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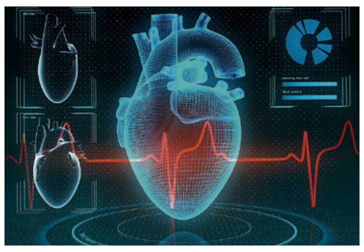

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- **A round-up of reports and interviews from this summer's scientific gatherings and congresses**
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Instituting hybrid care

Will telehealth replace traditional in-person healthcare? Healthcare and digital health professionals around the world have moved beyond this question.

Report: Dr Christina Czeschik

Telehealth scenarios are here to stay, and so is traditional healthcare. The relevant question is how both can be combined for optimum results. This is the focus of hybrid care models. Jonah Comstock of HIMSS recently presented a webinar on opportunities and challenges in hybrid care, with Kristi Henderson, CEO of MedExpress at Optum, and Scott Shreeve, MD, CEO of Crossover Health.

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Jonah Comstock

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Kristie Henderson

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Scott Shreeve

Telehealth on the rise

The pandemic has accelerated the acceptance of telehealth services, such as video consultations, around the world. In the USA, 11 more telehealth services have been added to the list of Medicare-reimbursable items.

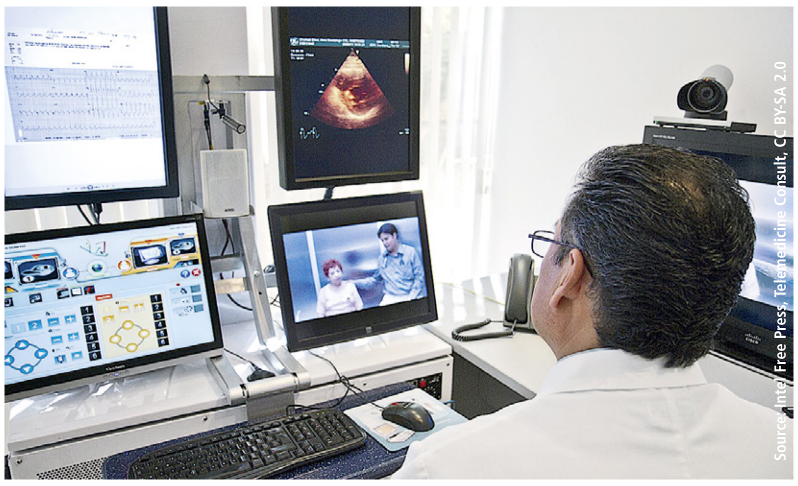
In Germany, the recent DVMPG legislation will soon permit doctors to treat up to 30% of their cases via video call (formerly 20%) and see patients via video call outside office hours (medical after-hours services), and also allows other independent medical professionals, such as midwives, to offer video consultations.

Telehealth services address a wide range of current challenges to patients and medical professionals: They decrease infection risk, lower barriers and increase accessibility to healthcare for patients with limited mobility or, in infrastructurally underdeveloped regions, provide new opportunities for healthcare providers to work location-independently and with a family-friendly schedule, and increase efficiency all over the healthcare system.

However, in-person visits cannot be replaced by telehealth services wholesale, regardless of context. Knowing which indications are most suitable to telehealth vs. traditional consultation is key to maintaining patient safety and satisfaction.

From emergency care to mental health

A recent study by US-based telemedicine provider Amwell revealed that, in the future, 76% of patients expected to use telehealth services at the same level or more frequently than before the pandemic and 92% of physicians were planning to provide them. Telehealth adoption varies with subspecialty. Psychiatrists are among the vanguards of digital services while emergency physicians are near the lower end of the spectrum of telehealth adoption.



Source: Intel Free Press, Telemedicine Consult, CC BY-SA 2.0

Telehealth services, such as video consultations, are on the rise

Physicians already have thoughts about the best ways to combine telehealth and traditional consultation in a hybrid model: They were most comfortable to provide prescription renewals and regular chronic care check-ins via video call (94% and 93%), but were more conservative about urgent care consultations and initial meetings with patients.

In the HIMSS webinar, Henderson and Shreeve disagree. 'Digital first, strategically in person'. Brick-and-mortar medical centres might go from having an exploratory to having a confirmatory focus. If all patients are seen digitally first, in-person facilities do not need to be prepared for all eventualities.

Both the Amwell research and the HIMSS experts suggests that, in the future, hybrid care models will be pervasive and increasingly seamless throughout the continuum of care. Telehealth will not be confined to certain siloed indications or subspecialties. Some services have to remain in-person, for example the taking of blood and other samples, vaccinations, surgical procedures. Others will be digitised almost regardless of the medical specialty – such as monitoring of vital parameters and medical-administrative work like the renewal of prescriptions. Hybrid healthcare of the future may come to resemble today's banking landscape between online banking, ATMs and office visits.

Challenges: reimbursement and digital skills

Developing adequate workflows comes with some challenges. Firstly, reimbursement regulations are often lagging behind technological opportunities. Only the in-person components of hybrid care are reimbursed, not the digital ones. If physicians and institutions want to establish new hybrid care workflows, they often have to rely on patients who are willing to pay out of pocket, find funding for pilot projects, or forgo reimbursement for months or even years.

Secondly, healthcare professionals are still in the process of acquiring the necessary digital expertise. That not only includes skills as a user of digital tools but also and, more importantly, knowledge about how to choose the right tool for the right indication, meet patient expectations and work in an economically viable way, all at the same time. For example, which kinds of patients are more likely to require in-person visits, even if at first they ask for a video consultation? How to reply to patients who request that their wearable device data is used for remote monitoring or diagnosis?

Fortunately, the time in which the individual physician or institution had to carry the burden of making all these decisions is coming to an end. Increasingly, pilot projects and regular hybrid care are evaluated scientifically, providing more and more evidence about the optimal ways of combining telehealth with in-person healthcare.

One cell's whole genome sequenced – even in hours

Advancing personalised health and genomics

A solid diagnosis is always the first step on any patient's journey to health. However, diagnostic categories are necessarily oversimplifications, says Dr Christina Czeschik.

In the last decades, medical professionals and scientists have begun to uncover the true variability in patients' physiological and biochemical make-up that is the principal cause for individual variations in the way diseases present themselves. A number of technologies have contributed to this massive increase in data and knowledge. In particular, radiology, histopathology and genetic sequencing are key fields in personalised medicine, and precision oncology is one of their top applications.

The different types of cancer (lung, breast) are in fact mixed bags of conditions that share only one feature: excessive cell growth. Chemotherapy and radiotherapy conventionally attack fast-growing and replicating cells. But as malignant and normal cells are still similar in many ways, such as their external structure and metabolic

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Making AI in dermatology

The need for us to quantify skin tones

Although artificial intelligence (AI) tools and smartphone apps that help identify suspicious moles and potential skin cancers are starting to proliferate, dermatology informatics has far to go before becoming a clinically adoptable technology. Many challenges need to be resolved, not least of which is the need for more image data representing people of colour.

Report: Cynthia E. Keen

Recently, three dermatologists working to advance informatics and the use of AI for dermatology discussed current challenges at the 2021 Society of Imaging Informatics in Medicine (SIIM) annual meeting. The scientific session raised more questions than answers, making it apparent that much more collaborative research needs to be undertaken as a global initiative.

The scope of dermatology photographs is broad, encompassing photos taken by patients and their primary care physicians, clinical photos, wound care photos, and histopathology CT scans. All of these need to be managed, labelled and stored appropriately, or else they cannot be used clinically or as reference data, said Veronica Rotemberg, MD PhD, of the Memorial Sloan Kettering Cancer Center in New York City.

'Standards for image acquisition are challenging. Many imaging standards need to be established, such as setting photography standards, standards for special considerations for sensitive sites, and standards for skin of colour.'

The use of DICOM, the international standard for medical imaging, for dermatological imaging has been limited. The ability of DICOM to encode relevant metadata and enable interoperability with electronic health records and clinical research software has driven the interest in its application to dermatology. A DICOM dermatology working group has developed dermatology-specific Information Object Definitions (IODs) for inclusion in the DICOM standard and future work will be for total body photography and reflectance confocal microscopy.

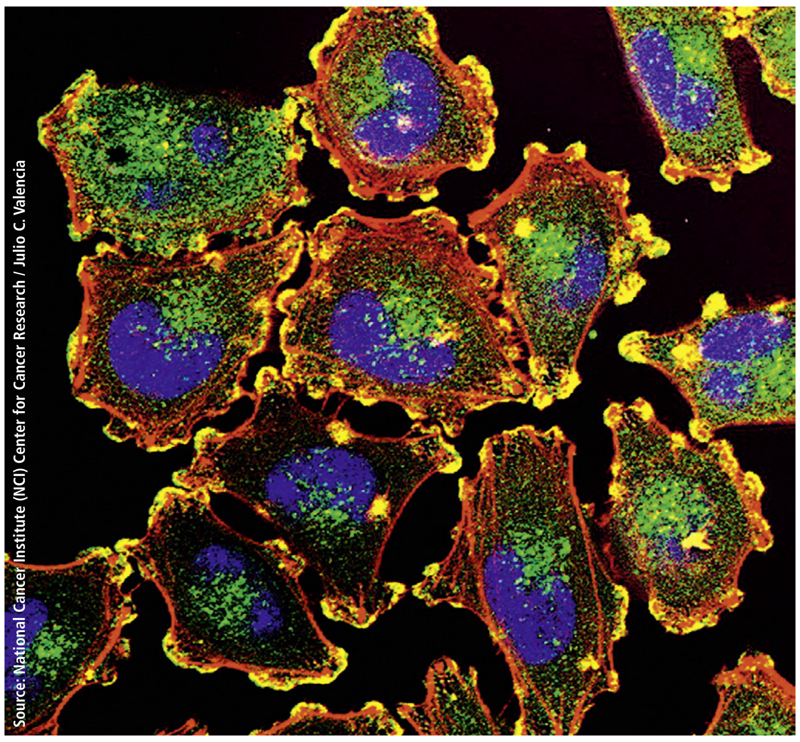
'There are numerous issues to resolve,' Rotemberg pointed out. 'No consensus exists yet on the specific fields to collect and store for every type of image. Patient level variables, such as ethnicity and skin type, need to be considered. Colour accuracy and fidelity are huge issues. In addition to lighting affecting colour, there is much variability in image sources from smartphones. Each acquisition device may code RGB values differently when capturing and storing images. With respect to standard file formats and colour fidelity, there is a wide variety on how to store images with uncompressed or compressed JPG, and the compression level used is not always encoded.'

Once image capture challenges are resolved, what should be done with the images? Research is underway in the fields of segmentation, wound measurement, and diagnosis using machine learning and AI, Rotemberg said, adding that a 2020 SIIM-ISIC Challenge for melanoma classification outperformed dermatologists, with a sensitivity of 79.3% for AI compared to 71.9% for dermatologists.

However, issues remain for clinical implementation of AI for skin cancer screening, such as identifying the appropriate evaluation criteria and appropriate users.

Image storage requirements for dermatology data can be another stumbling block, suggests Konstantinos Liopyris, MD PhD, of the University of Athens Andreas Syggros Hospital of Skin and Venereal Diseases. Dermatology data is massive, including patient demographics, anatomic locations

Metastatic melanoma cells



Roxana Daneshjou, MD PhD, is a clinical scholar in dermatology and a postdoctoral research fellow in biomedical data sciences at Stanford University School of Medicine in Redwood City, California. She is interested in bridging new technologies such as genomics and machine learning with clinical medicine and in the use of Twitter for scientific communication and medical education.

Continued from page 1

pathways, traditional cancer therapies are highly noxious to both normal and malignant cells. They cause a wide range of side effects, mostly in tissues with a naturally high proportion of healthy fast-growing cells, such as the gastrointestinal tract, bone marrow and skin. Their side effects may be as fatal as the underlying disease.

Thus, the holy grail of cancer medicine are therapies that are precisely targeted to eliminate malignant cells only. To develop such therapies requires a deep understanding of the cancer cell down to the molecular level.

Insights into the cancer cell

There are three main fields of medical science that contribute to an intimate knowledge of the workings of a cancer cell: radiology, histopathology and genetics/genomics. In recent decades, radiology has progressed from giving a rough orientation of a lesion's spatial dimensions and internal structure to providing detailed information almost on a cellular level.

In the newly developed field of radiomics or quantitative imaging, machine learning algorithms exploit subtle differences in signal strength that are invisible to the human eye. Similarly, histopathology has progressed from traditional H&E staining for visual examination under the microscope to far more sophisticated immunohistochemistry, using specific antibodies that bind to certain cell components.

Information on a sub-visual level is being utilised as well, on secondarily digitised or primarily digitally acquired slides, employing machine learning methods to identify patterns predicting malignancy.

While radiology and histopathology are approaching the cancer cell from a macroscopic to a microscopic level, genetic sequencing is working its way up from a submicroscopic level.

High-throughput sequencing methods have all but replaced the conventional Sanger sequencing approach and have made it possible to sequence a cell's whole genome in a matter of days or even hours. Massive genetic databases enable scientists to algorithmically identify pathogenic mutations within the overwhelming genetic variability of the human species.

Minimal collateral damage

Ideally, detailed knowledge about a cell population's genetic aberrations helps to identify pathways that are instrumental for the growth of a specific tumour and can be inhibited with minimal collateral damage to the patient's healthy cell populations.

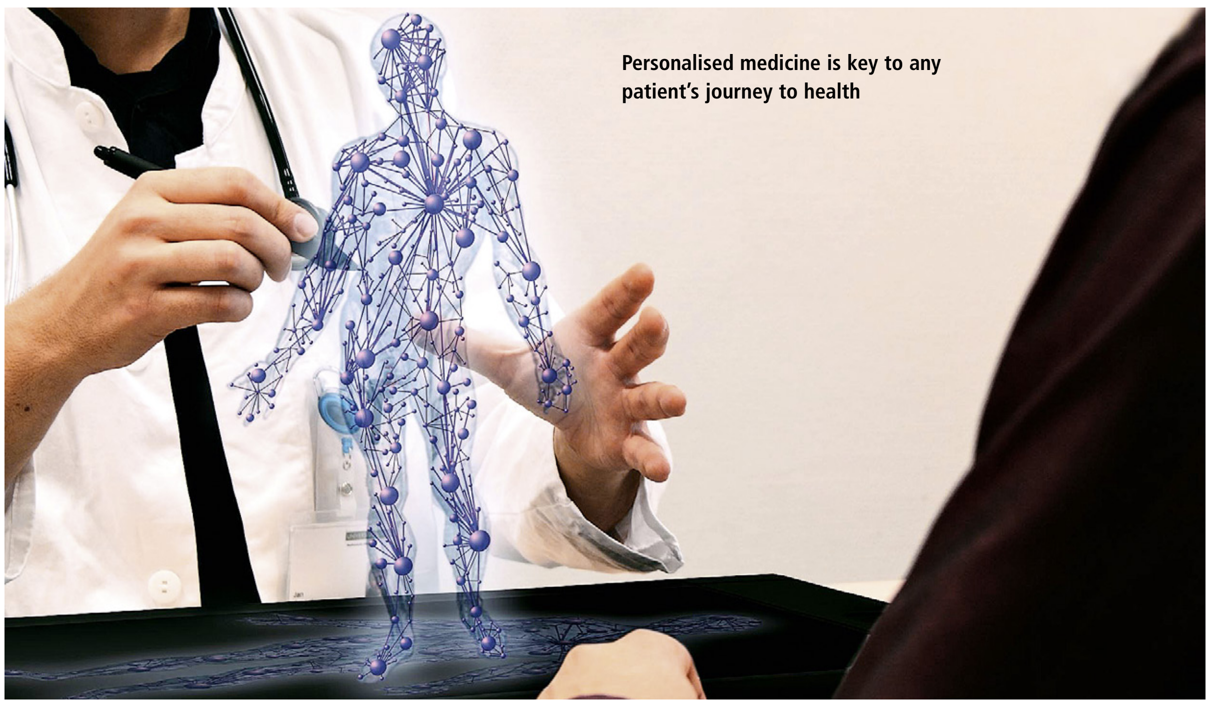
This so-called molecular profiling was implemented, among others, in the NIH-funded I-PREDICT trial. Of 83 patients with previously therapy-resistant tumours, 73 received an individual combination of drugs matched to their respective molecular profile, with encouraging results regarding prolonged stable disease. To make results like these accessible to the medical community, there is now even a journal dedicated to personalised and precision oncology, Nature Precision Oncology (npj).

The principle of tailoring therapies to a patient's genetic make-up is not limited to oncology: in pharmacogenomics, scientists investigate the influence of genetic variation on cellular pathways and thus the way that individual patients react to or metabolise drugs, finding out which drugs work best on a specific patient or subgroup of patients and which to avoid. However, personalised medicine poses a particular challenge to the way medical science has worked so far. In decades of evidence-based medicine and care, large, randomised studies have become the gold standard of medical knowledge acquisition. Their goal is to evaluate the effects of a therapy (or other intervention) with optimum reliability and precision, eliminating bias, confounding factors and just plain coincidence as far as possible.

In the age of randomised controlled trials (RCTs), an intervention is only considered effective if there is a statistically significant difference in outcome still visible after averaging hundreds or thousands of patients.

In this way, the RCT does not only eliminate coincidence but also the influence of individual genetic predispositions, unless the study population is chosen explicitly for a certain genetic trait. This, however, is possible only for the most frequent genetic variations. For example, breast and ovarian cancer patients are likely to profit from treatment with a PARP inhibitor only if they carry a BRCA-1 or BRCA-2 mutation. Such mutations are sufficiently frequent to include their carriers in large clinical studies.

However, there are many more genes more subtly involved in cancer risk, and once we start considering not only single gene mutations but also combinations of mutations, things get infinitely more complex. As we know, there are hardly two people in the world sharing the exact same genetic make-up. Thus, the RCT might even be considered



Personalised medicine is key to any patient's journey to health *work for every skin colour*

Dermatologist **Konstantinos Liopyris, MD PhD,** specialises in skin cancer at the University of Athens Andreas Syggros Hospital of Skin and Venereal Diseases, in Greece. Also a research fellow at the Memorial Sloan Kettering Cancer Center in New York City, he specialises in medical image processing AI in dermatology.

© Memorial Sloan Kettering Cancer Center

Dermatologist **Veronica Rotemberg, MD PhD,** specialises in skin cancer and directs the imaging informatics program at the Memorial Sloan Kettering Cancer Center in New York City. A biomedical engineer, her research interests include dermatology imaging standards, high resolution skin imaging and AI for diagnosis.

of lesions, biopsy results, treatment modality data, biopsy results, diagnoses, and outcomes. Image data can be clinical, dermoscopic, RCM images, and OTC images for both initial and all follow-up visits.

Universal and reproducible surface anatomy terminology is essential. In 2020, Liopyris participated in an initiative by the International Skin Imaging Collaboration to establish a standardised set of 513 terms to describe clinically relevant human surface anatomy for dermatologic documentation. More work is still needed, he said.

