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Physicians forecast benefits for healthcare providers and patients

The impact of technology in 2030

How will digital technology impact on healthcare in 2030? If challenges to acceptance and utilisation can be overcome, healthcare providers and patients will benefit significantly, according to physicians participating in a recent online seminar on this topic.

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Report: Cynthia E. Keen

'Smart' technology is already utilised today to personalise interactions with a person by an entity in the consumer and financial industries. One example: online clothes shopping services, which assess physical size, body characteristics, age, budget, and wardrobe preferences by a professional stylist, and then use algorithms to subsequently select and sell clothing for subscribers.

The healthcare industry was a laggard in converting from analogue to digital technology and, for many reasons, this still continues today. Digital technology can make healthcare better for patients, can enable physicians and healthcare providers to do a better job, increase efficiency, and lower costs. 'But what do we specifically want it to do, and how are we going to pay for it?' asked Bob Kocher MD, Senior Fellow at the University of Southern California's Schaeffer Center for Healthcare Policy and Economics and Adjunct Professor at Stanford Medicine.

Fee-for-service healthcare model

Kocher said the healthcare technology IT software that exists in the United States is designed to make the fee-for-service healthcare model work better and to optimise the net revenue for individuals/ organisations that deliver healthcare services. 'We need to change how healthcare is delivered. How do we get technology to do this? If we change the business model of healthcare, technology will rapidly adapt.'

Internal medicine physician **Bob Kocher MD** is a partner at Venrock where he focuses on healthcare IT and services investments. An Adjunct Professor at Stanford University School of Medicine and a non-resident Senior Fellow and advisory board member at the Leonard D Schaeffer Center for Health Policy & Economics at USC, he also serves on the advisory board of the National Institute of Healthcare Management.

To achieve this, it will be necessary to change the business model of healthcare. 'Payment models are most important. Healthcare is driven by the power of local hospitals and regional health systems throughout the U.S. because insurance companies need these organisations to be able to sell health insurance policies.'

Kocher noted that major problems include lack of standardised software that can be universally used, lack of invulnerable secure software, and the expense of getting patients and healthcare providers to purchase the technology.

Amy Merlino MD agrees. 'We are using technology to mimic old processes. We need to rethink how digital technology can be utilised, keeping in mind that human interaction is essential, and that technology must be used to support rather than obstruct this. The current healthcare model is based on intermittent care, usually initiated by a patient with a healthcare crisis.'

Future healthcare will be ever-present in life

She predicts that the future of healthcare will be one in which healthcare will be an ever-present part of a person's life, unobtrusively and securely collecting data that can be AI-analysed to keep a person healthy, as well as proactively predict and respond to a person's healthcare needs throughout their lifespan. Wearable devices providing data to artificial intelligence tools will alert specific caregivers to intervene appropriately if medical attention is needed and to provide proactive assistance to support best-practice outcomes.

More patient centricity

Eyal Zimlichman MD, Deputy Director General, Chief Medical Officer, and Chief Innovation Officer of Sheba Medical Center in Tel Hasomer, Israel, believes that healthcare is on the brink of major transformation.

Redesigned hospitals will need to be much more patient-centred, providing better personalised care at lower cost using best-practice-based AI decision support tools and

Continued on page 3


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Amy Merlino MD is Enterprise Chief Medical Information Officer and a staff physician in obstetrics and gynaecology for the Cleveland Clinic Health System. She directs a team of physicians who have dual appointments in clinical practice and technology, working to optimise electronic records data and to promote evidence-based best practices.

Eyal Zimlichman MD is an internal medicine physician, healthcare executive, and researcher focused on assessing and improving healthcare quality and value, patient engagement and patient safety. He is currently Deputy Director General, Chief Medical Officer and Chief Innovation Officer at Sheba Medical Centre, Israel's largest hospital.

Update

5G in German healthcare

This September, the symposium 5G4Healthcare, organised by the Technical University of Applied Sciences (Ostbayerische Technische Hochschule – OTH) Amberg-Weiden, Germany, explored how 5G can contribute to greater efficiency in healthcare.

Report: Cornelia Wels-Maugg

The event was based on the insights from the 5G4Healthcare project at OTH. Launched in 2020, it is one of six research projects in the 5G innovation programme funded by the German Ministry of Transport and Digital Infrastructure. 'We are looking at the effects of the 5G technology and how it interacts with hardware and software and we explore interoperability as well as the health economy effects 5G might be able to generate,' Dr Steffen Hamm, Professor for Digital Healthcare Management at OTH Amberg-Weiden, explained in his opening remarks. The project aims to further the development of solutions that might serve as a blueprint for digital healthcare approaches in rural areas.

5G in a nutshell

5G is the 5th generation standard for broadband cellular networks. It offers high-speed transmission of large data volumes and low latency. In addition, unlike other standards, 5G can integrate a much higher number of user devices. Benefits:

- Enhanced mobile broadband
  - Data transmission rate of up to 10 Gbit/s
  - Stable connection even with high speeds (up to 500 km/h)
- Massive machine-to-machine communication
  - Up to one million devices/km2
  - Energy savings of up to 90%; longer battery life
- Ultra-reliable and low latency communication
  - Latency <1ms
  - Ultra-high reliability and availability (99.999%)
- Network slicing: different requirements regarding speed, data rates and user/app capacities can be defined in each slice of a 5G network
- Massive multiple-input/output: spatial transmission of the radio signal is calculated, thus signal can be adapted.

While other network technologies offer some of these features, none offers them all to the same degree as 5G.

5G added value in healthcare

5G meets the demanding requirements of e-health in terms of capacity, bandwidth, reliability, availability, latency and security and thus presents itself for different use cases, such as telemonitoring, mass connectivity of sensors and devices in the internet of things (IoT), wireless application in augmented and virtual reality, real-time data transfer with emergency services, robotics-guided telesurgery, live streams of surgeries, telediagnostics, location of devices and building infrastructure, transport of medication organs, etc. with drones.

Hamm pointed out that the deployment of 5G depends on the overall requirements of each use case: when only a single device needs to be integrated, 5G does not make sense, but with many devices it does.

However, in German hospitals very few of the above-mentioned applications use 5G. 'In healthcare 5G hasn't evolved as quickly as in other areas,' explained Professor Dr Hans Dieter Schotten, Chair of Radio Communication and Navigation at the University of Kaiserslautern. The reasons are, inter alia, 'The high availability requirements, but also to the very specific regulation of the healthcare sector, the lack of experts and lack of market transparency. Moreover, financing 5G is very difficult. The public 5G networks, which are designed for 95% availability, don't meet a hospital's very high requirements regarding security, latency and availability.'

