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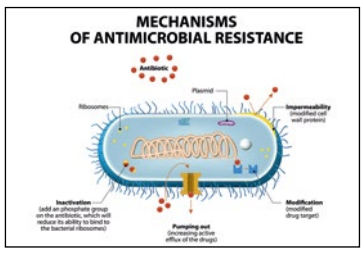

New regulation has a global impact

This May the updated Medical Device Regulation (MDR) was implemented, a year after a delay caused by the coronavirus pandemic. This, the first update in three decades, has implications for the MedTech and healthcare sectors, which was examined by experts during a special MDR conference.

Report: Mark Nicholls

Speakers included Erik Hansson, Deputy Head of the Unit of the European Commission responsible for the legislation on medical devices. He discussed the challenges and benefits of the regulations from a European perspective and focused on two of the main EC tasks under the new regulation – to develop implementation enactment and guidance documents – and the new European Database on Medical Devices (EUDAMED).

'The new legislation is very ambitious and needs a lot of effort and resources from all actors involved – manufacturers, notified bodies, Member States and the Commission – and will have an important impact on relevant stakeholders, such as healthcare providers,' Hansson explained, speaking with European Hospital ahead of the event.

Uniform implementation

A series of guidance documents developed by the Medical Device Coordination Group, the EC and stakeholders, will help deliver a uniform implementation of the new regulations across Member States, he added. The MDR aims to bring EU legislation in line with technical advances, changes in medical science, and progress in law making.

'They create a robust, transparent, and sustainable regulatory framework, recognised internationally, which improves clinical safety and creates fair market access for manufacturers. In contrast to directives, regulations do not need to be transposed into national law. The MDR will therefore reduce the risks of discrepancies in interpretation across the EU market.'

Wide-reaching impact

The legislation revision is the first since the EU acts were drawn up 30 years ago, and will have a broad-reaching impact.

'The legislation will be applied in the EU as well as certain countries with which the EU has agreements and therefore will be applied in not far from half of the countries worldwide that are regulating medical devices,' Hansson pointed out. 'Therefore, it will also have a global impact.'

Compared to the current Directives, the new regulations emphasise a life-cycle approach to safety, backed up by clinical data and add more stringent rules for the designation of the certification bodies and also add more control and monitoring requirements.

Greater transparency

In terms of the impact on healthcare, he said: 'The main objective is to ensure efficient and safe medical devices for use in healthcare. It will also bring more transparency for healthcare professionals as the new EUDAMED database includes information on devices which will also be accessible for healthcare professionals once finalised.'

Traceability of devices will also improve through a Unique Device Identifier (UDI) system based on the use of barcodes.

Factors that healthcare providers need to consider, Hansson said, should be to make sure that devices are CE-marked, ensuring that the requirements of the legislation are fulfilled.

The Regulation contains specific provisions on when health institutions can manufacture, modify and use devices 'on a non-industrial scale' in-house when equivalent ones are not available commercially.

It also clarifies the obligations of manufacturers, authorised representatives, importers and distributors, and both device and manufacturer must comply with the MDR.

Patient safety

Manufacturers need to assess the conformity of a device, while other important points of the MDR include requirements on clinical evaluation, risk management, quality management systems, post-market surveillance, technical documentation and other reports and liability for defective devices. 'One of the more important aspects for improving patient safety are the reinforced requirements for clinical evaluation,' he said. 'As under the old Directives, it includes the collection of clinical data already available in the literature as well as the setting up of any necessary clinical investigations.' Patient safety is a key aim of the new regulations and the strengthened legislation has improved safeguards to achieve this. 'The overall objective is to ensure that patients are treated with safe and effective medical devices,' said Hansson, adding that, in general, the MDR retains all the requirements of the old directives, while adding new measures. 'The regulations will not completely reshape the medical device regulatory landscape, but will ensure that devices manufactured and used in the EU will fulfil the highest standard.'

Continuous process

While all new medical devices certificates will have to be delivered according to the new regulation from May 26, there is a transitional provision under certain conditions for devices covered by the previous Medical Device Directive. Additionally, new regulations on in vitro diagnostic medical devices will become applicable.

'Despite the challenges related to the implementation of the new requirements, in particular, during the Covid-19 pandemic, important progress has been achieved and the new legislation is now ready to be applied in practice. However, the work will not stop here because the development of guidance documents is a continuous process that will last for many years to come,' Hansson concluded.

Erik Hansson is Deputy Head of the Unit for Medical Devices and Health Technology Assessment of the European Commission Directorate General for Health and Food Safety (SANTE), which is responsible for the legislation on medical devices.

New responsibilities for the European Medicines Agency

The MDR is introducing new or revised responsibilities for the EMA (European Medicines Agency). These affect:

- medicines with an integral device, such as pre-filled syringes and pens, and pre-filled inhalers;
- medical devices containing an ancillary medicinal substance to support the proper functioning of the device. Examples: drug-eluting stents, bone cement containing an antibiotic, catheters coated with heparin or an antibiotic agent and condoms coated with spermicides;
- medical devices made from substances that are absorbed by the human body to achieve their intended purpose;
- borderline products for which there is uncertainty over which regulatory framework applies. Common borderlines are between medicinal products, medical devices, cosmetics, biocidal products, herbal medicines and food supplements.

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The gender gap adversely affects AI

Data holds a legacy of discrimination

Report: Karoline Laarmann

Technologies based on artificial intelligence (AI) are considered the epitome of progress. However, the data AI algorithms use to draw their conclusions is outdated. It ignores the existence of biological sex and socio-cultural gender and their effects on individual health and disease states. Thus, the 'thinking machines' not only reproduce discriminating bias and prejudices but also produce suboptimal and even outright wrong results.

German experts discussed the gender problem in healthcare AI at the Econ Forum by TK at virtual. MEDICA 2020. This was a women-only panel, underlining that it is mostly women who are interested in the gender issue. More so, the audience reflected the panel composition, as Dr Christiane Gross, Chair of the Medical Committee on Telematics North Rhine Westphalia and President of female physicians' association Deutscher Ärztinnenbund, pointed out: 'In training sessions on gender issues I often mainly see women. But the moment you call the session 'men's healthcare' the audience is split evenly in 50 percent women and 50 percent men.' The word 'gender' is still widely considered a women's niche topic, although gender-specific differences concern all humans. Men, however, have fewer reasons to feel excluded in medical sciences because they are over-represented


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at all levels. After all, the majority of participants in medical research projects are men, thus the training data fed into AI systems is either focused on men or neglects the gender dimension altogether.

When machines think like men

'The gender bias in medicine has been known for years but it took the research community quite a while to catch on,' said Brigitte Strahwald, the Chair for Public Health and Health Services Research at Ludwig Maximilian University, Munich. During development of AI technologies, legacy data was used that carry the gender-related distortions from the analogue into the digital world. 'This is due, among other reasons, to the gender gap in AI research and development,' Strahwald pointed out. Algorithms are not only the product of the data sets on which they are based, they are also the product of the humans who program them – the majority of whom are men. Since most healthcare AI applications do not differentiate between sexes and genders, it can be assumed that the IT experts in charge either consider this aspect irrelevant or are not even aware of it.

Gendering as a success factor

Neglecting the gender dimension is not only a matter of discrimination against women – it undermines the usefulness of AI. Take the digital health applications that are being reimbursed by health insurers under the German Digital Care Act (DVG), which came into effect last October. Barbara Steffens, former health secretary of North Rhine Westphalia and current head of regional policy support of a large health insurer, Techniker Krankenkasse, points out that the 'non-differentiating apps' help neither men nor women, but only generate costs: 'In the first certified apps we are aware of five health areas in which we know men and women are affected differently, not to mention different perceptions and courses of disease.' More men than women, for example, suffer from chronic tinnitus, but women experience the disease more intensely. Thus it can be expected that the success of a tinnitus app also hinges on the question of whether contents are prepared and communicated in a gender-sensitive manner. Currently, this is not the case.

Gender was, and is, the big unknown, not only in digital healthcare but also in teaching, training and research. There appears to be an easy way to strengthen awareness of gendered healthcare, said Dr Christiane Gross: 'If we manage to get men on board we will have reached a major milestone.'

Dr Christiane Gross is Chair of the Medical Committee on Telematics, North Rhine Westphalia, and President of the Deutsche Ärztinnenbund, the female physicians' association.

Former health secretary of North Rhine Westphalia, **Barbara Steffens** currently heads regional policy support of Techniker Krankenkasse.


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Medicines work differently in men and women. However, women are under-represented in most studies.

Inclusion of women in studies and guidelines must increase

Gender medicine

Women and men are different – nobody could argue against that. However, in medicine, gender plays a subordinate role. Neither research, prevention nor therapy adequately reflect this difference. 'This is no longer acceptable,' Professor Vera Regitz-Zagrosek emphasises. At the 127th Congress of the German Society for Internal Medicine, the internist and cardiologist emphatically demanded that females should be more included in studies and that guidelines should consider gender aspects.

Report: Sonja Buske

The biggest problem is lack of data. 'When studies are designed, frequently no thought is given to the fact that women and men may have different reactions to medication, which is also why no research is carried out into potentially different dosage requirements,' explains Regitz-Zagrosek. 'We then obviously cannot expect that doctors will treat men and women differently and in the best possible way, given that there are no studies and guidelines available.'

The cardiologist used a study on the low dose administration of colchicine to reduce cardiovascular events after myocardial infarction as an example to illustrate this neglect of women's needs. This study of 5,000 patients included only 900 women. However, the effectiveness of colchicine was confirmed for the entire study group and the risk reduction was quoted as being 23%. 'But only after reading the electronic appendix of the manuscript and taking a closer look did it become clear that the risk reduction in women is only 1%, and that it's therefore not effective,' Regitz-Zagrosek points out.

According to this cardiologist the case is no exception. Only 11% of cardiovascular studies itemise side effects by gender, and only 30% list effectiveness by gender. Current Covid-19 studies are no different. The proportion of women in three quarters of treatment studies is less than 45%. In vaccination studies the percentage is slightly higher at 45 – 55%, but the side effects are not itemised by gender. 'This is a mistake,' Regitz-Zagrosek stresses, because 'ninety percent of allergic reactions after vaccinations occur in women.'

Why the gender imbalance in studies? The Berlin-based expert points to one reason: a lack of awareness in research within the pharmaceutical industry. 'It's simply assumed that there are no major gender differences and, subsequently, there is also no interest or analysis. Allegedly, it is also too complicated for doctors to consider gender when determining dosage. This attitude is a catastrophe.'

She also believes the licensing authorities should be obliged to demand an appropriate proportion of women and gender-specific evaluation in studies. 'There are guidelines for this, but they are not being implemented,' Regitz-Zagrosek points out. She recommends that doctors should consistently ask companies to publish gender-specific dosage guidelines and urge professional medical associations to reflect gender-specific differences in their guidelines.

The under-representation of women is a recurring theme in medicine as well as in cardiology training. Regitz-Zagrosek: 'Women in cardiology earn less money for the same amount of fulltime work and receive less support than their male colleagues, and thirty percent of female cardiologists also suffer sexual harassment – and all this against a background of a persistent, highly competitive work environment and inflexible working hours. All this leads to women being pushed out of the competition for leading positions at university,' she concludes. Whether or not there is a connection between the proportion of women in studies and the proportion of female medics in leading positions remains to be proved.

Vera Regitz-Zagrosek MD is an internist, cardiologist and senior professor at the Charité Medical University Berlin, as well as a professor at the University of Zurich. She was a founding director of the Berlin Institute for Gender in Medicine (GiM) at the Charité and founding president of the German and the International Society for Gender Medicine. Regitz-Zagrosek researches molecular, clinical and sociocultural bases of gender differences in heart disease and their importance for treatment. In November 2018 she was awarded the Order of Merit of the Federal Republic of Germany, First Class, for her achievements in Gender Medicine

Medical oncology

Covid-19 and gender parity: a worrisome scenario

The pandemic could challenge what little achievement has been made so far in the field, a prominent Spanish medical oncologist explained during the virtual European Lung Cancer Conference (ELCC 21) organized by the European Society of Medical Oncology (ESMO) last March.

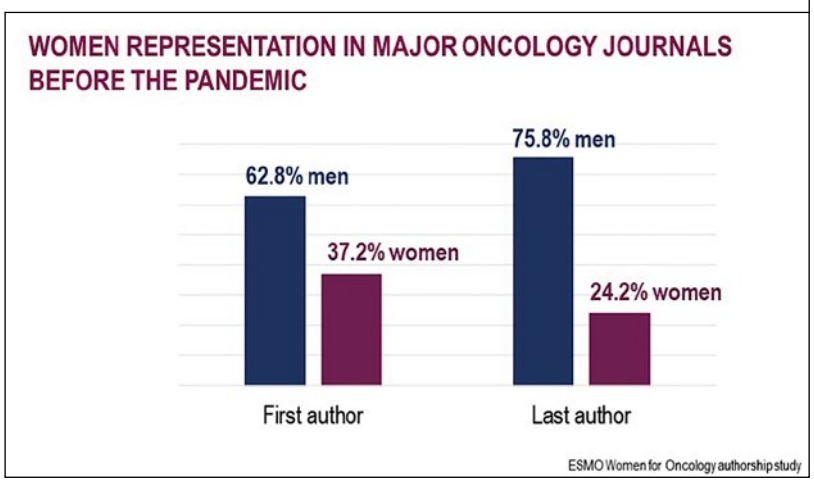
Report: Mélisande Rouger

Covid-19 and its economic fallout have made women more vulnerable. They are likelier to lose their jobs than men, partly because the crisis significantly increases the burden of unpaid care, which is disproportionately carried by women.

Women have also published less during the pandemic and about the pandemic, data shows. Women's posting rates on preprint servers has slowed during the first two months of the crisis. When compared with March and April 2019, the number of male authors who posted on those servers has grown faster than the number of female authors in the same period in 2020.

Besides, women account for only one third of authors who published on topics related to Covid-19. 'Maybe that's why we're losing a part of the gender dimension of Covid-19, even from the research area,' said Dr Pilar Garrido, an associate professor of medical oncology at Alcalá University near Madrid, in her online presentation.

Garrido is chair of the ESMO Women for Oncology (W4O) committee. The group launched a survey last year to assess the impact of the Covid-19 crisis on work and home life for both women and men in oncology. 'Our special concern was also related to the potential influence on the potential career in young oncologists,' she said.



Preliminary results show that the pandemic affected the careers of the respondents in a negative way. But there was little participation of men in the survey.

Early data also reveals that women have been less present than men on Covid-19 advisory groups, as recently highlighted by the European Commission. More men than women declared having spent more time on science, research and publication, while more women declared having spent less time on these activities.

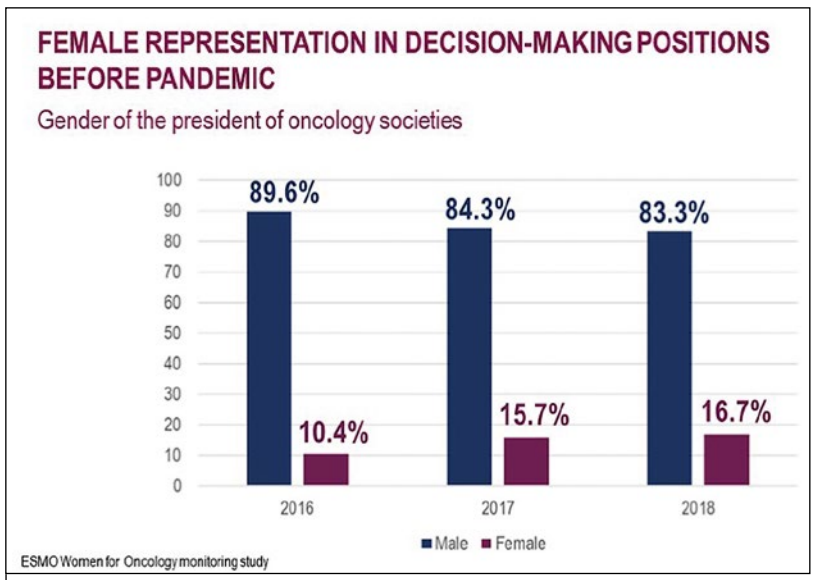
The definitive results of the W4O survey will be available later this year, along with another survey on perception of gender challenges and an exploratory study in Asia.