Skin colour

A major roadblock in developing AI tools for dermatology is that dermatology datasets have focused on Caucasian 'white' skin, said Roxana Daneshjou, MD PhD, of Stanford University School of Medicine. It is imperative to address biases in image-based dermatology, which for decades has underrepresented darker skin tones. Without appropriate representation of all human skin colours, disparities can get exacerbated when transferred to AI datasets, Daneshjou explained. 'Bias exists at every stage of algorithm development.

'We are working in a "black box" about whether a training algorithm for an AI tool has enough representation of range of skin tone. Not knowing this means there is no way to determine how well an AI algorithm works in darker skin colours.'

Daneshjou agreed that colour balancing of photography has favoured lighter skin, and that digital cameras may still have differences in colour balancing that can affect skin tones, creating a discordance between real life and the colour captured. Because natural light, room light and overhead light can also change colours, the lighting in a clinic can affect how a colour is represented and what is captured as a dermatologic image.

What should be done?

The experts concurred that more representative samples are needed to develop AI tools and researchers need to understand the technical challenges with photography and image capture. How to quantify skin tones to include the total range of human skin colour Is essential. As the experts summed up, 'There's lots of work to do and lots of work being done right now to make this a better reality.'

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the antithesis of personalised medicine.

Working on new solutions

But the scientific community is already working on new solutions for patient populations as small as n=1. Experts of the US-based Translational Genomics Research Institute have coined the term 'rapid learning systems' (RLS) for infrastructures that collect complex and real-world data on patients and their treatment outcomes.

The goal of RLS is not, as in RCTs, to have as little heterogeneity in study populations as possible, but to record this heterogeneity as detailed as possible and use it to detect previously unknown associations between patient characteristics and treatment success.

In an even higher-level approach, not the efficacy of individually tailored drugs or drug combinations is investigated, but rather the quality of algorithms used to match a patient's genetic profile to the optimum personalised drug regimen.

Baby steps are being taken, for example, by comparing the performance of different machine learning algorithms in the prediction of efficacy and toxicity of chemo and radiotherapy. Meaningful progress will require massive amounts of precise clinical data as well as computing power, interdisciplinary collaboration and a further breaking down of barriers between medical, biological and computer sciences.

Women in medical R&D

Innovation depends on more than technical skills

Cécile Geneviève is one of the few women who lead research and development (R&D) at a major company and her increasingly female team reflects women's growing interest in the field. But while gender balance is an important criterion, it takes a broad palette of skills to innovate to alleviate pain for millions of patients, she explained in an interview with European Hospital.

Report: Mélisande Rouger

Eagerness is what emerges from a conversation with Cécile Geneviève, a French mechanic and development engineer who leads system engineering at Zimmer Biomet Robotics. It's easy to imagine how she inspires her team of 20 engineers to follow in her footsteps and deliver their best to innovate in surgery robotics. 'I like to understand a complex subject and detail it, dissect it, and then control and learn from it,' she said. 'This is what attracted me to physics and mathematics, and science in general. R&D presents a dynamism and energy in which I can constantly evolve.' She started working in the automotive industry in the late 1990s, drawn by the many opportunities to learn and grow in a complex and technical world. In 2010, her focus switched to the medical device industry and robotic-assisted surgery and she never let go. 'The pace of innovation and opportunity to deliver a service to patients and users is very exciting; it's an area where so many things are happening right now.'

What makes a good team?

Leadership positions continue to be dominated by men in many industries, often more so in technical departments. But the world is changing. An increasing number of women are taking an interest in R&D leadership, such as Liane Teplitsky, Vice President and General Manager of Technology & Data Solutions at Zimmer Biomet's. 'Gender divide is fading out,' Geneviève said. 'I don't notice a difference in the way we work between France, Canada and the United States. An HR publication was sent out recently that showed almost no difference in salaries between men and women in our company. I think this helps to inspire more women to work in this field.'

Geneviève witnessed the change early on. When she studied mechanical engineering at the National Institute of Applied Sciences (INSA, in French) in Lyon back in the 1990s, 30% of her classmates were women. 'This was the first time so many women joined that course,' she said. 'Some areas, for example software engineering, remain male-dominated. There are just not enough female students in the pipeline.'

Geneviève's team now comprises 40% of women system engineers. The proportion wasn't an objective but reflects a sense of fairness and desire to attract the right skills in her department, she explained. 'I am very sensitive to the question of equality and, for me, it's crucial to offer equal opportunities to all qualified applicants, regardless of gender or background. Technical and soft skills, motivation and respect for others is what really matters.' Geneviève and her team work closely with healthcare professionals to speed the pace of innovation and expand the possibilities for successful treatment outcomes. 'Collaborating with physicians, we've created a comprehensive inventory for joint reconstruction, bone and skeletal repair, sports and spinal injuries, and dental procedures available.'

Below: A surgeon interacts onscreen and with the ROSA robot

Cécile Geneviève leads a team of R&D engineers at Zimmer Biomet Robotics, a global musculoskeletal healthcare leader. Based in Montpellier, France, Cécile and her team are developing robotic solutions that assist surgeons to treat patients suffering from disorders of, and injuries to bones, joints its supporting soft tissues and performing complex neurosurgical procedures.

Launched: The Woman in Orthopedics program

There are more women in orthopedics than first thought and the number is growing. The Zimmer Biomet Institute has recently launched the Woman in Orthopedics program to support the trend. Surgeons are very demanding partners regardless of gender. 'They have very high expectations and that's why the development of a product such as the ROSA robot is so interesting for engineers,' she said. 'The key challenges are related to the variety of surgical techniques used by surgeons. We need to develop features that are flexible enough for good adaptability to these techniques, while achieving the highest level of quality for performance and safety.'

'Patient and user safety is at the center of our activities, and risk management and quality are a daily focus for R&D teams,' she said. 'ROSA ONE Brain is a good example of this patient-focused work frame.' The robot assists surgeons in planning and performing complex neurosurgical procedures through a small drill hole in the skull. The technology enables surgeons to perform less invasive procedures than traditional craniotomies – enabling smaller incisions and potentially enhancing patient comfort. 'The device may give access to a therapy for patients who could not have supported a conventional procedure, because of the operating time, for example the SEEG, which aims to identify epilepsy foci for drug resistant patients,' Geneviève said.

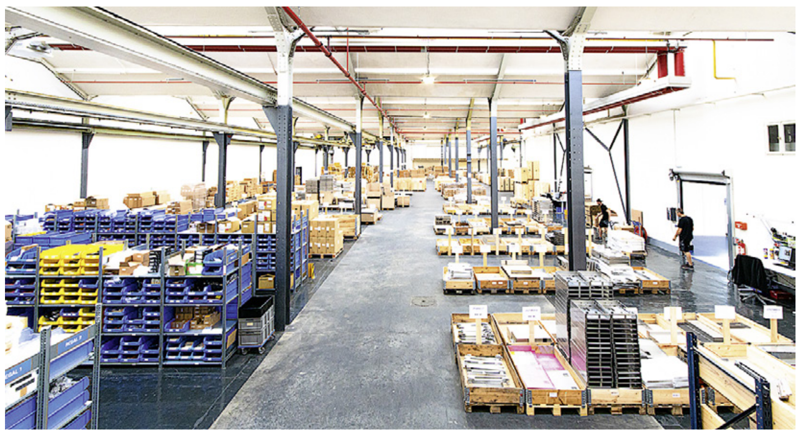
Another innovation, ROSA ONE Spine, enables to perform minimally invasive surgeries and has been proven to significantly reduce blood loss, lower infection rates and reduce complications. Studies show that use of robotic guidance during spinal fusion significantly reduces radiation exposure and length of stay. Technology is increasingly integrated in the operating room and robots are only one part of the equation. In the future, there will be a stronger integration between implants and technology, artificial intelligence and data insights, she believes. 'Many devices and products are now robotic, connected and/or equipped with sensors: operating tables, lighting, imaging systems, microscopes, drills and reamers. All these devices will work as integrated units, delivering new sources of data insights to further improve patient care.' Robotics is a part of ZBEdge, Zimmer Biomet's suite of integrated digital and robotic technologies, which has been engineered to deliver data-powered clinical insights, shared seamlessly across the patient journey.

'Data processing and artificial intelligence make it possible to rerun surgeries for training purposes, share a specific technique with other surgeons or train young surgeons. The possibilities are endless,' Geneviève concluded, 'and that's what makes it so exciting.'

Changing processes increased output by 30 percent

Streamlining and higher quality

Rein Medical, a leading supplier of customised all-in-one computer systems, high-resolution displays, customised OR wall modules and video and image management software solutions across Germany and Europe, produces high-quality, robust products. 'To maintain these high standards going forward, the JVC subsidiary has enlarged and redesigned the warehouse and production area and optimised the processes,' the company reports.



The company's enlarged and redesigned warehouse and production area

'We are focusing on two separate production areas. The mechanical components are manufactured in the separate pre-production area, which keeps most of the dust and impurities outside the electronic assembly.

'In the production area, which is protected from electrostatic discharge (ESD) and air-conditioned, the assemblies are created on mobile workstations and then inserted into the pre-assembled housings. This protects the devices from uncontrolled electrostatic discharges, which can cause invisible damage inside the components.

'Thanks to this more efficient production process and the enlargement of the production areas, we could increase production output by 30 percent, with less work for the production technicians and with the same number of production days.

'We have also improved quality assurance with the new ESD area,' said Stephan Rein, founder and managing director of Rein Medical, when describing the new processes and their advantages.

During the redesign, special attention was paid to ergonomics at the workplace, he added. 'After all, we want to create the best working conditions for our employees, and improve the quality of their work and products.' The Mönchengladbach-based company benefited from the experience of its colleagues at JVCKenwood Corporation in Nagaoka (Japan) in regard to more efficient production and logistics processes.

Details: www.reinmedical.com

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!

ATEM Mini........**265€***
ATEM Mini Pro........**439€***
ATEM Mini Pro ISO........**695€***

Learn more at www.blackmagicdesign.com/nl

Blackmagicdesign

*Recommended retail price excludes VAT and shipping and delivery costs. ATEM Mini for use in training, conferencing and teaching purposes only.

3-D printed titanium-alloy knee plates

High tibial osteotomy simplified

3-D metal printing technology is producing personalised medical-grade titanium-alloy plates that perfectly fit individuals suffering arthritis of the knee.

Engineers at the University of Bath's Centre for Therapeutic Innovation (CTI) working with 3-D Metal Printing Ltd, are using the TOKA (Tailored Osteotomy for Knee Alignment) treatment to improve the surgical procedure and fit of high-tibial osteotomy (HTO) plates to realign a patient's knee. The system improves stability, comfort and weight bearing over existing generic plates. The technique also simplifies high tibial osteotomy (HTO), making operations quicker and safer.

The HTO plates have been safety tested in a computer-based virtual 'in-silico' trial using CT scan data from 28 patients. The in-silico clinical trial, globally the first to demonstrate the safety of an orthopaedic device, modelled the stresses that would be exerted on the bespoke plates and showed these would be comparable in safety to the standard treatment.

'Knee osteoarthritis is a major health, social and economic issue and does not receive as much attention as it should,' Professor Richie Gill, from the Centre for Therapeutic Innovation, pointed out. A quarter of women over 45 have it, and about 15 percent of men, so it's a significant burden that many live with. Knee replacement is only useful for end-stage osteoarthritis, so you can be in pain and have to live with a disability for a long time, potentially decades, before it's possible. We hope that the new TOKA process we've developed will change that.'

Knee osteoarthritis patients receiving TOKA will undergo a 3-D CT scan of their knee, before a personalised 3-D printed surgical guide and plate, both shaped to their tibia (shin bone) is created. The surgical guide simplifies the surgery and is designed to improve accuracy.

The process also sees the first implementation of 3-D printed screw threads into the HTO plates, meaning they can be optimally positioned to help secure them against the bone.

Upcoming trials

When clinical centres return to carrying out elective surgery, expected later this year, trials will begin. UK hospitals in Bath, Bristol, Exeter and Cardiff will take part in a randomised control trial to compare patient outcomes with an existing generic HTO procedure.

Tests of the TOKA technique have already begun in Italy where, so far, 25 patients received new personalised HTO plates as part of a trial at the Rizzoli Institute in Bologna.

HTO surgery realigns the knee joint by making a cut to the tibia and opening a small gap, which needs to be stabilised by a metal plate. This realignment moves the loading to a less worn part of the knee. Patient outcomes depend on how accurately the cut is made and the gap opened.

'HTO surgery has a long clinical history and has very good results if done accurately. The difficulty surgeons have is achieving high accuracy, which is why we have created the TOKA method,' Gill explained. 'This starts with a CT scan and digital plan. 3-D printing the custom knee implant and doing the scanning before operating means surgeons will know exactly what they'll see before operating and where the implant will go. In addition to a surgeon being able to precisely plan an operation, a surgical guide (or jig) and a plate implant, each personalised to the patient, can be 3-D printed automatically, based on the scanning data. Importantly this type of treatment relieves the symptoms of knee osteoarthritis while preserving the natural joint.' Pre-planning greatly simplifies surgery and could cut time on the operating table from two hours to around 30 minutes. (SKE)

© University of Bath

The implant preserves the existing joint and can be used at an earlier stage of arthritis, that means before a knee replacement becomes necessary.

Modern cementing technology

Cemented hips help preventing

For decades, hip arthroplasty has been a routine procedure. In Europe, both total and partial hip replacements are the most frequent surgical interventions for patients with hip fracture or osteoarthritis. The treatment relieves pain and has good long-term outcomes. In cemented hip replacement, the artificial acetabulum and/or the femoral stem are fixed with bone cement and implant and bone bond immediately.

To prevent infections, the cement contains one or two antibiotics. Comprehensive studies have confirmed many benefits of this method.

The trend towards uncemented implants

Nevertheless, in Denmark, currently around 70 % of the patients receive uncemented implants, whereas Norway and Sweden are more conservative, but the use of uncemented implants has increased even in these countries, in Sweden from 3% in 2000 to 28% in 2019.

According to the German Arthroplasty Registry's (EPRD) annual report 2019, in Germany, the number of cemented total hip replacements decreased from 8 % to 5 % between 2014 and 2018 across all patient age groups; at the same time, the percentage of entirely cement-free replacements increased from 75 % to 79 %. 'Comprehensive studies have confirmed the many advantages of cemented hip replacements, such as a reduced fracture risk. Particularly certain patient groups, above all older patients or patients with hip fractures, profit from this type of implant. 'However, in many countries, clinical practice does not follow scientific evidence,' says Professor of orthopaedic surgery Søren Overgaard of Copenhagen University Hospital, Bispebjerg, Denmark. The reasons for this trend, he assumes, might be the fact that surgeons are not familiar with the current evidence and the differences in training and culture in healthcare systems.

A sustainable bonding solution

The goals of any surgical intervention are pain reduction, maintaining long-term function and avoiding complications and revision surgery. The outcome is shaped by several factors – which can be partially controlled by the surgeon and the patients. 'Advanced patient age is a given,' says Overgaard. But 'consumption of tobacco, alcohol or medication and the willingness to undergo surgery are issues that patient and physician can discuss.'

In addition to patient selection, perioperative care and rehab, the choice of bonding components plays a crucial role. This decision should always be based on reliable data. 'There is plenty of evidence from high-quality studies,' says Overgaard and adds that his team 'chooses the individual suitable fixing methods based on this evidence.' The high percentage of uncemented implants shows that this is not best practice in all hospitals. Overgaard underlines a lack of experience particularly among young physicians. 'We surgeons only teach what we can do,' he says, but 'the objective should be to decide on the basis of reliable evidence in order to achieve best outcomes for the patient and reduce complications.'

Periprosthetic fracture is more common in uncemented stem fixation

The most common complications after hip replacement are loosening of the components, infection, periprosthetic fracture, and dislocation. Among these complications, periprosthetic fracture (PPF) had the highest mortality, according to the Swedish Arthroplasty Register. 'Thus, prevention of a PPF not only can increase the quality of life, but also might save lives,' concludes Dr Georgios Chatziagorou from the University of Gothenburg in Sweden.

'It's therefore, important to identify the patients most at risk of PPF,' he emphasises. Increasing age is a known risk factor, and uncemented femoral components resulted in higher risk of revision surgery, according to a large register study. Among male patients aged 60-69 years who received an uncemented stem, the risk of PPF was four times as high as among the same age group with cemented stem. However, among women of the same age-group, the risk was thirteen times higher for those with uncemented stem fixation compared to women with a cemented femoral component.

Women older than 55 years should receive cemented hip replacements, according to data from the Norwegian Arthroplasty Register. A Danish study showed positive effects of changing from uncemented to cemented fixation.

The number of periprosthetic fracturea decreased from 4.1 % to

Dr Georgios Chatziagorou, University of Gothenburg, Sweden

Professor Nils Hailer, Uppsala University Hospital, Sweden

Professor Søren Overgaard, Copenhagen University Hospital, Bispebjerg, Denmark

Orthopaedic advances

Virtual training by hip implant simulator

Trainee trauma or orthopaedic surgeons have limited chances to practice hip replacement surgery before their first hands-on case. To change this, a team in the Dynamic HIPS project aim to improve this by creating a dynamic hip replacement simulator for future surgeons to practice the intervention and develop a reality-based feel for the procedure, Sascha Keutel reports.

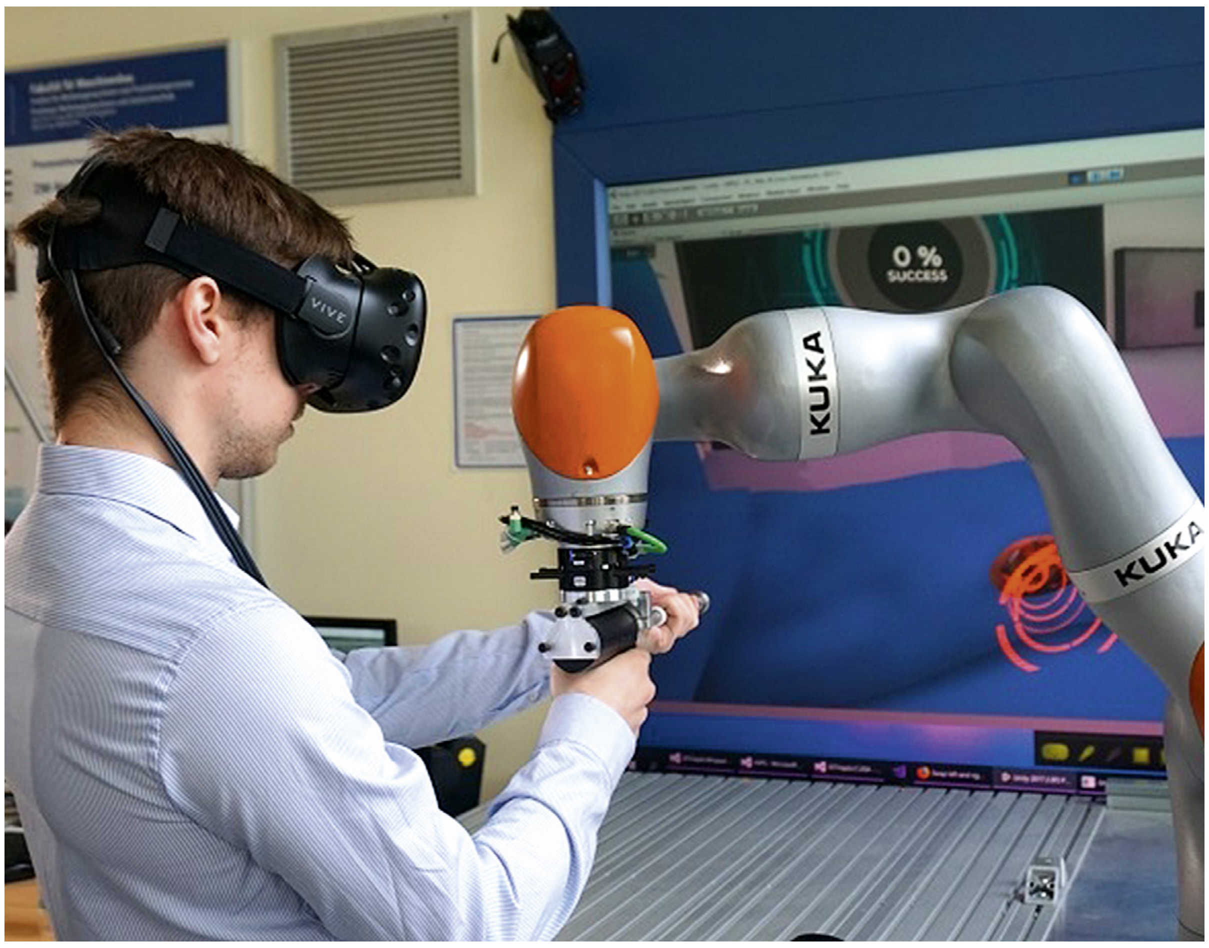
With an ageing population it is inevitable that the number of hip replacements is increasing – as is the demand for well-trained orthopaedic surgeons. The surgical procedure requires precision and physical strength.