5G in German hospitals

Holger Mauerer, Executive Customer Solution Architect for Vodafone, confirmed that 5G in German healthcare is still a rarity: '5G is used particularly where huge data volumes need to be transmitted – in telemedicine, for VR headsets in the OR or by emergency services that have to access patient records or need the support of hospital physicians during patient transport.' Moreover, according to Mauerer 5G is used for asset management, particularly asset tracking such as beds, and vital signs transmission via IoT sensors. 'During the pandemic, 5G helped move the check-in area outside the hospital proper. This entailed mobile solutions, such as face mask recognition or measuring body temperature,' he added.

Tobias Friedrich, Account Manager at Nokia, expects 5G use to go beyond asset tracking in hospitals and will include robotics and telemedicine: 'Robotics is a major case for 5G as latency is required, for example to disinfect potentially contaminated surfaces in the OR. 5G is also important for teleconsultation and teleboards in the hospital or radiological remote diagnostics.' He added that 'Logistics' is another important area which might include many aspects such as the transport of medicatio.'

Start-ups and 5G

Several start-ups that are interested in 5th generation wireless networking were present at the symposium. ProCarement developed an app that helps patients manage chronic diseases. 'The app is installed and personalised on the patient's smartphone. It reminds the patient to measure vital signs, attend appointments and take medication. At the same time, the app offers lifestyle advice based on current medical guidelines. Our proprietary algorithms detect changes in the health status and direct the patient to the right person in the healthcare system. This reduces the number of unnecessary trips to physicians and hospital admission,' explained Sebastian Eckl, founder and Managing Director of ProCarement.

inContAlert aims to help manage incontinence by collecting data on bladder fullness with non-invasive sensor technology and transmitting it to a mobile device. In addition, the app calculates when the bladder needs to be emptied again. 'Thus, patients regain control over their bladder – which means improved quality of life,' said Jannik Lockl, co-founder and CEO of inContAlert.

After 5G: 6G

'We expect new wireless technology to be introduced every ten years. Thus 6G will arrive around 2030,' predicted Dr habil. Ivan Ndip, Head of Department at the Fraunhofer Institute for Reliability and Microintegration. 'The crucial differences,' he predicted, 'will be that 6G will offer 50 times higher data rates and one tenth of 5G latency,'

6G promises to provide healthcare services, despite staff shortages, thanks to robots and the internet of medical things – capabilities that are important for rural areas. According to Ndip, 'Sensors can measure vital signs and transmit data wireless to medical staff. Robots can hand out medication.' 6G bandwidth enables the large-scale connectivity between 6G and robots. Moreover, the very low latency and the high reliability will most likely allow real-time monitoring of patients. Additionally, AI-based algorithms might lead to enhanced diagnostics and therapies. At this point however, that's still pie in the sky because there is no 6G hardware, and 6G signals might be blocked by things, people and rain.

A propos people: In addition to the technical challenges which need to be overcome on the road to 6G, the 'people' factor might play a vital role in 6G adoption. What has to happen for patients and clinicians to accept 6G? Hamm is convinced that the German Minister for Health, Jens Spahn, was right when he said 'Digital health has to be fun, otherwise it won't be used'. So far the fun factor with 5G has been low – as has been the adoption rate.

The ‘bio space race’. Who will win the day?

Cybersecurity professionals are scarce

The Covid pandemic swung a spotlight onto the increasing role of cyber-attacks and weaknesses in healthcare. In healthcare as in other industries, cybercrime does not stop at national borders. With this in mind, the United States consulate general in Düsseldorf and the US embassy in Vienna recently invited interested parties to their Cybersecurity in Healthcare briefing.

Report: Dr Christina Czeschik

The meeting kicked off with a keynote talk by Supervisory Special Agent Edward You (FBI), who presented the US perspective on current cybersecurity threats and countermeasures in healthcare and the wider bio-economy.

Perhaps not surprisingly, Special Agent You saw the most significant threat to information security and patient safety of US patients in the activities of Chinese companies. He even made the Cold War analogy explicit by calling the competitive race between Chinese and US companies the ‚bio space race‘, with data as its fuel.

In You’s words regarding genomics and other big data-powered bio sciences: ‘Whoever generates the largest, most diverse dataset is really gonna own the day’. As early as 2015, 30% of the world’s genetic sequencing machines were located in China; the proportion is increasing. Many healthcare providers in the US and internationally contribute to China’s dominant position on the market by sending samples to the BGI Group (formerly Beijing Genomics Institute), the incumbent on the genome sequencing market and provider of the popular NIFTY prenatal test.

Another important Chinese player is the WuXi conglomerate: one subsidiary invested in 23andMe, the personal genomic sequencing company, and another, the WuXi NextCode Sequencing Facility, was accredited by the American College of Pathologists, now accepting samples directly from US patients.

However, the generation and analysis of genomic data seems to be a one-way street to Chinese corporations and governments, You reported. China’s state council order demands that foreign entities analysing the material of Chinese citizens must cooperate with a Chinese company and must share all data and patents with their Chinese partners.

US institutions managing the risks and threats associated with the Chinese predominance in the bio-economy include the FBI and the National Academies of Sciences, Engineering and Medicine. While the former is concerned with cybersecurity and protection against economic espionage, the latter published a report titled ‘Safeguarding the Bioeconomy’ in 2020, focusing less on cybersecurity issues than on issues of the competitive fitness of the US economy and the contributions of the sciences.

EU: Directives and regulations

In the second keynote, Maria Papaphilippou, Cybersecurity Officer of ENISA, reported on the policy and regulatory frameworks of cybersecurity in healthcare in the EU. The European Union Agency for Cybersecurity (**ENISA**) counts the increasing frequency and differentiation of ransomware attacks, the increase in teleworking due to the pandemic and last but not least the enduring lack in skilled cybersecurity professionals among the most important threats to healthcare cybersecurity.

In incident reporting and analysis, ENISA has identified systems failure as cause for 59% of incidents, human error and malicious intent for 19% each and natural phenomena as cause for only 2% of incidents. Data breaches and leaks, with 49%, are the most frequent type of incident in healthcare, followed by ransomware attacks with 26%, other malware with 7%, threats targeting e-mail with 4% and fraud with 2%.

As two of the most important regulations safeguarding cybersecurity in EU healthcare Papaphilippou cited the NIS directive (in full: Directive […] concerning measures for a high common level of security of network and information systems across the Union) and the EU MDR (Medical Devices Regulation). NIS implementation is guided by the NIS Cooperation Group and its various working groups, one of which is dedicated exclusively to cybersecurity in healthcare (WS12).

