulnerabilities. I don't know of any large security company offering products to secure these devices at the point of care; most companies offer products that increase the security of the network, but not the device itself.

'Devices are not monitored enough. I think that monitoring the devices' operations at the point of care may be an important layer of security that can significantly reduce the risk of attacks. I have developed a detection and prevention framework that monitors the instructions sent with these devices. It uses advanced AI algorithms to detect anomalies within these instructions, and can alert the technician operating, for example if a CT scanner receives the instruction to deliver an excessive radiation dose. This kind of security layer is highly effective as it can block the attacks just in time before they affect the patient, no matter from where the attack originated.'

Do you have recommendations to make medical devices more secure?

Mahler: 'In my research, I determined that the modality workstation that a technologist uses to configure and control the imaging device is extremely vulnerable to attacks. The detection and prevention framework that I developed monitors the actual instructions sent from the workstation to the scanner. As far as I know, this was the first time anyone tried to look inside a CT device and analyse the instructions sent from the host control PC.

'The anomaly detection and prevention framework can be installed outside the host control PC and still block potentially malicious instructions from reaching the CT scanner, or for that matter, any type of digital imaging or radiotherapy device. Automated anomaly detection AI software can do this with an accuracy to date of up to 99.5%. After receiving an alert, a CT technologist can cancel the exam or override it if there is a clinical reason for the anomaly, such as imaging an extremely obese person. The system can even suggest automatically how to correct the instruction and fix the anomaly.'

What other types of protection do you recommend?

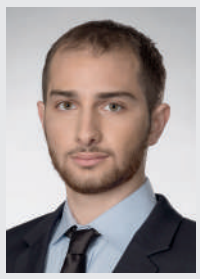
Mahler: 'My colleagues and I have shown how images from medical devices can be manipulated by adding or removing cancerous tumours in a way that radiologists cannot detect. Adding a digital signature is a secure way to make sure that the data received originated from a secure participant. If that data has been manipulated, the recipient would be alerted to this. Digital signature is very easy to implement, and this feature could be offered by modality and PACS vendors. However, offering such a feature is not enough. It should also be implemented and used by the hospital in which the PACS is deployed. I've often found security features provided by vendors that simply were not enabled.

'I also strongly recommend encryption of data in motion between a modality workstation and a PACS. The transmission of non-encrypted data is a huge vulnerability and is one that is very easy to fix.'

What should the role of radiologists and radiology administrators be in assessing security risk?

Mahler: 'The risk assessment process should be done by IT security personnel or a company specialising in these services, under the organisation of the hospital's chief information security officer. Radiology professionals can play an important role by assessing the impact of attacks, such as malicious sabotage. They also need to advocate for increased security of medical devices to their organisation's IT staff, computer security team, and to senior hospital administration.'

Interview: Cynthia E. Keen



Tom Mahler

Tom Mahler, PhD, is a researcher at the Ben-Gurion University of the Negev (BGU) in Israel. He completed the combined PhD track for outstanding graduate students as the youngest in his class. Mahler's research focuses on the cyber-security of medical devices and how to protect them using state-of-the-art machine learning and deep learning techniques. He is also the co-founder of FlowHow (p.k.a. CyberMed), a startup company that, based on his research, develops a secure workflow monitoring and optimization solutions for medical imaging devices and radiology departments.

Sponsored • New products presented live

Successful post-pandemic return at ITEM

After a two-year break due to the pandemic, the International Medical Imaging Exhibition (ITEM) of the Japanese Radiological Society in Yokohama once again offered exhibitors the opportunity to present their solutions, live to an inquisitive audience.

'Even though only about half as many visitors as in 2019 attended ITEM, we are satisfied with our presence at the exhibition,' said Mamiko Katagiri from JVC Kenwood Corporation's Healthcare Business Division. 'We were able to welcome many customers and interested parties to our stand and present our new products to them. Our new CL-R813 8-megapixel monitor was particularly in demand.'