Currently, training junior surgeons depends on donor bodies and animals before the intervention can be performed in the OR supervised by an experienced colleague. 'The use of virtual reality (VR) combined with haptic simulation would enable future surgeons to practice the intervention as often as necessary, without having to rely on donor bodies or animals and without having to put real patients at risk,' according to Dr Mario Lorenz, research associate at the Institute for Machine Tools and Production Processes (IWP), at the Technical University (TU) Chemnitz. There, a simulator is being designed to complement current training methods and save scarce training resources.

Dynamic HIPS is the successor project of HIPS (HüftImplantat–PfannenfräsSimulator), which was completed in 2019. 'At the end of HIPS, we had developed a technically fully functioning system that could simulate milling the acetabulum and implanting the replacement hip with haptic feedback in virtual reality,' Lorenz explained. But, he added, something was amiss. 'The hard contact when placing the mill on the bone has to be generated by the robot within milliseconds to make the situation real for the surgeon.' However, in the first clinical tests the haptic feedback was outside the time range envisaged by the scientists.

Project aims

This is how Dynamic HIPS was born, Lorenz explained. 'We want to develop a haptic simulator that offers the surgeon the same sensory experience as real surgery. Above all, we want to map the forces at play when sawing or milling a bone.' With the exception of opening the body and closing the wound, the researchers want to include all steps of hip replacement surgery in their expanded simulator – removing the femoral head with a bone saw, shaping the socket and placing the implant in the reshaped socket.



The hip simulator system at work

In a real operating room, the surgeon works on the femur and the acetabulum to fit the implant. In the virtual OR, the surgeon sees the virtual body and 'feels' it because the tools give mechanical feedback. The scientists want to identify the forces, torques and speeds that occur during each step of the procedure. On the basis of this data, they plan to develop a robotic arm and to further optimise current haptic tools.

First, the project partners create a mathematical model that more precisely simulates the resistance and the bone tissues removal. Furthermore, the team aims to develop a virtual OR where the trainee surgeon is supervised by an experienced senior physician. Such a remote training session could be performed across long distances and would facilitate knowledge transfer to newly developed and developing countries.

'We want a collaborative multiuser system,' Lorenz said. To this end, the project partners are developing a mathematical model that simulates the resistance and material removal on the bone even more precisely. Due to travel restrictions caused by the Covid-19 pandemic, material tests had to be postponed to autumn 2021. Nevertheless, the project partners could finish all individual components. 'We expect to be able to join all the components, that is to completely finish our extended prototype, by spring 2022,' he said.

The project partners

In addition to the Chemnitz University of Technology, the University of Bremen and several companies are involved in the project. FAKT Software GmbH will integrate the components and build the training system, as well as the multi-user system.

CAT Production GmbH developed the 3-D models of patient anatomy and of the OR. Haption GmbH will contribute an enhanced haptic system and a module for user safety.

YOUSE GmbH will ensure the user-centred approach of the project and monitor the ethical, legal and social implications of Dynamic HIPS. The medical experts on the project are the Department of Orthopaedic, Trauma and Plastic Surgery at the University Hospital Leipzig, the Centre for the Study of the Musculoskeletal System (ZESBO), the Division of Macroscopic and Clinical Anatomy at the Medical University Graz (Austria) and the med-tech department of the Fraunhofer Institute for Machine Tools and Forming Technology (IWU).

g infections

2 % when the number of women above 60 receiving cemented hip replacements increased from 12.3 % to 82.5 % during the same period of time.

Hip fracture patients are particularly at risk due to comorbidities

For Nils Hailer, Professor of orthopaedics at Uppsala University Hospital in Sweden, older patients who receive a partial or total hip replacement following a femoral neck fracture are a high-risk group due to their comorbidities and high early mortality.

Despite the risk of bone cement implantation syndrome, he recommends cemented implants for this group since the benefits of cemented fixation vastly outweigh the disadvantages.

'Uncemented hemiarthroplasty patients require second surgery twice as often as other patients,' because 'the risk of PPF and infections is increased, and the life span of the implant is decreased.' Moreover, patients with a cemented hip replacement regain mobility much faster.

In addition, the infection risk can be reduced with a cemented hip, Hailer points out: 'We have solid evidence that infection protection is achieved when we use cements loaded with antibiotics.

'There is also emerging evidence that dual antibiotic cement can further reduce the risk of periprosthetic joint infection in hip fracture patients, but several ongoing randomised trials need to confirm this theory.'

A randomised controlled study conducted in Newcastle confirms this view: The use of high dose dual-antibiotic impregnated cement in these patients reduced the infection rate by 69 % compared with standard low dose single antibiotic loaded bone cement.

Thus, Hailer concludes, 'Uncemented hemiarthroplasty should by all means be avoided in patients with hip fractures, both to reduce the risk of periprosthetic fracture and infection.'

The experts agree that evidence-based treatment decisions would significantly improve outcomes.

In view of the study results and the fact that, in Denmark, 50 % of the hip fracture patients receive uncemented hemiarthroplasty, Professor Overgaard has and aims for a clear goal: 'We will try to change that.'

Scientific references available on request.

RTI: Ensuring X-ray quality for 40 years

Triple celebrations in Sw

The Swedish RTI Group reports three notable milestones in 2021, including its 40th year in specialised X-ray safety manufacturing.

In 1981, the DIGI-X model – the first commercially available multimeter to measure non-invasive kV – was launched. 'Subsequent developments have included world firsts, in both quality assurance (QA) hard- and software, of the Mini-X, PMX-II, Barracuda and oRTIgo,' the firm reports. 'Today, RTI's trademark Piranha and Cobia meters are used by a plethora of hospitals, major manufacturers of X-ray equipment, service providers and government authorities worldwide.'

Early in 2021, RTI launched its own Scatter Probe, a combined leakage and scatter detector, an upgraded version of its industry-leading QA software Ocean.

At the forefront of these key developments in X-ray QA have been Olle Mattsson (Area Sales Manager Nordic & Rest of the World) and Sören Sturesson (Product Management & Technical Manager Calibrations), both RTI's longest-serving "veterans", now celebrating 25 years of service in the Gothenburg HQ Sales and R&D departments.

What drew them to RTI?

After graduating as an electrical engineer, Mattsson saw a RTI job advertisement. 'Like many others, I'd never heard of the concept of measuring on X-ray machines non-invasively. RTI, therefore, sounded like a very open-minded, creative and forward-thinking company.' The job interview was a resounding success.

In the early '90s, during Sturesson's studies in Medical Physics at Sahlgrenska University Hospital, Gothenburg, he was working on dosimetry in diagnostic radiology departments. 'After reading about the X-ray developments at RTI, I applied for work there as part of my master's thesis evaluating solid-state detectors and scintillating materials for radiation protection in medical X-ray. I graduated in '95 and worked part-time at the University Hospital and at RTI, before joining the latter full time,' bringing him understanding and schooling in clinical and manufacturing in dosimetry.

How has RTI's 'firsts' impacted on the X-ray market and influenced your own work?

'If RTI has been the first to do something, most of my time in Sales has been spent explaining our unique solution,' Mattsson said. 'Customers are very keen to get the latest and best on offer. Thanks to RTI, the X-ray QA market has advanced significantly in user-friendliness and meeting new demands. Naturally, this will continue to improve in future.'

Research and development has been challenging, but working with generations of X-ray multimeters has been exciting, Sturesson pointed out.

'There have been increased demands for user-friendliness to meet the new technical innovations within diagnostic imaging. When the company released DIGI-X in 1981, every X-ray tube/filter combination was almost the same, whereas today there's a large variety in X-ray spectra, narrow-beam geometry.'

Scatter probe from RTI

How did the X-ray industry respond to RTI's breakthrough developments?

'Due to all its "firsts", many times our competitors simply had to follow us,' enthused Mattsson.

'The Barracuda meter release in 2001 was a major paradigm shift for the X-ray multimeter market,' Sturesson observed. 'Our in-depth research and testing resulted in a meter without the shortcomings present in other non-invasive X-ray multimeters then available. Our competitors followed ever since, while we've continued to lead in the simplification of using our meters, not least with software tools like Ocean.'

Sören Sturesson, Product Management & Technical Manager Calibrations

How has X-ray testing technology changed in 25 years?

'The X-ray machines and QA solutions available have moved the focus away from hardware towards different software solutions to help the users,' Mattsson explained. 'Consequently, QA testing standards had to change due to new regulations in the X-ray market, often after the industry has already developed the new hardware to meet demands.

'In RTI Sales, we have a far bigger and more active global distributor network – more than 100 contacts – since I joined. Since the early 2000s, beginning with the formation of RTI Group Inc. in the USA and, more recently, with Group APAC in Singapore, our presence and exposure in North America and Asia-Pacific also increased significantly.'

Sturesson: 'The basics are still the same – safety and proper functionality of the X-ray equipment. The major change was when X-ray film was phased out and replaced with digital detectors, opening the door for major development of X-ray diagnostics, which has led to a wide range of applications with which the X-ray multimeters of today must comply.'

How will the increased implementation of software shape future X-ray QA?

'I don't think anyone could foresee how big the focus on software would be, nor how many different software programmes would be available today to assist users in so many ways,' Mattsson noted. 'Software has become essential, and will continue to grow to ensure compliance, easy management of measurements and the integration of other important data. Therefore, RTI has invested in its Academy training and online presence to increase accessibility of the Ocean software portfolio.'

'In the late '80s, RTI launched oRTIgo, the first software tool for X-ray QA,' Sturesson added. 'This continued to develop and has now evolved to the Ocean software we offer today.

Supercomputer creates 3-D brain models

The Synthetic Brain Project

Scientists are using artificial intelligence and the Cambridge-1 supercomputer to synthesise artificial 3-D MRI images of human brains and create models that show disease states across various ages and genders, Mark Nicholls reports

The Synthetic Brain Project is focused on building deep learning models which have been developed by King's College London (KCL) and NVIDIA data scientists and engineers as part of The London Medical Imaging & AI Centre for Value Based Healthcare.

Computing power

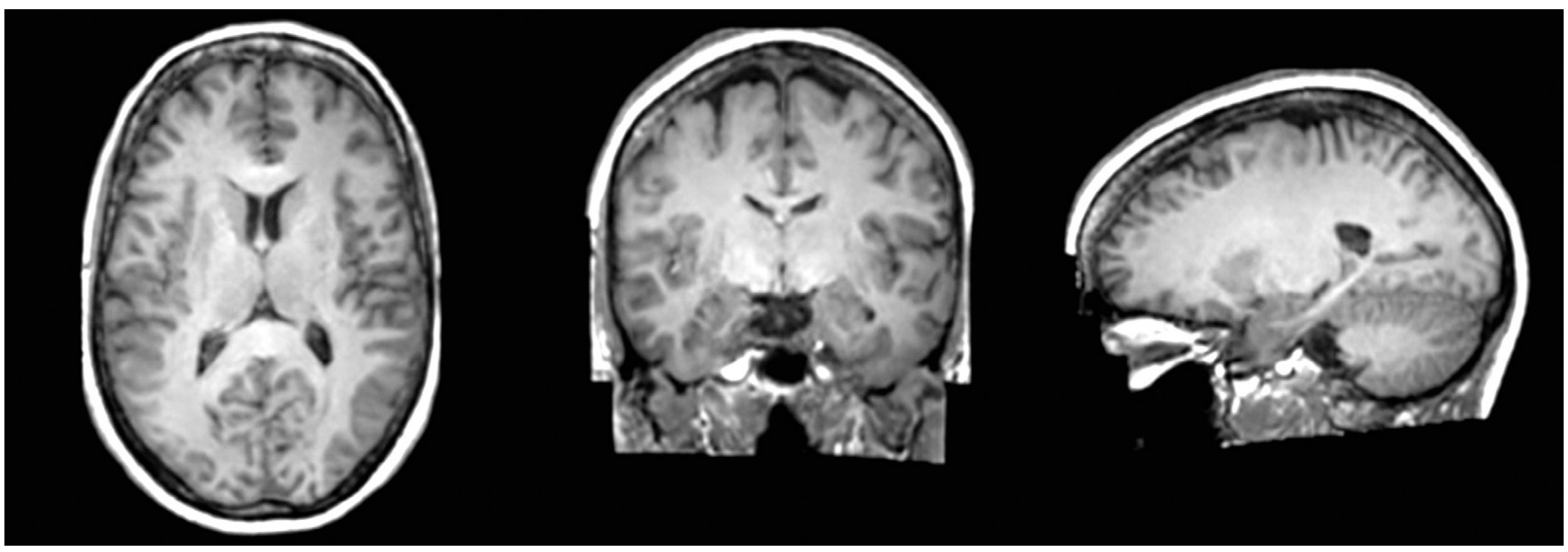
Dr Jorge Cardoso, Senior Lecturer in Artificial Medical Intelligence at KCL and CTO of The London AI centre for Value Based Healthcare, said that the Cambridge-1 supercomputer has the necessary computing power to train models of the size needed for this process, along with the speed to make development cycles fast and feasible.

The AI model has learned what human brains look like by examining many images, Cardoso explained, with Cambridge-1 being used to teach AI models to generate synthetic brain images from previous MRI brain scans from the UK Biobank and NHS. 'We can then sample from this model by providing the subject characteristics, such as age and sex, and retrieve the newly-generated images.

'This solves the problem of scarce data, as we can generate as much data as we want, and also the problem of privacy, because we can learn from synthetic data rather than real data.

'As the models learn to generate brains with/without pathologies, and in young and old age, we can then study these images to better understand the effects of pathology and ageing to give us a better understanding what actually changes in these brains.'

Synthetic brain model created by KCL and NVIDIA using Cambridge-1 supercomputer



Disease diagnosis

This, he added, will help to diagnose neurological diseases, such as stroke, dementia, brain cancer and multiple sclerosis, based on brain MRI scans – or predict diseases that a brain may develop over time and enable preventive treatment.

Researchers hope that by generating an infinite number of images with/without pathology from many ages, genders and ethnicities, they can then train other AI algorithms to learn to identify which images are pathological and which are not.

Cambridge-1 enables accelerated generation of synthetic data that offers an understanding of how different factors affect the brain, anatomy, and pathology.

Scientists can 'ask' the models to generate an almost infinite amount of data, with prescribed ages and diseases and, from there, help tackle problems such as how diseases affect the brain and when abnormalities might exist. 'This could mean better and earlier diagnosis, which would be naturally beneficial to most patients, because early treatment commonly improves outcomes,' Cardoso pointed out. 'A better understanding of how diseases affect the brain can also help develop new therapeutics.'

Data availability

The Cambridge-1 supercomputer has been pivotal in this aim, because the previous biggest computers – albeit very substantial in computing power – could not scale to the AI model size needed to produce good quality data.

Data availability can be a major issue, but Cambridge-1 is helping to solve that via its massive computational power to generate the large synthetic datasets for research and algorithm development.

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Olle Mattsson, Area Sales Manager Nordic & Rest of the World

'It's much more than storage of measured data because it provides organisation, compliance and efficiency for the entire X-ray QA process. As an innovative organisation, we are experienced enough to research and develop the rapidly changing software needs of our customers and partners.'

Mattsson: 'RTI will continue its holistic view and strengthen its focus on complete solutions. Our drive to work even closer together with our distributors and users to be their QA partner will doubtless receive even more interest within the X-ray industry!'

'RTI's determination to develop even more efficient QA solutions will be a huge determining factor in our progression,' Sturesson predicted. 'Software will continue to be even more important in supporting the users in their daily QA work, but we will also certainly see new dosimeters on the market that meet new technical demands.'

With more than 12 years expertise in advanced image analysis, big data, and artificial intelligence, **Dr Jorge Cardoso** is senior lecturer in artificial medical intelligence at King's College London, where he leads a research portfolio on big data analytics, quantitative radiology and value-based healthcare. He is also Chief Technology Officer of the new London Medical Imaging and AI Centre for Value-based Healthcare.

Cambridge-1 is one of the world's top 50 fastest supercomputers, built on 80 DGX A100 systems, integrating NVIDIA A100 GPUs, Bluefield-2 DPUs, and NVIDIA HDR InfiniBand networking.

KCL researchers are leveraging NVIDIA hardware and the open-source MONAI software framework supported by Pytorch and NVIDIA's software solutions like cuDNN and Omniverse for visualising brains in the Synthetic Brain Project.

Dr Cardoso, who led the research team and developed and trained the artificial intelligence model, said a next step will be to expand the process to other body parts and disease, and in a longitudinal progression.

UPCOMING EVENTS

- **German Congress of Radiology (DRK)**
  27 March-8 November 2021, online
  www.roentgenkongress.de
- **Swiss Congress of Radiology (SCR)**
  26 June-16 December 2021, online
  www.congress.sgr-ssr.ch
- **Journées Francophones de Radiologie (JFR)**
  8-10 October 2021, Paris, France
  www.jfr.radiologie.fr
- **Radiological Society of North America (RSNA)**
  28 November-2 December 2021, Chicago, USA
  www.rsna.org
- **Joint International Congress of Emergency Radiology (JICER)**
  5-6 February 2022, online
  www.jicer22.com
- **European Congress of Radiology (ECR)**
  2-6 March 2022, Vienna, Austria
  www.myesr.org/congress/ecr2022

Reduce MRI scanner anxiety

Float off into virtual reality

Claustrophobia or anxiety can overwhelm small children and people with cognitive difficulties, especially in a confining and noisy MRI scanner tube. Their restless reactions can then render scan images useless.