'Our mission is to raise awareness and promote equal access to career-development opportunities for women oncologists, while providing a platform for networking with other women oncologists and national groups,' she said.

Potentially widening the gap

Before the pandemic, the committee found that very few women held decision making positions, although things had slightly improved recently. 10.4% of presidents of oncology societies were women in 2016, vs. 15.7% in 2017 and 16.7% in 2018 (see graph).

There was also a gender divide in research and publications before Covid. In 2019, women only represented about 30% of all research grants PIs. In high impact journals, they only made up 38% of first authors and 24% of last authors (see graph).



In 2019, the Lancet asked if the academic publishing system was gendered and looked at internal processes. Women represented 79% of the editorial staff and 57% of the editors in chief across the group's 14 journals. However, women only accounted for 30% of the editorial advisory board members and there were fewer women in the peer review and commissioned content sets.

'This is a vicious circle,' Garrido said. "Women have fewer publications, so they probably have fewer opportunities for funding, being promoted and advanced. There is a risk of poor representation in decision-making, poor participation in peer review and fewer publications. There is a clear bias and unconscious bias and a large room for improvement."

To narrow the gap, the W4O committee will continue to observe, support and report about the situation in medical oncology.

'With the crisis comes the risk of losing what little achievement we have made so far. We need to explore new ways of collaborating and networking, including mentorship sessions, forums at virtual congresses and roundtables in social media. We need to advocate for gender balance to remain a priority in the agenda,' she concluded.

Equal opportunity in orthopaedics and trauma surgery

Skull & bones? Female specialists fear not

In the past few years the number of women going into orthopaedics and trauma surgery has increased. Currently, 25 percent of the junior physicians in Germany are female – which in international comparison puts the country in one of the top spots. However, after their initial years many of them do not complete specialist training, only five percent of head of department positions in German university hospitals are held by women and not even 10 percent of orthopaedics professors are women. Annika Hättich, specialist physician for orthopaedics and trauma surgery at the University Hospital Hamburg-Eppendorf, wants to change that: her aim is to make her discipline more attractive for women and to improve equal opportunity.

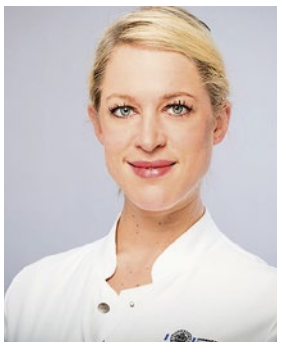
Orthopaedic surgery – women in 'a man's world'. From left: Specialist physician Annika Hättich, operating room technical assistant Betül Koz and junior physician Dr Alonja Reiter

Report: Sonja Buske

Orthopaedics and trauma surgery are still often considered 'men's work'– backbreaking jobs with extremely hard physical work and brute force. Many women, afraid of failing in the OR because of lack of physical strength, body size or physique, forego this discipline. A groundless fear, as Annika Hättich underlines. She points out that in her eight years in the OR at most five times she found herself physically incapable of performing the surgery at hand. 'No doubt, you start to sweat. But that happens in every discipline. After all, stamina is something one can train. In addition, you are never alone in the OR. If indeed you falter, there is always someone on the surgical team to support you.' Moreover, the length of orthopaedic surgery has been decreasing steadily as Hättich explains: 'In the olden days ten hours in the OR was no exception but today with modern technology and minimally invasive procedures surgery takes about two hours on average.'

OR schedules and part-time jobs are compatible

Shorter surgery times are important with regard to compatibility of family and profession as a two-hour procedure can be integrated much more easily into a part-time schedule than ten hours. But few hospitals offer part-time models.



Annika Hättich is specialist physician for orthopaedics and trauma surgery at the University Hospital Hamburg-Eppendorf where on 1 July 2021 she will assume her new responsibilities as senior physician. She has been an active member of the Junge Forum O&U since 2013 and will be chairing the organisation as of summer 2021.

'Unfortunately, there is a persistent prejudice that part-time physicians don't perform as well and miss too much,' Hättich says and also adds 'in hospitals, however, where staff do not have to work overtime and where the heads of department make sure that work schedules are adhered to, the part-time staff are more satisfied and indeed often better performers.' This does not apply only to mothers – increasingly fathers demand parental time off; they are no longer prepared to work full-time. The conditions that enable work/life balance have to be actively created.

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Longer term impact of Covid-19 revealed

A new insight into the longer-term impacts and recovery time for patients hospitalised with Covid-19 has been revealed in a UK-based study.

The PHOSP-Covid study found that seven in 10 patients have still not fully recovered five months after discharge and many face continuing impacts on their physical and mental health, and their ability to get back to work.

It also highlighted that those who experience the most severe prolonged symptoms tend to be white women aged 40-60 with at least two long-term health conditions such as diabetes, lung or heart disease.

Led by the National Institute for Health Research (NIHR) Leicester Biomedical Research Centre (a partnership between Leicester's Hospitals, the University of Leicester and Loughborough University), the research also found that 20% of participants had a new disability, while cognitive impairment was also a predominant symptom in some patients.

Burden of symptoms

Dr Rachael Evans, an associate professor at the University of Leicester and respiratory consultant at Leicester's Hospitals, said: 'Our results show a large burden of symptoms, mental and physical health problems and evidence of organ damage five months after discharge with Covid-19. It is also clear that those who required mechanical ventilation and were admitted to intensive care take longer to recover.'

The study analysed 1,077 Covid-19 patients who were discharged from hospital between March and November 2020.

The most common symptoms were muscle pain, fatigue, physical slowing down, impaired sleep quality, joint pain or swelling, limb weakness, breathlessness, pain, short-term memory loss, and slowed thinking but many patients had several symptoms at the same time.

The study also found a quarter of participants had anxiety and depression and 12% had symptoms of post-traumatic stress disorder after five months.

In addition, of the 67.5% of participants who were working before Covid, 17.8% were no longer working, and nearly a fifth experienced a health-related change in their occupational status. The study team underlined the need for employers to understand this and acknowledge Covid patients may take a long time to fully recover.

Proactive approach

Dr Evans, the study's lead co-investigator, said that much of the wide variety of persistent problems was not explained by the severity of the acute illness, indicating other underlying mechanisms

'One of the most striking findings of the study is just how few people are fully recovered five months down the line,' she said. 'This demonstrates how healthcare services will have to re-think strategies to deal with this post-Covid burden and how they will offer support to this group of patients. We have highlighted the need for a proactive approach.

'With both mental and physical impairments at five months, wider access to mental health and physical health interventions is required as well as a co-ordinated approach so patients are not seeing several different specialists.'

Dr Rachael Evans is an NIHR Clinical Scientist at the University of Leicester and an Honorary Consultant Respiratory Physician at Leicester's Hospitals and a co-investigator of the study PHOSP-Covid. Her areas of expertise include exercise physiology, training and rehabilitation for people with long-term cardiorespiratory conditions.

Dr Evans said health systems face a long-term legacy from Covid-19 and will need a range of strategies and interventions to cope with this.

Recovery clusters

The research has also uncovered a potential biological factor behind some post-Covid symptoms. A biological marker associated with inflammation, C-Reactive Protein (CRP), is elevated in all but the mildest of post-hospital cases.

Professor Louise Wain from the University of Leicester, and also a co-investigator for the PHOSP-Covid study, said: 'From previous studies, it is known that systemic inflammation is associated with poor recovery from illnesses across the disease spectrum.

'We also know that autoimmunity, where the body has an immune response to its own healthy cells and organs, is more common in middle-aged women. This may explain why post-Covid syndrome seems to be more prevalent in this group, but further investigation is needed to fully understand the processes.'

Researchers classified the types of recovery into four different groups or 'clusters' based on the participants' mental and physical health impairments.

'The evidence for different recovery clusters, and ongoing inflammation, really is important in guiding how we conduct further research into the underlying biological mechanisms that drive Long-Covid,' Professor Wain added.

Largest study

The PHOSP-Covid study also measured the impact of medicines given during hospitalisation to see if they affect patients' recovery. Early indicators show that while giving corticosteroids is a factor in reducing mortality in hospital, it does not appear to have an impact on longer term recovery.

There are more than 300,000 post-hospitalisation survivors that have been discharged from UK hospital's following Covid-19 and while the study only represents a small sample of these patients, it is the largest study to report in detail on prospectively assessed outcomes across multiple UK centres to describe the impact of Covid-19 on the medium-term health of survivors.

The study will see participants followed-up at 12 months, as well as blood samples analysed, and ongoing effects on mental health and their immune systems assessed. (MN)

Professor Louise Wain is the GSK/British Lung Foundation Chair in Respiratory Research in the Department of Health Sciences at the University of Leicester. As a genetic epidemiologist, her research is geared towards understanding the genetic factors that contribute to risk of developing respiratory disease.

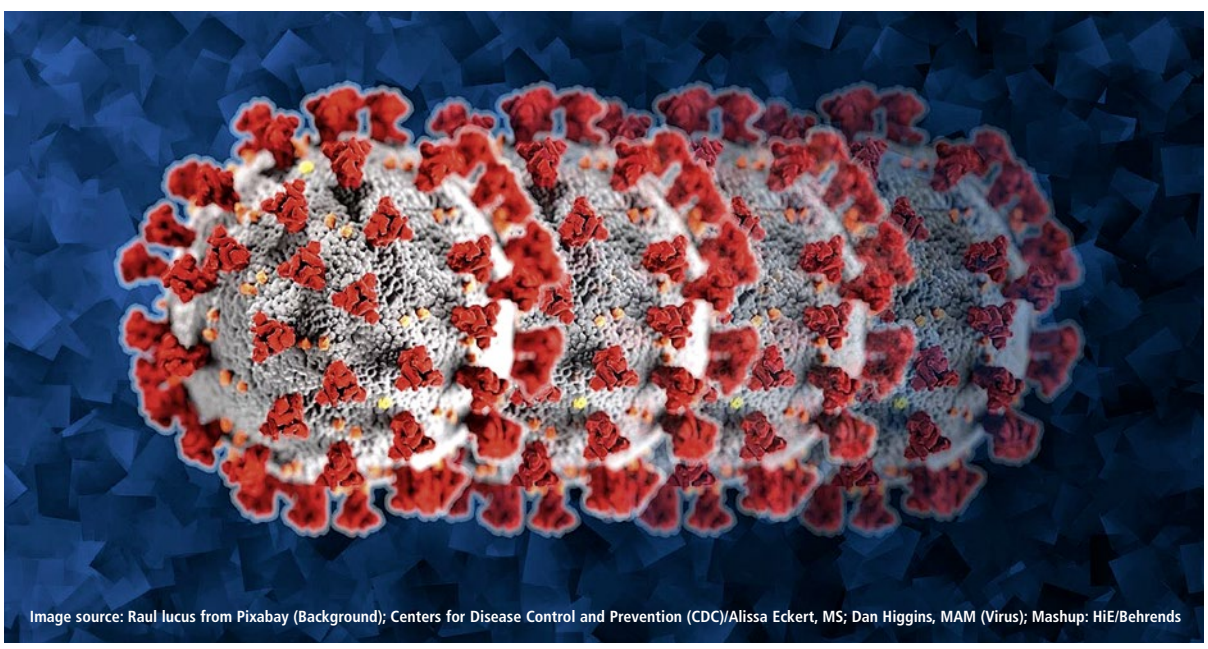

Image source: Raul lucus from Pixabay (Background); Centers for Disease Control and Prevention (CDC)/Alissa Eckert, MS; Dan Higgins, MAM (Virus); Mashup: HiE/Behrends

Skull & bones? Female specialists fear not

Continued from page 3

Family or career?

Hättich has seen many female colleagues throw in the towel: 'Very often it is during the specialist physician training that a decision has to be made: do I want to start a family or do I want to stay on the career track towards senior physician or even head of department?' Female physicians who opt for the family tend to abandon their specialist physician training or transfer to an off-hospital physician's practice where work schedules are more compatible with being a mother.

The Hamburg-based orthopaedist blames – among others – the lack of support for and by women: 'Men support each other more, be it in mentoring programmes or in networks. While indeed there are a few universities that offer mentoring programmes for female surgeons – albeit not specifically in orthopaedics and trauma surgery – we women are such a minority that we have the feeling we have to fend for ourselves.'

This is where the Junges Forum O&U – a forum for junior physicians in orthopaedics and trauma surgery – comes in. The group was founded about 20 years ago to represent the interests of the young generation of orthopaedists and trauma surgeons. Hättich is heading the chapter dealing with support for junior physicians and she is involved in issues surrounding training, family and career, science and interdisciplinary cooperation. While both men and women are targeted, the majority of members as well as leaders are women. A topic which is close to Hättich's heart is surgery during pregnancy – which has long been a taboo. 'Today, studies confirm that under certain conditions working in the OR is not associated with particular risks for pregnant women,' Hättich explains and ads that 'when no gas and x-rays are involved there is no reason to exclude pregnant surgeons. Many of my pregnant colleagues are indeed grateful for the opportunity to perform surgeries because thus they lose less time during their further training.'

In early 2021, another organisation was founded to provide a platform for female surgeons to exchange knowledge and experiences. 'Die Chirurginnen' – the female surgeons – arose from the women's desire to network, to learn from each other and to grow together.

Working as a team – on equal terms

Hättich wants the women to organise, to find ways to be more visible and to further their careers. Nevertheless: 'Our aim is to work in a team and on equal terms, no matter which time model. We want the team to function as a unit rather than being split into different groups with differing interests.' Annika Hättich herself has successfully taken the next step: as of 1 July she will be senior physician at her Hamburg hospital.

Introducing ATEM Mini Pro

The compact television studio that lets you create presentation videos and live streams!

Blackmagic Design is a leader in video for the medical industry, and now you can create your own streaming videos with ATEM Mini. Simply connect up to 4 HDMI cameras, computers or even technical equipment. Then push the buttons on the panel to switch video sources just like a professional broadcaster! You can even add titles, picture in picture overlays and mix audio! Then live stream to Zoom, Skype or YouTube!

Create Training and Educational Videos

ATEM Mini's includes everything you need. All the buttons are positioned on the front panel so it's very easy to learn. There are 4 HDMI video inputs for connecting cameras and computers, plus a USB output that looks like a webcam so you can connect to Zoom or Skype. ATEM Software Control for Mac and PC is also included, which allows access to more advanced "broadcast" features!

Use Professional Video Effects

ATEM Mini is really a professional broadcast switcher used by television stations. This means it has professional effects such as a DVE for picture in picture effects commonly used for commentating over a computer slide show. There are titles for presenter names, wipe effects for transitioning between sources and a green screen keyer for replacing backgrounds with graphics!

Live Stream Training and Conferences

The ATEM Mini Pro model has a built in hardware streaming engine for live streaming via its ethernet connection. This means you can live stream to YouTube, Facebook and Twitch in much better quality and with perfectly smooth motion. You can even connect a hard disk or flash storage to the USB connection and record your stream for upload later!

Monitor all Video Inputs!

With so many cameras, computers and effects, things can get busy fast! The ATEM Mini Pro model features a "multiview" that lets you see all cameras, titles and program, plus streaming and recording status all on a single TV or monitor. There are even tally indicators to show when a camera is on air! Only ATEM Mini is a true professional television studio in a small compact design!