Entry into high-quality multimodal reporting

With the CL-R813, JVC Kenwood offers radiologists the ideal colour monitor for reporting images of all modalities, such as DR, CT, MR and pathology. The 32-inch TFT LCD display impresses with a maximum brightness of 500 cd/m² and a contrast ratio of 1000:1. The entry-level device reduces eye strain due to its high resolution and offers a comfortable reporting environment for diagnostic imaging. In addition, the diagnostician can open different application windows on the screen in parallel, such as a viewer, findings and results of a separate AI software. In addition, the monitor features a slim and space-saving design with a narrow frame.

The 30.9-inch colour monitor CL-S1200 with 12 megapixels can also display medical images of different modalities such as CT, CR/DR, MR, ultrasound or mammography and pathology side by side on one monitor. The arrangement of the windows can be freely configured, and the large screen without a centre bar creates a comfortable environment for radiological diagnostics. With its maximum brightness of 1200 cd/m² and a contrast ratio of 1500:1, it is also suitable for mammography. The smooth, flat design of the CL-S1200 ensures that both the monitor and wide-angle base can be disinfected and thus kept hygienically clean.

Six megapixels for diagnostic radiology

The CL-S600 6-megapixel monitor from JVC Kenwood supports every modality except mammography. With its 30-inch display, it is predestined as a PACS monitor. The arrangement of the windows is also freely selectable here. With a high brightness of 1300 cd/m² and a high contrast ratio of 2,000:1, as well as an antibacterial housing, the display supports the doctors' work in image interpretation. The large screen without a centre bar creates a comfortable environment for radiological diagnostics.

With the PM Medivisor Cloud solution, JVC Kenwood offers administrators a secure and efficient way to record, analyse and store the operating status of monitors – installed inside or outside the facility – via the Internet. This allows management and monitoring of quality status remotely and comprehensively, regardless of location, greatly simplifying work and reducing maintenance costs. In addition, secure remote management can be carried out via the internet using secure communication protocols.

Sponsored • RFID technology

Modern authentication solutions for clinics

A system for user authentication and access management is key for simple, as well as transparent, processes in everyday hospital life. It thus contributes to an optimal working environment for staff and the best treatment conditions for patients. Because of this role, such a system can help clinics stand out from the competition.

Whether accessing electronic patient records or gaining access to sensitive areas: a modern, uniform system for user authentication and access control based on radio frequency identification (RFID) ensures that permissions are exclusively granted for authorized personnel. Not only does this simplify compliance with legal requirements, but it also ensures smooth processes. An RFID card, which staff members often already carry as an employee ID, is all that is needed to quickly gain access and entry to predefined areas. Authorizations can be managed centrally by the hospital IT with little effort. This, along with the simple authentication processes for staff, increases the efficiency of clinics and helps to reduce costs. Similarly, RFID cards may be issued to patients, to facilitate cafeteria payments, access to entertainment programs and more, in an easy and convenient way.

The access to sensitive areas is only possible with a modern, uniform system for user authentication.

Sustainable and secure

Universal readers are at the heart of modern access control systems. While hospital staff authenticate with cards, for example, patients can use their smartphones. To ensure that confidential information is protected, a reader that supports advanced security protocols and encryption is also required. Furthermore, the reader's design must reflect the demands of a modern clinical environment, with an appealing aesthetic and the possibility for hygienic cleaning of the housing.

Those in charge for the successful implementation of an access control system should consider further important points beyond the choice of reader. For example, it is necessary to include the complete system in the hospital's security concepts in advance. Further crucial points are in the flexibility and future viability of the system. It should be compatible with existing solutions, allow adaptations to changing requirements and be able to handle future technologies. Still, the system must be as user-friendly as possible to manage authorizations. Given the complexity of these requirements, seeking advice from specialized solution providers is recommended in order to avoid bad investments. For example, Elatec GmbH, one of the world's leading providers of user authentication and identification solutions, offers comprehensive consulting.