Report: Mark Nicholls

To help such patients to relax during scanning, a team from King's College London (KCL) has designed an immersive environment with a special virtual reality (VR) headset for use with MRI scanners.

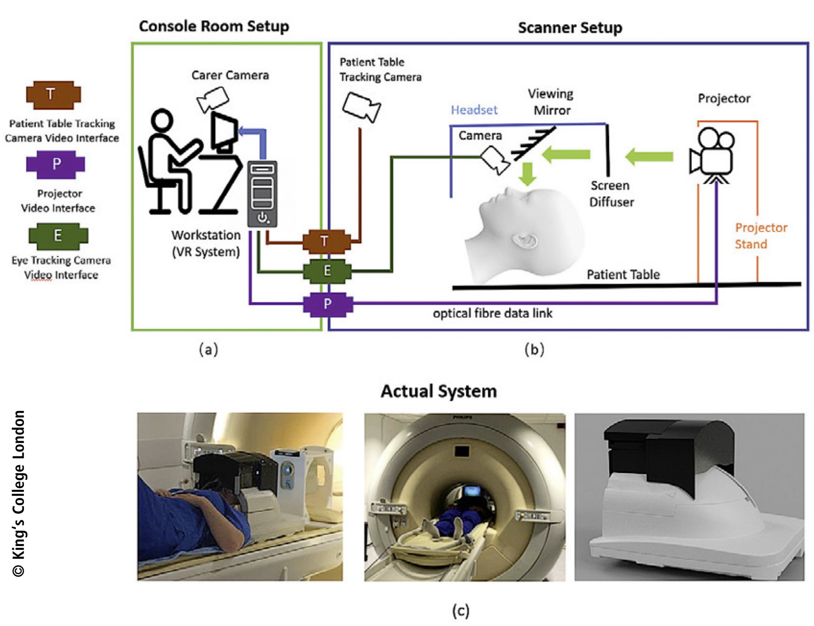
Christmas gift inspiration

The idea for this distracting system originated when Dr Tomoki Arichi, a Clinician Scientist and Clinical Senior Lecturer in the KCL Centre for the Developing Brain, presented Jo Hajnal, Professor of Imaging Science in the Centre, a Christmas gift of VR goggles. 'Professor Hajnal realised that whilst using the goggles, the strong immersive experience meant he was completely unaware of what was going on around him and this inspired us to create similar technology for use inside an MRI scanner,' lead researcher Dr Kun Qian explained. 'We then went on to develop the technology through a multi-disciplinary collaboration of colleagues with a background in computer science, engineering, optical science, clinical and physics.'

Qian, a research associate in the Centre for the Developing Brain at KCL's School of Biomedical Engineering & Imaging Sciences, acknowledged that having an MRI scan can be an 'alien experience', with scanning failure rates in under five-year-olds as high as 50 percent.

Time and resource wastage can delay clinical decision making, he pointed out. 'Even in those children who manage to complete the scan, movement artefacts can significantly degrade image quality and affect interpretation. Whilst this can be alleviated with sedation or anaesthesia, these are resource heavy and carry their own associated clinical risks.'

The researchers had observed that, when fully immersed in a virtual reality environment, people become unaware of what occurs in reality around them. Thus, they developed a system to replace a patient's actual visual scene when having a scan with tailored VR content that is immersive and interactive, Qian said. 'This removes the sensation of being inside an MRI scanner. We believe that it can potentially benefit all groups having a MRI scan, but in particular will help vulnerable populations with anxiety problems, and those with cognitive difficulties.'



The VR headset can be used safely inside an MRI scanner. The device is designed to be light tight, so that the user cannot see their surrounding environment at all.

The key component

This is a custom-built 3-D printed MR-compatible VR headset; a pair of MR-compatible cameras (for eye tracking) and a MR-compatible projector for VR content display, which can be set up and removed between patients.

The research team also designed the system to precisely match existing scanner hardware – in the case of King's College London, the head coil in a Philips Achieva 3T system.

With everything connected to a standard PC in the control room, patients control the system by using their eyes. They also can communicate with a carer outside the scanner. The aim is for the system to transform the MR examination from a passive and isolating experience into an active, engaging and interactive one.

'Our VR headset is designed to be entirely light tight, so that the user cannot see their surrounding environment and is unaware of visual reminders of their position inside the MRI scanner,' Qian added.

Immersive content

With the patient positioned in the scanner, the projector's system immediately shows immersive 3-D images which appear to surround the user. This continues till the examination ends. 'Crucially, it means that a patient may be completely unaware of their surroundings during their whole time inside the scanner,' said Qian.

The research team has incorporated real-life sensory experiences into the VR environment, such as the visual scene moving when the examination table moves, or animated characters responding to scanner noise.

Using their eyes, the user can navigate through the virtual world to select content, such as films or games, and initiate, or terminate, a video link to their carer, meaning they can interact at any time during the scan with a companion via a webcam with microphone and a display monitor.

Value in studies of cognitive processes

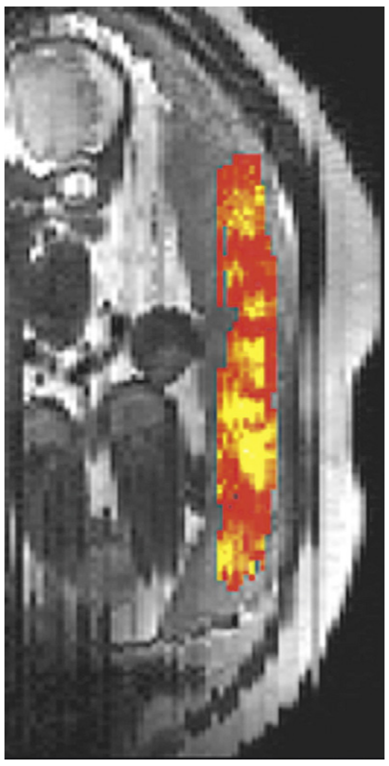
While the proposed system has clinical applications for the populations who find MRI stressful, the team believe it also has potential for neuroscience as a platform for MRI experiments studying fundamental

30-second MRI scan to estimate placental health

Detecting early signs of pre-eclampsia

From routine MRI scans, a machine learning algorithm is being used to model the normal distribution of placental tissue properties and show deviations from normal placental ageing and signs of pregnancy complications.

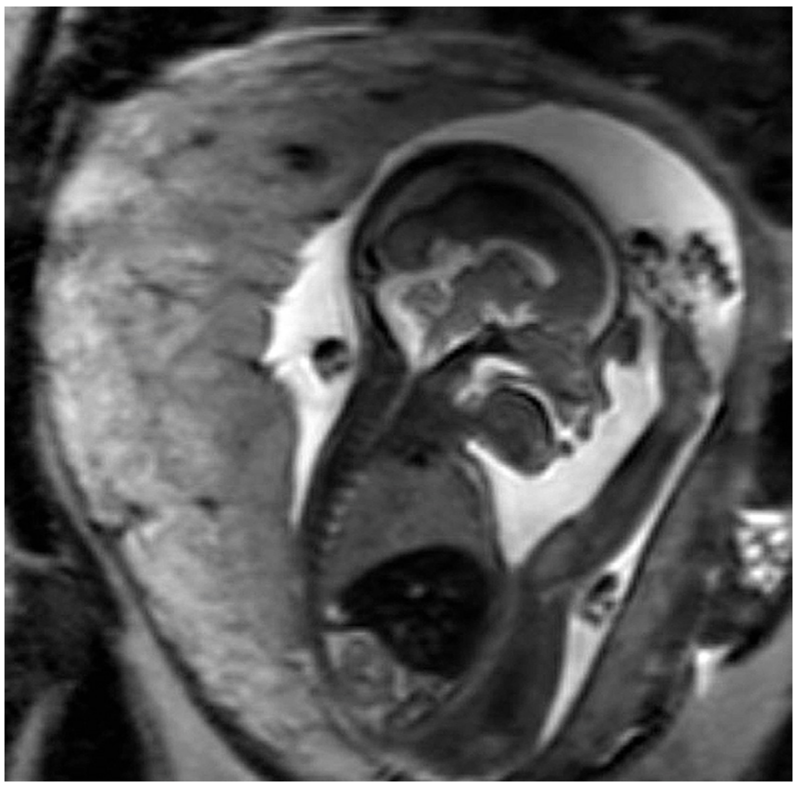
To identify adverse conditions in pregnancy, researchers at the School of Biomedical Engineering & Imaging Sciences at King's College London (KCL), united with the women's health department at the city's St Thomas' Hospital, where the emerging technique was devised in collaboration with obstetricians, physicists, radiologists, midwives, engineers and pathologists.



Overlay of a placental T2* map (functional MRI) on an anatomical MRI image. Bright yellow indicates high oxygen content, dark red low oxygen content.

Patients are scanned with a T2* sequence MRI, with imaging data fed into the neural network pipeline, which rapidly performs automatic segmentation before a regression model delivers a placental health score. The scan, combined with the automatic pipeline, can be included as part of any foetal MRI examination but has the benefit of acquiring additional information not available under routine obstetric screening using ultrasound.

Lead researcher Dr Maximilian Pietsch explained that the method is most sensitive early in the second half of pregnancy – also typically when the onset of pre-eclampsia begins – thus allowing early detection and monitoring. The method develops a clinical marker and automates its extraction, which would otherwise be prohibitively time-consuming in clinical practice.



Anatomical MRI image of the placenta (left side) and the foetus (right side) in the 2nd trimester

Oxygenation levels

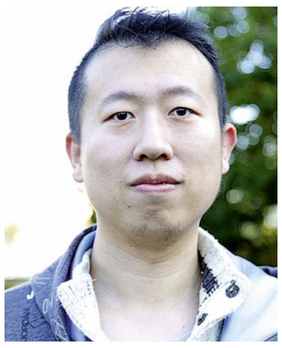
Research Fellow Dr Jana Hutter said the approach may provide additional information to ultrasound, which cannot acquire information from inside the placenta. 'We use MRI because it has no ionising radiation, so is completely safe to use in pregnancy, and the T2* imaging technique allows us to look at oxygenation in the placenta.'

Dr Jana Hutter is a Senior Research Fellow at KCL and UKRI Future Leaders Fellow based at St Thomas' Hospital. After gaining her PhD in Erlangen, Germany, she moved to KCL, where she now leads her own research to focus on functional foetal and neonatal MRI.

Chronic hypertension in pregnancy is increasingly common, raising the chance of pre-eclampsia.

'This technique allows us to look for this before any clinical symptoms start in this high-risk population,' Hutter said. 'This gives obstetricians additional valuable information to closely monitor the mother and baby to optimise the time point of the birth – late enough for the baby but early enough to avoid any effects to the mother.' The technique may assess the health of an unborn child and the mother, so as to introduce interventions to prevent possible complications from growing more serious.

Other applications could be to identify evidence of foetal birth restriction, in which a baby does not grow as big as it could, plus late stillbirth, and other complications, such as gestational diabetes.



Dr Kun Qian is a post-doctoral researcher in the Centre for the Developing Brain, at the School of Biomedical Engineering & Imaging Sciences, King's College London. His research focuses on developing a non-intrusive MR-compatible VR system which avoids disturbing the magnetic environment and uses eye tracking as the main interface.

cognitive processes, such as social communication, opening the way to gain new insight into how patterns of brain function, behaviour and social skills develop.

Increasing content

With positive initial feedback from participants, the next step is to test it on a larger and more varied group of users and patients. 'We would also like to develop more content, specifically for some of the vulnerable groups and potentially tailor the environment for them if needed,' Qian added.

'As this content is likely to be very different, depending on age and cognitive capabilities, getting this right and tailoring it for different clinical and study populations is a key next step.'

Dr Maximilian Pietsch is a Research Associate in The Institute of Psychiatry, Psychology, and Neuroscience (IoPPN) at King's College, London (KCL). He also conducts research in a clinical setting at St Thomas' Hospital. Research interests: using machine learning combined with advanced diffusion MRI data to study the developing brain.

Solving clinical need

A next step is to recruit targeted groups to test the machine learning algorithm for other conditions and add technical improvements.

However, Pietsch already can emphasise its current value: 'This solves a clinical need in a way that's feasible to achieve in standard clinical care. The time to obtain the information is reduced drastically. Before, it would have to be manually segmented to extract this information. To assess the health of the placenta, the data flow is quite simple, and results are immediately intuitively interpretable.

'Whereas a lot of medical machine learning research is somewhat detached from clinical needs,' Pietsch pointed out, 'this system has a strong immediate application in a hospital setting.' (MN)

AI in radiology

Unexpected benefits, unintended consequences

Artificial intelligence (AI) could match the impact of PACS on radiology. Covid-19 stimulated the development and testing of AI diagnostic-aiding tools in radiology, an unintended consequence of the pandemic. More image data sets have been created to train AI software, an unexpected benefit for radiology research, Cynthia E Keen reports.

The Samuel Dwyer Memorial Lecture at the virtual 2021 Society of Imaging Informatics in Medicine (SIIM) annual meeting, in May, focused on the exponential development of medical AI research and 'approved' radiology AI tools, as well as the challenges to achieve expected quality, safety, and performance attributes. Adam E Flanders, MD, Professor

Continued on page 12

Continued from page 11

of Radiology at Thomas Jefferson University Hospital, Philadelphia, delivered the 'Serendipity and Unintended Consequences' lecture, it reflected the visionary perspective of the late PACS pioneer Professor Samuel J Dwyer III, whose seminal research on the retrieval rates of radiology exams formed the basis for PACS storage systems.

Flanders likened the surge in AI tool development, and image data set expansion, to the 1960s space race, which launched the digital age, and to the global campaign to end the use of DDT.

The latter produced a negative unintended consequence: injury to wildlife was reduced, including mosquitoes, which then caused a large increase in cases of malaria.

The promise of AI technology to radiology

This is huge – potentially it could improve diagnostic quality, to efficiently extend access and be a panacea to major cost reductions in medicine. Flanders referenced experts who predict that healthcare AI overall will be a US$36 billion industry by 2025, generating a US$150 billion annual savings in AI-enabled healthcare by 2026. HealthITAnalytics reported, in 2019, that the top three areas of healthcare AI investment were robot-assisted surgery ($40 billion), virtual nursing assistants ($20 billion), and administrative workflow ($18 billion). By comparison, AI for preliminary diagnosis and automated image diagnosis ranked at the bottom of its list, at $5 billion and $3 billion respectively.'

Artificial intelligence is fundamentally limited

Nonetheless, there has been a tremendous surge in interest in AI in radiology. 'But is diagnostic AI on the right track? Is it happening too fast? Are image databases used to train AI software diverse enough, inclusive enough? Is there enough information?' Flanders asked. 'AI needs guardrails. It doesn't know when it doesn't have enough information when making a decision.'

Flanders cited an example of a brain CT angiogram, whereby the AI interpretation was a technical error of insufficient contrast material when, in fact, the patient was brain dead. While a radiologist can infer the correct diagnosis in this instance, it underscores the fact that AI is fundamentally limited to entities for which it is trained.

As of 2021, 222 AI medical devices were cleared by the FDA. Of these, 129 were for radiology applications, with 77% manufactured by small companies. But there is no agreed definition of an AI device or specific regulatory pathway, either in the USA or Europe. Is there enough rigorous evaluation? Flanders thinks not, nor do many other radiologists now speaking out publicly.

Researchers from Radboud University Medical Centre in Nijmegen, the Netherlands, evaluated 100 CE-marked AI software products for clinical radiology from 54 vendors listed in www.aiforradiology.com.

They reported in *European Radiology* that sixty-four products had no peer-reviewed evidence of efficacy, and that only eighteen of the hundred had evidence of efficacy rated as 3/6 or higher, validating impact on diagnostic decision-making, patient outcome or cost.

International standards for performance are needed

Between January and October 2020, 320 published papers described new machine learning-based models to detect Covid-19 in chest CT images and chest radiographs. Writing in Nature Machine Intelligence, researchers from Cambridge University reported that none of these models were of potential clinical use due to methodological flaws and/or underlying biases.

Most failed to describe a reproducible methodology or failed to follow best practice for ML model development, and/or failed to show sufficient external validation to justify wider applicability of the method.

Flanders said a recent editorial in Radiology *'Artificial Intelligence of Covid-19 Imaging: A Hammer in Search of a Nail'* was even blunter. 'To a large extent, the large quantity and rapid publication of articles on AI for Covid-19 are emblematic of current trends in other areas of radiology AI.

'It's now so much easier to design and conduct a radiology AI experiment. The only prerequisite seems to be possession of a large data set,' observed Ronald M Summers, MD PhD, of the National Institutes of Health Clinical Center's Imaging Biomarkers and Computer-Aided Diagnosis Laboratory of Bethesda, Maryland.

'International standards to enable meaningful comparisons of the performance are needed for AI software,' emphasised Flanders. 'Prospective outcomes studies are necessary to determine whether use of AI leads to changes in patient care, shortened hospitalisations, and reduced morbidity and mortality.'

Governments support image data collection

Access to data is critical, but has historically been monolithic, isolated, and difficult. Governments are now starting to support image data collaboration. Covid-19 brought a huge opportunity, because significant R&D funds became available to facilitate image data sharing and collaboration. One example is the Medical Imaging and Data Resource Center (MIDRC), a consortium formed by the American College of Radiology (ACR), the Radiological Society of North America (RSNA), and the American Association of Physics in Medicine (AAPM) for image collection, curation and distribution of Covid-19-related imaging data for AI research.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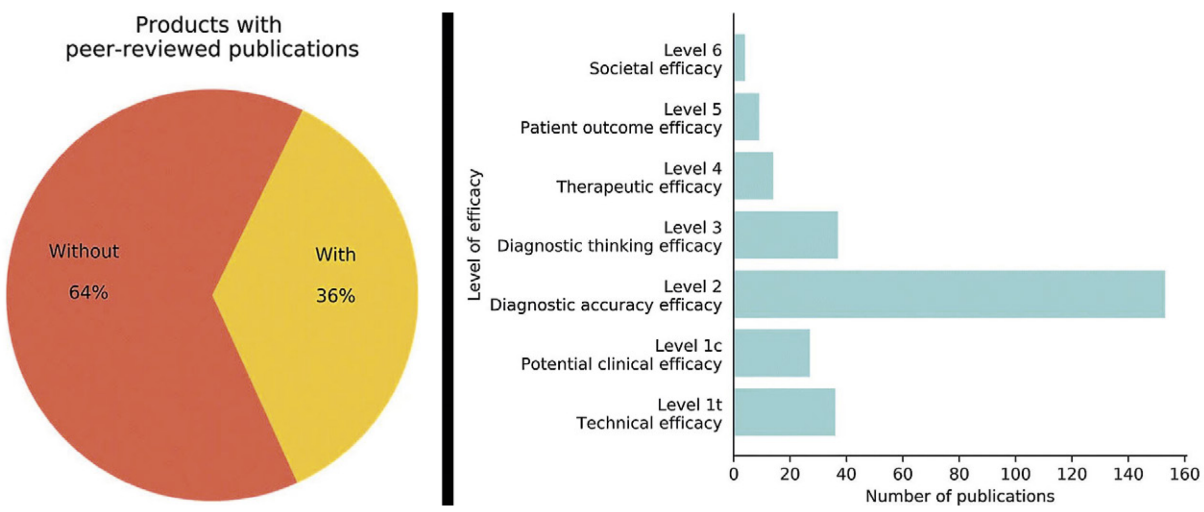
Adam E Flanders MD, Professor of Radiology and Rehabilitation Medicine at Thomas Jefferson University Hospital in Philadelphia, is co-director of neuroradiology/ENT radiology and vice chair of imaging informatics, also chairing the Imaging Informatics Council for the Enterprise Radiology and Imaging Service Line for Jefferson.