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Implantation of cartilage or stem cells

Remarkable cartilage regeneration

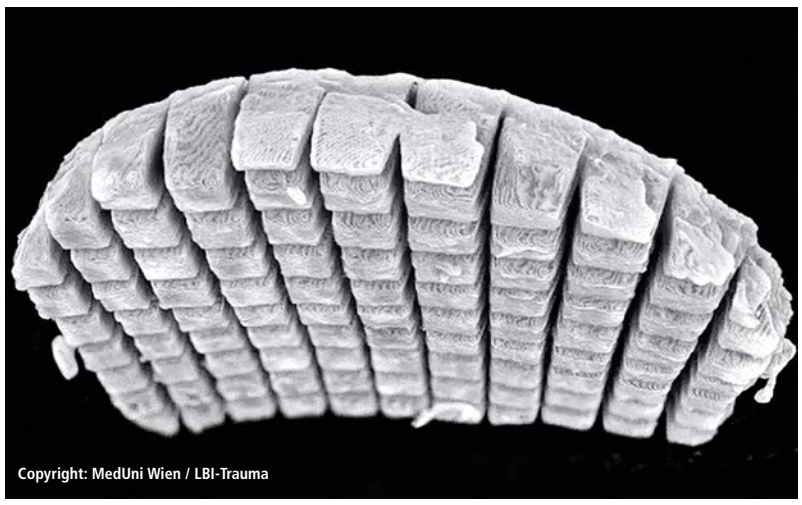
Report: Michael Krassnitzer

Joint cartilage usually regenerates very poorly. The matrix of cartilage (scaffolding) contains very few cells in deep layers. Moreover, joint cartilage is highly isolated: there are neither regenerative cells in the immediate vicinity that could migrate into the site of the defect and trigger repair, nor vessels that could transport regenerative cells to the cartilage. Unsurprisingly, researchers all over the world are experimenting with different approaches to transporting biomaterials to the joint to make cartilage repair more robust.

In pre-clinical trials a research team* at the Medical University Vienna (Department of Orthopaedics and Trauma Surgery, Division of Trauma Surgery) could achieve remarkably extensive regeneration of joint cartilage from cartilage matrix as biomaterial. The matrix used was harvested from surgery patients who had consented to have their tissue examined for this study.

All cartilage cells were removed from the donor matrix leaving native cartilage tissue consisting of collagen type II fibres und glycosaminoglycans. This material, called CartiScaff, is transported to the defective sites in the joint, to create an ideal environment for cartilage cells or stem cells.

'The challenge here is to insert native cells into the tissue,' explains Private Docent Dr Sylvia Nürnberger, the project leader. 'Cartilage cells are indispensable for cartilage repair,' she pointed out, because cartilage cells build collagen type II and have to respond to different types of stress. Cartilage matrix without cells would suffer from wear and tear over time. 'Cartilage cells keep the cartilage intact,' she explained. 'They are the maintenance crew of the cartilage.'



µCT scan showing a 3-D view of the laser incisions. The material is implanted tip-down, i.e. perpendicular to the defect. The (implanted) biomaterial covers the defect to the joint cavity

Laser opens the door for helper cells

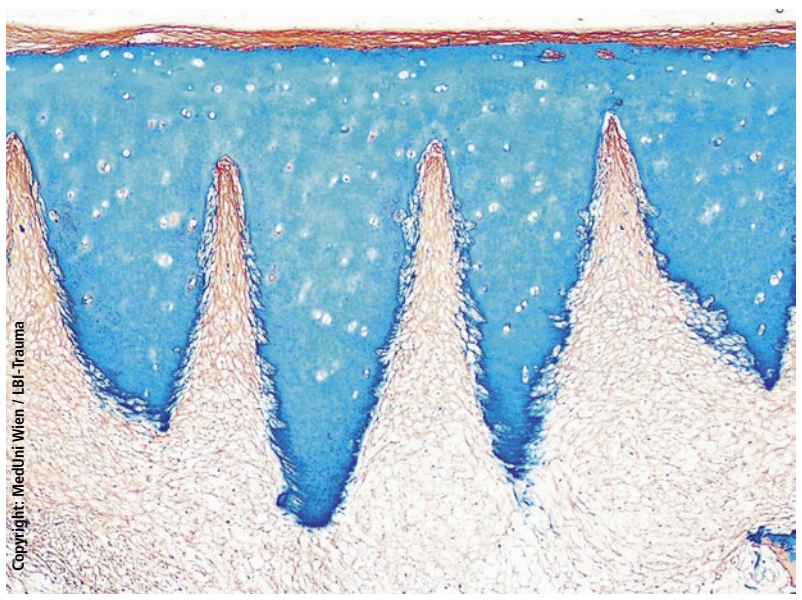
Laser beams have long been a surgical tool, e.g. to correct pathologies in the ear or eye. Nürnberger's team perforate the cartilage matrix with a laser beam to create an opening for the cells. Tiny grooves were engraved in the matrix, with high precision and all equal in size and distance. These served as access for the regenerative cells, which could thus migrate even in deeper tissue layers.

There are three ways to transport the cells to the matrix: either a hole is drilled to the bone marrow and the stem cells can enter the site of the defect, or the matrix and bone marrow harvested from the iliac crest are inserted into the joint in one go. The stem cells then develop into cartilage cells. The third option: the matrix is seeded with stem cells or cartilage cells prior to implantation.

The laser incisions offer another advantage: they provide the cartilage tissue with a high degree of flexibility so it can be more easily fitted onto the rounded surface of the joint bone – comparable to the flexibility of a concertina, Nürnberger observed. 'The cartilage tissue that grows in the grooves is of rather good quality considering that it's regenerated tissue.' Collagen II fibres are orientated perpendicular to the bone and, since the surface is created by the implanted biomaterial, it has the same structure as native cartilage. 'With the biomaterial being so similar to native cartilage, it can stay inside the defect as a part of the regenerated tissues. Alternatively, it can degrade and be replaced with new matrix,' Nürnberger explained, adding that follow-up studies will show how the implants develop over time.

* 'Repopulation of decellularised articular cartilage by laser based matrix engraving'. S. Nürnberger, C. Schneider, C. Keibl, B. Schädl, P. Heimel, X. Monforte, A.H. Teuschl, M. Nalbach, P.J. Thurner, J. Grillari, H. Redl, S. Wolbank. doi:10.1016/j.ebiom.2020.103196

Dr Sylvia Nürnberger is a researcher in the Department of Orthopaedics and Trauma Surgery, in the Trauma Surgery Division, at the Medical University of Vienna, Austria, where she heads the Tissue Regeneration group. Her research focus is biomaterials, chondrocytes and alternative regenerative cells (e.g. fat stem cells) in biological therapeutic substances.



Histochemical section of the implanted biomaterial. The tips are shown in blue; the gaps are filled evenly with neo-tissue (brown).

Low-cost tech for missed ge

Report: Mark Nicholls

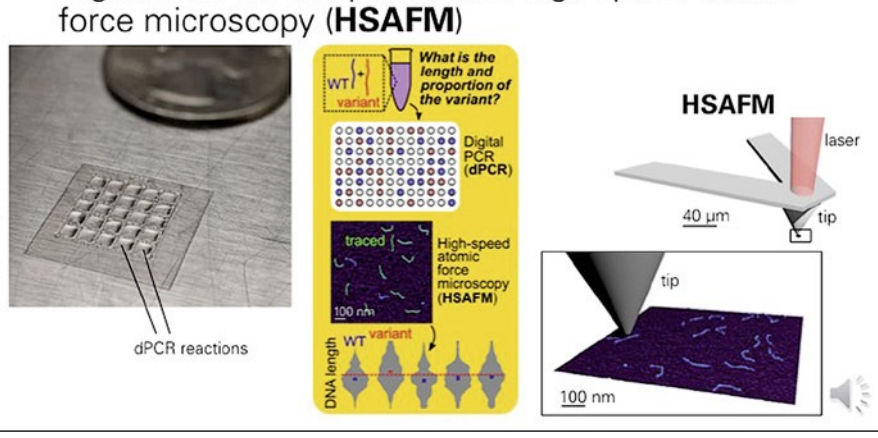
A new low-cost method targeting genetic mutations often missed by existing diagnostic approaches has been developed.

Researchers at Virginia Commonwealth University (VCU) in the United States noted that most rearrangement mutations implicated in cancer and neurological diseases fall between what can be detected by DNA sequence reads and optical microscopy methods.

The new technique combines digital polymerase chain reaction (dPCR) and high-speed atomic force microscopy (HSAFM) to create an image at a nanoscale resolution, which allows technicians to measure differences in the lengths of genes and identify these missing mutations.

Nanoscale resolution

Dr Jason Reed, an associate professor in the department of physics at the VCU College of Humanities and Sciences, said: 'Our approach is the first to combine dPCR with HSAFM to create an image with such nanoscale resolution that users can



EUROPEAN HOSPITAL
European Hospital Verlags GmbH
Theodor-Althoff-Str. 45,
45133 Essen, Germany
Phone: +49 (0)201 87 126 850
Fax: +49 (0)201 87 126 864
E-mail: info@european-hospital.com
www.healthcare-in-europe.com

Editor-in-Chief:
Brenda Marsh (BM)

Editorial team:
Wolfgang Behrends (WB),
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Correspondents

Austria: Michael Krassnitzer (MK), Christian Pruszinsky (CP)

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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: rm@european-hospital.com

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

Israel: Hannah Wizer, International Media Dep. of El-Ron Adv. & PR Co., Ltd., Phone: +972-3-6 955 367
E-Mail: ronin@netvision.net.il

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

Roxsy Mangiante
Phone: +1 21 469 48542
E-Mail: mangiante@european-hospital.com

Shaping better health and care

AI launches across the UK's NHS

Artificial Intelligence in healthcare is being launched across the United Kingdom via a major national project which already produces a range of innovations.

Developments were outlined during the online Intelligent Health conference in a presentation by Dr Indra Joshi, Director of AI at NHSX, a unit bringing together teams from NHS England and NHS Improvement, and the Department of Health and Social Care, to drive the digital transformation of health and care.

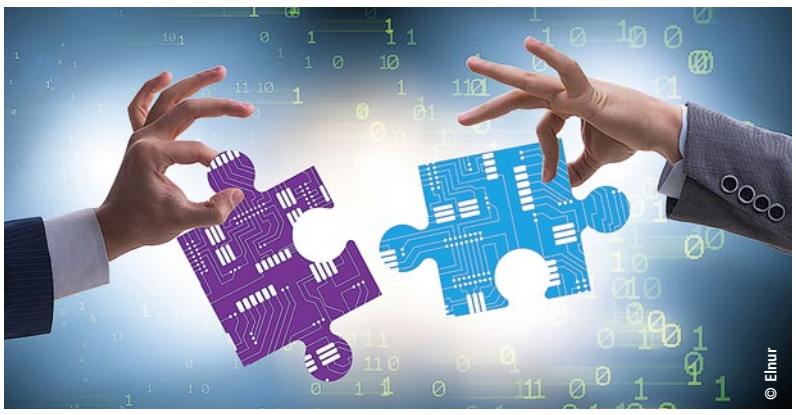
Core aims

In her presentation 'The NHS AI Lab – How the NHS is enabling the safe, ethical and effective adoption of AI in health and care,' Joshi explained that the AI initiative had three core aims: Digitise, Connect and Transform. 'We aim to level up the NHS and social care services to ensure they have a core level of infrastructure, digitisation and skills,' she explained.

This means joining services together through technology to allow health and care providers to share information and take a shared approach to procurement and planning, and then use the platform of a 'digitised, interoperable, connected health and care system' to deliver services more effectively.

Confidence in AI

With the AI Lab a 'focal point for accelerating AI technology' in the NHS, Joshi continued: 'We want to ensure we build a system that enables AI technology to be deployed and used on the frontline in everyday practice. To do that, we need to ensure the infrastructure works, and we need to work alongside the workforce and users of that technology.'



The NHS AI Lab is seeking to drive change by bringing AI technologies into use with access to high quality data sets, to encourage staff to understand AI benefits, and develop the expertise to use it. 'Clinicians and the public must have the confidence in the AI-driven technologies and systems they are using to use them to their full potential,' she added.

NHSX is working with professionals across health and adult social care to highlight where AI can make a difference, efficiently and safely. 'We're using experts across the field to ensure we get best tools, and also that it has all we want to see in clinical technology; efficiency, safety, and that it's working for the economy,' Joshi pointed out.

Delivery programmes

There are five delivery programmes: the AI in Health and Care Awards (with £140m for development and deployment of technologies from early stage to market-ready technologies); Skunkworks (a small team working with developers and technical experts on a well-defined problem towards delivery); AI Regulatory Programme; AI Ethics Initiative; and Imaging. These are underpinned by supporting programmes that ensure different outputs are embedded strategy and policy, collaboration and engagement, and programme management. To win funding awards for projects, the technical feasibility of a product or concept needs to be demonstrated and undergo real-world testing and prototyping towards adoption.

Early-stage technologies

Examples of early-stage technologies include SamurAI, which uses AI to combine historical data for patients prescribed antibiotics with the findings of specialists in infections as they review prescriptions; and Woubot, which is automated software for wound clinics. A more advanced project is focusing on automating early lung cancer detection.

'It's not just about deploying those technologies,' Joshi added. 'It's about evaluating them and making sure they do what we need them to do on the frontline, but also working with commissioners and procurers to understand how we add longevity to this.'

Joshi also highlighted the Data Lens project, which helps to address the issue of the large amounts of NHS health data held on incompatible databases and brings it together to give wider access.

Next step

NHS AI Lab, she said, has initiated a programme with regulators to enable a clear, safe, and ethically robust regulation ecosystem for AI-driven technologies in health and care, while also striving to counter any inequalities that may arise from AI deployment.

As part of the imaging stream, in response to the Covid-19 pandemic, NHSX worked with a number of institutions to develop the National Covid-19 Chest Imaging Database containing X-ray, CT and MRI images for clinical use. 'The NHS AI Lab is investigating building a National AI Medical Imaging Platform to safely and securely collect and share imaging data on a national scale, helping AI screening technologies to be developed and tested more quickly,' she explained.

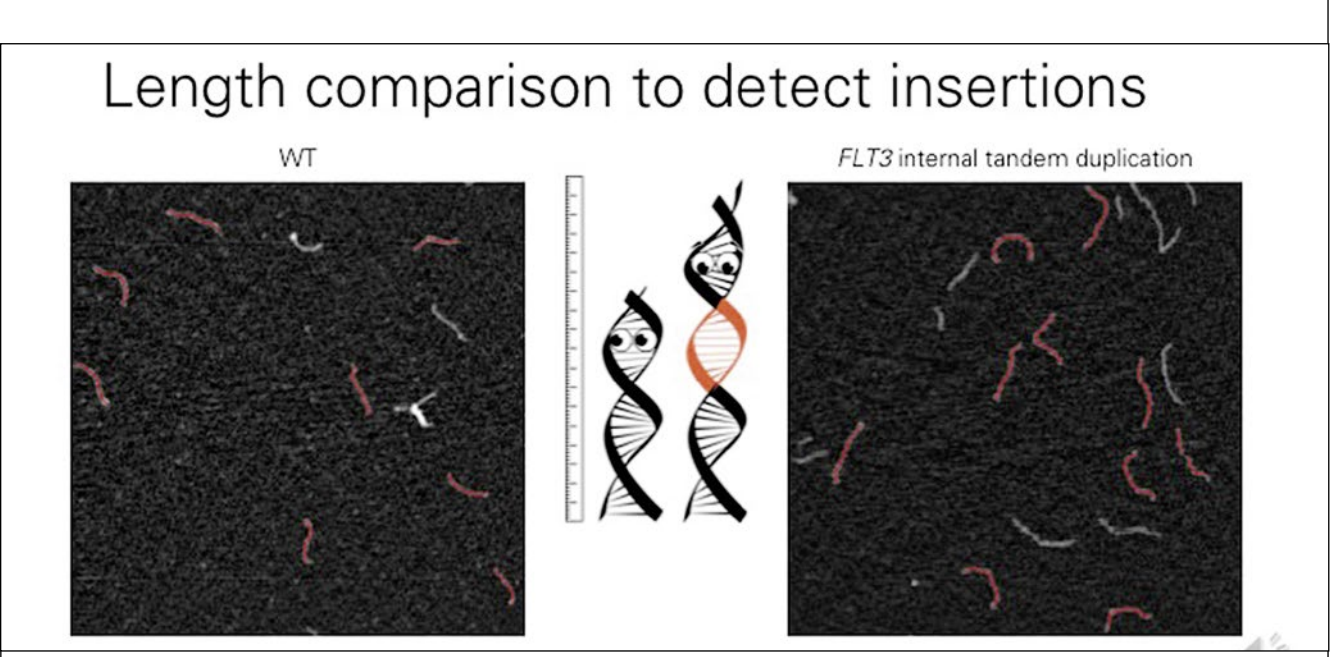
Future plans for AI in health and social care in 2022 include the launch of the National AI Strategy for Health and Adult Social Care, further awards for projects, ethical AI research, and clarifying regulation protocols.