Disinfection safely regulated

The example of the American company UV-Concepts shows how safety, flexibility and appearance requirements can be successfully met. The company specializes in innovative, non-contact disinfection solutions, including a chamber that uses ultraviolet UV-C waves to kill germs on large items such as wheelchairs. To ensure disinfection performance and avoid health hazards from UV-C rays, access to the equipment must be limited to trained personnel. To achieve this, UV-Concepts relies on Elatec's TWN4 Palon Compact Panel solution. The reader features a durable, high-quality panel display and is compatible with up to 60 transponder technologies. Certified for sale in up to 110 countries worldwide, it offers exceptional flexibility. For example, the high level of compatibility benefits hospital associations that use a range of different technologies at their sites. In addition, activating new card technologies and updating firmware by remote configuration are easily possible. The reader is integrated into the UV chamber's digital tagging system and backend software, allowing for tracking of the time and trigger for each disinfection cycle. In this way, the reader contributes significantly to the correct application of the disinfection solution and protects patients and staff alike. ■

Sponsored • Fast-tracking research results into clinical practises

Clinical evidence workflow solution

The path from evidence-based research to clinical implementation is straightforward in theory but taxing in practice: Research groups must be coordinated, relevant published material identified, classified, and prepared, to shape findings into a comprehensive SOP for clinical use. To facilitate this complex process, Wolters Kluwer developed a new suite of applications, called Ovid Synthesis. It streamlines research workflows and the implementation of quality improvement measures into clinical practice. We spoke with Vikram Savkar, Senior Vice President & General Manager, Medicine Segment, Health Learning, Research & Practice, about the new solution, its development, and unexpected benefits for clinical education and onboarding.

'We want to facilitate the process of continuous quality improvement, which is highly relevant for any hospital,' he says. 'Applying the best practice is essential for better clinical outcomes for patients and also benefits financial performance. But it can also be very tedious and time-consuming. With Ovid Synthesis, we have developed a workflow tool that helps make that process efficient, successful, collaborative and more accurate.'

Only trained personnel can use the disinfection chambers.

Coordination of research groups is an enormous challenge, especially in bigger institutions: teams are scattered and communication about ongoing projects often happens in parallel over emails, offline documents and spreadsheets. 'This is inefficient and makes it hard to find the relevant evidence,' Savkar says. 'Findings are challenging to share across teams in other departments or hospitals. As a result, much time is wasted on research that has already been done before.' To solve this, Ovid Synthesis offers a cloud-based space to conduct research activities, provides access to all relevant published evidence and ensures that all teams involved have visibility into current projects in a comprehensive dashboard. 'The system also allows teams to track previous unsuccessful research projects to avoid duplication of efforts.'

AI classification streamlines search for sources

To accumulate relevant sources for research projects, the Synthesis solution is built upon the Ovid platform, which, according to Savkar, is the largest database of medical literature in the world. However, for teams searching for specific content, this wealth of information can be challenging to process: 'Even the most accomplished and earnest researcher can't possibly read all the articles that are published in a particular field,' he says. 'This is where our solution comes in – technology can help to make the selection and evaluation more efficient.'

To achieve this, Ovid Synthesis uses artificial intelligence (AI) to classify publications by their relevance. This is determined by scientific criteria, such as study design, sample size, or frequency of external citations. 'If this were done manually, this classification alone may take up to an entire year, but our tools can reduce the process to a period of weeks.'

Not only does the system help pulling the relevant papers, but it also helps users extract their key insights and generates citation lists. 'This process ensures that the template for any clinical improvement plan will be created in a rigorous, evidence-based way,' Savkar stresses. Originally intended as a tool to bring the latest evidence into clinical practice, the suite has also proven to be helpful in other, unexpected ways, Savkar reports: 'We didn't build Ovid Synthesis as an educational or training tool. But the hospital systems we work with find that this is a very useful way to help residents and new doctors quickly assimilate to evidence-based practice culture in those hospitals. Because it is such a structured tool and it templatises the process of evidence-based practice, it helps teach them what that looks like.'