Left: Peer-reviewed articles were present for 36 of the 100 commercially available AI products; Right: Levels of efficacy of the included papers. The search strategy yielded 239 peer-reviewed publications on the efficacy of 36 out of 100 commercially available AI products. A single paper could address multiple levels. (Image source: van Leeuwen et al., European Radiology 2021)

The world's largest open Covid-19 images database

MIDRC supports 12 internal Covid-related research projects. Its repository is expected to be the largest open database of anonymised Covid-19 medical images and associated clinical data globally.

'There's no organ system in the body not affected by Covid-19. I predict this image repository, which welcomes image data contributions from throughout the world, will be of tremendous benefit to AI research and innovations for radiology,' said Flanders.

Continuing AI radiology research

He advises contribution of data to public data repositories to mitigate bias and strength diversity in AI research and development. He recommends promotion of new international evaluation checklists for testing, and radiologists should retain an appropriate level of scepticism when assessing products for clinical use, and when purchasing radiology artifical intelligence tools, mandate vendors to provide a complete account of performance.

'Most importantly, remain engaged in this very exciting, accelerating, and ever-changing process.

'Just as radiologists' input helped to perfect PACS to become the utilitarian technology it now is, most likely they will do the same for radiology artificial intelligence tools as they become ubiquitous.'

Hospital pathologists recognise the advantages

Digital pathology adoption accelerates

Professor Anil V Parwani is the vice chair and director of anatomical pathology at Ohio State University, and the director of pathology informatics at The James Cancer Hospital. His expertise includes the design of quality assurance tools, bio banking informatics, clinical and research data integration, applications of whole slide imaging, telepathology, image analysis and lab automation. He is also editor-in-chief of Diagnostic Pathology and an editor of the *Journal of Pathology Informatics.*

Digital pathology (DP) is a game-changer in the workflow, functionality and accessibility of a hospital's pathology department. As pathologists understand the benefits, and the availability of commercial products and systems increase, alongside data transmission and storage costs decreasing, DP deployment in hospitals is accelerating.

Report: Cynthia E. Keen

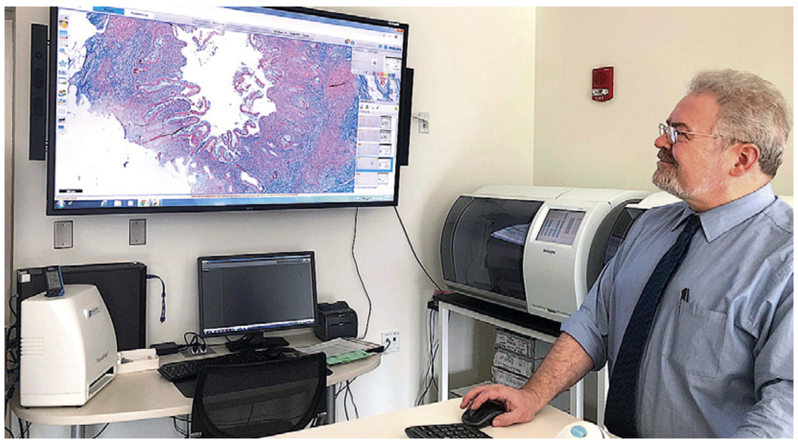
Pathology informatics expert Anil V Parwani, MD PhD, discussed DP advantages and implementation at the Ohio State University Wexner Medical Center in Columbus during the 2021 annual meeting of the Society of Imaging Informatics in Medicine (SIIM). Digital pathology was launched in July 2016. Currently, over two million pathology slices have been scanned, and 41 of the 104 pathology faculties are approved for DP reads.

Like X-ray film digitisers, whole-slide imaging (WSI) systems were the catalyst for digital conversion. A WSI scanner is comparable to a digital microscope outfitted with special high-resolution cameras which, combined with optics and software, serve to produce diagnostic quality images. The image is an accurate representation of the scanned glass slide, which may be manipulated, transmitted for primary diagnosis or second opinions, stored, and linked with a patient's electronic medical record (EMR). Digitised images of glass slides can also be analysed using deep learning and artificial intelligence (AI) tools.

'Pathology is ready for a digital disruption,' said Parwani. 'It offers so many advantages, including increased productivity through improved workflow distribution, information of management, and integration of data. Quality is better because DP enables efficient second review and transmission to sub-specialists. Operational costs are reduced, because slides and associated paperwork do not have to be moved about and, also for this reason, delays in diagnosis can be eliminated. In addition, the technology helps compensate for a shrinking pool of pathologists in the workforce because the workload can be distributed remotely to where pathologists are and help enable them to work more efficiently.

'The value drivers of DP are significant,' Parwani added. 'Because digital workflow enables the transmission of images to pathologists, both the speed of diagnosis and the quality of reviews increase. There is access to an expansive pool of specialist pathologists. Interoperability across EMRs enhances continuity of care. DP provides more power to clinicians, who can show pathology images and discuss findings better with patients, as well as review images easily at tumour boards and meetings.'

In 2016, the OSU pathology department initially began digital scanning of retrospective oncology cases, mostly for research and archival purposes. After the USA's Food and Drug Administration (FDA) approved the first pathology image management system (the Philips DP, Royal Philips, Amsterdam) in 2017,



the department offered its pathologists the opportunity to develop a DP workflow at their own pace. Use of the DP system was optional.

A laboratory information system (LIS; Epic Beaker, Epic Systems Verona, WS) was implemented in September 2019, whose barcode-enabled workflows facilitated prioritisation and the ability to sort slides in various ways. OSU built a new histology laboratory, with six Philips UFS systems installed adjacent to the histology staining machines. This significantly improved DP workflow.

There are three layers of storage, to provide fast retrieval for the most recent studies, and for older studies to be archived at lower cost. The LIS is seamlessly integrated into the hospital's EMR.

The Covid epidemic

Digital pathology proved invaluable with the onset of the Covid-19 pandemic. After analysing the steps involved in creating and delivering glass slides, the pathology department staff identified many potential risk points for cross-contamination of touch points for glass slides, cardboard slide folders, and the paperwork generated to accompany the slides on each case. Whole slide imaging processing and reporting required far fewer. Since the pandemic began in early 2020, the number of pathologists using WSI increased significantly.

'One significant advantage of DP to our department is better prevention of errors during slide scanning and case entry when reviewing slides and completing reports,' Parwani pointed out. 'Our system verifies the barcode label on the glass slides digitally, prior to attaching the image to the case. We have WSI annotation capabilities and a measurement tool allowing precise microscopic measurements of tumour size, invasion depth, and distance to surgical margins.

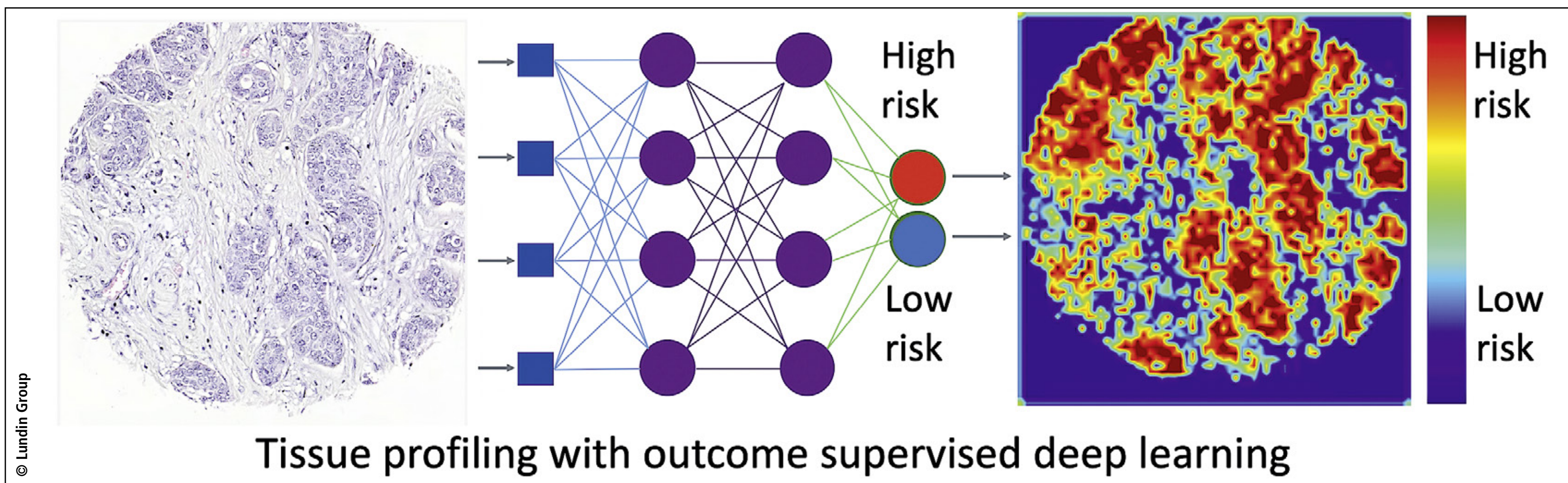
'Slides can be viewed side by side, enabling easier comparison of an H&E (haematoxylin and eosin) stain image and its corresponding immunohistochemical or special stained slides. Our system enables two pathologists to collaborate together, each with the ability to simultaneously move the slide, change magnification, or annotate the slide remotely in real time.'

'Intraoperative consultation,' Parwani said, 'did not see significant changes in the use of DP tools as a result of the pandemic. But we believe that DP contributed to reducing the risk of virus transmission to our staff because we could decrease the number of in-person interactions, as well as the number of individuals handling slides and other material. We look forward to the continuing development of AI tools which will help us do our job even better.'

Training AI to predict outcomes for cancer patients

ERBB2 gene amplification status

Predicting cancer outcome could help with a clinical decision regarding a patient's treatment. In his keynote speech during the online '7th Digital Pathology and AI Congress: Europe', Johan Lundin, Research Director at the Institute for Molecular Medicine Finland (FIMM) at the University of Helsinki and Professor of Medical Technology at Karolinska Institute, discussed 'Outcome and biomarker supervised deep learning in breast cancer to predict survival and efficacy of adjuvant treatment', citing his team's investigation into whether a machine learning algorithm, trained with images of tumour tissue morphology only, can predict breast cancer ERBB2 gene amplification status and whether this prediction is associated with patient outcome.



Outcome Supervised learning

'**Our hypothesis is** that training a machine learning classifier, supervised by outcome and biomarkers instead of expert-defined entities, has the potential to help discover new prognostic factors,' Lundin explained.

Our results show that morphological features learned by the deep learning algorithm predict survival, molecular status of the tumour and efficacy of ERBB2-targeted therapy in breast cancer.' While AI promises much in support, assistance, improved speed and accuracy, it will be interesting to see what happens when it goes beyond what the human clinician can do and starts making discoveries, he pointed out. 'However, while AI and digital pathology can overcome human weakness, we are still far from overwhelming human strengths.'

What expert-supervised machine learning can do is identify features on a cellular and tissue level, although, once AI gets into the realms of predicting disease outcome and response to treatment, the question will be how much the subjectivity of the expert annotating the samples affects the predictive accuracy.

AI is just as good as the annotator

'The challenge here,' Lundin explained, 'is the ground truth that you provide. For most of the supervised learning in digital pathology today, AI is just as good as the annotator, so the quality of the annotations is crucial.' Already, there is potential to bypass the subjectivity; he outlined a recent study from his centre where an antibody supervised learning method, using stained samples from thyroid cancer, was used as ground truth

Continued on page 14

Genomics, transcriptomics, proteomics, metabolomics

Molecular profiling boosts personalisation

Matthias Schwab is Professor and Chair of Clinical Pharmacology and heads the Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology in Stuttgart and the Department of Clinical Pharmacology, University Hospital, Tübingen, Germany. His major clinical and research activities are personalised medicine and pharmacogenomics with focus on cancer.

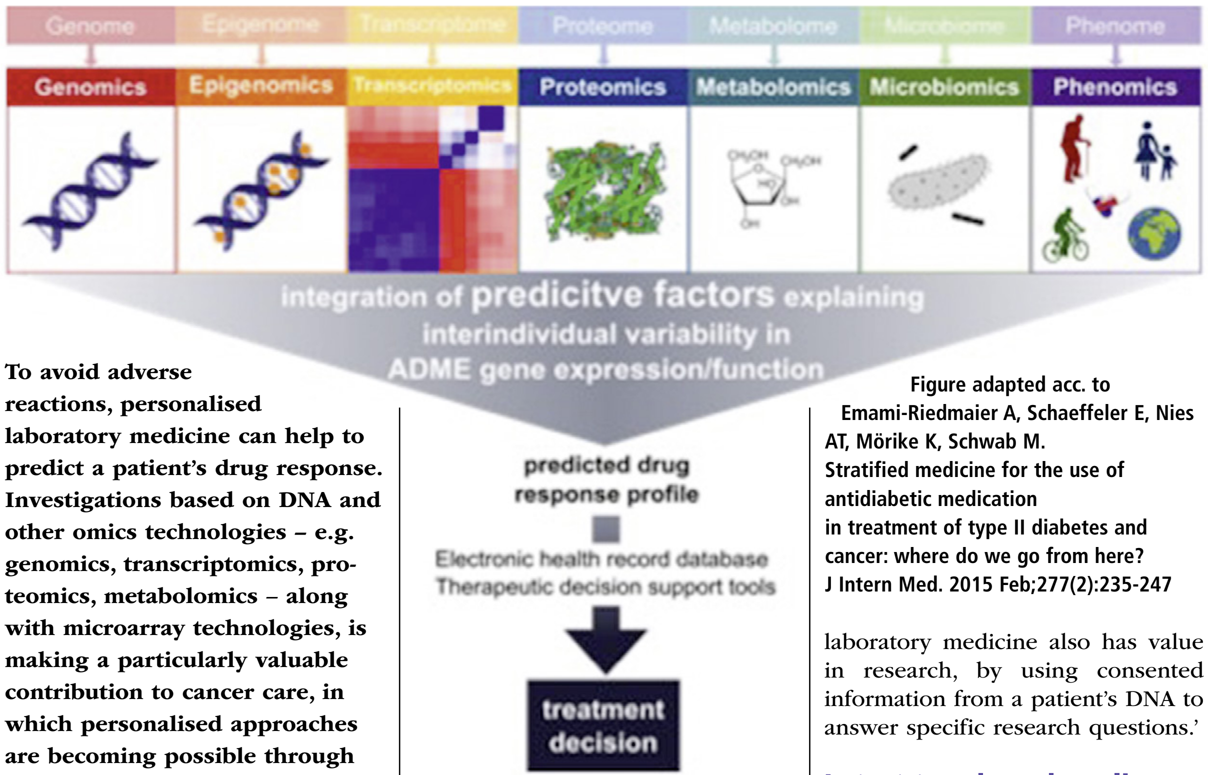


Figure adapted acc. to Emami-Riedmaier A, Schaeffeler E, Nies AT, Mörike K, Schwab M. Stratified medicine for the use of antidiabetic medication in treatment of type II diabetes and cancer: where do we go from here? J Intern Med. 2015 Feb;277(2):235-247

To avoid adverse reactions, personalised laboratory medicine can help to predict a patient's drug response. Investigations based on DNA and other omics technologies – e.g. genomics, transcriptomics, proteomics, metabolomics – along with microarray technologies, is making a particularly valuable contribution to cancer care, in which personalised approaches are becoming possible through molecular profiling.

Report: Mark Nicholls

Matthias Schwab, Professor and Chair of Clinical Pharmacology at the University of Tübingen, who also heads the Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology in Stuttgart, Germany, believes that personalised laboratory medicine will have an increasingly important role in patient care over the next decade.

However, he emphasises that the technique must be used in line with guidelines and recommendations – and where there is a clear consequence to the action, such as in drug selection or adjustment of the dose.

Cancer drugs and pharmacogenomics

This is particularly important in drugs that have a narrow therapeutic window, where the dose used is close to that which may result in drug-related toxicity. 'Personalised laboratory medicine in healthcare is currently mostly implemented for treatment of oncology patients to avoid adverse drug reactions,' he explained, adding that, in some areas, such as colorectal cancer, the approach is clearly defined – and where drugs (e.g. 5-Fluorouracil) to be used in clinical practice should be laboratory tested with a personalised medicine approach, for example to prevent haematoxicity and/or gastrointestinal side effects. '

Personalised laboratory medicine – a crucial step towards correct doseage

'Personalised laboratory medicine is a crucial step in ensuring the dose is correct, that the treatment is correct, and matches the patient's DNA, genetic profile and condition,' Schwab emphasised.

'Guidelines for healthcare implementation, that are regularly updated and publicly available, are there for doctors to select the right drug and adjust dose, or in some cases choose another drug. Personalised laboratory medicine also has value in research, by using consented information from a patient's DNA to answer specific research questions.'

Latest trends and applications

Trends and applications in personalised laboratory medicine involve the application of newer drugs in cancer therapy, such as epidermal growth factor receptor (EGFR) inhibitors in lung cancer and can support genetic testing in therapy selection.

With around 15 different drug targets (e.g. genes) and genetic variation, the technology can help clinicians select the right drug and dose in a process mostly conducted together with a pathologist using lung tissue.