(MN)

Emergency medicine specialist **Dr Indra Joshi** is Director of AI for NHSX, overseeing the NHS AI Lab project. Her experience extends across policy, governance, digital health and marketing, national project strategy and implementation. She is also the Clinical Director of One HealthTech – a network that champions and supports under-represented groups in health innovation, particularly women.

Cancer and neurological diseases

nique enetic mutations



measure differences in the lengths of genes in a DNA sequence. These variations in gene length, known as polymorphisms, can be key to accurately diagnosing many forms of cancer and neurological diseases.'

The dPCR uses the DNA polymerase enzyme to exponentially clone samples of DNA or RNA for further experimentation or analysis. The sample is then placed on an atomically flat plate for inspection using HSAFM, which drags a sharp microscopic stylus across the sample to create precise measurements at a molecular level.

'Our technique,' he continued, 'uses easily accessible and affordable optical lasers, like those in a DVD player, to process samples at a rate thousands of times faster than typical atomic force microscopy.'

From there, the team developed computer codes to trace the length of each DNA molecule. Dr Reed said genetic mutations can be missed by existing diagnostic approaches as DNA-length polymorphisms are difficult to diagnose due to their repetitive or variable elements. For example, within the FLT3 gene, internal tandem duplications (ITDs) range from <30 bp to >200 bp (base pairs) in length and are associated with poor prognosis in acute myeloid leukemia.

Strong interest

The VCU team believe their approach could have applications in a number of areas of medicine. Dr Reed explained that many forms of cancer and inherited neurological diseases involve insertions or deletions of DNA material that can be difficult to characterise with DNA sequencing.

The current standard test for diagnosing FLT3 gene mutations is the Leukostrat CDx FLT3 mutation assay.

'Our approach shows variant allele fraction, which the current approach does not, and we are able to stitch together multiple images to show the lengths of extremely long molecules,' he added. 'The speed, low cost, and flexibility of dPCR–HSAFM to detect long, repetitive insertions (>200 bp) make it an attractive alternative to sequencing or other more costly assays in the clinical diagnosis of length polymorphisms.'

Clinicians and researchers who work on neurological disorders like Huntington's disease, Fragile X syndrome, movement disorders such as Parkinson's, have already expressed interest.

Fast and cost-effective

For patients, the new approach could lead to more accurate diagnoses and the potential to diagnose future diseases distinguished by DNA length polymorphisms.

But a big appeal is that it is fast and cost-effective and at less than $1 per sample to scan as dPCR is a common and affordable process for amplifying genetic material for analysis capable of being performed in most clinical laboratories.

'We have made HSAFM analysis of the sample affordable by adapting common optical lasers and creating computer code to trace the DNA molecule,' said Dr Reed. 'If commercialised, this process could offer a significantly cheaper alternative for detecting and diagnosing DNA length polymorphisms.'

He also emphasised that the method does not have any more complexity than a PCR assay and can easily be performed by most lab technicians.

As this technology will allow for more accurate and affordable diagnoses of genetic diseases, the next step for the VCU team is to test the technology in other settings where DNA structural mutations are relevant

Dr Jason Reed is associate professor in the Department of Physics at the Virginia Commonwealth University College of Humanities and Sciences in Richmond, Virginia, and a member of the Cancer Biology research program at VCU Massey Cancer Center. His current research focuses on bio-mechanical systems, microfabrication and surface metrology for biological material characterisation.

Preventing blood cu

Specimen diversion devices l

Blood cultures are among the most important laboratory tests a patient can have, especially to diagnose serious infections. Contamination is a constant concern – a patient could be misdiagnosed due to a false-positive test. Even with the most diligent quality control measures to limit contamination, including rigorous skin disinfection, contamination may occur from skin fragments colonised with bacteria that are dislodged with venipuncture. However, when initial specimen diversion (ISD) techniques are used, potential rates of contamination from skin fragments can drop to near zero.

The effectiveness of using an ISD device to reduce blood culture contamination (BCC) rates and a new national movement in the USA to reduce the BCC hospital benchmark to 1%, or less, were topics of an April 2021 *Dark Daily* webinar featuring two experts in infection control.

They discussed the impact that an ISD device that separates the initial blood draw from the laboratory samples can have in significantly reducing BCC rates in hospitals, referencing findings of numerous clinical trials.

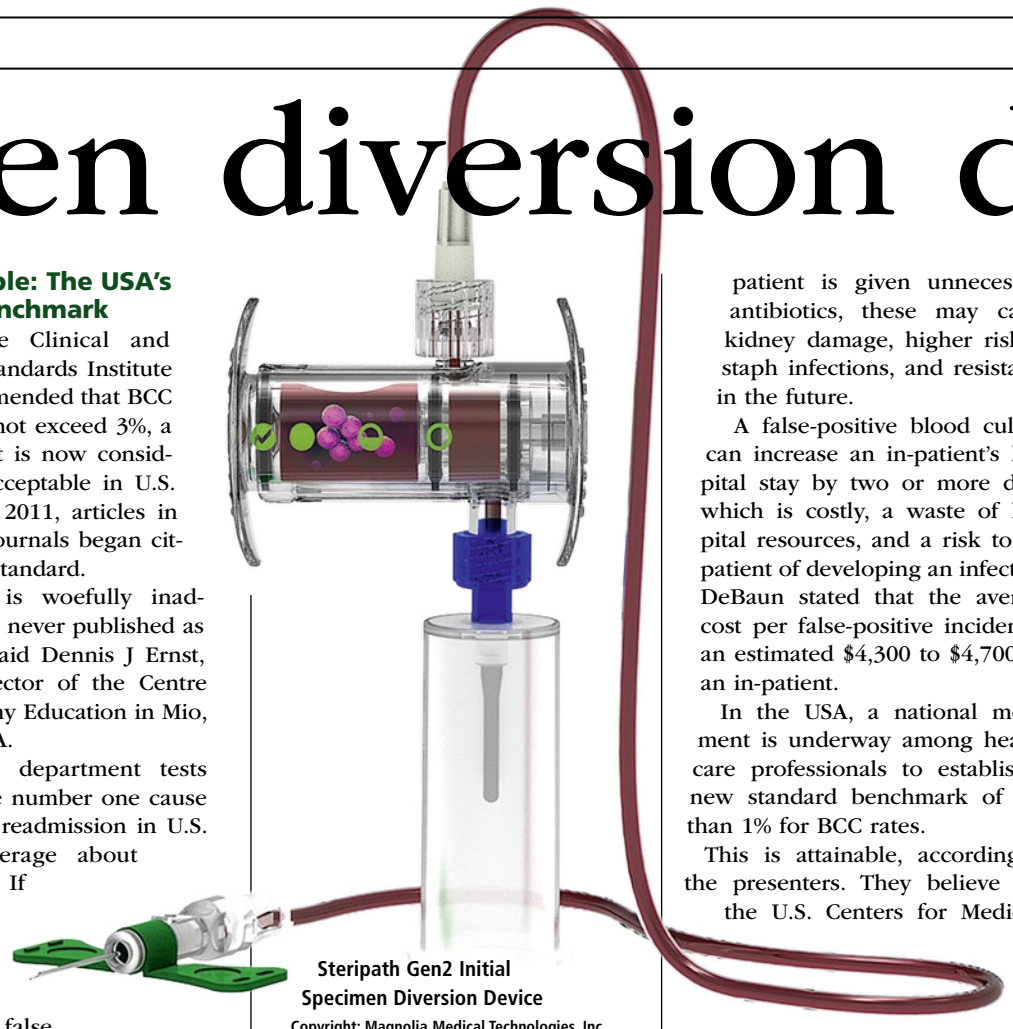
Unacceptable: The USA's 3% BCC benchmark

In 2007, the Clinical and Laboratory Standards Institute (CLSI) recommended that BCC rates should not exceed 3%, a threshold that is now considered to be acceptable in U.S. hospitals. By 2011, articles in peer-review journals began citing this as a standard.

'This rate is woefully inadequate. It was never published as a standard,' said Dennis J Ernst, founding director of the Centre for Phlebotomy Education in Mio, Michigan, USA.

'Emergency department tests for sepsis, the number one cause of death and readmission in U.S. hospitals, average about 8% positive. If you factor a 3% contamination rate, 40% of these are false positives,' said Barbara DeBaun, RN, of Cynosure Health in San Francisco.

'As a nurse,' she added, 'I cannot think of any other test performed in a hospital that is incorrect 40% of the time.'



Steripath Gen2 Initial Specimen Diversion Device

Copyright: Magnolia Medical Technologies, Inc. Seattle, USA.

When a patient has a false-positive test for sepsis the implications are huge, she pointed out. If a patient is given unnecessary antibiotics, these may cause kidney damage, higher risk of staph infections, and resistance in the future.

A false-positive blood culture can increase an in-patient's hospital stay by two or more days, which is costly, a waste of hospital resources, and a risk to the patient of developing an infection. DeBaun stated that the average cost per false-positive incident is an estimated $4,300 to $4,700 for an in-patient.

In the USA, a national movement is underway among healthcare professionals to establish a new standard benchmark of less than 1% for BCC rates.

This is attainable, according to the presenters. They believe that the U.S. Centers for Medicare and Medicaid (CMS) should make this a quality measure and reportable.

It is imperative for hospital healthcare providers to rigorously practice and enforce proven techniques and quality control measures associated with BCC prevention. These include skin disinfection, strict aseptic practices and quality control, the use of a pre-packaged blood culture kit, and ample education and training. 'But, when a hospital is doing everything right, contamination may still be caused by skin fragments. Active diversion of the initial 1.5 to 2.0 mL of blood using a closed system has been repeatedly clinically proven to reduce BCC,' Ernst said. 'Manual diversion to a waste tube will not solve the problem as effectively. In the best case-controlled clinical study scenario, the lowest published contamination rate achieved was 2%.' uality measure and reportable.

Reducing BCC rates

Use of a pre-assembled, sterile blood culture system (Steripath Initial Specimen Diversion Device, Magnolia Medical Technologies) designed to divert and separate the initial 1.5 to 2.0 mL of blood from the rest of the sample, combined with rigidly enforced quality control measures, can reduce BCC rates to 1% and less.

This device, which is U.S. FDA approved, is preassembled and ster-

Mass spectrometry

Skin swabs can detect Covi

Skin swab samples analysed using mass spectrometry could be used to detect Covid-19 in patients, according to research conducted at the University of Surrey in the UK.

Current Covid-19 testing is via a polymerase chain reaction (PCR) test, which involves taking a swab of the back of the throat and inside the nose, but the team from Surrey – working with Frimley NHS Trust and the Universities of Manchester and Leicester – have used sebum samples from the outer layers of skin (stratum corneum) to identify the presence of Covid-19.

They collected samples from 67 hospitalised patients – 30 who had tested positive for Covid-19 and 37 who had tested negative – by swabbing skin between the shoulder blades. This area of the body is rich in sebum, the oily, waxy substance produced by sebaceous glands.

Samples were then analysed using liquid chromatography (to separate the lipids) and mass spectrometry (to identify the lipids). The Partial Least Squares Discriminant Analysis (PLSDA) statistical modelling technique was used to differentiate between the Covid-19 positive and negative samples. Patients with a positive Covid-19 test had lower lipid levels – or dyslipidemia – than those with a negative test.

Study co-author Matt Spick said: 'The test differentiates between positive and negative Covid-19 results by looking at sebum lipids in the outer layer of skin. 'We found that participants infected with Covid-19 had markedly reduced levels of many triglycerides and ceramides in particular. Although no single lipid gave a definitive signal, by looking at the overall lipid profile through multivariate machine learning, we could differentiate between positive and negative results.'

Sebum sampling

The team believe sebum sampling has the potential to support diagnosis and prognosis, as well as for investigation into the impact of Covid-19 on the host metabolism, by looking at what the virus does to patients, rather than looking for the virus itself. A challenge faced by researchers was that comorbidities also dysregulate the skin, making it difficult to differentiate between Covid effects and conditions such as Type 2 Diabetes. However, this was addressed with medication and additional health conditions factored in.gative results.'

Differentiating lipids is a challenge

'We controlled for this by matching comorbidities,' added Mr Spick, 'for example, looking at the difference between Covid-19 positive and negative within the subgroup of participants with T2DM. We found that when controlled for comorbidities our model was 82% accurate.'

In addition, with thousands of different lipids present in the human body, differentiating between them proved a further challenge.

However, co-author Dr Melanie Bailey explained: 'Mass spectrometry lets us identify the individual lipids, both by accurate molecular mass and also by breaking the molecule apart and identifying characteristic fragmentation patterns.'

PCR remains the gold standard in Covid testing in terms of accuracy, and there is no suggestion that sebum-based tests can replace them, but certain researchers believe sebum swabs may provide an alternative, although they acknowledge the test is not yet suited to clinical settings. At present they think the work is more likely to inform research into skin health and how this may be influenced by infection. Dr Bailey said: 'The most obvious implication of our findings is that skin can be added to the list of organs that are dysregulated by Covid.

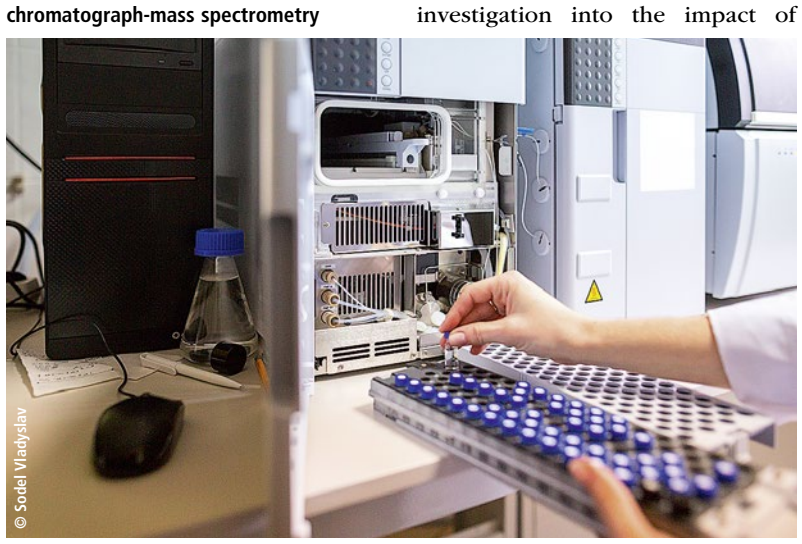
Researcher Mike Wilde is processing an extracted gauze sample ready for analysis.

Understanding skin health

Another feature of Covid-19 is the range of symptoms that those infected may present with. We do not yet fully understand how this variation might translate to skin, but it does appear that the reduction in sebum triglyceride and ceramide levels is a consistent feature across the population that we sampled. 'More broadly, understanding how diseases interact with other comorbidities in influencing the metabolism of the stratum corneum can only help us understand skin health.'