However, while these regulations may serve as a good start and foundation of healthcare cybersecurity, Papaphilippou had to admit, upon questions from the audience, that ENISA does not currently pursue any collaboration with institutions outside of the EU, and that it does not concern itself with genomics and the associated threats to personal data at the moment.

Hospitals are ‘target rich and cyber poor’

After several of commercial entities had the chance to present their products and services during the event, the Cybersecurity in Healthcare Briefing concluded with a panel discussion of government officials from Germany (Jeffrey Fleischle, German Federal Ministry of Health), Austria (Robert Scharinger, Austrian Federal Ministry of Health) and Switzerland (Marc Henauer, National Cybersecurity Centre Switzerland), as well as Josh Corman of the US Cybersecurity and Infrastructure Security Agency (CISA).

Participants in general agreed that international collaboration is key to fighting cybercrime in healthcare. However, regulatory measures seem to be on the forefront of thinking for many EU member institutions.

Jeffrey Fleischle set out by explaining how regulatory holes were closed by including smaller hospitals in critical infrastructure regulations.

Corman suggested that maybe the patient safety aspect of cybersecurity was neglected in the past, concentrating on personal data security instead. Time and again, the discussion circled back to the lack of trained professionals in cybersecurity. Corman described many hospitals in the US and abroad as ‘target rich and cyber poor’ or even living below the ‘infrastructure poverty line’. Even if sufficient funds were available, Scharinger added, the cybersecurity professionals who could be paid with those funds are presently extremely scarce.

Continued from page 1

patient-specific precision medicine treatments.

‘AI developments today, such as automated interpretation of screening mammograms to aid radiologists, show its potential. Radiology has always been an early adopter of new technology, and digital pathology is close behind.

Like mammography, artificial intelligence deployed in pathology can analyse digital slides to accelerate rapid decision-making but, in five years,’ he added, ‘may independently make new discoveries to revolutionise diagnoses.’ Zimlichman believes that AI will transform early detection of disease. Much like at airports, he predicts that AI-driven ‘control towers’ will manage hospital operations, directing patient flow for diagnoses and treatment, and monitoring/alerting when change is needed, such as transferring an inpatient to an ICU.

‘Today nurses capture vital data in hospitals. What is going to happen when we have ambulatory patients with patches on their chest that generate hundreds of parameters of data? Who is going to analyse and make sense of this? We need to develop detailed processes to determine what is vital and what is noise,’ Zimlichman pointed out. He believes that patients who require chronic disease management or have chronic pain will be the initial beneficiaries of new AI tools.

With respect to artificial intelligence healthcare-related apps that exist today, he recommends regulatory assessments to verify their quality, and which are most appropriate for specific medical conditions. ‘These need to be used better. I predict these may even be prescribed like drugs in the not-too-distant future.’

Interview with Professor Maciej Pech, Director of the Department of Radiology and Nuclear Me

Histotripsy: Mic destroy tumours

Focused ultrasound waves create microbubbles in a fluid – a phenomenon called cavitation. In a current study this process is used to destroy liver tumours and metastases. In this MEDICA-tradefair.com interview, Professessor Maciej Pech discussed testing cavitation events generated during histotripsy, describing the process and its advantages.

Professor Pech, what is the purpose of the Hope4Liver study?

This phase I clinical trial investigates the safety and efficacy of the histotripsy method in the treatment of liver lesions. This includes primary and metastatic liver tumours.

What is histotripsy?

Histotripsy is a method based on sound waves that induce cavitation. During a low-pressure cycle, high-intensity ultrasound waves lead to the formation of small vacuum bubbles or cavities in the liquid. When these bubbles reach a volume at which they can no longer absorb the energy, they implode when subjected to higher pressure. The bubbles form within a narrow region via the superposition of ultrasonic waves and destroy tumour cells at the cellular organelle level.

After creating the treatment plan, a robotic arm performs point-by-point ablation in the targeted tumour area and respective clearance zone. This is a very precise maneuver as the ultrasound is focused with millimeter-precision.

How long has this technique been around?

The method has been used in experiments and in research laboratories for the past 15 years, but clinical trials are just now underway. The forerunners of this technique include lithotripsy, a procedure that applies shock waves to break up stones in the kidney and parts of the ureter, or thermal ablation using focused ultrasound. Histotripsy is non-invasive and does not produce heat in the tissue. Cavitation destroys the targeted area completely.

Where can the technique be used?

In theory, you can use the method anywhere in the body for all types of tissues that can be radiated with focused ultrasound. However, there are some physical limitations. It is difficult to use the process behind a bone because the ultrasound is reflected off the structure. It is also not an ideal technique for air-filled organs.

Once the accuracy and safety of this technique have been proven, I could envision its application to treat the affected lymph nodes, bladder tumours, and kidney cancers.

Does imaging accompany the procedure?

Imaging is primarily used for treatment planning during which the tumour is highlighted using the ultrasound image. The liver ultrasound scan is available during the exam. It does not have the same quality as we see in primary diagnostics, but you can detect the bubble cloud shape in the tumour, giving you direct control over the sound waves to trigger cavitation in the targeted area. This facilitates online monitoring during the procedure and provides added visualazion and safety.

What are the advantages of this method?

It is a non-invasive technique, which means it carries no risk of infection and there is no need to tend to or

NEW: Controlled high power ultrasound

A new device for ultrasound therapy, Fisiosonic Plus, uses an innovative output stage called Class E, reported to deliver mechanical efficiency notably higher than that obtained via traditional output stages. This allows the operator to issue high powers on a patient in a constant and controlled way in relation to impedance of the tissues and with a limited thermal effect, the manufacturer reports.

The producer, Fisioline, adds that the system is a last generation ultrasound device that uses 1-3MHz multifrequency applicators. 'These frequencies can be used separately, or in joint mode, during the treatment. Besides traditional methods, Fisiosonic Plus has introduced two innovative functions: sequential treatment and automatic frequency switching. 'The sequential treatment offers the operator the opportunity to use multidisc scanning applicators with a wide contact surface to be applied by common elastic straps. The ultrasound emission is sequential, so the operator can carry out an automatic treatment on a wide surface with no need for a manual dedicated intervention.'The automatic frequency switching is obtained by the exclusive A.F.S. (Automatic Frequency Switching) device, to exploit the various focalisations of 1 and 3MHz frequencies at the same time and set different supplying times for each frequency. This feature enables the operator to obtain a focalised action.