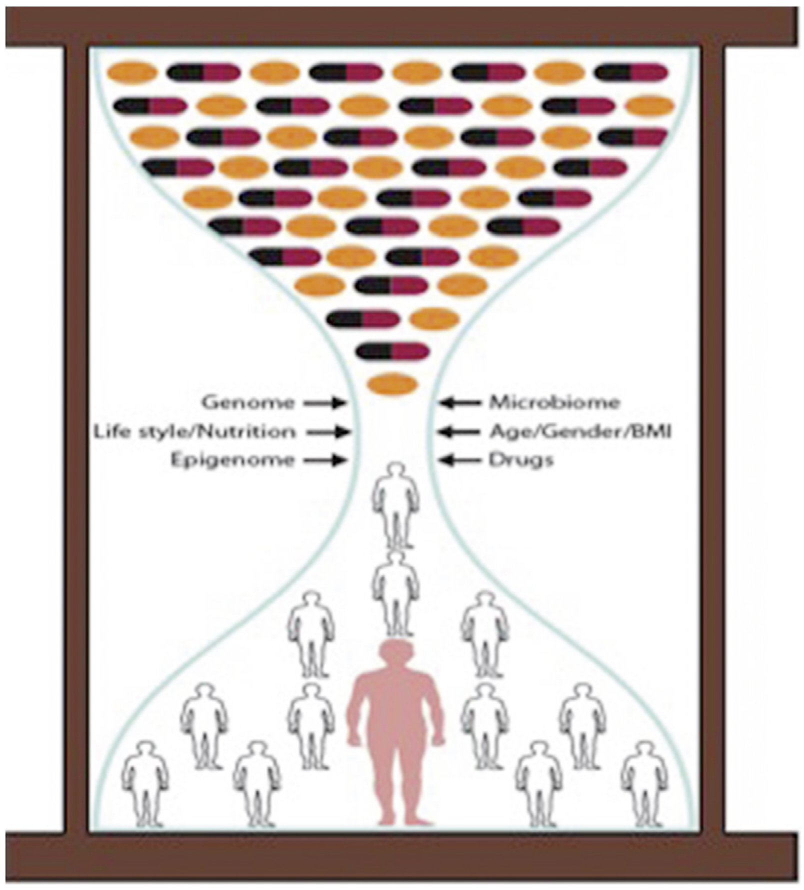
Schwab feels this is the most promising application, but he foresees a move towards pre-emptive testing, not only in cases of drug failure after conventional cancer therapy, but also at the onset of therapy, where genetic information will be available when prescribing. When discussing personalised laboratory medicine in genomics, he emphasises that it is important to clearly define the genome variation. Germline DNA from individuals will ease this pre-emptive approach while, in cancer patients, personalised laboratory medicine must focus on DNA from the tumour.

For patients with a tumour, where Next Generation Sequencing is currently mainly conducted only in cancer relapses, he suggests that, within the next decade, this will be a routine pre-emptive pharmacogenetic test.

Better treatment and drugs that work

To Schwab, the benefits of personalised laboratory medicine are clear. 'It's about better treatment and selective drugs that will work if you carry a specific mutation, meaning patients will receive individualised treatment and not suffer toxicity.' Such a medical approach promises more effective diagnostics with more effective and safer treatment, as well as faster recovery and restoration of health and improved cost effectiveness.

'Personalised medicine in the genomics area is the future,' Professor Schwab concluded, but, he added, 'in the next few years we will also talk about liquid biopsies because we can also use this information for epigenetic or metabolomic markers.'



Matthias Schwab & Elke Schaeffeler. Pharmacogenomics: a key component of personalized therapy Genome Medicine volume 4, Article number: 93 (2012)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Johan Lundin is Research Director at the Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Finland and Professor of Medical Technology at the Department of Global Public Health at the Karolinska Institute, Stockholm, Sweden. He is also co-founder of Aiforia Technologies, a FIMM spin-off company developing a cloud-based platform for AI-supported digital diagnostics within pathology.

Continued from page 13

instead of annotation by an expert. 'This also allowed us to create high amounts of training data in a very short time and we showed, in a validation set of 250 images, including immune cells, that the accuracy on a pixel level was very high, which shows that this method should work,' he added.

However, the big question remains as to whether AI is going to be just another subjective expert. 'How you select and annotate training data is crucial, especially for expert-supervised algorithms,' Lundin continued.

'Ground truth is provided by human observations and will always be subjective. To get more reliable ground truth, should we,' he questioned, 'use alternative and more objective endpoints than the expert annotations?

'Maybe it's time for a paradigm shift, as most of the algorithms so far created for pathology are based on expert interpretation. The whole idea of performing those are often that we want to make a prediction, a diagnosis, but that could also be a prediction of survival, risk of cancer recurrence and evaluation of the treatment efficacy.'

Learning with 1,300 breast cancer patients

Lundin's question was whether a middle step of human annotation is needed, or could that be replaced with machine learning, going directly from the sample to the prediction? He detailed how this has been examined by his team for direct outcome supervised learning with 420 colorectal cancer (CRC) and 1,300 breast cancer patients using microarrays where the long-term outcome was known. Pathologists performed a risk prediction visually before the images were put through a neural network trained to directly predict outcome. High discrimination was achieved using this outcome-supervised learning and in CRC, it was better than the consensus score of three experienced pathologists, demonstrating that valuable information can be extracted from the tissue. Further, the centre's ERBB2 study of breast cancer patients was based on nationwide data from Finland, and saw the team train a set of 700 samples where they knew the ERBB2 status. Having shown it is possible to predict ERBB2 status from the morphology with supervised learning, this was validated in samples from a randomised trial study on the effect of Trastumuzab treatment.

Here, the algorithm predicted ERBB2 status from the morphology and also discriminate the patients who received Trastumuzab into two different prognostically different groups. 'This is among the first studies to show that an improved efficacy of a molecularly targeted therapy can also be predicted from the morphology based on features learned by AI,' the professor noted.

'From these studies, we see that, using morphology and patient status as endpoints, you can clearly predict the survival and do it at the level of a highly-trained expert, and in some circumstances even better.'

VACUETTE® EVOPROTECT safety blood collection set

The gentle touch

Evoprotect presents a new, higher level for blood collection. The semi-automatic safety mechanism protects the user from needlestick injury risk and makes the daily task of blood collection easier.

'Vacuette Evoprotect enables gentle blood collection and safety from injury because we believe that every needlestick is one too many,' the manufacturer Greiner Bio-One reports. 'The safety blood collection set meets current safety recommendations and requirements and provides substantial support for safe blood collection and infusion with the same set.'

The device has a winged needle, specially developed for one-handed use. Potential needlestick injuries are minimised by the activation of the safety mechanism while the needle is still in the vein. This system is also suitable for blood collection and following infusion with the same set.

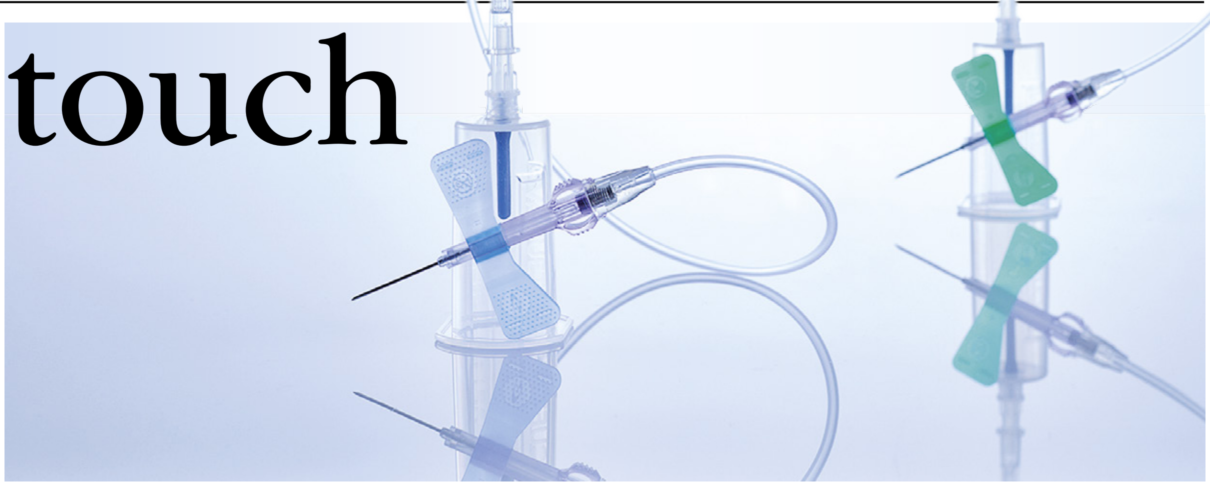
Maximum safety

'The Vacuette Evoprotect Safety Blood Collection Set has a semi-automatic safety mechanism,' the manufacturer adds. 'The triggers for the one-handed activation are located on the side of the product, thereby supporting a straight and gentle retraction of the needle. The needle is then automatically retracted and, at the same time safely and irreversibly enclosed in the body of the device. A clearly audible click confirms that the safety mechanism is successfully activated.' This takes place while the needle is still in the vein, providing an even higher level of safety. The design of the safety mechanism promotes a straight retraction of the needle from the vein, therefore offering more patient comfort.

Designed for patient comfort

'The ultra-sharp, triple bevel needle tip ensures optimal patient comfort during penetration. A view window between the needle and the tubing gives an immediate visual indication that vein entry was successful. 'The tubing is designed to ensure that the needle stays as still as possible in the vein. The location of the safety mechanism triggers, on the side of the device, minimises the risk of the needle moving in the patient's vein during activation. Because the same device can be used for taking blood and for a subsequent infusion immediately afterwards, a second puncture is in such situations not needed.'

Details: www.gbo.com or www.power4safety.com



A need for deep learning attention maps

Next steps will use deep learning attention maps to understand better what AI has learned in this context.

'With the breast cancer study I have presented, we have shown that the deep learning algorithm trained on tissue morphology and supervised by molecular status can predict the efficacy of adjuvant therapy in patients with breast cancer,' Lundin pointed out.

'We have also shown that it's possible to extract the predictive information from routine tumour sections performed on every new patient, which means this is an interesting approach that can complement the molecular tests,' the professor added. (MN)

Demand for molecular LIMS increases

Lab interoperability is essential

Fast, flexible laboratory information management systems (LIMS) that cope with data and workflow complexities of molecular and genetic testing now work in laboratories internationally. Here, in the first in a new Lab Pinnacle Series, experts from the CliniSys Group, Sunquest Information Systems and Data Innovations (all owned by Roper Technologies), discuss the value of a LIMS in molecular and genetic testing.

'**When precision medicine** initiatives gained momentum in the USA,' observed Laura Voeghtly (Sunquest), clinicians focused on molecular testing, which was new to many of them. Thus, higher volume and greater test complexity needed support, and clinicians needed to know the diagnostic, prognostic, and therapeutic implications of test results. Thus, LIMS automation, instrument integration and general laboratory interoperability became essential.'

To deliver a genomic medicine service, NHS England commissioned seven Genomic Laboratory Hubs (GLHs) and developed a National Genomic Test Directory for GLHs. 'The initiative includes goals for standardisation, equity of access to testing, economies of scale, and volume growth that are collectively increasing demand for well-integrated LIMS technology,' said Steve Abbs (CliniSys). 'NHS labs also do a lot of genetic testing for infectious disease,' Tony Oliver (CliniSys) pointed out. 'Just think of Covid-19 to grasp the volume of molecular PCR amplification techniques and sequencing events. Those are generally done in metropolitan teaching hospitals, but with the commoditisation of molecular testing, we see a greater need for specialised LIMS technology.'

Stéphane Decap (CliniSys/MIPS) pointed to a sharper distinction between molecular and genetics tests in the EU. Molecular techniques are routine for human genetics and by other labs, for example for virology. University hospitals mostly cover human genetics testing but genetics markets vary greatly between countries, e.g. in Germany many private labs do human genetics tests, but France has only a few, and only two genomics hubs do full genomics testing. 'The need for GLIMS – our lab information system that supports genetics – has not been as high in France or Belgium; but, as those countries follow the UK's increased testing, demand will grow. Genetics and genomics tests are very complex and specialised, which calls for specialised technology that integrates with all necessary databases and systems from order to invoicing.'

LIS or LIMS?

'LIS are built to accommodate clinical pathology, so they can be fairly rigid in their database structures,' Shirley Li (Sunquest) underlined. 'With molecular and genetic testing, applying different ways to sequence new modules requires a flexible, agile workflow solution. The application of different assay technologies varies among laboratories and even for a given instrument there can be differences in analysis and data interpretation needs.'

Next generation sequencing (NGS)

This needs more sophisticated analysis for bioinformatics, which can also differ from one lab to another. LIMS can be key to supporting the right level of configurability and modularity for labs to define their own plans and strategies in this field.'

'We can work with middleware partners to support molecular workflows,' said Filip Migom (CliniSys/MIPS), adding, 'within the human molecular testing domain, if your focus is testing with yes/no results, a traditional LIS can handle that. However, if you want to do more complex procedures, it's better to manage this outside the standard LIS.' 'Techniques change rapidly, but generic approaches are possible, as done in Europe with our GLIMS. We've built a special purpose module, GLIMS Genetics, to support the flexible workflows needed in those environments. Instead of dedicated haematology or biochemistry modules, we have a more general approach, so we can support some complex workflows.'

Automation of processes and cross-discipline data availability can produce maximum efficiency

Middleware

'Across the board, interfacing gives you efficiency, quality, and scalability,' said Carol Beth Casto (Data Innovations). 'For molecular and genetic testing, instrument interfacing is in its infancy. Different molecular and genomics labs have different workflows. At Data Innovations, we are making inroads with workflow variability by establishing that standard, lower-level protocol for the output, and able to tweak here and there. We work with instrument vendors and LIMS systems to provide standardised translation from the system to the instrument and back with our Instrument Manager middleware.' 'In Europe, test orders come in and results go out through different systems with different protocols, formats and languages,' Filip Migom explained. 'Middleware enables our GLIMS to manage all those variables. We must translate all types of requests to standardise within our database, and then we must translate again for the reporting and business side. In the middle, we must also translate all the interoperability with the instruments because performing a download of a plate depends on the instrument technique and reporting code. Middleware plays a key role in facilitating this level of integration and interoperability.'

When should molecular testing be brought in house and LIMS be implemented?

'For private labs, when it can be profitable,' answered John Lebon (CliniSys/MIPS). 'Plan early,' he advised; volumes grow beyond the capabilities of the current LIS. Interfacing with variant analysing systems within healthcare systems is difficult and often performed manually.

Shirley Li agreed, profitability is the primary driver in the USA – i.e. scalability and reimbursement above cost. Looking at NGS, about two-thirds of lab costs are for reagents. Additional efficiencies in staff time and resource allocation are worthwhile. 'Moving from paper-based, offline systems into something like Sunquest Mitogen LIMS helps understand where lab costs are and how to improve cost analysis measures.'

Holding power within an institution

'Testing within the system, sometimes even before it's profitable, can be better for the overall business strategy than sending samples out to a private lab,' Stéphane Decap reasoned. Various diseases are tested in different lab specialties, such as pathology and genetics. In a one lab system, using a sophisticated LIMS to automate the workflow, processes can be streamlined, with higher volumes and fewer people.

Laura Voeghtly: 'If a testing method emerges that drastically reduces lab costs, labs will often make the case to bring it in – that's easier to do when you already have LIMS or other software that provides a process to manage testing.' An existing good volume of testing also underlines a need to introduce a LIMS.

Steve Abbs: 'Since the first big genetics push in early 2000s and still today, many UK labs use NHS funding to purchase LIMS. Under the current national genomic medicine initiative, labs are expected to deliver change by standardising and industrialising testing. To that end, NHS funding is available for purpose-built LIMS technology.'

Could LIMS take molecular/genetic testing beyond workflow into analysis, particularly for NGS?

Shirley Li: 'Molecular and genetic testing involves large volumes of complex data – especially true with NGS, where a typical whole exome sequencing identifies around 10,000 variants per patient, per sequencing run. Doing this manually carries risks error and data loss, and challenges information filtering. Today's LIMS help data files and assets move across the lab, corresponding to the testing and ultimately being translated for the different analysis pipelines laboratories use.'

Steve Abbs: 'The UK has independent bioinformatics and variant interpretation software providers; a current priority is interfacing those solutions with the LIMS. With the bioinformatics process being so complex, interfacing is necessary to get that output into the LIMS and ultimately into the diagnostic report, which then goes into the electronic patient record. For more basic genomic tests that require a simple genotype and produce a positive/negative result, LIMS users can apply rules-based logic to automatically generate a report based on the result.'

'Inside the LIMS, we collect a lot of data about the phenotype, clinical information and family history, which can be very useful for NGS techniques,' added Stéphane Decap. To manage all that data, connectivity must be beyond the instrument, beyond the wet lab. 'It needs to connect to a Human Phenotype Ontology (HPO) database to manage the NGS information, and needs to connect to the variant analysis informatic pipeline.'

Covid-19 challenges

'Many existing interfaces were available for PCR instruments that were connected directly to our LIMS,' said John Lebon. 'But suddenly every lab bought new instruments and wanted to increase PCR capacity significantly. Our team made it work through remote installation and a lot of logistical problem-solving.' Reagents were not available for the instruments they had, noted Tony Oliver, thus labs bought many additional instruments, resulting in an exploding need for interfacing in the UK. 'We deployed to data centres, but cybersecurity regulations make processing text files problematic when data-centre-deployed interfaces are involved. The sudden surge in new labs and instruments caused a surging need for text file interfaces. That was really the only notable technical challenge we faced in the UK.'

Interfacing demand also spiked in the USA, Laura Voeghtly said – not just for new instruments but also for existing platforms as new reagents received emergency use authorisation (EUA). 'Standard regulations were not yet in place for these EUAs, creating a "wild west" situation with many moving parts – particularly as we worked to support the many Covid-19 labs that were entirely new to molecular testing.'

Pop-up labs

'The Belgian government created a pop-up lab for faster testing of the entire population,' added Filip Migom. 'Everything was centralised and prelabelled with barcodes through the LIS, but the lab had many different instruments using a range of techniques for Covid-19 testing. In a normal lab workflow, you know in advance which instrument you will use, but the LIS is not designed for molecular testing workflow and does not know upfront which instrument to use for any given plate. Every instrument has its own plate structure format, so an urgent need arose to select and correctly upload a file for the plate configuration. We were all very motivated; we achieved it, but it was a big challenge.'

'We had to be nimble to support USA pop-up labs,' said Laura Voeghtly. 'We encountered two main types: (1) pop-up labs in health systems and physician practices focused on acquiring specimens and clients from across the region and country and (2) brand new laboratories at academic institutions to test students, faculty and staff.

For healthcare organisations we provided quick integration with our ordering process through Sunquest Atlas, providing a physician portal to acquire countrywide specimens. For the academic institutions, we managed the integration of necessary components to support Covid-19 testing for new and potentially inexperienced labs.'

Prediction:

Next Generation Sequencing may become the highest diagnostic yield assay adopted by labs.

ON THE BEAT: Everything's ticking over

IN THE HEART OF SUMMER … despite Covid-19 restrictions… internationally prominent cardiologists and researchers exchanged their news and views. By the same electronic means, EH reporter *Mark Nicholls* compiled reports and interviews with speakers and experts taking part in the following virtual events: The British Cardiovascular Society annual congress, ESC Preventive Cardiology 2021 and ESC 2021 congress.

Small plaque assessment is vital

AI device predicts future heart attack

An artificial intelligence-led device to assess coronary CT angiographs has been designed to assess cardiac plaque that may lead to myocardial infarction (MI).

In his presentation 'Vascular inflammation and cardiovascular risk assessment using coronary CT angiography' (CCTA), Charambalos Antoniades, Professor of Cardiovascular Medicine at the University of Oxford, presented the research team's findings during the European Society of Cardiology Congress.

Plaque ruptures: small, but deadly

For our EH interview Professor Antoniades explained that whilst heart attacks happen when plaque ruptures, blocking arteries, in around half these cases myocardial infarction is caused by a small plaque rupture. 'However, these are plaques that have never caused any symptoms before or have been dismissed in previous angiograms as of limited importance and non-obstructive; but rupture of these minor plaques leads to the most dangerous heart attacks.'