The work is one strand of research into skin health as a diagnostic tool, with work at the University of Manchester, for example, looking at how sebum sampling followed by mass spectrometry can be used to diagnose Parkinson's disease. Because the skin is so rich in lipids,

A laboratory scientist prepares samples for high-performance liquid chromatograph-mass spectrometry



© Sodel Vladyslav

lture contamination

lower BCC

ile. After actively diverting potentially contaminated blood, it collects cultures through a second flow path, creating a closed vein-to-bottle collection system.

Researchers at the University of Nebraska Medical Center in Omaha conducted the first clinical trial of the Steripath device in 2016, reporting their findings in Clinical Infectious Diseases. Professor Mark E Rupp MD and colleagues collected 1,808 blood cultures from 904 emergency department patients during a six-month time period. Each patient had two blood draws, one with the standard method and one with the ISDD.

They reported a positive rate of 8.4% among the patients. The contamination rate using the ISDD was 0.21% compared to 1.8% for the standard method.

The phlebotomists who used the ISDD reported it was easy to use. It offered the advantages of being able to easily draw additional tubes of blood and eliminated the need to transfer blood from a syringe to blood culture vials.

The presenters discussed 18 additional clinical studies using the ISDDs, all of which achieved at least a 75% reduction of BCC. One of the most impressive was a 120-day hospital-wide phlebotomy study conducted at Stanford University Hospital to compare standard blood culture collection methods with the use of ISDD.

This 2019 clinical trial produced dramatic findings. None of the nearly 4,500 collections with ISDD were contaminated, achieving 0%. By comparison, the BCC rate by nursing staff using standard methods was 1.98% and 3.15% by phlebotomy.

Magnolia Medical Technologies plans to launch the Steripath ISDD product portfolio in the European Union a and United Kingdom markets in the near term, according to Bob Gerberich, the company's chief commercial officer. (CK)


© Kateryna Kon

Sepsis: 3D illustration with rod-shaped bacteria, red blood cells and leukocytes

d-19

Dr Melanie Bailey is a Reader in Chemistry at the University of Surrey, and is currently working on a EPSRC funded fellowship.

Matt Spick is a post-graduate researcher at the University of Surrey within the Bailey research group.

and also because sebum is non-invasive and quick to sample – and can be sampled in a home setting – the Surrey team believe the method shows promise for diagnostics and monitoring of Covid-19.

'Our study suggests that we may be able to use non-invasive means to test for diseases such as Covid-19 in the future,' Bailey added. (MN)

AI algorithm reads patterns of Covid-19 infection in blood

‘Barcode’ brings quicker test results

Report: Madeleine van de Wouw

When patients are admitted to a hospital emergency room (ER) it is immediately vital to determine whether s/he has Covid-19. However, with a regular PCR test a result can take up to a few hours. Thus, initially, the patient must be isolated. During the height of the corona pandemic last year, researcher Ruben Deneer from Eindhoven University of Technology (TU/e) and clinical chemist Arjen-Kars Boer from the Catharina Hospital were asked whether they could find a quicker way to rule out Covid-19. The answer was ‘yes’.

‘During the first period of Covid-19 no quicker PCR tests were available; results sometimes took up to four hours,’ Boer explained. ‘Now there are faster tests on the market, but they are expensive – in the Netherlands about €110 per test. We knew that patients admitted to the emergency room have their blood taken as standard for a so-called quick scan. The blood is tested for as many as 30 different values. So we wondered if an infection might be visible in the blood, appearing as a sort of recognisable barcode that is characteristic of Covid-19.’

The researchers worked on that idea and their studies showed that, with the help of a calculation algorithm, it was indeed possible to show these changes in the blood. This led to the CoLab score. Unlike a PCR test, which indicates the presence of virus particles, the CoLab score analyses the changes the virus causes in the blood. Those changes are present even before a patient notices or knows that he or she is infected. The CoLab analysis rules out the signs of an infection so a PCR or LAMP test is only necessary when infection cannot be ruled out.

CoLab screening does not replace a PCR test but is an additional tool for quick initial Covid-19 screening and is – with an accuracy of almost a hundred percent on the absence of the ‘barcode’ in the blood – extremely suitable for application in the emergency room. There are several advantages: expensive PRC-tests are needed less often and, because the results are back within an hour, patients with a negative result can leave isolation quickly. Also, the medical staff will know in a short time frame whether they can approach the patient without extensive personal protective equipment.

How the test score works

The CoLab score is software based on an artificial intelligence (AI) algorithm. With this algorithm, patterns – the ‘barcode’ that indicates a Covid-19 infection – are recognised in the blood. If no patterns are present, an infection is virtually excluded.

‘During the search for that barcode’, Boer explained, ‘the data of more than 10,000 patients entering the emergency room were digitised to develop the algorithm. The data were both from infected and non-infected people. To analyse this data manually would be an almost impossible, painstaking and laborious process, so we used AI to draw the right conclusions from those data. ‘We looked for the smallest set of results that makes a good prediction and we managed to identify ten laboratory tests that together form the best predictors of Covid-19.’

Results are expressed as a cut-off value from 0 to 5 – a value used to determine whether a result is abnormal. The number indicates the values found. With 0, 1 and 2, the chance of corona is almost zero. At 3, 4 and 5, a subsequent PCR test is needed to demonstrate infection.

Because a PRC test is not a routine procedure if people do not show symptoms, missing a very small portion of patients has more consequences when the prevalence is high rather than low. The cut-off value, the value used when a result is called abnormal, is therefore prevalence dependent.

Arjen-Kars Boer PhD, who has worked in the Catharina Hospital, in Eindhoven since 2006, is listed in the European register of specialists in laboratory medicine, as well as an endocrinologist. Besides this specialty he is known for using big data solutions in clinical chemistry, bariatric surgery, cardiology, and emergency medicine. He also trains various laboratory specialists and co-promotes several PhD students.

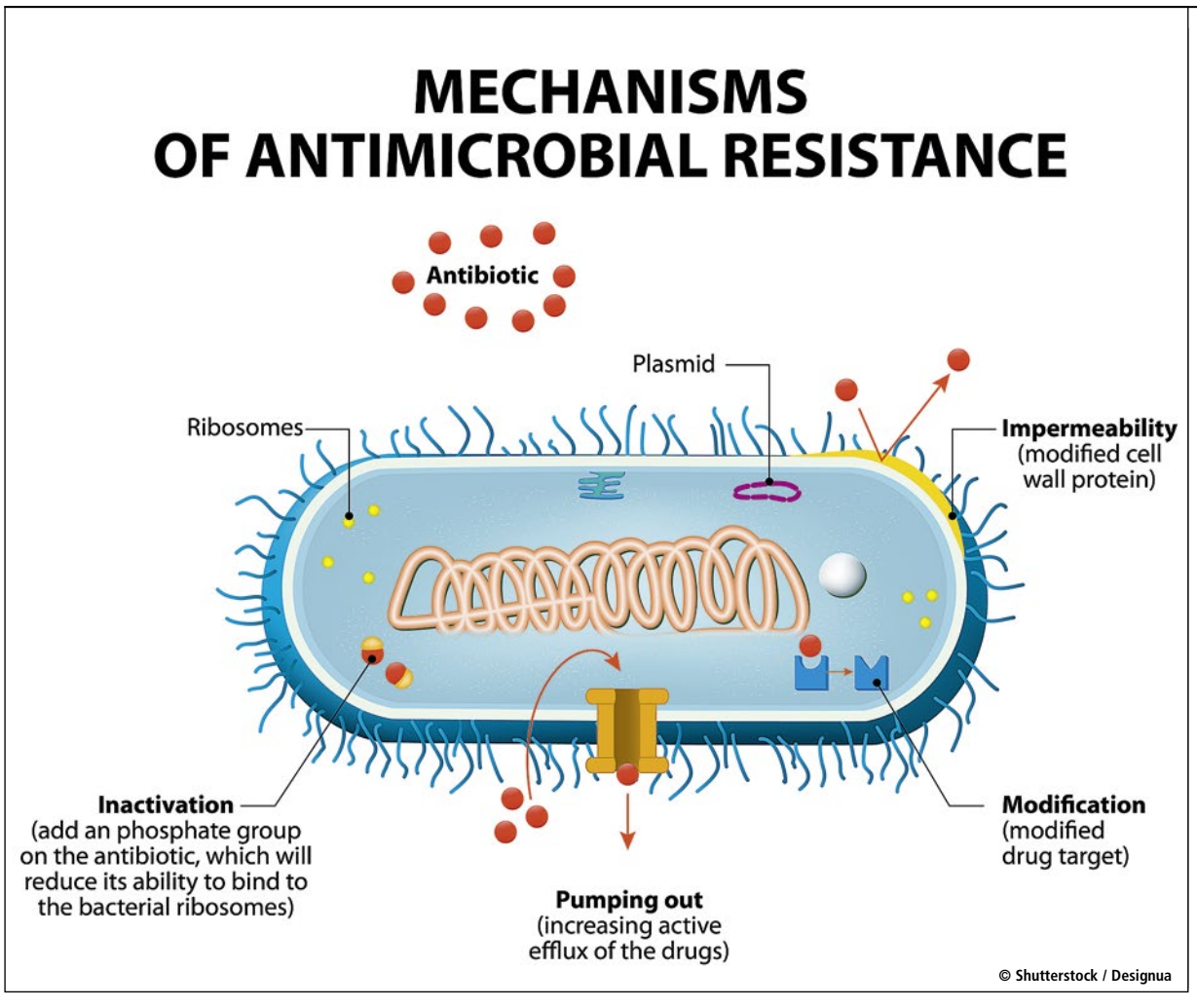
A €150,000 grant

Recently these Dutch researchers received a grant of €150,000 to accelerate the introduction of the CoLab score in European hospitals. ‘That’s quite a challenge,’ Boer observed. ‘Every hospital carries out different tests in the emergency room. We are therefore going to make our CoLab score ‘ smarter’ so that it can be used in every hospital in Europe. We’re working hard on that along with the company Gaston Medical. Every hospital in Europe should be able to use it very simply: plug and play. It’s easy if they already use Gaston Medical’s software, but a connection must also be sought for hospitals that use other software.’

The grant comes from the COVID-X programme which aims to beat Covid-19 with data solutions. There were 112 applications submitted and only 15 were honoured, including one from the Netherlands.

Funded by the EU within the Horizon 2020 programme, the Covid-X program aims to make data solutions ready for the European market in nine months.

Speeding up diagnostics to detect antibio



New goals w continuous i

Infectious disease diagnostics are notoriously slow. The gold standard for laboratory diagnosis of bacterial and fungal infection involves growing the pathogen from a clinical specimen – an overnight event, or even longer. The healthcare focus is on improving the use of antibiotics for better patient outcomes and reducing the environmental pressures that drive antibiotic resistance. To impact antibiotic use, diagnostic tools need to be faster without compromising the performance characteristics necessary for definitive therapy decisions – a lot to ask, but this is a new era of innovation and companies are driven to fill this need.

Antimicrobial susceptibility test results enable definitive treatment decisions. This test traditionally takes three or more days from specimen collection to result, but technology is chipping away at the timeline. Molecular tests can identify the pathogen and detect resistance mechanisms from a positive blood culture in less than two hours. Knowing the infectious aetiology is powerful. This information alone can significantly reduce the time to de-escalate empiric therapy decisions to more targeted therapies *[1].

Detecting resistance mechanisms is most helpful for Gram-positive bacteria where a limited number of acquired resistance mechanisms are responsible for the most important phenotypes, like *mec*A in *Staphylococcus aureus* and *van genes* in *Enterococcus*. Assays to detect resistance mechanisms in Gram-negative bacteria can provide early evidence of what drugs will not work, but failure to detect a resistance mechanism is insufficient evidence to de-escalate antibiotics because many acquired resistance

Researchers develop aptasensor swabs

Five-minute MRSA detection

The international research team from Saudi Arabia, Germany and Jordan

An international research team from Saudi Arabia, Germany, and Jordan has developed a novel pathogen aptasensor swab designed to qualitatively detect, within five minutes, any methicillin-resistant *Staphylococcus aureus* (MRSA) contamination that remains in a hospital isolation room or other surface following standard decontamination and cleaning.

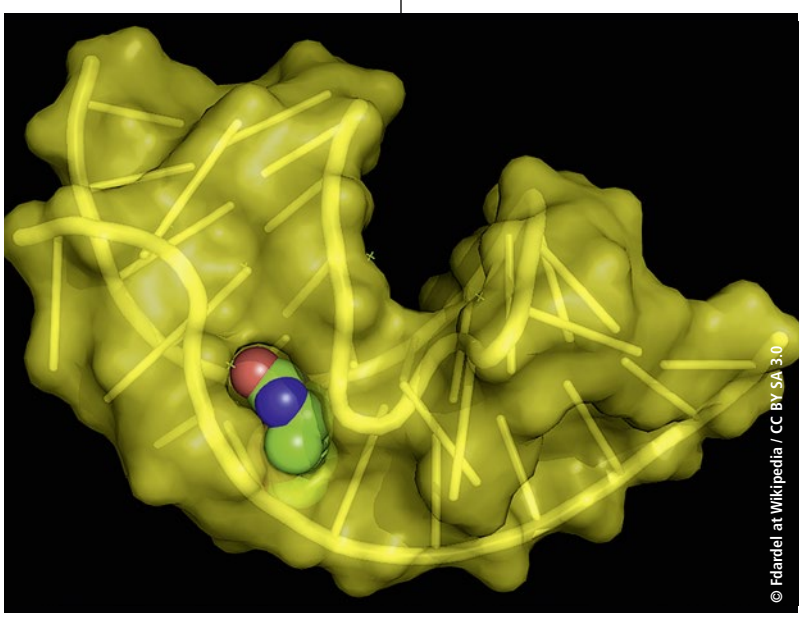
Aptasensors are small, synthetic nucleic acid-based affinity binders with high selectivity and specificity to a specific target. They are easy and inexpensive to mass produce and have very little variation from batch-to-batch. 'Our engineered aptasensor targets MRSA selectively and does not bind to any other bacterial pathogen on a multi-contaminated surface,' explain the researchers in *Biosensors and Bioelectronics* (issue: 15/3/2021).

'We believe the engineered aptasensor holds great promise for the rapid and multiplexed detection of MRSA and other life-threatening infectious pathogens in the hospital environment.... It offers a means to rapidly detect residual viable bacteria, such as MRSA, on frequent touch surfaces that may have survived after being cleaned.'

The researchers explain that aptamers, oligonucleotide or peptide molecules that bind to a specific target molecule, have important advantages compared with antibodies. In addition to being easier and cheaper to mass produce or modify, and without batch-to-batch variation because they are synthetically produced.

They can be incorporated into assays that need heating because they have better thermal stability. Additionally, they can better detect small, poorly immunogenic biomolecules independent of carrier molecules.

Structure of the biotin RNA aptamer (yellow) complexed with biotin – created with pymol using PBD entry 1F27



MRSA contaminated swabs turned from white to blue

For the validation study, principal investigator Professor Mohammad Zourob PhD, and co-researchers, prepared sterile cotton swabs that were infused with MRSA-targeting aptamers.

The swabs were placed in tubes containing MRSA of differing concentrations and a sterile control tube for three minutes and then washed with a phosphate-buffered saline (PBS) solution. Testing was also performed on glass slides and plastic containers, but no absorbable surfaces.

Swabs contaminated with MRSA changed from white to blue, with more vivid colour correlating with greater levels of MRSA. Qualitative and quantitative analysis showed that MRSA was detected in the concentration range of 10^2 to 10^8 CFU/ml.

Because the cotton swab serves as both a collection and concentration tool, it eliminates the need to be sent to a lab for both enrichment and culture.

The rapid turnaround time enables users to identify MRSA rapidly, before another patient or staff come in contact with the contaminated surface and to prevent spread and cross-contamination. It also is a quality control tool to show if more stringent environmental cleaning protocols are needed.