The process-oriented approach is also beneficial in creating greater job satisfaction for doctors and nurses, as user feedback shows: 'They feel a sense of agency, that they can participate in a process to help improve clinical outcomes of their hospital. This is very meaningful for doctors and nurses, so it's another by-product that we are thrilled about.'

Feedback loops fuel further development

Ovid Synthesis launched in January 2022, after a two-year development phase. 'We have worked closely with selected hospitals to make sure that all the innovation we put into this suite is driven by customer needs. We engaged many of our large hospital customers to help us design this so that it genuinely met their needs.' Since the solution is cloud-based, it can be implemented into any pre-existing clinical IT infrastructure, says Savkar, adding that 'cybersecurity is a top-level issue for us, so we implement the best practices to protect our customer's data.'

Feedback loops are also to be a driver of the regular expansions to the suite, which are scheduled for release in six-month intervals; for example, a new institutional dashboard allowing users to identify and build on previously successful projects and automated integration with external research platforms. 'So far, we have been very successful with this product; many major hospital systems adopted it on the first day it launched. The reason for this success is that we're choosing to take a steady customer-based path to building out the full solution over time.' (WB) ■

Vikram Savkar

Vikram Savkar is the Senior Vice President and General Manager, Medicine Segment of the Health Learning, Research & Practice business at Wolters Kluwer. Previously, Mr Savkar served as General Manager for several businesses in the Legal & Regulatory division before joining the Health Division in late 2019. Prior to joining the company, he held senior positions at Nature Publishing Group and Pearson Education, and has earned degrees in Physics and Classics from Harvard University.

Cyberattack collaterals

War in Ukraine also threatens German hospital IT security

Hospitals in Germany may end up in the line of fire during the Russian invasion of Ukraine: As the conflict extends to the digital realm, cyberattacks against websites of Ukraine authority even predated the first conventional military moves. According to Deutschlandfunk information, digital attacks targeted the Ukrainian Foreign Office, as well as the nation's Ministries for Emergencies and Research as early as January 2022.

However, these were not the first cyberattacks in the long-smouldering conflict between Russia and Ukraine. In 2015 and 2017, several serious attacks were attributed to Russian hacker group "Sandworm", which is said to be close to the Russian domestic intelligence service FSB. While the attack in 2015 paralysed the power grid in the Ukrainian capital Kiev for several hours, a more widespread attack took place in 2017 with the malware NotPetya. The Trojan purged stored data from hard drives and caused financial damage amounting to 0.5% of Ukraine's GDP. Among the affected were also Russian companies such as the listed energy company Rosneft. The company is headed by Igor Sechin as CEO, a close confidant of Russian President Vladimir Putin (as well as former German Chancellor Gerhard Schröder as chairman of the supervisory board).

This collateral makes it clear how difficult it is, even for professional attackers, to direct a malware-based cyberattack strictly to the intended targets – and how easily such an attack gets out of control. So-called wipers, i.e. malware tools that delete hard drives and servers, are currently in circulation again. For example, IT security firm ESET reports that three new wipers have already been discovered in Ukrainian computer networks since February 23: HermeticWiper, IsaacWiper and CaddyWiper. The former was already detected by IT security researchers on the eve of the invasion.

Hospitals get caught in the digital crossfire

The analysts suspect that many of the Ukrainian systems that have been attacked by these wipers in recent weeks had already been infiltrated beforehand. This lines up with a notorious practice known as Advanced Persisting Threats (APTs): Intruders gain access to a foreign system and initially remain dormant without causing any noticeable damage. In this period, they spy on the system and tap into access and user data. This unnoticed intrusion can also be used to place targeted malware such as the wipers described above. This M.O. ensures that the intended targets are infected by the malware – even if an uncontrolled spread of the malware cannot be prevented afterwards, also damaging unintended institutions and companies on both sides of the conflict.