Currently, the only way to find these plaques is via standard CCTA when patients present with mild chest pain. However, even then the scan cannot show which plaques will rupture and which will not. 'We have developed a technology called "fat attenuation indexing", which uses artificial intelligence to analyse standard, routine coronary CT angiograms and produces a prediction about the risk of the patient having a fatal heart attack over the next eight years. By knowing who is going to have a heart attack, you know who to treat more aggressively.'

The technology works by non-invasively quantifying the degree of inflammation in the arteries from the standard coronary CT angiograms, Antoniades explained.

By uploading the patient's scan on a cloud platform, clinicians can obtain the quantification of coronary inflammation. Additionally, this medical device combines that information with the coronary atherosclerotic plaque burden and the risk factors of the patient to generate the personalised absolute risk of the patient of having a fatal heart attack, thus informing treatment decisions. 'By knowing which arteries are inflamed,' the professor pointed out, 'you can predict which artery is going to develop disease in the future and also tell which artery with disease is going to give a heart attack. Then you know which is the vulnerable plaque but, most importantly, who is the vulnerable patient that needs treatment.'

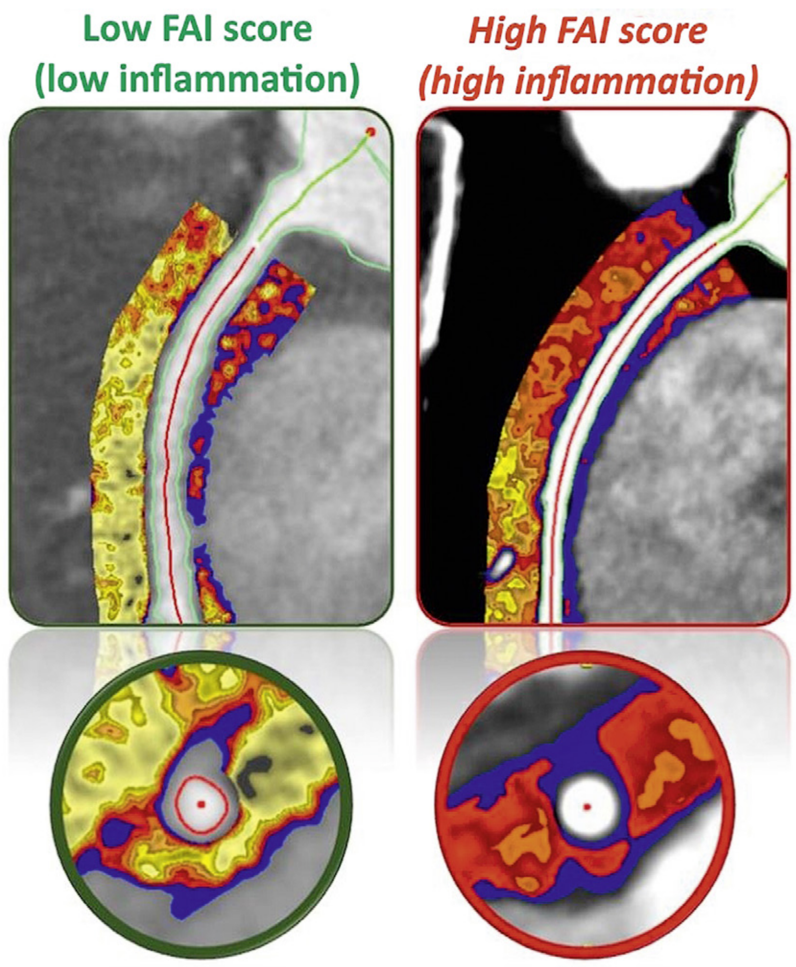
Charambalos Antoniades, Professor of Cardiovascular Medicine at the University of Oxford

Developed over the last three years, the technology has been successfully used in a research setting in large prospective trials and has already received clearance by European regulators as a medical device under the new Medical Device Regulations (CE mark). It is now used in clinical practice in hospitals.

Identifying at-risk patients

The AI approach will advance CCTA for chest pain investigation – a first line of investigation in the United Kingdom and increasingly so in the rest of Europe and the USA. However, in up to 80% of cases, the result will still come back negative, showing no significant sign of disease and the patient is discharged. 'The new technology analyses all cases, with or without disease, and quantifies the inflammatory burden inside the arteries,' Antoniades said. 'Then it tells you whether this patient who has no disease will develop the disease in the next few years, or if a patient who has had minor disease is likely to have a heart attack because that minor disease is unstable and may lead to plaque rupture in the next 2-5 years.'

By identifying patients most at risk of future heart attacks, prescribing an inflammatory agent such as colchicine – shown to be effective in preventing heart attacks – or even initiation (or escalation) of statin treatments, can be implemented.



Low and high FAI (fat attenuation indexing) scores, which are used to predict the patient's likelihood of having a fatal heart attack.

Accurate prediction

The new medical device, called CaRi-Heart, allows clinicians to upload scans through a cloud gateway for analysis.

The device then extracts information from the scans about coronary inflammation and atherosclerotic plaque burden, while it also considers existing ESC risk scoring criteria, to generate a refined, personalised absolute and relative risk of the patient for a fatal heart attack.

This allows more efficient use of the ESC clinical guidelines to prevent future heart attacks in the specific population of patients who undergo coronary CT angiography.

The AI algorithm for the device has a very high negative predictive value for fatal cardiac events (99.8%), and it is continuously validated and refined in a large cohort – the ORFAN study – of 100,000 patients who had CCTA and were followed up for up to 15 years. 'In the ORFAN study, Antoniades added, 'we are now at the stage of analysing data from all continents to project predictions in much larger populations, with representation of more ethnic groups.'

5G tech and AI combine to help chronic HF patients

Tackling remote monitoring

5G telecommunications technology plus artificial intelligence are expected to monitor seriously ill heart failure patients remotely and continuously.

An increasing number of chronic heart failure (HF) patients are receiving Left Ventricular Assist Devices (LVADs) to ease their severe condition, but this needs remote monitoring and that's restricted due to lack of technology. Now, however, 5G the offers the possibility of constant monitoring of the LVAD function along with a patient's physiological data.

Within the three-year 5GMedCamp project, a study in Germany will monitor chronic heart failure patients 24 hours a day. Study leader Dr Friedrich Köhler, who heads the Centre for Cardiovascular Telemedicine at the Charité, explains that artificial intelligence is crucial to support the analysis of the data generated by constant monitoring.

The 5GMedCamp project is led by the Charité – Universitätsmedizin Berlin with the German Heart Centre Berlin (DHZB), the Fraunhofer Heinrich Hertz Institute (HHI), and two technology companies (SectorCon GmbH and SYNIOS Document & Workflow Management GmbH). 'Telemedicine offers great potential for early diagnosis and treatment of any complications that may arise, such as bleeding, infections or technical problems with the implant,' Köhler pointed out. 'Therefore, 24-hour telemedical support on all weekdays is medically very relevant for this group of patients, but this requires continuous transmission and monitoring of the data.'

Previously seen as a temporary support for the circulatory system before a heart transplant, LVADs are increasingly fitted in patients as permanent treatment options. In Germany, more than 1,000 chronic heart failure patients a year receive them.

However, due to the need for close monitoring, the consortium is researching how to improve the follow-up care using modern telemedicine and 5G mobile communications standards for continuous vital data transfer, combined with an AI-based clinical decision support system for telemedical care after implantation of a permanent LVAD. Köhler said current remote monitoring measures data, such as blood pressure or ECG at certain time points; the 5G-capable non-invasive measuring devices will constantly record blood pressure, ECG, anticoagulation status and renal failure.

'Patients with LVAD are a good use case and our project could be the first to pioneer this and to move from single, short, measurements in remote patients to continuous monitoring.'

The study will assess how effectively telemedicine monitoring delivers technical data direct from the device, alongside patients' physiological data.

Complexity lies in the transmission and management of continuous data from patients who move between different 5G campus networks, public networks and home networks that

Dr Friedrich Köhler is Professor of Cardiology and Head of the Centre for Cardiovascular Telemedicine at the Charité. He is also project leader of 5GMedCamp with research interests in heart failure, digital cardiology and congenital heart defect in adults.

Continued on page 18

AI elevates imaging of coronary arteries

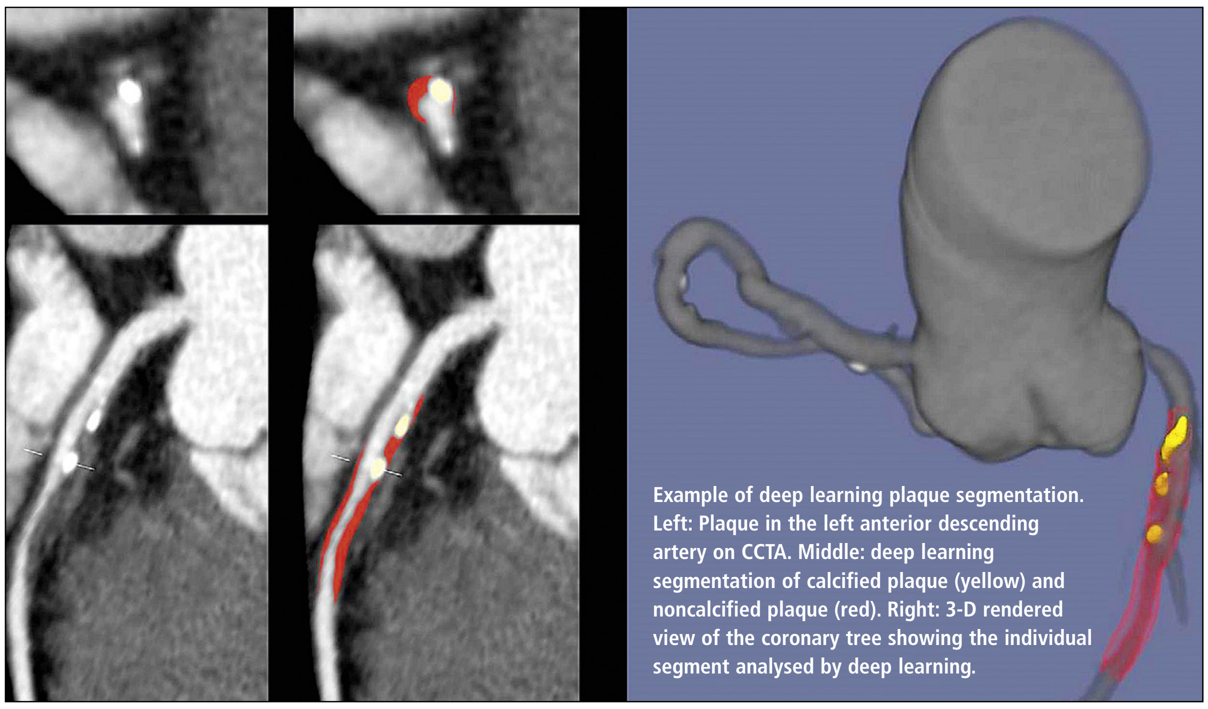
Coronary plaque scanned in six seconds

Coronary computed tomography angiography (CCTA) is a non-invasive imaging test which can be used to evaluate coronary artery stenosis and measure plaques. Current plaque analysis is time-consuming and needs expert readers in order to help assess a patient's heart attack risk. That's about to change.

Report: Mark Nicholls

During a session focused on artificial intelligence in imaging, at the forthcoming virtual European Society of Cardiology Annual Congress 2021, Dr Andrew Lin will explain how using artificial neural networks, AI can generate automated predictions directly from medical image data. Healthcare in Europe spoke with the post-doctoral researcher about his work at the Biomedical Imaging Research Institute at Cedars-Sinai Medical Center, in L.A. California. Research aims? To develop a deep learning system for plaque quantification from CCTA and compare it with expert readers and intravascular ultrasound.

A dataset of 921 patients was used to train an automated deep learning neural network to measure plaque volume and coronary artery stenosis from CCTA images. The deep learning network was then applied to an independent test set of 275 patients, where its diagnostic performance was evaluated. 'There was excellent agreement between deep learning and expert readers for measurements of total plaque volume and coronary artery stenosis,' Lin confirmed. 'Deep learning also performed in close agreement with intravascular ultrasound, which is the invasive gold standard for plaque measurements.



Example of deep learning plaque segmentation. Left: Plaque in the left anterior descending artery on CCTA. Middle: deep learning segmentation of calcified plaque (yellow) and noncalcified plaque (red). Right: 3-D rendered view of the coronary tree showing the individual segment analysed by deep learning.

Speed and high accuracy

The time taken for deep learning analysis per scan was around six seconds, compared with 25-30 minutes taken by experts.'

Deep learning offers significant promise for plaque quantification from routine CCTA images, by automatically detecting and contouring the heart arteries and underlying atherosclerotic plaques. This, Lin pointed out, enables measurements of plaque volume and coronary artery stenosis directly from standard CCTA images, with high accuracy compared to expert readers and at a fraction of the usual analysis time.

Lin also noted that deep learning from CCTA agreed with the invasive reference standard of intravascular ultrasound for measurements of total plaque volume and minimum luminal area.

Dr Andrew Lin is a postdoctoral researcher in the Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, California, (Mentorship: Dr Damini Dey). His research focuses on the application of artificial intelligence and advanced analytics techniques to plaque imaging with CCTA.

Workflow integration

He now believes a deep learning system that rapidly and accurately estimates coronary artery stenosis could potentially be implemented into clinical practice as a 'second reader' and clinical decision support tool. 'By providing automated and objective results, deep learning may reduce inter-observer variability and interpretative error among physicians. The system also could be used to pre-screen CCTA scans, flagging patients with obstructive disease to be prioritised for clinical reporting.' When integrated into clinical decision-making, CCTA guides the use of preventive therapies, improves event-free survival, and reduces unnecessary downstream testing. AI-enabled image analysis has the potential to improve the efficiency of CCTA workflow and enhance patient risk stratification.

Continued from page 17

will transmit the large amounts of data quickly and in real time.

Diverse expertise

Diverse expertise is vital in the consortium, with HHI as a technical partner alongside technology companies, and the LVAD experience of DHZB.

Dr Slawomir Stanczak, Head of the HHI Wireless Communication and Networks Department, stressed the obvious need to integrate data protection and security into the data transmission. This research is in the earliest stages. It will assess the technology and compare conventional datasets with those offered by the 5G campus map, before leading to a patient study and a clinical trial.

LVAD patients still need support from specialised centres for what remains a complex therapy and while remote monitoring of class 2 or class 3 heart failure patients is being conducted, the hope is that this technology will enable more severe heart failure patients to be monitored remotely, beyond the specialist centres, and improve total mortality outcomes.

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Risk reduction

The role of AI in preventive cardiology

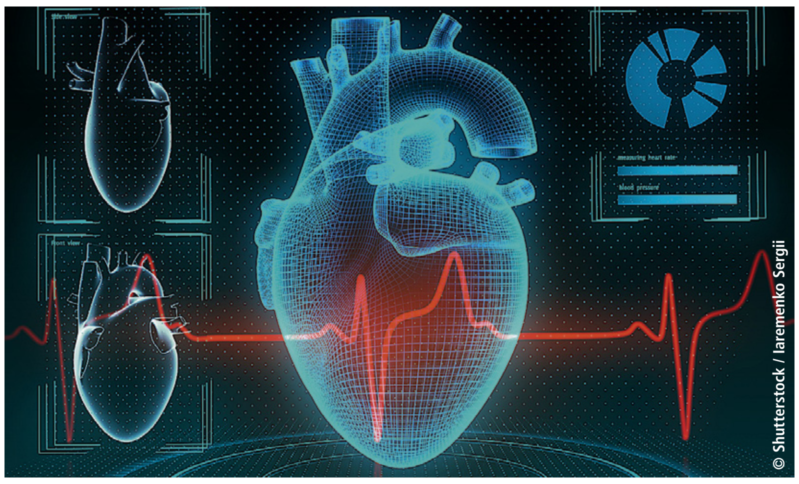
Artificial Intelligence and Big Data in cardiovascular risk reduction and cardiac rehabilitation are offering new opportunities for increased diagnostic accuracy and more personalised exercise prescription.

Experts believe it can be harnessed to design tools to enable cardiologists to make better decisions, and have more confidence in the decision-making process.

The topic was featured at ESC Preventive Cardiology 2021, highlighting the latest developments in preventive cardiology. In a session entitled 'Artificial intelligence and big data: what can they do for us?,' speakers examined the potential value of AI in cardiovascular risk reduction and cardiac rehabilitation.

In his presentation 'Big data: does it always improve decision-making in imaging?', Paul Leeson, Professor of Cardiovascular Medicine at the University of Oxford, suggested that AI can improve on the accuracy of human readers, reduce variability between readers, and give them more confidence in findings.

He said that medical AI is being driven by its use within imaging, with modalities such as echocardiography offering huge amounts of data to develop new algorithms. He said traditional analysis that relies on the operator to perform measurements can introduce a lot of variability. 'However, as soon as you start to automate it, you take away variability in these measurements in a reproducible way. Each time you take an image and analyse it with AI you get the same reading,' said Professor Leeson.



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Some of the areas that still need addressing are ensuring that high quality evidence underlies the new AI methods and understanding to what extent use of AI and Big Data can help aid disease diagnosis. Cardiovascular imaging is at the forefront of clinical applications of AI and big data; tools are being developed for image quantifications and are now available for use

Professor Leeson, who has a specific research interest in pioneering AI to improve clinical tools already available to identify those at risk, such as echocardiography, and identify next generation imaging and management approaches, said use of AI to aid diagnosis could change clinical practice forever by influencing how doctors make decisions. He pointed to an example where the technique is already being applied to look at how use of AI for automation of image analysis could help in understanding management of Covid-19. Meanwhile, another trial involved a series of stress echo images where image readers 'did well' but that performance improved when they were supplied with an AI opinion. 'So, AI can improve their accuracy, plus they became more confident,' he continued. 'This is beginning to suggest that actually not only can AI interpret these images but if supplied to doctors you can start to improve decision making.'

In conclusion, he said: 'Cardiovascular imaging is at the forefront of clinical applications of AI and big data; tools are being developed for image quantifications and are now available for use. Some of these can improve consistency of reporting, accuracy (of decision-making) and confidence of decision-making.'

The next step is prospective trials to test whether implementation into practice leads to measurable improvements in patient outcome.

Entering the era of the 'digital nurse'

Professor Leonard Hofstra (Amsterdam UMC) said that big data can be used to mimic randomised controlled trials and then help design tools to enable cardiologists make better decisions, while Professor Lis Neubeck (Edinburgh Napier University) looked at the evolving role of nursing in a digital world. Posing the question 'are we entering the era of the digital nurse,' she said there are challenges about how nurses utilise data and in preparing the work force to embrace the digital environment, while underlining the need to continue to keep the patient at the centre of digital health. 'This is why nurses should have a very central role in developing systems and ensuring they are linked,' she added.