The applicators are waterproof for underwater treatments. The instrument can be operated in two modes: continuous and pulsed. The pulsed operating mode enables energy modulation (duty-cycle from 10% to 90%) to reduce the thermal effect and keep the peak pressure applied by the acoustic wave on the tissues steady. The output power density can be adjusted from 0 W/cm2 and 3 W/cm².

Fisionic Plus has self-calibration and a visual and sound contact control system. The appliance is equipped with an inlet for electrotherapy device connection (Modulo series); the operator can then carry out a combined therapy with any applicator. Fisiosonic Plus is also equipped with a library of pre-set therapeutic protocols focused on severe and chronic pathologies. 'It provides the operator with the option to create customised programs for a patient and indicated for specific pathologies or areas to be treated, for rapid and efficient therapies,' the manufacturer reports.

Fisioline is at Medica Hall 9 / D34

edicine at University Hospital Magdeburg

robubbles s

monitor wounds. That is why this is a conceivable outpatient treatment that does not require an overnight stay at the hospital. The patient could simply return to the hospital the next day for a checkup if he lives near the facility.

Are there any known risks?

So far, we are not aware of any. In theory, there is always the risk of poor planning, or that the energy is applied at the wrong spot. This is why visual tracking during the procedure is key. The robotic arm is far more accurate in applying the energy than humans.

Another risk is that the patient could make involuntary movements by breathing or coughing, for example. You would have to stop and reschedule the intervention immediately, which is why anesthesia is used for the purpose of this study. However, one might also consider simple sedation in the future.

What follows next?

It is currently a classic phase I clinical trial that seeks to evaluate the safety and efficacy of the process. In the next phase, the mechanism of histotripsy would be tested in a randomed setting against an established method. This could be thermal ablation, radiofrequency ablation, or stereotactic radiation therapy.

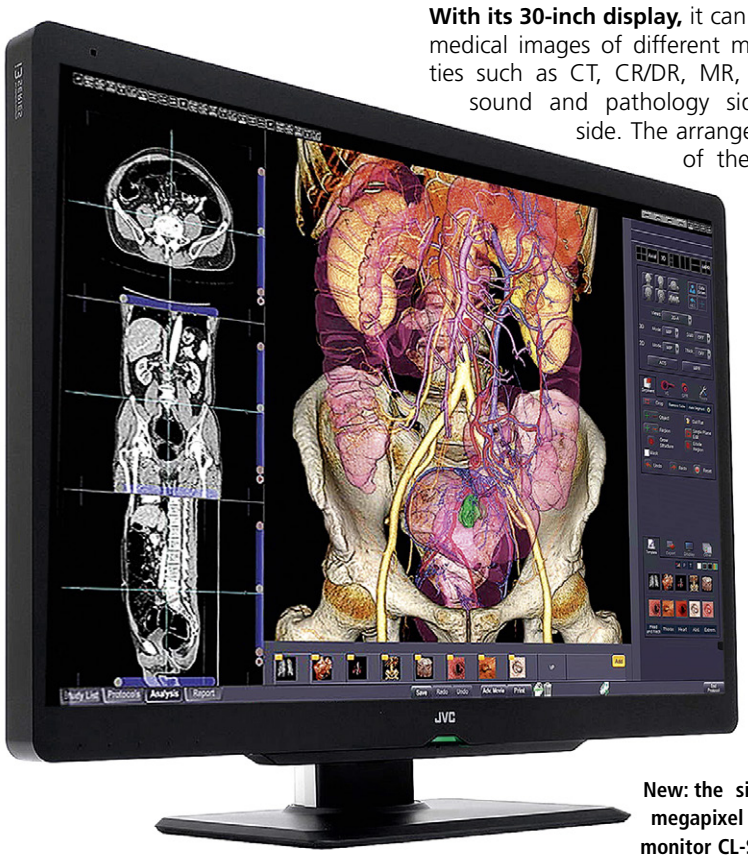
This interview was conducted by Timo Roth and translated from German by Elena O'Meara. MEDICA-tradefair.com

Professor Pech performing histotripsy. Image: (c) Christian Morawe. Universitätsmedizin Magdeburg

Monitor CL-S600

Six megapixels for diagnostic radiology

Everything but mammography, that's what JVCKENWOOD's new CL-S600 6-megapixel monitor can do.



New: the six megapixel monitor CL-S600 (c) JVCKenwood

With its 30-inch display, it can show medical images of different modalities such as CT, CR/DR, MR, ultrasound and pathology side by side. The arrangement of the windows can be freely selected. The large screen without a center bar creates a comfortable environment for radiological diagnostics.

The monitor is equipped with the latest technology. The patented Dynamic Gamma function, for example, analyses the entire screen content and selects the correct gamma curve for each individual pixel in real time. This applies to all images – whether ultrasound, endoscope, pathology or nuclear medicine – and always results in an optimum representation. 'This works without problems even with moving images, although millions of operations per second are necessary here,' explains Marcel Herrmann, Marketing Manager for Medical Imaging at JVCKenwood.

The novel turbo luminance function can increase the brightness and contrast of the screen for a maximum of 30 seconds to magnify recognisable gray scales. This allows the radiologist to reliably assess even the finest calcifications. The effect is further enhanced by the Visual Point mode. This increases the contrast in certain areas controlled by the mouse pointer. Luminance and color temperature are automatically adjusted in real time on the CL-S600. 'The built-in color front sensor on the screen constantly measures the color temperature and adjusts changes over a long period of time,' says Herrmann. This is easy on the eyes of the person reading the images – as is the built-in lighting on the back of the monitor and the indirect lighting of the keyboard and mouse.

JVCKenwood is at Medica Hall 14 / A17

Fully synchronised group measuring

Bittium NeuroOne

'Bittium NeurOne is one of the quickest and most accurate EEG measuring devices in the world designed for clinical and research use,' the manufacturer reports. 'Bittium NeurOne system enables fully synchronised group measuring of up to 30 people simultaneously, for example in different types of psychological studies.

'The solution is optimised for use with transcranial magnetic stimulators (TMS-EEG), with optional possibility to use it during magnetic resonance imaging procedures (fMRI-EEG).'

Bittium Biosignals Oy is at Medica Hall 9 / C15

Saving lives

Mobile stroke units

Speed in treatment of ischemic stroke can mean the difference between successful recovery versus permanent disability or death caused by brain tissue damage.

Report: Cynthia E. Keen

Time is of the essence to perform thrombolysis with a tissue plasminogen activate (tPA), a protein that can dissolve blood clots causing the stroke or intra-arterial thrombolytic therapy (IAT) because of large-vessel occlusion.