Zourob told *European Hospital* that real-world validation is being planned in several hospitals in Saudi Arabia.

'We'll conduct this study on actual patient samples in hospital environments. We expect this validation procedure to take approximately six months.' (CEK)

tic resistance

von through nnovation

mechanisms and various chromosomal mutations can result in clinically significant phenotypic resistance. Sequence-based technologies can also identify pathogens, detect acquired resistance mechanisms, chromosomal mutations, and capture detailed isolate epidemiological features to map transmission dynamics (e.g., data to identify a common source of transmission).

Sequence-based assays are in development for clinical laboratories, but there are practical concerns like whether the price and complexity of testing are suitable for clinical laboratories. There is also a concern that molecular tests are limited to detection of known resistance and cannot detect resistance that is new or poorly characterised at the molecular level. With this limitation, how can molecular test results provide enough information to improve patient outcomes and antibiotic use?

Overnight phenotypic antimicrobial susceptibility testing is the gold standard test for definitive therapy decisions. Rapid AST systems have come to market, and more are in development. These aim to test positive blood cultures and the time to result ranges from two to six hours for the most common bacterial pathogens. The following three examples are rapid AST systems that use very different technology.

- The Accelerate Pheno (www.acceleratediagnostics.com) systems will identify pathogens and perform rapid AST for the most common pathogens in positive blood culture and this is available in multiple markets. The method uses microscopic examination of cells in the presence of antibiotics as the detection method. The time to result for ID and AST is about seven hours. Over time, this system's performance was improved to increase MIC accuracy and adding new drugs for reporting *2. The throughput is one specimen per instrument and the cost is greater than $100/specimen.

Detecting volatile organic chemicals from bacteria during growth

New to the European market is the Specific Diagnostics Reveal technology (www.specificdx.com). This test looks like a conventional MIC panel, but a lid is placed on the panel. This lid includes a small molecule sensor array to detect volatile organic chemicals produced by bacteria during growth. Changes in the array detection indicate growth or no growth in each well, thereby producing a MIC. The time to result is 4-6 hours and the stackable instrument can test two panels at a time. The Reveal assay is in development for the United States market.

- Flow cytometry, like the FastInov assay, is another detection method, which may be the fastest technology with results available in about two hours (www.fastinov.com). The throughput is lower because a single instrument queries each well of a microtiter plate.

A single specimen can take 30 or more minutes to read. However, with an overall time to result of two hours, this throughput may work well. This test is still in development.

These are just three examples. There is so much innovation in progress that one or more of these systems is sure to impact on medical practice significantly. Rapid phenotypic AST for positive blood culture is likely to become the standard of care. The winning tests will have an accuracy rate that can drive a definitive therapy solution in a single work shift and replace overnight AST. Where does the pathogen identification come from? The most likely answers are Maldi-TOF or molecular systems. Workflow and compatibility with rapid AST systems will determine each laboratory's solution.

The next question worth answering is: Will rapid phenotypic AST replace all conventional AST? This would be an excellent win for patient care, but some technical breakthroughs are needed. Continuous innovation can get us to the goal.

Dr Jean Patel joined Beckman Coulter after nearly seventeen years at the Center for Disease Control (CDC) in the Antimicrobial Resistance Reference Laboratory and the Office of Antimicrobial Resistance.

Before this she was Assistant Professor of Pathology and Laboratory Medicine, and Assistant Director of Clinical Microbiology at the University of Pennsylvania.

*1 (Banerjee R, Teng CB, Cunningham SA, et al. Randomised trial of rapid multiplex polymerase chain reaction-based blood culture identification and susceptibility testing. Clin Infect Dis 2015; 61:1071–80)

*2 (Sikorski A, Shamsheyeva A, Gamage D, Oppermann N, Bhalodi AA, Humphries RM. 2021. Performance of antipseudomonal β-lactams on the Accelerate PhenoTest BC kit against a collection of *Pseudomonas aeruginosa* isolates. J Clin Microbiol 59:e01781-20)

Identifying cancers in symptomatic younger women

DBT shows superiority

Report: Cynthia E. Keen

Digital breast tomosynthesis (DBT) increases detection of breast cancer in symptomatic women under the age of 60, especially in dense breasts. A large, multi-institutional study conducted in the United Kingdom to compare the sensitivity of full-field digital mammography (FFDM), DBT, and FFDM plus DBT supports findings of two similar published studies, both conducted in China within the same time frame.

Much research has been carried out to confirm the increased cancer detection capabilities of DBT technology as a breast cancer screening tool, but very little has been undertaken to evaluate and quantify the accuracy of DBT in symptomatic patients.

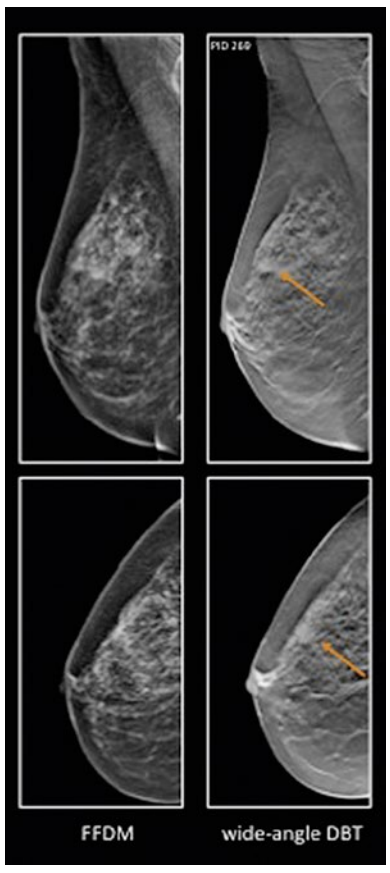
The rigorous double-blind retrospective study, led by researchers at the University of Dundee in Scotland, utilised images acquired from a different mammography system than that used by the Chinese researchers. Because DBT technology differs significantly, findings of a single-vendor study do not necessarily apply when other equipment is used. This new study published online in the *British Journal of Radiology* complements the research in China with similar data for a European population.

The participants included 300 women with symptoms or signs of breast cancer representing a 20% or greater likelihood of malignancy following a clinical examination. They had both FFDM and DBT at five UK hospitals' specialist breast centres within a five-year period, starting in 2011. All sites used MAMMOMAT Inspiration units from Siemens Healthineers. Images were acquired at all sites. The study cohort included all 152 women recruited who were diagnosed with cancer, plus a randomised selection of half of the 209 recruited women with benign lesions and half of the 76 women with normal breasts.

The MAMMOMAT Inspiration from Siemens Healthineers is equipped with 50° Wide-Angle Tomosynthesis and offers high-quality results using up to 30% less dose in FFDM, with MoodLight and OpComp personalised compression to improve patient experience.

The mean age was 47 years, but some participants were as young as 24 years. None of the patients had breast implants, as DBT had not yet been approved for use. Masses, at 89%, were the dominant radiological feature in malignant breasts, and 85% were unifocal tumours. The majority of cancers were Grade 3 or 2 invasive ductal tumours (42% and 33% respectively) and invasive lobular carcinoma (12%). Ductal carcinoma *in situ* (DCIS) represented only 1% of the 157 cancerous breasts.

Twelve breast imagers experienced with Siemens DBT independently analysed a batch of 50 cases for each category, for 150 readings, two readers per batch. Each batch had similar distributions of different aged patients, and cancerous, benign, and normal cases. To replicate real-life practice conditions, they were provided with the patient's age and clinical records.



Case 1. A symptomatic woman was screened with both FFDM and wide-angle digital breast tomosynthesis. Imaging revealed an 8 mm spiculated mass that was more visible on wide-angle digital breast tomosynthesis as compared to FFDM. Biopsy samples from this lesion demonstrated an invasive ductal carcinoma on histopathology.

The imagers made their interpretations using FFDM images only, DBT images only, and FFDM+DBT images, marking regions of interest, measuring lesions they identified, and describing abnormalities. They scored suspicious lesions on a 1-to-5 scale (normal to malignant). For FFDM images, the readers categorised breast density using a BI-RADS density 1-4 category score, and used an on-screen 0-100 mm visual analogue scale to assign an area-based percentage mammographic density. The percentage of volumetric breast density was also assessed using Volpara Data Manager software (Volpara Solutions, Wellington, NZ).

Andy Evans MD, Professor of Breast Imaging at the University of Dundee and honorary consultant radiologist in NHS Tayside, and co-authors, compared the 1,800 case findings with the diagnosis of each patient, based on clinical exam, medical imaging, and histopathology. Readers identified 260 unifocal malignant lesions on DBT images compared to 214 on FFDM.

Highest sensitivity

The FFDM+DBT combined exams had the highest sensitivity in detecting breast cancer, at 97%, followed by 89.1% for DBT alone, and 86.6% for FFDM alone. In the densest breast category, FFDM+DBT identified 10.3% more cancers than FFDM alone, but DBT alone was most accurate for breasts in the third BI-RADS breast density category.

Overall specificity was highest for DBT alone (84.6%), followed by FFDM (81.4%), and then FFDM+DBT (79.6%). The researchers attribute the lower FFDM+DBT reader results as a function of needing to interpret two exams instead of just one. Tumour measurement accuracy was comparable for all three groups.

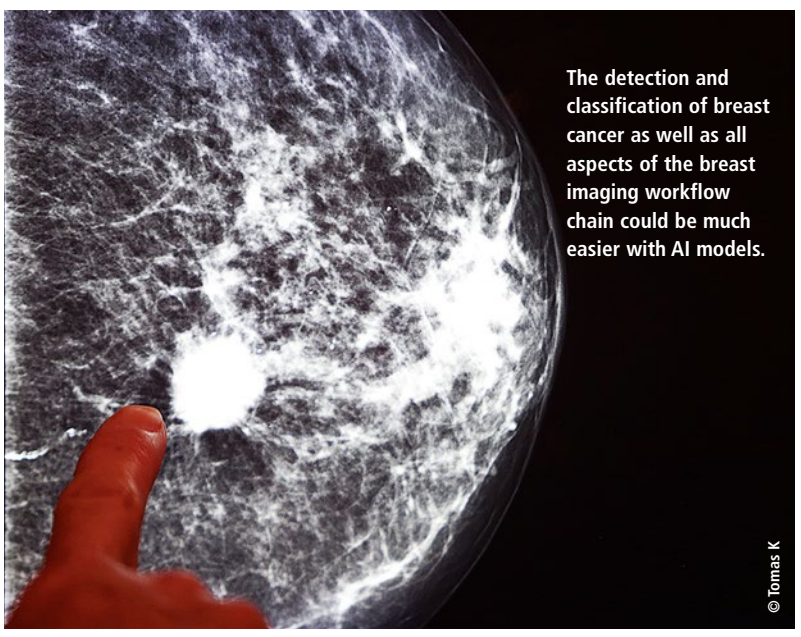
Based on their findings, the authors recommend that DBT be used for symptomatic younger women with known very dense breasts, or as a second-line exam following a negative FFDM. And, in view of increasingly available contrast-enhanced digital mammography (CEDM), they also recommend that the performance of DBT be evaluated in clinical studies with this breast exam.

'With respect to additional research, the Dundee team is currently conducting a UK multicentric study called CONTEST, comparing the diagnostic accuracy of CEDM with FFDM, DBT and MRI,' lead author Patsy Whelehan, a researcher at the University of Dundee School of Medicine and a consultant radiographer at NHS Tayside, told *European Hospital*. 'The study started as single centre in 2018, but we now have several centres on board and recruitment is ongoing. Another major current UK-wide project from the Dundee team is MEDICI, which aims to assess whether a reduction in mammographic density in women taking adjuvant endocrine therapy following breast cancer surgery is associated with a lower risk of recurrence and/or a lower risk of dying.'

After leading the mammography training service at King's College Hospital in London, since 2009 **Patsy Whelehan** has researched clinical breast imaging in Dundee alongside Professor Andy Evans. As well as radiology research, she has a strong interest in patients' mammography experience. Clinically, she exemplifies the extended role opportunities available to radiographers in the UK, whereby with rigorous additional training radiographers can undertake advanced practice, such as reporting mammograms and performing breast biopsies.

Malignancy detection as good as radiologists

AI potential in breast imaging efficiency



The detection and classification of breast cancer as well as all aspects of the breast imaging workflow chain could be much easier with AI models.

The contribution of Artificial intelligence (AI) has great potential in breast imaging efficiency, Professor Linda Moy MD told attendees at the 2021 Society of Breast Imaging/American College of Radiology (SBI/ACR) Breast Imaging Symposium this April. AI models for breast imaging have focused mainly on the diagnostic classification and detection of breast cancer. However, AI applications for workflow optimisation can provide support for interpretation tasks and increase overall operational efficiencies in all aspects of the breast imaging workflow chain.

'There are currently numerous AI applications in development that have the potential to benefit breast imaging, from test ordering to report communication,' said Moy, who is professor of radiology at New York University's Grossman School of Medicine. 'At a time when there's a shortage of breast imagers, there's increasing patient volume, and with increased utilisation of digital breast tomosynthesis (DBT) and breast MRI, an increasing number of images in an exam. Radiologists can benefit from intelligent, automated, time-efficient tools to perform or expedite repetitive tasks. These can help increase efficiency for breast imagers.'

The workflow chain in imaging includes multiple segments, starting with an order for the patient. This needs to be reviewed for imaging appropriateness and the protocol to be used, scheduled, performed, managed, reported with results communicated, and billed. A staff member is needed at each step to integrate information and accurately pass the information along to the next step. AI can potentially address every aspect of the workflow, Moy believes, 'enhancing practice workflow efficiency, reducing variability, and improving quality.' 'Most attention for AI in breast imaging goes to pixel-based image analysis, with a focus on narrow AI tasks including detection, classification, segmentation, prepopulating a report, prediction of breast cancer risk, and treatment response prediction,' she explained. 'Less attention is being paid to radiology workflow, but I think the greatest potential for AI lies in making these back-end processes more efficient. The current limitation and dif-

DeepCAT

AI tool improves high volume mammography

A new deep learning system to help radiologists improve their workflow efficiency when reading high volumes of screening mammograms is being developed at Johns Hopkins University's Radiology Artificial Intelligence Lab (RAIL) in Baltimore, MD. DeepCAT (Deep Computer-Aided Triage) is focused on workflow prioritisation. 'Improvement in the radiologists workflow may be just as important as breast cancer detection,' write the software developers in the February 2021 issue of the *Journal of Digital Imaging*. 'The topic of workflow improvement has received much less attention than breast cancer detection rates.' DeepCAT is designed to automate prioritisation of images likely to contain cancer and to discard images unlikely to contain cancer. It is a triage system that focuses on two key elements for mammogram suspicion scoring: discrete masses and other image features of cancer, such as architectural distortion. The software has two components, a mammogram classifier cascade which uses AI to classify images as potentially normal, benign, or malignant, and a mass detector. These components are combined in a sequential workflow of image processing to generate an overall priority score. The priority score is used to order studies for review by the interpreting radiologist. DeepCAT's components were trained using the Digital Database for Screening Mammography (DDSM), a dataset of 3,034 2D film mammography images from 2,620 patients at four U.S. hospitals. The mass detector was trained to detect benign and malignant masses, and background breast tissue while generating a bounding box around any potential malignant lesions. In addition to classifying images, the mammogram classifier cascade was trained to maximise malignancy recall (sensitivity) and non-malignant precision (positive predictive value).

To improve workflow in radiology, a new AI tool should automate prioritisation of images likely to contain cancer and to discard images unlikely to contain cancer.

Lead author Paul H Yi MD, and co-researchers describe the performance and validation of their prototype software using a 595 testing image dataset in the February 2021 issue of the *Journal of Digital Imaging*. It achieved 100% precision for normal studies, classifying 53% as normal without missing a single cancer. The authors report that they are currently training a DeepCAT system for DBT and 2D digital mammography. They also are discussing training the system to identify and classify microcalcifications.