IT security researchers point out the dangers of this type of digital warfare for healthcare systems, also in Germany: According to WHO data, Russia is responsible for a total of 197 conventional military attacks on Ukrainian hospitals and practices (as of May 24). with 70 people killed and 55 injured. The UN considers such attacks to be war crimes. Targeted cyberattacks on healthcare facilities, on the other hand, have not been reported so far – in all cases, these are likely to have been collateral damage rather than intended targets of the Russian armed forces.

Malware does not respect national borders

Such collaterals had already been reported in 2017, when NotPetya was deployed: First, Ukrainian hospitals were infected and had to restrict or stop patient care. Later, the malware spread worldwide via the Ukrainian branch of the software company Nuance, also to US hospitals, which frequently use speech recognition software from Nuance, for example for documentation in digital patient records. However, the loss of existing data was not the whole story: Because the NotPetya infection initially went unnoticed, clinicians and nurses continued to work with the speech recognition software, resulting in numerous dictated epicrises and reports never appearing in the designated patient records. It cannot be determined with certainty how many diagnostic and therapeutic decisions were influenced or delayed as a result.

A current concern is that collateral damage could hit the already severely weakened healthcare system in Ukraine and also affect medical care in other countries, since malware does not respect national borders. The American Hospital Association (AHA) therefore issued a warning at the end of February 2022, stating that the war in Ukraine also justified a heightened alert level in US hospitals. Threats to hospitals are categorised in three levels: Targeted attacks on healthcare infrastructure, collateral damage from uncontrolled malware, and thirdly the disruption of supply lines and external services that are essential for hospitals to maintain patient care.

BSI warns against Kaspersky, CISA recommends geo-fencing

The US Cybersecurity & Infrastructure Security Agency (CISA) almost simultaneously issued a so-called "Shields Up" directive, raising the alert level for threats to the digital infrastructure for all domestic organisations. Concrete instructions from the AHA and CISA include specific measures for the current conflict, such as geo-fencing (a geographically defined blockade) of internet traffic from Ukraine and neighbouring regions. Most important, however, are general information security measures, from systematic monitoring of potential vulnerabilities to ongoing awareness campaigns and staff training on IT security.

Since March, the German Federal Office for Information Security (BSI) warns of increased danger from cyberattacks on hospitals. The agency communicated the second-highest warning level, orange – explicitly not only for hospitals classified as critical infrastructure (KRITIS; meaning hospitals with more than 30,000 full inpatient cases per year), but for all hospitals in Germany. As a consequence, these institutions must tighten their IT security (or introduce general measures in the first place). This is a challenge in itself, given the financial and personnel bottlenecks in the clinics still affected by the coronavirus. In addition, a specific warning was issued against antivirus solutions from Russian company Kaspersky, which are frequently used in Germany – also in the health sector. However, the BSI cautioned against a sudden deactivation of Kaspersky antivirus software without sufficient replacement, but rather switching to alternative products after prudent planning while accepting 'temporary losses in comfort, functionality and security'. ■

Report: Dr Christina Czeschik

Antimicrobial resistance development

AMR and climate change: a worrying dual threat to global health

Climate change and antimicrobial resistance (AMR) are forming an alarming alliance: Global warming creates new breeding grounds for resistant bacteria, which challenge human, animal, and environmental health systems globally. A serious and very real threat to public health – but not quite the doomsday scenario some might make it out to be, says Prof Sabiha Essack from the University of KwaZulu-Natal in Durban, South Africa.

'Antimicrobial resistance and climate exacerbate each other,' Prof Essack says. 'Studies have shown that rising temperatures together with high population densities lead to higher AMR in bacteria – maps that show increases in temperature correlate with areas where more resistant bacteria are found.' Because the transfer of resistance genes is facilitated at higher temperatures, the bacteria can acquire and spread AMR genes more easily. As global warming progresses, these high-risk areas become more common, creating new breeding grounds for resistant pathogens.