CT imaging to rule out intracranial haemorrhage is essential to determine if this treatment is appropriate. In 2003, Professor Klaus Fassbender MD, Director of the Neurology Clinic at Saarland University Medical Center in Homburg, Germany, proposed the idea of expediting CT imaging by bringing a CT scanner to the stroke victim in a specially configured 'stroke ambulance'. His idea to shift acute stroke examination, including brain imaging, to a prehospital setting became reality with the 2008 launch of the world's first mobile stroke unit (MSU) at his hospital, which serves mixed urban and rural communities in a 20 km radius.

MSUs incorporate a compact CT scanner, a complex point-of-care laboratory equipped with small, commercially available portable laboratory devices to quantify haematological, clinical chemistry, coagulation markers, and renal function markers; real-time bidirectional audio-video communications, and a PACS workstation. Clinical staff onboard typically include a paramedic, CT technician, and physician plus a registered nurse trained in stroke medicine. A neuroradiologist should be accessible via PACS, and telemedicine connects with a hospital's laboratory staff, emergency physicians, neurologists, and/or neurosurgeons.

Blood clot-busting medication: Sooner in MSUs

MSUs shorten time to treatment, improve prehospital triage, and can increase thrombolysis rates. A study presented at the 2021 American Stroke Association's International Stroke Conference from Memorial Hermann Texas Medical Center in Houston reported that stroke patients treated in MSUs received blood clot-busting medication more frequently and sooner than patients who received initial care from emergency medical technicians in a standard ambulance. James C Grotta MD, director of the Houston Mobile Stroke Unity Consortium, called MSUs 'a stroke centre on wheels'. Grotta reported that 53% of patients treated on an MSU in his study made a complete recovery, compared to 43% who were not treated on an MSU. Memorial Hermann Health System is sponsoring an ongoing randomised interventional clinical trial, the BEST-MSU Study, which began in August 2014 with an estimated enrolment of 1,038 patients.

The completed study will provide data on outcomes and cost of MSUs compared to standard ambulances, and will help determine the value of integrating MSUs into hospital stroke programs in the USA.

'This study will provide critical information that will be needed to determine if and how a subsequent more definitive study should be conducted. It is a necessary first step in a process which may dramatically modify the way that acute stroke patients are managed in the United States,' Grotta pointed out.

The Houston Mobile Stroke Unit

Currently there are fewer than 30 MSU programs in operation in the USA. Major roadblocks to implementation include cost, staffing, and the ability to identify individuals who have had a stroke by emergency telephone call dispatchers.

Clinical trials performed in Europe

A number of clinical trials have been conducted in Europe, all of which produced data supporting the benefits of MSUs to stroke victims.

A randomised clinical trial performed in Homburg between 2008 and 2011 showed that MSU-based stroke management significantly reduced time to treatment from 153 minutes for ischemic stroke patients receiving standard care to 72 minutes with an MSU. Nearly 60% of patients in an MSU had therapy decisions for or against thrombolysis based on diagnostic work-up, including laboratory and imaging studies, made within 60 minutes, compared to only 4% who received standard care.

A newly published study in the Journal of the American Medical Association (JAMA) conducted in Berlin between February 2017 and November 2019 also produced impressive results, with stroke victims who received MSU care having less disability after 90 days. The objective of this non-randomised controlled intervention study of 1,543 patients was to evaluate the functional outcomes at three months among patients with acute ischemic stroke who received pre-hospital care by a conventional ambulance or by an MSU.

Heinich J Audebert MD from the Centre for Stroke Research Berlin, Charité-Universitätsmedizin Berlin, and co-researchers reported that 80.3% of MSU-dispatched patients had none-to-moderate disability at 90 days compared to 78.0% of the conventional ambulance-dispatched group, 12.6% compared to 13.3% had severe disability, and 7.1% compared to 8.8% died.

Erik Freitag MD and colleagues at the Klinik und Hochschulambulanz für Neurologie, Charité–Universitätsmedizin Berlin, provides useful recommendations in a newly published article in Stroke 'How to set up a successfully running mobile stroke unit program'. In addition to technical, staffing, and logistical requirements, they discuss if an MSU program makes sense in the area a hospital serves.

A million people catchment area for one mobile stroke unit

'We estimate a one million people catchment area to be a proper population covered by one MSU,' they advise. 'In health systems with hospitals competing for stroke cases, it's vital to start with intensive communications. MSU services can work smoothly if they are operated in close collaboration with the dispatch centre and EMS.' Allies, such as politicians, will be needed to support the system if it is to be paid by public funds. Legal issues also need to be investigated in advance.

'Organising an MSU service is not an easy task,' Freitag observes. 'But enjoy the pleasure of thrombolysing patients in the 'Golden Hour' of stroke, with many patients experiencing rapid recovery.'


(© Universität des Saarlandes)

Professor Klaus Fassbender MD is Director of the Neurology Clinic in Homburg, Germany.

James C Grotta MD, is Director of the Houston Mobile Stroke Unity Consortium, called MSUs 'a stroke centre on wheels'


(© American Heart Association)

Heinich J Audebert MD works at the Centre for Stroke Research Berlin, Charité-Universitätsmedizin.

Haptic feedback

Smart Shirt guides neurosurgeons

The NeuroShirt, developed by Elitac Wearables in collaboration with the University Medical Centre Utrecht (NL), is a patent-pending smart shirt that helps guide neurosurgeons during complicated skull-base surgeries. It connects to the neuronavigation system and continuously indicates both the distance and direction of critical structures through haptic feedback (vibrations). 'This way,' the manufacturer reports, 'surgeons no longer have to split their focus between patient and screen. They can stay focused and operate more safely. Elitac Wearables CEO and co-founder Merijn Klarenbeek explains, 'We believe that wearable technology can play a major role in improving medical fields like rehabilitation, surgical assistance, patient mobility, etc. The benefits of haptic feedback and wearable sensors range from augmenting or even replacing impaired senses and reducing sensory overload to capturing real-time, accurate data.

'Until quite recently, the practical implementation of wearable technology was held back due to issues such as washability and wearability. But by combining new technological advances (miniaturisation, smart textiles, stretchable electronics, etc.) with our extensive experience developing wearables, we can utilise this new technology to its maximum benefit. For example, with our NeuroShirt, we have demonstrated that haptic feedback can be intuitive, precise and distinct enough to complement complex brain surgeries.'

The NeuroShirt, developed by Elitac Wearables in collaboration with the University Medical Centre Utrecht (NL)

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A potentially devastating impact on non-Covid patients

Covid-19 alters antibiotic use

The long-term impact of the coronavirus pandemic on antimicrobial resistance (AMR) remains difficult to predict, Mark Nicholls reports.