© University of Oxford

Paul Leeson is Professor of Cardiovascular Medicine at the University of Oxford and Head of Oxford Cardiovascular Clinical Research Facility. He is also a Consultant Cardiologist at the John Radcliffe Hospital, where he provides expertise in Cardiovascular Imaging, as well as General Cardiology and Cardiovascular Prevention through the Oxford Specialist Hypertension Clinic.

Another role for AI is in shaping cardiac rehabilitation programmes for patients to make them more consistent. At present, patients with similar cardiovascular disease profiles may be given widely varying exercise regimes by different clinicians.

Decision support systems for exercise prescription in cardiac rehab are rising and can help address this but Dr Dominique Hansen, Professor of Exercise Physiology at Hasselt University, Belgium, said there remains a need for more data to 'unequivocally confirm the practical and clinical benefits and feasibility.'

Machine learning can study statistics to foresee events

Prediction: Sudden cardiac death

Could machine learning (ML) help to predict sudden cardiac death (SCD)? According to Dr Sanjiv Narayan, Professor of Medicine at Stanford University, California, many exciting studies are using ML to predict sudden death in ways not previously possible.

'Complex data, such as MRI geometry, very large electronic health records or continuous data streams from wearables, are difficult to probe meaningfully with statistics, yet can be studied by machine learning to make predictions.' Narayan, who directs the university's Computational Arrhythmia Laboratory, and co-directs the Stanford Arrhythmia Center, will question 'Sudden cardiac death: Can we move from prediction to prevention?' during his ESC 2021 presentation this August.

Sanjiv Narayan is Professor of Medicine at Stanford University, Director of the Computational Arrhythmia Laboratory, and Co-Director of the Stanford Arrhythmia Center. He oversees and directs several NIH-funded studies to develop machine learning and computer models for arrhythmias, to bring them directly to the care of patients.

Novel wearables

Speaking with our European Hospital reporter, the professor said ML applications can now use simple measures of heart and breathing rates to detect imminent collapse or hypotension within minutes. This could become the basis for novel wearables to predict SCD a few minutes before it happens and alert emergency services, hopefully to prevent the event.

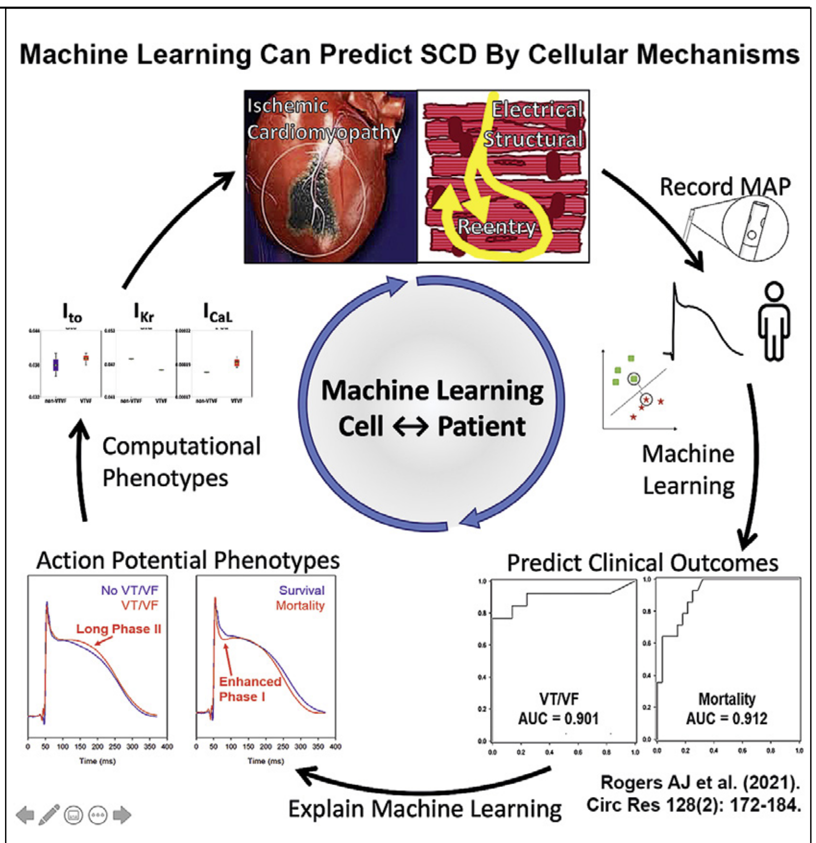
'This would be revolutionary,' he continued. 'In other applications, machine learning has been used to extract features from the detailed structure of the ventricles and granular distributions of scar imaged by Gadolinium-enhanced MRI to predict SCD better than existing clinical tools.' Other studies have used ML to predict which drugs could be pro-arrhythmic from their molecular structure alone, or whether ML of the ECG alone could improve on current risk models, while his group has shown that signals from inside the heart that indicate cellular remodelling in heart failure can predict SCD.

Personalised medicine

To enable personalised medicine, ML can be trained to learn patterns in an individual, rather than in a population, Narayan explained. Examples: Do LV (left ventricular) geometry, scar on MRI, or electrical remodelling indicated by action potential shape (see figure), predict sudden death?

'These questions are difficult to frame for conventional statistical analysis, which is better suited to linear data than complex data (of high dimensionality). ML can also be used for very large data – such as continuous streams from wearables,' Narayan added.

Whilst the professor points out that ML will never replace the clinician, it will provide better tools for personalised medicine – an evolving trend for over a decade. 'MRI and CT scans have ML tools to help the clinician interpret them, or that flag potential abnormalities,' he pointed out. 'Even ECG machines have forms of ML to provide the automated diagnoses. This will enable the clinician to make better management decisions and be more efficient.'



Smart analysis

Patients also win where machine learning automates tools, e.g. focused analysis of continuous large data from an Apple watch, activity monitors or smart devices in the bathroom, elsewhere at home or even in a care home. 'This can empower the patient, reduce delays in the healthcare system, and potentially off-load some of the health system burden,' Narayan pointed out.

ML can provide simple automated tips; patients can benefit from better and safer drug prescribing and, he believes, many other benefits have yet to be realised.

Other presentations in the session will examine digital heart rate analysis and question whether we can predict sudden cardiac death as well as prevent sudden cardiac death in heart failure.

Digital innovation in cardiology

What's new?

Triage HF Plus, highlighted in the BCS conference session 'Digital Innovation in Cardiology - What's new?' is a digital heart failure care project that uses a customised algorithm to detect early signs of deterioration in patients with implanted devices.

During her presentation 'Digital solutions to identify worsening heart failure', consultant cardiologist Dr Fozia Ahmed discussed the UK's NHS heart failure burden (c. one million patients). In recent years, HF hospitalisation has risen by 33 per cent, three time faster than all other hospital admissions, she said, adding that predictions from 2010 indicated the UK would see a 50 per cent increase in HF admissions by 2035 – but this milestone was reached by 2018 in the Greater Manchester area.

'That highlighted the need to do things differently,' Ahmed noted, 'to identify unstable or decompensating patients earlier, in order to improve outcomes, reduce admissions and decrease overall costs.'

The traditional approach was reactive, but using risk-based data from implanted devices to help identify decompensating patients sooner and intervene earlier to prevent a 'problem turning into a crisis'.

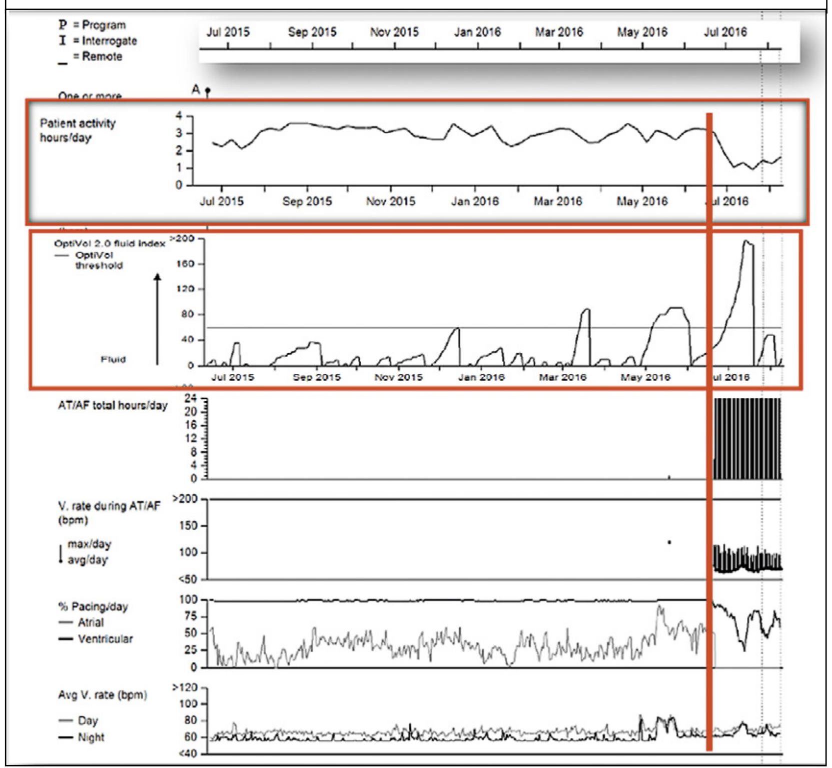
Clinical alert

The Manchester team developed Triage HF Plus: a remote management HF care pathway which combines the TriageHF risk score with a structured telephone-based remote clinical patient assessment.

The validated Triage HF score is a feature of Medtronic cardiac implantable electronic devices, which use data from up to nine monitored physiological parameters to classify patients as low, medium, or high risk of HF hospitalisation in the next 30 days. Once enrolled, all high-risk episodes are managed via the Triage HF Plus pathway and patients received a structured telephone assessment to assess both HF and non-HF related acute issues.

The data in the accompanying report summarises a patient's general health, highlighting any significant reduction in activity levels, a change in heart rate or rhythm and increasing indicators of congestion. 'Without seeing this patient, the remotely monitored data can provide an indication of whether the patient is less active, more symptomatic, and in need of clinical review, just from the remotely-monitored data,' Ahmed explained. 'Combined with the telephone assessment, it's then possible to obtain a more comprehensive picture of how stable or unstable the patient is.' The nurse-led system is patient-centric and has transformed care for more than 1,000 patients in the Manchester region. Other issues, such as acute respiratory infections and worsening COPD (chronic obstructive pulmonary disease), have also been identified.

Health report showing abnormal data



The team has redesigned services and delivered real-time rapid triaging and automated specialist management in the home environment. 'By implementing this, we could reconfigure and redesign our clinical services in such a way that patients get assistance on the basis of clinical need between scheduled appointments,' Ahmed explained.

'The digital solution is hi-tech, low-labour and low-cost, designed so that it complements existing heart failure care pathways and can augment guideline-directed interventions. It's also Covid-proof and delivers end-to-end remote monitoring management and intervention.'

Risk prediction in cardiomyopathy

Delegates also heard from Professor Declan O'Regan (Imperial College London), who spoke of future precision phenotyping and risk prediction in cardiomyopathy, and the added value that machine learning can bring to every stage of cardiovascular imaging. 'That starts from the point of image acquisition and reconstruction, to image enhancement like super resolution, to labelling images, and also identifying pathology and new imaging biomarkers of disease, such as the concept of radiomics, and also moving beyond conventional diagnosis towards prediction tasks, which really drives management decisions in the clinic.' O'Regan covered three main topics – how computational imaging can be useful in cardiovascular medicine, ranging from integrating data, and bringing imaging and non-imaging data together; using AI and imaging for discovery science and understanding new mechanisms of heart disease; and for early diagnosis and risk prediction.

Finally, on the vexing issue of overload, Professor Tim Chico (University of Sheffield), questioned and suggested how to cope with the amount of data being generated a in his presentation 'A cardiovascular digital twin; the brain assist device we need to make sense of data overload?'

Dr Fozia Ahmed is a consultant cardiologist at the Manchester Heart Centre, part of Manchester Royal Infirmary, where she specialises in heart failure and cardiac devices. In December 2020 she received a major UK award for her outstanding contribution to heart failure services and excellence in HF care. Her research interests include risk prediction models, remote monitoring in heart failure, and prevention of cardiovascular infection; with a focus on re-designing clinical pathways to improve patient outcomes.

C-arm adds accuracy to cardiovascular interventions

Flexibility and freedom of movement

Alongside the worldwide increase in longevity, inevitably with chronic health conditions rising, cardiovascular procedures and OR utilisation have surged. Thus the efficient and safe performance of surgeries is even more important.

The intraoperative use of mobile C-arms increase, accuracy, improving clinical outcomes, which can significantly reduce revision rates and thus overall healthcare spending, the manufacturer Ziehm reports, also noting: 'Mobile X-ray imaging devices also have lower acquisition and installation costs, which results in a faster return on investment in comparison to fixed installed systems.'

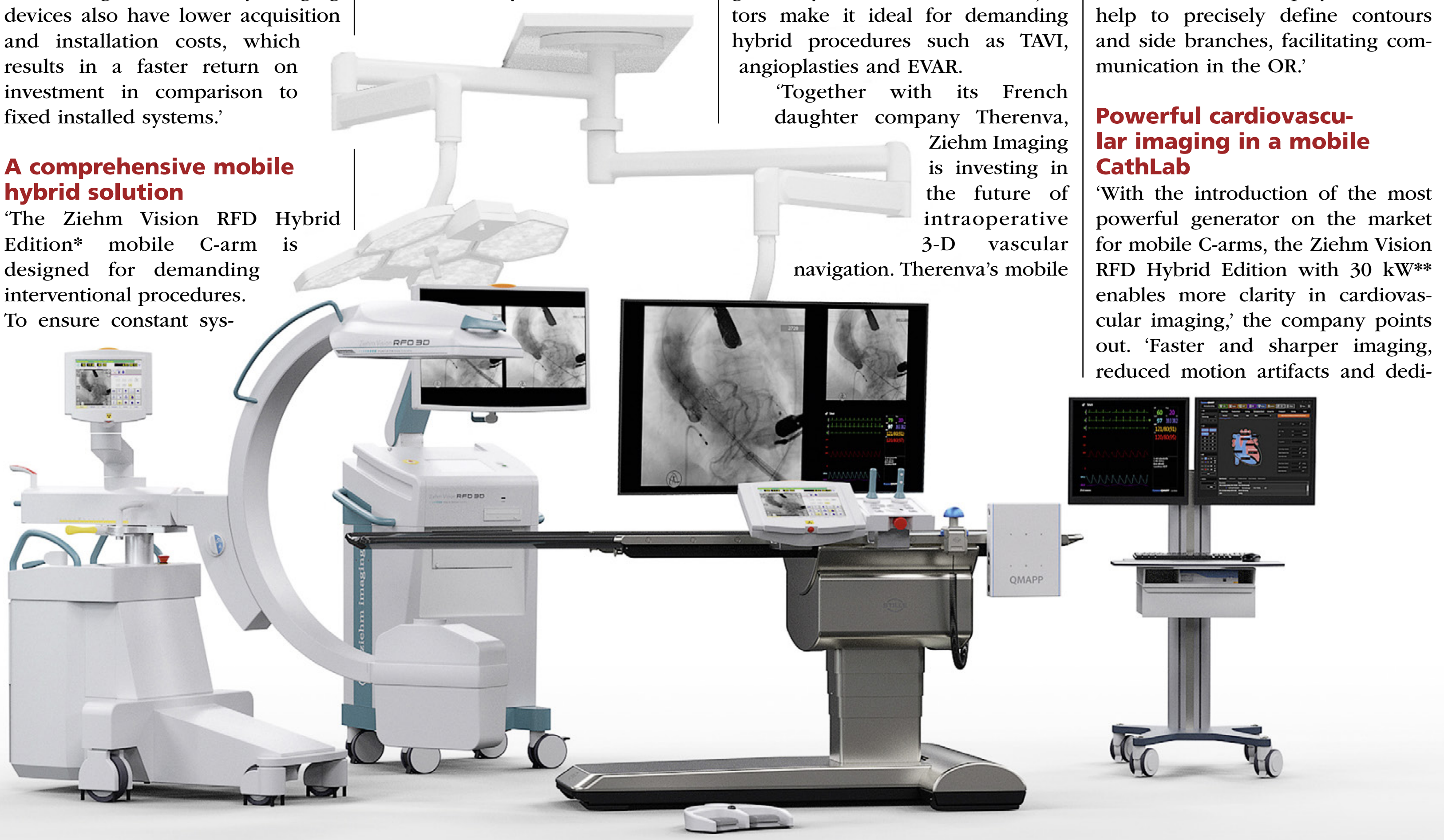
A comprehensive mobile hybrid solution

'The Ziehm Vision RFD Hybrid Edition* mobile C-arm is designed for demanding interventional procedures. To ensure constant system temperature and avoid system failures due to overheating, it is equipped with Advanced Active Cooling. Additionally, it is the only system on the market to offer motorisation of all four axes for easy control. 'The system meets all the requirements to transform conventional ORs into hybrid rooms in no time,' Ziehm continues. 'With versatile display options, ceiling-mounted monitors, wireless solutions and a unique Usability Concept, it does not require any changes to the OR and is ready for use immediately – without extensive construction work.

'Connectivity to 3-D vascular navigation systems and contrast injectors make it ideal for demanding hybrid procedures such as TAVI, angioplasties and EVAR.

'Together with its French daughter company Therenva, Ziehm Imaging is investing in the future of intraoperative 3-D vascular navigation. Therenva's mobile image fusion system EndoNaut enables physicians to achieve better accuracy during challenging hybrid surgeries. Combining preoperative CT data with intraoperative images from the mobile C-arm on the EndoNaut system reduces X-ray dosage and contrast media usage for even more precise results.

'Software features such as Enhanced Vessel Visualization with automatic colour display of vessels help to precisely define contours and side branches, facilitating communication in the OR.'



Powerful cardiovascular imaging in a mobile CathLab

'With the introduction of the most powerful generator on the market for mobile C-arms, the Ziehm Vision RFD Hybrid Edition with 30 kW** enables more clarity in cardiovascular imaging,' the company points out. 'Faster and sharper imaging, reduced motion artifacts and dedicated parameters allow more details to be displayed. Dedicated functions for coronary interventions and electrophysiology provide the best possible support during demanding procedures.

'Furthermore, special display and transmission options suitable for cath labs are available. These have become well-known and established through many years of practice in hybrid rooms.

'Together with its Dutch partner company, Fysicon, Ziehm Imaging is going one step further. To meet the needs of interventional cardiologists worldwide, they offer a dedicated mobile haemodynamic measurement station. The mobile CathLab solution provides more flexibility and freedom of movement and represents an alternative to conventional setups.'

Reflecting on the use of Ziehm Vision RFD Hybrid Edition CMOSline in his mobile CathLab, Dr Rajaram Prasad concluded: 'Our mobile concept has only advantages for me, my staff and my patients. I have not yet had a case that I could have solved better with a fixed system.'

** Ziehm Vision RFD Hybrid Edition represents a group of optional hardware and software that creates an option package on the device named Ziehm Vision RFD.*
*** 30 kW generator is available in combination with dedicated cardio packages.*