'Our work is currently focused on radiologist workflow, using AI to modify the reading worklist to prioritise cases more likely to contain a malignancy, and to potential remove normal cases from the worklist. Both of these actions would focus the radiologist's effort toward higher priority cases, and could decrease time spent on interpretation of normal cases,' co-principal investigator and breast imager Lisa Mullen MD told *European Hospital*. 'Combining these workflow enhancements with computer-assisted diagnostic tools would be very powerful. This combination could help the radiologist to be more efficient and may assist the radiologist with interpretation of difficult cases.'

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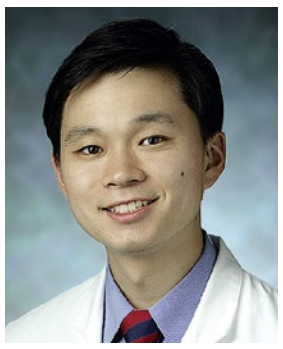
Assistant professor of radiology Lisa A Mullen MD who works in the Breast Imaging Division of the Russell H. Morgan Department of Radiology and Radiological Science at Johns Hopkins Medicine, is also Director of the Breast Imaging Fellowship Program.

She emphasises 'We are not looking to replace radiologists, but rather to assist with workflow and to provide a second interpretation or consultation,[she ephasised. 'A combined AI system may have the potential to replace a human second reader where double reading is the norm.'

Co-principal investigator Professor Gregory Hager adds, 'Personally, I think the right way to think about AI is as a second reader, potentially blinded from the radiologist. We can train algorithms to be complementary to humans -- that is, make them more sensitive to cases the human gets wrong, so that combination of human and machine has maximum value. That, combined with optimising workload, would have the biggest impact, in my opinion.'

The developers invite collaborators so that they can train DeepCAT on a dataset of images from various low-resource countries, because they believe these systems could be of great benefit in areas with an inadequate number of breast imaging radiology specialists. (CK)

Gregory D Hager PhD, is the Mandell Bellmore Professor of Computer Science and founding director of the Malone Center for Engineering in Healthcare at Johns Hopkins University. His research interests include collaborative and vision-based robotics, time-series analysis of image data, and medical applications of image analysis and robotics. Professor Hager is a fellow of the ACM, IEEE and AAAS for his contributions to Vision-Based Robotics, and a Fellow of the MICCAI Society and of AIMBE for his contributions to imaging and his work on the analysis of surgical technical skill.



Paul H Yi MD.is a radiology Instructor and Fellow in the Musculoskeletal Imaging Division at Johns Hopkins Medicine and is the founding co-director of the Radiology Artificial Intelligence Lab (RAIL).

ficulty are in integrating these tools into our RIS and PACS, because both can be quite inflexible.' PACS worklists have limited prioritisation capabilities, such as exams flagged as STAT.

A deep learning tool with the ability to screen breast studies for potential abnormalities and malignancy could flag these exams as priority for interpretation. Studies have been conducted that show AI can identify such exams as accurately as a radiologist. Moy cited published studies that compared accuracy and interpretation times between radiologists and AI tools in mammography interpretation. As a group, radiologists tended to perform more accurately and efficiently with the aid of an AI interpretation tool.

However, the effectiveness of such AI tools ultimately depends on how well the individual radiologist can use them. In fact, one study Moy cited revealed that interpretation time and recall rate actually could increase for some radiologists. Natural language processing is being used to perform automated text mining and data analytics of a patient's electronic health record. This capability combined with AI can help verify the appropriateness of an order, prepopulate or augment clinical information in the order entry process, and 'harvest' clinical information relevant to the exam. 'An unintended consequence of computerised physician order entry is that radiologists don't receive detailed relevant clinical history that pertains to the exam being ordered, and radiologists don't have time to review a patient's medical record to try to identify this information,' Moy pointed out. 'An AI tool could do this, and be very beneficial.' In addition to automating protocols for high frequency, low variability orders, AI tools could also identify patients who in all likelihood will need routine spot magnification images when they are having a mammogram. An example could be patients being followed for previously identified calcifications. Moy explained that this capability could decrease interruptions related to add-on studies.

Another opportunity for AI is to improve patient exam and staff scheduling, and to identify patients most likely to be 'no shows' and initiate additional intervention measures. This would benefit human and imaging modality utilisation in multiple ways. Another type of targeted intervention would be to improve follow-up rates of patients having a BI-RAD 3 assessment. And rule-based AI algorithms could check for inaccuracies such as duplicate patient orders or allergy histories and create automated alerts. 'AI software is being developed for each step of the imaging value chain. Radiologists may potentially leverage these products to provide more value and better patient care in their clinical practices,' she concluded. (CK)

Linda Moy is a Professor of Radiology at the NYU School of Medicine and at the NYU Center for Advanced Imaging Innovation and Research. Her area of expertise is breast MRI and AI. She is the immediate past Chair of the RSNA's Scientific Program Committee on Breast Imaging and serves as a Deputy Editor of Breast Imaging and Senior Deputy Editor for Radiology. Moy also chairs the ACR Appropriateness Criteria and Practice Parameters on Breast Imaging, is a consultant for the Journal of Breast Imaging, and a member of the SBI Board of Directors.

ECIO 2021

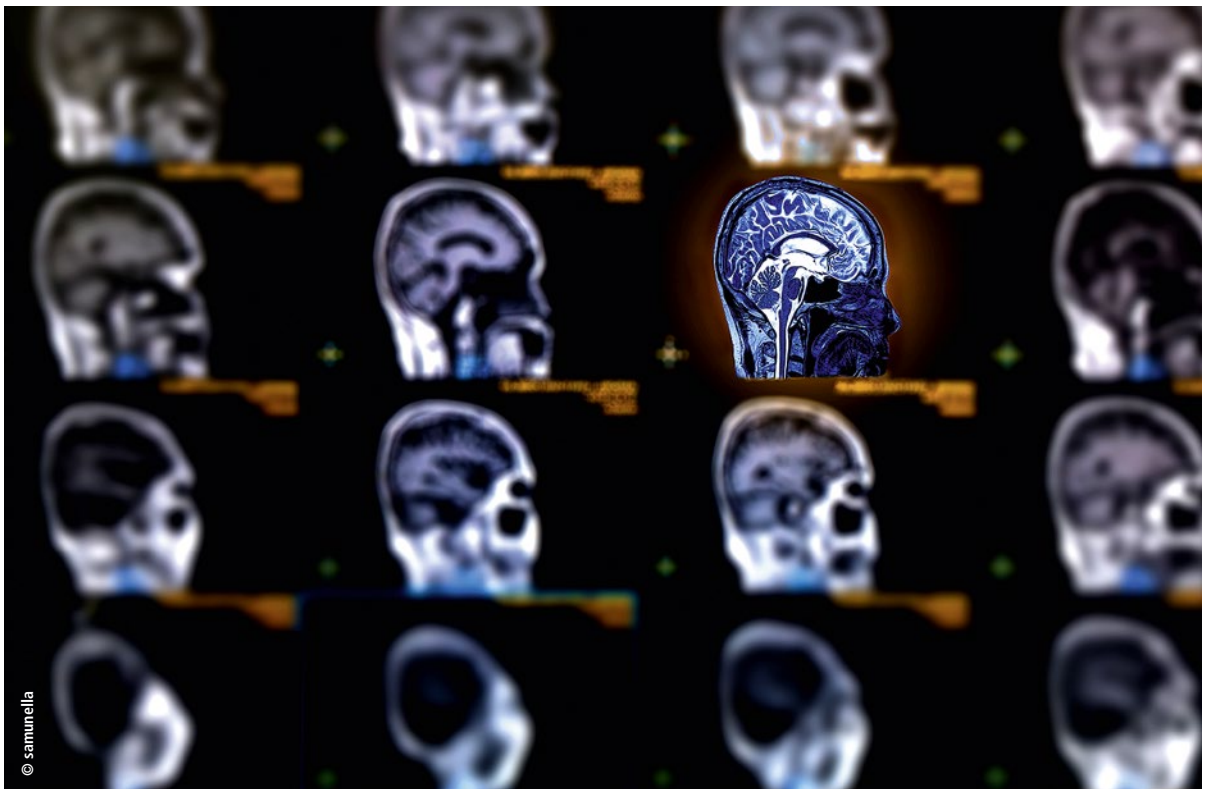
AI in interventional oncology: promise & reality

Report: Cynthia E. Keen

Is artificial intelligence (AI) technology ready to be utilised as a clinical tool by interventional oncologists? Not yet, but when it is, AI technology's clinical impact may be as profound as advanced imaging is today. This is the consensus of two leading researchers developing AI for interventional oncology use, who presented back-to-back scientific sessions at ECIO 2021 on both the promise of AI and current concerns and limitations about AI use today.

The potential impact of AI in clinical oncology is immense, according to Brad Wood MD, director of the National Institutes of Health Center for Interventional Oncology and chief of Interventional Radiology at NIH Clinical Center and the National Cancer Institute in Bethesda, MD. He leads a large multi-disciplinary team of NIH researchers and academic and industry partners that develops devices, software, and navigation approaches for cancer patients via novel local and regional minimally invasive image-guided therapies.

AI could help standardize and automate image interpretation and cancer detection



Potential capabilities

AI will help create accurate predictive models by integrating deep learning to genomic molecular, clinical, histology, imaging and radiomic data. It will be used for staging and response criteria and risk and outcome prediction. AI biomarkers will be used in drug discovery, with the ability to select drugs and predict side effects. This capability will shorten time to drug development, help determine where to biopsy and then correlate image to pathology, explained Dr Wood.

In imaging, AI will help standardise and automate image interpretation and cancer detection in face of widely variable radiology and pathology human practices. Examples of this include tumor stratification and cost-effective classification, and auto-segmentation and registration for interventions and followup.

Dr Wood cited an investigation of the impact AI could have on clinical trial eligibility. Researchers Genetech and Stanford University's Department of Electrical Engineering evaluated AI software called Trial Pathfinder to emulate completed clinical trials of advanced non-small-cell lung cancer using data from electronic health records of over 61,000 patients. AI-defined inclusion criteria doubled the number of eligible patients and improved the hazard ratio, suggesting that many patients who were ineligible to participate in the clinical trials could have potentially benefitted from the treatments. AI has the ability to navigate through a huge number of images that is infeasible for a human researcher and has the potential to make clinical assessments. These will include detection of abnormalities and characterisation of them, such as segmentation defining the boundary extent of abnormality for subsequent diagnosis and treatment. AI tools will be able to evaluate and classify abnormalities as malignant or benign, and to stage them into multiple predefined categories.

AI will aid change analysis, by tracking object characteristics across multiple temporal scans and across multiple modalities for diagnosis as well as evaluating treatment response. 'All this will happen, but it is easier said than done, and there are a lot of pitfalls,' Dr Wood said.

AI: A 'data wrangler' of the future

Julius Chapiro MD PhD., co-director of the Yale Interventional Oncology Research Lab of the Department of Radiology and Biomedical Imaging at the Yale University School of Medicine in New Haven, CT, agrees. He leads an interdisciplinary team of basic, translational, and clinical scientists who are developing new quantitative imaging biomarkers, predictive instruments, and imaging techniques for the diagnosis, characterisation and image-guided therapy of hepatocellular carcinoma (HCC).

Tumour treatment management today is based on inadvertent biased interpretation of evidence. Decisions are made based on evidence accrued from experience and knowledge reflective of an individual physicians' perceptions. There are more than 25 unclear, varying, and inconsistent diagnostic imaging guidelines. No unified staging system for HCC exists, and the wide variety of loco-regional therapy options are all supported by different data.

'The hypothesis of utilising AI is that it is exclusively data driven and therefore neutral to the personal cognitive bias of a physician. But is this really true? Can AI help us break out of the vicious unintended circle of bias? The problem is that any AI decision support tool will only be as good as the data that we use to train it,' Dr Chapiro explained.

Large amounts of high-quality, annotated curated data are needed from multiple sources. Selecting the data to use is very complex; the quality of data is key. A large data volume alone does not guarantee success. The question of explaining what decisions are made, why the AI tool does what it does, and why it is needed also must be addressed. No algorithm will be clinically applicable unless it can be independently verified.

AI cannot solve every problem

'Is the problem that an AI tool resolves worth solving?' queried Dr Chapiro. 'AI cannot solve every problem in medicine, and certainly not in IO. AI tool developers need to start with problems that have sufficient data to begin with, of frequently encountered pathologies with high incidence rates rather than rare findings.

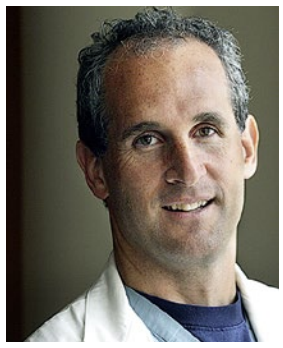
Other questions to ask include when evaluating an AI tool for IO: Was standardised reporting used? Is the study methodology respecified? What are the sources of data and what were the measurement benchmarks for quality? How is data split between AI tool development and validation? Was the dataset used in model training reflective of clinical reality and intended use case? Was the output of the model interpretable? Is the performance reproducible and generalisable?

Dr Wood discussed similar issues. 'To realise the promise of AI in IO, we must define the clinical task, which is easier said than done. We must determine where AI is most likely to have a positive impact. We need multi-disciplinary teams to create AI tools. And most importantly, uniformly standardised data needs to be shared throughout the world, through registries, research databases, and reporting.'

Predicting future oxygen requirements

Federated learning is one method to train AI models that are generalisable and reproducible with data from multiple sources while maintaining anonymity of the data. Dr Wood cites a collaboration by 20 institutions to create an AI tool that predicts future oxygen requirements of patients infected with Covid-19. He also explained how a CT AI Covid-19 detection and classification model was trained to be generalisable across nations. Simple AI models can be building blocks that feed larger blocks to create more complex AI models, he emphasised. This is happening now.

Like diagnostic imaging, AI tools offer immense promise to improve IO. This is starting to happen now, and probably will steeply accelerate in ensuing years. Right now, however, it's important to keep knowledge about AI utilisation in perspective.



Brad Wood, M.D., is director of the National Institutes of Health Center for Interventional Oncology and chief of Interventional Radiology at NIH Clinical Center and the National Cancer Institute in Bethesda, MD.

Julius Chapiro MD PhD, is co-director of the Yale Interventional Oncology Research Lab of the Department of Radiology and Biomedical Imaging at the Yale University School of Medicine in New Haven, CT.

Low-field M

The battle o

Source: Hitachi Medical Systems Europe

New interdisciplinary approaches

Intervention & immuno-oncology

Over recent years interventional oncology (IO), as a subspecialty of interventional radiology, has become a standard component of many cancer therapies. The broad range of minimally invasive methods – and their results – are often comparable to those of traditional approaches, such as surgery, chemotherapy or radiotherapy, e.g. with regard to hepatocellular cancer (HCC), oligometastatic diseases of the liver and the lung or small renal cell carcinoma. However, IO procedures have significantly fewer unwanted side effects as their traditional counterparts and patient acceptance is much higher.