Infectious diseases consultant Professor Alison Holmes said Covid-19 has impacted on antibiotic use in hospitals and across the wider community, but more research is needed to fully assess the extent and implications.

Holmes discussed the subject in detail in her presentation 'Healthcare associated infection, antibiotic use, drug resistance and Covid-19', to the 73rd annual congress of the German Society for Hygiene and Microbiology, with a focus on bacterial infections, antibiotic use, hospital-onset Covid infection and how that should be tackled, and healthcare associated infections (HCAI) in individuals with and without Covid-19.

'Bacterial infection and Covid-19 were a major concern, particularly at the beginning of the pandemic in terms of driving antibiotic use and potential AMR,' said Holmes, who is also Director of the NIHR Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, as well as the Centre for Antimicrobial Optimisation (CAMO) at Imperial College London.

Antibiotic prescribing

Emphasising the importance of looking at the effect, directly and indirectly, of other clinical activity related to infections on Covid and non-Covid populations, Holmes said: 'There were many consequences that could impact on infection that could fuel antimicrobial resistance, or indeed reduce it significantly, and it is important that we consider this across multiple levels.' Further considerations included the potential for bacterial infection risk on new therapies, particularly immunological; the pressures on different healthcare systems, and patient backlogs.

Holmes, who has contributed to the national Covid-19 response in the UK, noted that early in the pandemic, experts were keen to conduct a rapid review in terms of bacterial and fungal infections, but particularly how it could support antibiotic prescribing.

Initial research

Low levels of coinfection in Covid-19 patients (8%), but high rates of antimicrobial use (70%), were suggested in initial research, but there were research limitations: studies often did not differentiate whether patient populations were in critical care or not; there was limited microbiology, risk factors such as whether patients were being ventilated were not reported; and complications of excessive prescribing were not identified. She said the evidence at the time supported use of antibiotics only in suspected or confirmed serious infections and with regular review, short duration and the need to maintain strong antimicrobial stewardship programmes, although more recent evidence has 'expanded the level of understanding of co-infection'. Critical care has been highlighted as the main focus for coinfection, with organisms linked predominantly to local epidemiology. However, while the majority of coinfections were hospital-acquired pneumonia or ventilator-associated pneumonia, there was a need for these risk factors to be collected in a standardised way to 'understand risk of Covid in terms of coinfection'.


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Covid-19 has impacted on antibiotic use in hospitals

Non-Covid patients

More recent study findings, however, were not dissimilar to the early research, with 8.6% of bacterial infections seen versus 74.6% of patients on antibiotics. But she added: 'We are not doing well enough in terms of understanding what is going on in low resource settings and we need to do much better around that to understand the potential devasting impact this is having on our non-Covid patients.' Holmes also discussed the impact of Covid on bacteremias, notably a major drop across the two waves of Covid and particularly in e.coli bacteremia, though this was tempered by the change in the patient mix.

In the USA, she noted, there was a rise in hospital-acquired infections in 2020 compared to 2019, after years of reductions, mainly catheter- associated urinary tract infections, ventilator associated events, and MRSA, but notably no increase in surgical site infections (with surgery being cancelled), and there was no increase seen in C.diff rates.

Community prescribing

With concerns about AMR in acute care, the implications of a fall in antibiotic use in the community – traditionally an area of higher usage – remain uncertain. 'That's a major concern because we don't know if people could access treatment appropriately, or if patients with infections are going untreated. There is a need for better evidence on this,' Holmes said and emphasised the need for 'strong, robust surveillance' of hospital-onset Covid for future pandemic preparedness, and recovery of healthcare resilience and safety.


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Alison Holmes is Professor of Infectious Diseases and Director of the NIHR Health Protection Research Unit in Healthcare Associated Infections and AMR, as well as the Centre for Antimicrobial Optimisation (CAMO) at Imperial College London. She leads an international, multidisciplinary infectious disease research programme focusing on optimising antimicrobial use by developing innovative approaches and technologies to manage and prevent infections.

Health systems need to understand that non-Covid patients can be well looked after and health systems be run effectively and safely with the appropriate level of capacity in terms of beds and staffing, she underlined.

Local epidemiology

While bacterial infection in Covid patients is relatively low, with the majority in acute care due to HCAIs, she said understanding the local epidemiology is critical and that a strong foundation of effective prevention and control practice is vital.

Antibiotic stewardship is also crucial given the high rates of prescribing, and there is a need for a better framework for prospective reporting to inform clinicians in providing safe healthcare for HCAIs associated with Covid, for hospital-onset Covid infections, and for antibiotic use within the Covid pandemic.

'By recognising that the AMR pandemic is happening already, we need to be able to understand and make the most of the information, so that we can learn from the Covid pandemic,' the professor said.

'The long-term impact of the pandemic on AMR is still difficult to predict and it's important to have a whole health system perspective, looking at what is happening in the community and in acute settings at the same time.'

Disinfection lamp

UV-C lamps combat viruses

The Covid-19 pandemic has generated an increased interest in methods and means of combating viruses and bacteria in human environments. 'UV-C technology is a very effective means to this end, which can help protect people from airborne diseases,' Ultraviol reports, adding: 'During the Covid-19 pandemic, the firm has launched two new lines of modern and highly effective UV-C products.

'Asepto Basic flow UV-C germicidal and virucidal lamps are designed for flow sterilisation of air in large areas, such as operating rooms, patient areas, halls, waiting rooms, open-space offices, auditoriums, public facilities etc. The devices provide fast and effective microorganism reduction, noiseless operation (whisper quiet) and are safe for people and animals. 'GermiProtect Industrial flow UV-C germicidal lamps dedicated for disinfection of the air in the large volume rooms and halls in the food processing industry, pharmaceutical industry, cosmetic industry, laboratories, pharmacies, railway stations, hotels, cinemas, restaurants, kitchens, gyms, lobbies and any kind of gatherings. The devices achieve a high level of purity in the production process, and enable intensive air disinfection during personnel presence.

'The high germicidal effectiveness of Aseptor Basic and GermiProtect is verified and confirmed by scientific and laboratory testing.'

Since 2020 the company has increased its production capacity to enable deliveries of the UV-C disinfection systems to many countries internationally.


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Lessons learned in hospitals

Covid-19 accelerated digital transformation

Digital transformation has been a significant factor in the way hospitals have responded to the challenges posed by the Covid-19 pandemic.

Report: Mark Nicholls

The ability to rapidly share data, monitor patients, and forecast future patterns has helped tackle the coronavirus crisis. However, during a presentation on the subject of Digital Transformation for Hospitals at the online HIMSS21 European Health Conference, a panel of experts were also quick to point out that the approach of the 'human resource' to the challenges and changes was a key factor.