Hunger for meat fuels AMR development

The growing demand for meat protein and other animal products is another major driver of AMR, especially in low and middle-income countries. Animals are raised on a large scale, with regulations on antibiotic use not being very strict. The practice of prophylactic antibiotic supplementation of feed – which is cheaper than vaccinating the animals – is especially problematic in this regard, Prof Essack points out. 'Not only does this promote escalation of AMR, but the larger number of animals also leads to increased methane emissions, speeding up the greenhouse effect.' Also, without proper preparation of the food produced from these animals, humans run risk of ingesting resistant bacteria themselves.

Biosecurity is a key element to mitigate AMR in food animal production, the expert says: This concept includes the use of vaccines, establishing "all in/all out" systems and thorough disinfection in production sites to prevent resistant pathogens from emerging and spreading from one herd or flock to another. Shifting from intensive to extensive and organic farming models may further reduce the need for antibiotics and the subsequent risk of AMR development. 'This is more expensive, but it is a vital step to reduce AMR,' she says.

Emerging from origins hot and cold

'Along with the rising temperatures, the ecosystems are changing,' Prof Essack continues. 'This leads to floods, droughts, and other natural disasters. Microbes adapt and spread to new areas, as do insects that serve as vectors for new diseases. As a result, more antibiotics are used, increasing selective pressure on pathogens and thus promoting the development of AMR.'

However, global warming not only facilitates the development of new resistance but might also bring back old ones: 'Climate change accelerates glacier melting and thawing of permafrost, which may contain antimicrobial resistance genes. Increased oceanic currents further help the spread of these AMR traits from Siberia and the Arctic to other parts of the world.'

For Prof Essack, the re-emergence of ancient resistant strains does not come as a surprise: 'Antimicrobial resistance has existed for millennia. It is our overuse and misuse that has severely tipped the balance and turned resistant pathogens into a significant global threat.'

Increasing health literacy without fearmongering

To counteract the self-propagating effects of AMR and climate change, public awareness is essential, the expert says: 'Antimicrobial resistance is a very intangible concept, so most people will not make the connection between the deaths from hospital infection and resistant pathogens.' The main objective for awareness campaigns is to clarify the consequences of AMR in an engaging way: 'If we allow this development to continue, it will fundamentally change our healthcare standards. Many common surgical procedures such as C-sections or implant surgeries will become impossible to perform, and untreatable infections will lead to premature death.'

Despite this, doomsday scenarios and fearmongering are not necessarily the way to go, Prof Essack believes: 'We can achieve a lot with just little changes in our behaviour – sparing, prudent use of antibiotics and running diagnostic tests to determine the type of pathogen before administering antibiotics – to ensure that our supply of effective antibiotics do not run out.'
To further loosen our dependency on antibiotics, a number of innovative and promising approaches aim to not only develop new antibiotics, but also antibiotic alternatives, such as bacteriophages. 'Our arsenal of antibiotics is limited, not least because development of new antibiotics is not very profitable,' the expert points out. To be prepared for the future, financial models should be established to incentivise research and development of new antibiotics, independent from the current return-on-investment model.

Report: Wolfgang Behrends

Sabiha Essack

Professor Sabiha Essack, PhD, is Vice Chair of the WHO Strategic and Technical Advisory Group for Antimicrobial Resistance (STAG-AMR) and Advisor for several international initiatives on antimicrobial resistance. She further serves as expert consultant on antimicrobial resistance (AMR) and antimicrobial stewardship (AMS) to the WHO. Professor Essack's current research interests include evidence-informed strategies for the prevention and containment of antibiotic resistance, characterization of the molecular epidemiology of resistance in humans, food animals and their associated environments, as well as health policy and health systems strengthening to optimise the management of infections in the context of antibiotic resistance and stewardship.