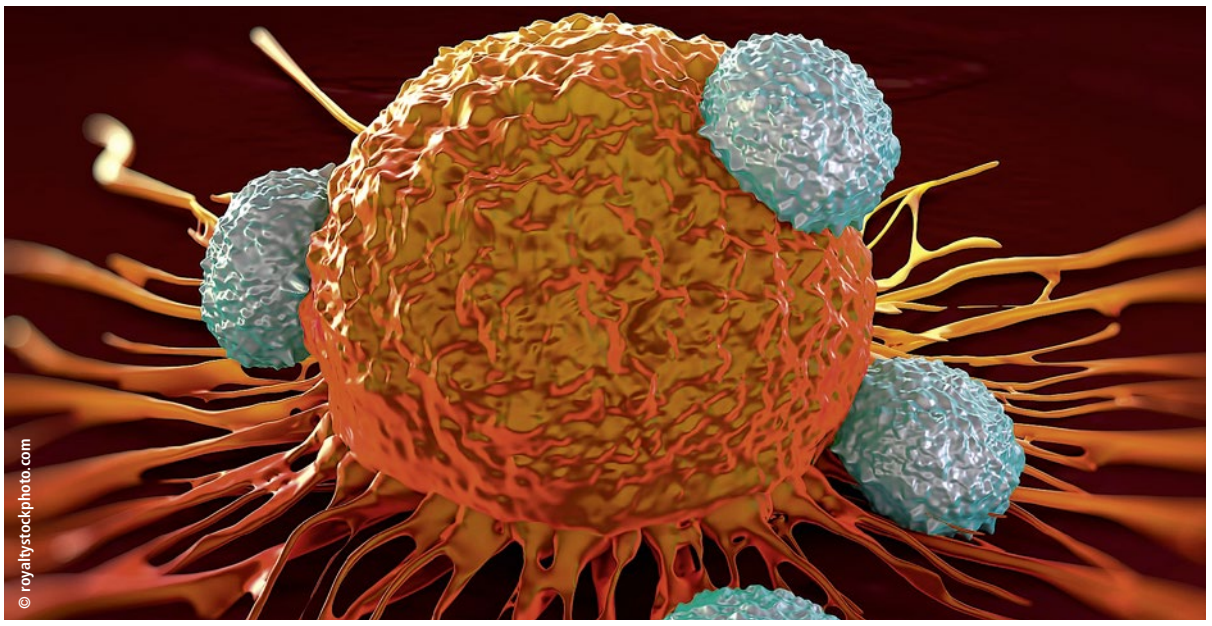
Professor Thomas Helmberger, Medical Director of the Institute for Diagnostic and Interventional Radiology, Neuroradiology and Nuclear Medicine at Munich's Klinik Bogenhausen, in Germany, outlines advances in tools for interventional oncology.

In the past decade, in addition to treatments using enzyme inhibitors, such as tyrosinkinase inhibitors, immune-modulating oncological therapies have progressed in leaps and bounds. They can support the patient's own immune system in entirely new ways and detect and destroy tumour cells. To date, however the effects of these selective therapies remain limited and are associated with often significant side effects.

'Interventional oncology procedures, whose immune-modulating effects so far have been considered negligible, in fact might offer substantial synergy effects when applied in combination therapies. We expect the combined application of interventional oncology and immune-oncology to overcome the limitations of the individual therapies such as merely local effects and a high degree of side effects,' Helmberger explains. He predicts the treatment of a defined disease to continue to move towards precision medicine with the different therapy components more finely tuned to the individual patient. This hypothesis is currently being tested in several studies. 'In these combination therapies,' the radiologist stresses, 'traditional surgical and minimally invasive procedures work hand in hand with individualised therapies.'

The orchestra of therapy options is increasingly complex – as is the radiologist's task. Detailed knowledge is essential, Helmberger points out: 'The tumour response during immuno-therapy can be quite different from the response to a conventional treatment', thus it is crucial 'to know these differences to be able to correctly interpret effects, such as pseudo-progression or therapy-induced pneumonitis, and take appropriate measures.' Moreover, immuno-therapies are developing at a rapid speed – every few months new and promising immune-medication is launched that claims more specific responses or fewer side effects. 'It's quite a challenge to stay up-to-date,' Helmberger admits.

Immuno-therapies are developing at a rapid speed. They are an option in the fight against cancer.



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From linear treatment plans to a complex therapy continuum

Increasingly complex treatment protocols are a logical consequence of better understanding of tumour biology. 'Today we know that, on the cellular level, tumours respond differently to therapies,' he points out. 'Consequently, we now abandon treatment plans that assume linear courses of treatment and simple yes/no evaluations of the response in favour of more a complex therapy continuum. This means the patient is accompanied over a longer period of time and the therapy is adjusted in a more nuanced way to the actual course of the disease.'

This development has made traditional walls between disciplines more porous, he observes. 'Oncologists, pathologists, surgeons, radiotherapists and diagnostic and interventional radiologists don't see each other as rivals any longer, at least in larger clinics, but use interdisciplinary approaches that benefit from shared synergies.' While this approach has not yet trickled down to every clinic, Helmberger is optimistic: 'When the safety belt was introduced several decades ago it also took some time for everybody to be convinced of its benefits.'

KI supports human skills – if the groundwork is done properly

Helmberger expects artificial intelligence (AI) to be a game changer: 'AI will enable us to analyse complex interdependencies and recognise links between diseases and tumour profiles that traditional statistical-analytical methods were unable to reveal.'

Today, some AI tools are being used and help, inter alia, to detect lung lesions, the extent of emphysema, or to identify the perfusion characteristics of different organs and tumours. 'These assistants will be integrated deeper and deeper into clinical routine,' the professor is convinced. This will yield supporting information, for example whether a suspicious spot in an MRI scan is more likely to be a tumour or a scar. In the future, patient data from different sources – radiology scans, blood analyses or histopathological information – will, Helmberger predicts, 'be linked by intelligent algorithms that provide individualised insights into the specific course of the diseases. Processing and standardising the data required for these computational procedures will be a crucial task of medical institutions and the industry partners.'

Radiologist **Professor Thomas Helmberger** MD is Medical Director of the Institute for Diagnostic and Interventional Radiology, Neuroradiology and Nuclear Medicine at Munich's Bogenhausen hospital. His research foci are on oncological diagnostics and interventional oncology, abdominal imaging and vascular imaging and intervention. He is a member of several German and international professional associations such as the German Society for Interventional Radiology (Deutsche Gesellschaft für Interventionelle Radiologie – DeGIR), the European Society of Radiology (ESR) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). He is also an expert for several scientific publications; inter alia Hepatology, Interventional Oncology, Radiology and European Radiology.

MRI: quality images with patient empathy

f fields in MRI

Report: Michael Krassnitzer

A big advantage in open low-field MRI is the relief it brings to the one in twenty patients who suffer claustrophobia.

Following the launch of several low-field MRI systems, the technology offers major advantages, including relatively low purchase and operating costs, with few artefacts and image quality comparable to a 1.5T scanner. Another plus is improved patient comfort in low-field scanners. This, however, tends to attract little or no consideration.

The Aperto Lucent Plus* – an open MRI system for a relaxed patient experience and high-speed exams with motion-free images.

During the European Radiology Congress (ECR 2021) one industry session dealt with issues surrounding low-field MRI. Geared towards users, the panel included neither developers nor scientists. The panellists own or run private MRI practices.

Open system benefits

A low-field scanner is an open MRI system, i.e. it is not in a closed tube. For obese and claustrophobic patients this is the only option to have an MRI exam.

According to the four radiologists on the panel, roughly five percent of all MRI patients suffer anxiety and panic attacks in the narrow tube of a conventional scanner and may need full anaesthesia before a scan. 'In some, claustrophobia is so severe that they can't even enter the changing room,' said Dr Jan Veryser, who operates an MRI centre in Sluis, Netherlands. For physicians helping that five percent – one in 20 – is a major issue. 'A lot of attention, love and time,' is Veryser's approach to claustrophobic patients. 'When they make an appointment we ask them to have a look at our scanners to understand that there are no tubes. Before the exam, even before they enter the changing rooms, we show them the scanner again.' The radiologist is present during the entire exam to provide support. Moreover, patients can take along someone they trust, to hold their hand during the scan.

Even the design of the room considers the needs of claustrophobic patients by providing one large room, rather than having small changing cubicles. Also, the distance from Reception to the exam room is merely 10 metres.

Dr Carsten Figge heads a radiology practice in Paderborn (Germany) that focuses on claustrophobic

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0.05T to 0.5T scanners expand MRI potential

Low-field MRI: Less is more

Report: Michael Krassnitzer

Currently, two opposing trends can be observed in MRI: on the one hand 1.5T scanners are increasingly replaced by 3T scanners for standard clinical MRI applications. On the other hand scanners with lower and even significantly lower field strength have commercially available in the past two years. A session at this year's European Congress of Radiology (ECR 2021) took a closer look at low-field MRI scanners with about 0.5T and ultra-low-field MRI scanners with a field strength of 0.05T.

'The key challenge of those low and ultra-low-field MRI systems is the poorer signal-to-noise ratio,' said Professor Andrew G Webb, Director of the Centre for High-Field MRI at the University Hospital Leiden (Netherlands). The signal-to-noise ratio (SNR) of a 1.5T scanner is six times higher than in a 0.55T system and even 300 times higher than in a 0.055T system. Each MRI system aims to deliver a good ratio of true signal (i.e. reflecting actual anatomy) to unavoidable background noise. While low-field and ultra-low-field MRI scanners struggle with SNR, they do offer certain advantages over standard MRI scanners.

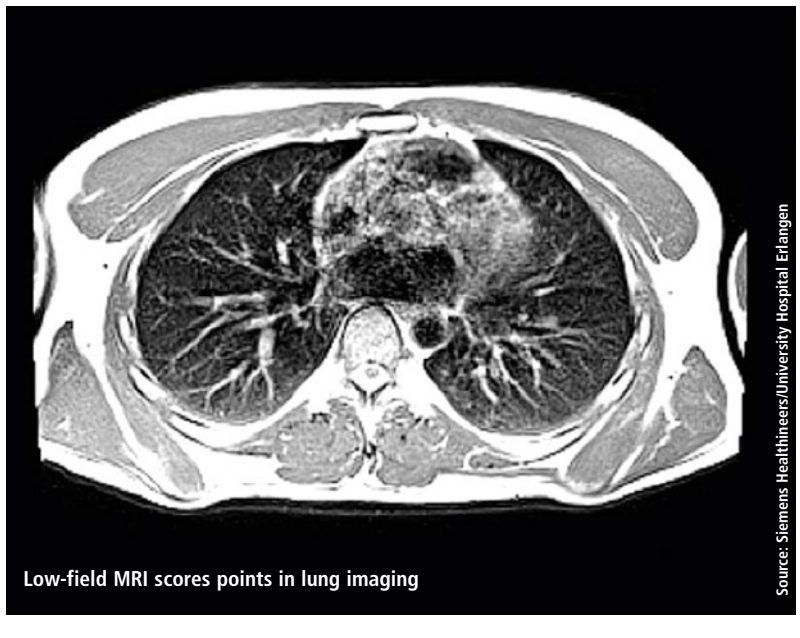
Webb pointed out the areas where low-field MRI scanners receive top scores: firstly, the low purchasing and site costs. Secondly, low-field MRI is less susceptible to artefacts caused by metal implants and unwanted effects caused by air-filled cavities (lungs, nose). The specific absorption rate (SAR) is about one tenth lower than in 1.5 T scanners, the wave lengths of the magnetic waves is above the critical value for implants. 'Therefore, we don't need to be worried about counter-indications,' Webb underlined. Since gradient acoustic noise is weaker, noise stress for the patient is significantly lower. Moreover, low-field MRI offers advantages with regard to relaxation times: T1 relaxation time is significantly shorter than in 1.5T scanners while T2* relaxation time is significantly longer.

With its Magnetom Free. Max Siemens Healthineers set a new standard. The 0.55T system, launched last year, is suited to examine lung, abdomen, brain and cardiovascular structures. In addition, image-guided interventions can be performed. 'This is basically a standard MRI scanner,' explained Professor Matthieu Sarracanie from the Department of Biological Engineering at the University of Basle. The system's benefits are light weight (3,200 kg) and a compact design with the large bore and closed helium-free cooling system. The drawbacks are the poorer resolution compared to 1.5T systems and that the system requires the same space and infrastructure as a standard scanner.

In the ultra-low-field MRI segment the Hyperfine scanner, launched in 2019, aims to be the new benchmark with a field strength of 0.054T. Weighing just 630 kg and being the size of a nightstand this mobile system can be used at the bedside, primarily in emergency settings. No site costs, no specific power supply, so specific cooling, even fewer artefacts caused by medical implants, no undesirable side effects caused by air – all are advantages, according to Webb.

'The magnetic waves are so long that the critical length for implants is 75 metres, which is irrelevant for clinical purposes,' the physicist pointed out. 'This system has enormous potential,' Sarracanie, a co-founder of Hyperfine. He also pointed at the low costs of approx. $30,000 plus a monthly fee. A dedicated site is no longer needed; the carbon footprint is comparatively small and the system can be powered by a standard wall outlet. However, he also points out drawbacks: the system is tailored for specific exams. Currently only brain and extremities can be scanned. Moreover, the Hyperfine is a proprietary system which means, for example, that images can only be stored in the company's own cloud.

50 mT human MRI system developed in the Department of Radiology at the Leiden University Medical Center.



Source: Siemens Healthineers/University Hospital Erlangen

Low-field MRI scores points in lung imaging

Open-source projects make MRI available for everyone

However, there are also non-commercial ultra-low-field systems. With his University Hospital Leiden team, Webb built a 0.05T portable system which is used for neuroimaging. 'Rather than using several large and heavy magnets we use many small ones – each about the size of a one-cent coin,' he explained. The dice-shaped 12 mm magnets are mounted on acrylic glass rings – 23 altogether with 2848 magnets. Costs: €4,000 plus a few thousand euros more for gradient and RF coils and amplifiers. 'This is an open-source project. Anybody who is interested can build such a scanner based on our construction plan.' These systems are also designed for one specific exam, for example paediatric hydrocephalus.

The system was designed primarily for use in developing countries. 'Seventy percent of the world population don't have access to MRI,' Webb pointed out. 'Due to low costs, mobility and standard power supply ultra-low-field MRI scanners can now make MRI available all over the globe.'

ESR/EFOMP – High-field vs low-field MRI: Time for a re-think?, ECR 2021, Vienna, 4/3/2021

The battle of fields in MRI

Continued from page 15

patients. His strategy includes the pleasant design of the scanner, sophisticated lighting and ceiling windows that open up to the sky. Additionally, the staff is trained to support patients before, during and after the exam. 'We aim to make their stay as pleasant as possible – from the first to the last second,' Figge underlined. This is more important to him than the technical specifications of the low-field scanner. He believes 'number crunching is irrelevant.' Nevertheless, he compared his low-field 1.2T with his 1.5T and reported that the 1.5T scanner yields slightly better results than the 1.2T scanner for prostate exams.

However, for musculoskeletal imaging and neuro-imaging he did not see relevant differences. In breast imaging the open scanner offers the advantage that women can lie flat on the chest.

Dr Mihaly Aradi, director of a private radiology practice in Pécs (Hungary), uses 0.4T as well as 3T systems. 'With low-field MRI you need to schedule more exam time,' he explained, adding that 'the new digital signal processing technologies compensate weaker signals well.'

In his experience, 0.4T scanners are as good for routine exams as the 3T system. 'For MRI scans of the spine both systems deliver pretty much identical quality,' the Hungarian radiologist said. He suggested that indeed 'every clinic that specialises in spine surgery should have a 0.4T scanner as well as a 3T scanner.' Aradi also pointed out that the low-field scanner's advantage is the reduced number of artefacts: 'Distortions are so minute that structures are clearly visible even when they are next to metal implants.'

No liquid helium cooling

Last, but not the least, Dr Liliana Rechmeier who, with her husband, co-heads a radiology practice in Bad Neuenahr, Germany, stressed the low operating costs of a low-field MRI scanner. Their private practice has to keep the costs under control, she pointed out. 'Due to the low costs for servicing and electricity and, since no liquid helium cooling is required, the operating costs are only about 60 percent of those for a conventional scanner. Over the course of eight to ten years of use, that's a substantial amount of money.' In view of the good image quality she also urges colleagues to rethink current prejudices: 'Low-field MRI is no amateur scanning; it delivers really good radiological images.'

Image comparison: MRI scans with Lucent Plus' IP-RAPID functionality ON/OFF