The session shared best practices from hospitals in the UK, the Netherlands and Portugal, highlighting lessons learned from the pandemic, and how HIMSS (Healthcare Information and Management Systems) models have supported digital transformation.

Digital maturity

Covid-19 highlighted the need to accelerate the digital maturity of health systems to improve patient health but also to be better prepared to respond to future public health crises.

The session, chaired by HIMSS Analytics regional director (Europe and Latin America) John Rayner, examined how to overcome major challenges through information and technology.

Katie Trott, Chief Nursing Information Officer at the Royal Free London NHS Foundation Trust, detailed the pandemic experience in London, particularly surrounding the creation of the 4,000-bed temporary Nightingale hospital in a large exhibition hall.

'One thing we learned from that was the ability to be able to share our information on patients that were transferred there,' she said. 'Staff at the Nightingale hospital were able to see everything about patients because of the electronic health records and the health information exchange we set up at the start of the pandemic.'

Rapid transformation

That demonstrated how quickly transformation could happen, and the appetite for doing this at speed and scale, not only from staff but patients too, she said, alongside a greater willingness to share information from organisations that were previously more cautious about doing so.

However, she stressed the importance of keeping the end users' preferences in view when switching to new technologies, and also of undertaking the right evaluation processes while trying to respond swiftly.

Going forward, Trott noted a renewed enthusiasm among staff at the Chase Farm Hospital – which is part of the Royal Free London NHS Foundation Trust group – and other medical units, in wanting to adopt new ways of working, and for quicker data sharing, but stressed the importance of ensuring personnel are included in discussions and decision-making and offered relevant training.

Good preparation

Vasco Antunes Pereira said that technology as a promoter of excellence in healthcare has been proven during the pandemic within his hospital in Portugal.

But he underlined the importance of good preparation in the ability to adapt fast, with technology as an enabling tool to deliver better health-

Continued on page 10

Interoperability: Insights from Down Under

We need government involvement

With interoperability stalled, participants (stakeholders) are seeking new ways to create an interoperable ecosystem. In an interview before Germany's Interoperability Day (25 October), IT specialist Jason Steen describes the state of interoperability in Australia and calls for more governmental commitment and international standards.

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Report: Sascha Keutel

Interoperability is crucial in healthcare – 'It matters for historical reasons and improves episodic care,' says IT specialist Jason Steen. 'The more a clinician knows about a patient, the better service he can give.

'Another reason is the number of parties involved in an episode of care. Multiple parties could work on different systems that need to share information. Furthermore, in a healthcare system where you're paying for tests, interoperability reduces costs.'

Making interoperability work in Australia

'Australia is a federation of fairly autonomous government entities, the States. Healthcare is a state-by-state exercise in governmental provision, but it is funded federally. We have multiple parties providing care. Private institutions provide some 40% of acute care. Then you have insurance and government paying. There are also government initiatives to get standardisation of healthcare information flow through the Australian Digital Health Agency.

'For interoperability, the stakeholders are governments and private companies providing care, international and local software vendors, and the patients themselves.'

The state of interoperability in Australia

'Compared to other nations, Australia is in pretty good shape. However, there is a lot to be done. Especially, when you compare it to other industries. 'In Australia, the patient can commute between different parties while in one hospital. At the end of the engagement, the clinician might hand them a letter of referral, the patients take that to the next clinician. They read that referral and re-enter the patient data into their systems.

'That's not how the banking system works. We are not walking around with pieces of paper between banks transferring money around. To me, healthcare information is more important but is transferred around less desirably.'

Why does healthcare lag behind other industries?

'The pace of change has been my biggest frustration in this industry. Particularly when most people know what the problems are. It is not a question of educating everyone on what needs to change. We're lacking the one organisation having the self-interest to make that change happen.

Other industries have adopted a more digital world faster than healthcare. If you are a bank, you want to know if your potential customer was late with previous mortgage payments from a different bank. One telephone provider wants your calls to connect to another provider. So, there is an incentive for the institutions to make interoperability work.

For healthcare, no country got the incentive model for making interoperability work right. If you are a software vendor, what is your incentive to make your software interoperate with other systems? If you are a hospital, where is the interoperability of information in your list of priorities?

'I don't see interoperability taking huge leaps until the incentives model changes – either by customer pressure or through government legislation.

'Patients can't enact the normal market forces on their suppliers like they would with a phone company. They don't exercise that power of customer-appointed care. They will not refuse to be treated in a hospital that lacks a certain level of interoperability.

'So, we require government engagement. We need a baseline across the industry to have certain software have a specific level of interoperability. In the US, Congress got involved with the Argonaut project and created bare minimums of interoperability. These were executed by software vendors.'

Should standards be international?

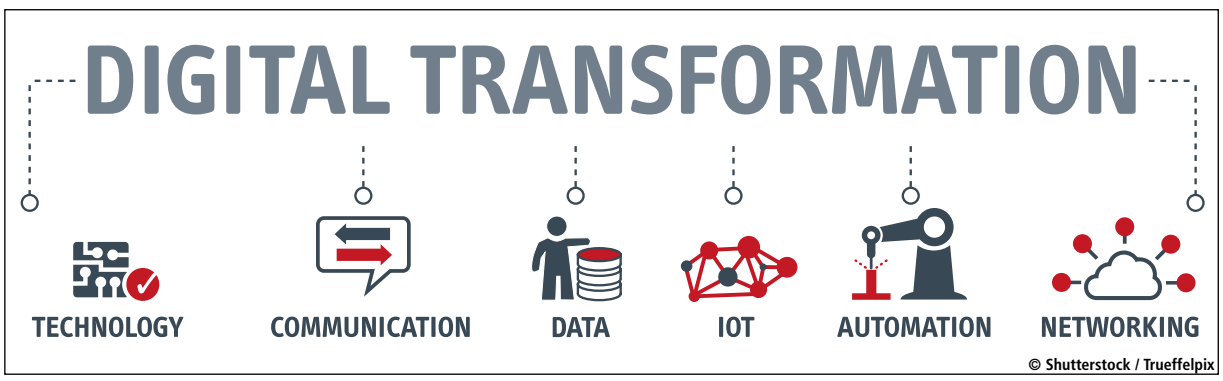
'Yes. We need international standards because we have international vendors. Some bodies exist already that could be leveraged. The FHIR standard emerged through the HL7 community.

'Australia has a population of roughly 26 million people. Most of our healthcare software comes from overseas. If we aren't conforming to some international standards the way we transfer information around, too much customisation would have to be done for a small population of people. Few countries could justify going out with their own standards and not bear massive costs from a software provisioning perspective.