Drug dose optimisation

Antibiotics: no more 'dosing in the dark'

Antibiotics are essential for keeping bacterial infections in check, but finding the right dose is akin to a Goldilocks problem: give too little, and the infection will persist; too much, and side-effects will override the benefits of the therapy. To get it "just right", Prof Dr Birgit Koch talked about dosing optimisation in the clinical setting at this year's ECCMID in Lisbon. We spoke with the Clinical Pharmacologist from Erasmus MC, Rotterdam, about the shortcomings of current methods and the benefits of patient-tailored dosing.

'The concept of "a lot helps a lot" clearly does not apply,' the expert points out: 'The higher the dose is, the more the toxicity of a drug becomes an issue.' Furthermore, incorrect dosage encourages resistance-building in pathogens, and excessive prescription is not a sustainable, cost-effective practice. 'This is why dose optimisation is so important.'

But getting the dosage of antibiotics right is a challenging matter, Prof Koch says: 'There is a range of factors that play a role. As a rule of thumb, anything that affects a patient's metabolic function should be considered, so the most important parameters are age, gender, and renal function.' Albumin levels in the blood are also relevant, as are pre-existing conditions and medication. Lastly, the type of targeted microorganism should be considered.

Models in need of greater diversity

Limited knowledge about a drug's pharmacokinetic (PK) and pharmacodynamic (PD) properties can add another layer of difficulty: 'Unfortunately, no PK/PD models exist for most drugs developed before 1995,' Koch reports. This includes antibiotics that are still in widespread use, such as amoxicillin. But even for newer drugs, PK/PD models often lack heterogeneity in patient data. 'A lot of times, references are only based on effects in young male persons.'

As a result, most patients receive the same antibiotic dosage – regardless of individual risk factors. 'We have discovered that for some beta-lactam antibiotics, most patients receive the same dose, but only 60% achieve site exposure,' the pharmacologist states. In other words, the drug does not reach its target in the intended quantity.

To establish more nuanced dosage models, researchers at Erasmus MC took a closer look at the blood of patients in the centre's ICU. The team gained insights into how drugs were metabolised by different patient groups. 'For example, impairment of renal function – due to advanced age or disease – affects the rate in which a drug is cleared from the blood,' Koch reports. 'We identified several of these risk factors for target non-attainment, so patients with these risk factors need to receive an adjusted antibiotic dose.'

AI to create more detailed connections

While the benefits of individualised drug dosing might seem rather self-evident, scientific evaluation of the concept is surprisingly sparse. The recently completed DOLPHIN trial is an effort to provide evidence and encourage clinical application of patient-tailored dose models, the expert says. In the Dutch multicentre, prospective, randomised study, outcomes were compared between critically ill patients whose medication dose was monitored and adjusted to reflect individual factors and patients who received the standard dosage. 'We hope that we will see more model informed precision dosing arrive in the clinical practice in the future,' says Prof Koch, who presented the findings of the trial at the ECCMID congress.

The expert also regards AI as a key technology. 'What is especially promising is that algorithms are not biased the way humans are. Because the AI will only process the raw data without knowing the context, it may establish correlations and identify risk factors that a human would have missed.' Prof Koch also advertises the practice of infection site measurement, which should replace current blood analysis to ensure more targeted results. 'We still have a lot of work to do,' she concludes, 'but getting the right drug in the right dose to the right patient could solve a lot of our current problems, so it's clearly worth the effort.'

Report: Wolfgang Behrends

Birgit Koch

Prof Dr Birgit Koch is a Clinical Pharmacologist and Full Professor of Clinical Pharmacometrics at the Erasmus University Medical Center, Rotterdam, the Netherlands. She focuses on Therapeutic Drug Monitoring (TDM), PK/PD and Toxicology and is also part of the management team of the pharmacy. The laboratory covers more than 70.000 TDM/toxicology samples per year and more than 100 assays, both in clinical care and in research. Since January 2020, Prof Koch is head of Research & Teaching of Pharmacy Erasmus MC.