'If a country doesn't adopt international standards, it hamstrings the local innovation and software development community. They might develop something very useful, but if it only interoperates in a proprietary way in your country, they limit their market solely on your country.

'It's easier for governments to come up with their own standards and match those to international standards later, because there is less engagement, and we can just progress at speed. However, history shows that by doing it that way, there is never a point when you're not updating or matching up to international standards.'

Continued from page 9



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care. 'A key element in this equation has to be the human factor and the team working together,' he said. 'We used the same knowledge and the same team but used technology that enabled us to reach a new standard of quality and care. It is always about the people.'

Clinical data scientist and pediatric intensivist Dr Ronald Petru from Radboud Medical Centre in The Netherlands said digitisation enabled the hospital to be adaptable and quickly switch between Covid care and regular, which was effectively conducted remotely from March 2020.

Staff flexibility

'This,' he continued, 'required flexibility from staff, and the need for an infrastructure that is preferably virtual and is scalable in capacity and security.

'There was also the need for flexible software solutions in a rapidly changing situation, which must be easily configurable to expand and adapt to new insights, drug regimes, and protocols.

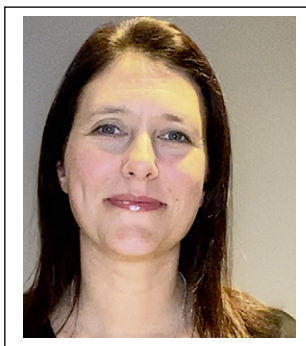
You also need great leadership; if you are to manage a crisis, you have to be in control.' Dr Petru, who was the hospital's Chief Medical Information Officer from 2014 to 2020, emphasised the need for situational awareness and real-time data to transform information into knowledge to quickly assess patient numbers, those with Covid and those who may have to move to intensive care, and to forecast future activities to be able to upscale or downscale quickly.

Change management

He said: 'At the core of digital transformation is change management. What we have seen in the pandemic is that everybody realised that change was necessary and if everybody wants to change, we can quickly achieve things that would normally take years.'

He also highlighted the need for IT and information management to be incorporated into the training of future health professionals.

In summing up the discussion, Dr Rayner stated: 'There is clear correlation between digital maturity and how hospitals have coped over the pandemic period; the more digitally-mature a hospital, the better the hospital has coped – but flexibility of the human resource is crucial.'



Katie Trott is Chief Nursing Information Officer at the Royal Free London NHS Foundation Trust. She has worked in the NHS for 27 years in nursing and midwifery and has a proven track record in managing and implementing clinical, operational and digital transformation.

Ronald Petru is a clinical data scientist and a pediatric intensivist at Radboud University Medical Center and an experienced programmer in several programming languages. He was the hospital's Chief Medical Information Officer from 2014 to 2020.

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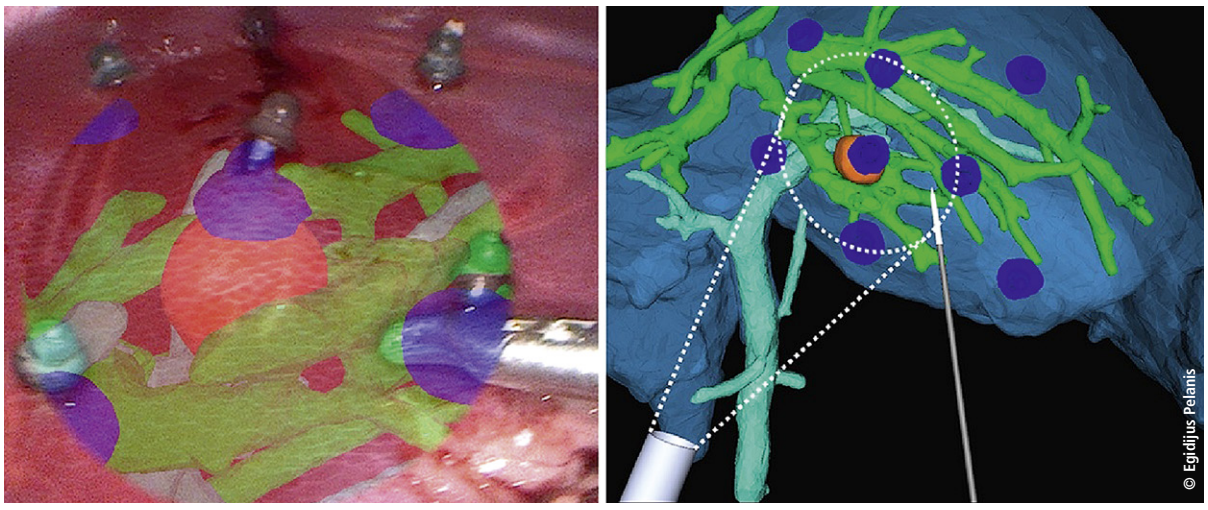
Vasco Antunes Pereira is CEO of Lusíadas Saúde, which is part of the United Health Group with 12 hospitals and clinics in Portugal. He began his career as a corporate lawyer and was director of the legal area at Hospital Amadora-Sintra before entering the private health sector.

'XR is fusing surgical reality with medical images'

Extended realities in the operating room

Leading medical extended reality (XR) experts gathered at Shift Medical to discuss developments on the use of immersive technologies in medicine. For European Hospital, Sascha Keutel interviewed Doctor Egidijus Pelanis of Oslo University Hospital about applying extended realities in the operating room.



Augmented reality laparoscopic image

'Virtual reality (VR) is often used for education and training, for example in anatomy teaching, where the students can examine the virtual models,' Egidijus Pelanis explained. 'In medical school, the students train on artificially created anatomical models. If it is not a cadaver, or comes from patients' images, the models are standardised. But that's not how it is in reality because patients have anatomical variations. In VR, you can create highly detailed and realistic patient-specific 3D models. The users can also be placed in life-like environments, simulations, and use controllers to get haptic feedback during interactions to train before the actual procedure.'

Augmented reality (AR)

'AR comes closer to the actual surgery because virtual images can be overlaid on top of the real-world object. In the Intervention Centre at Oslo University Hospital, we have tested AR for laparoscopic liver surgery. Here, the user can place 3D models and see these virtual elements in the 3D camera view. However, there are still some limitations related to the complex workflow, visualisation and how these virtual elements should be presented on the laparoscopic camera view.' 'In MR, the user views the digital images in the physical world and interacts with them. At our hospital, we're working with Microsoft's HoloLens 2, which allows us to put virtual objects into our environment. We create holograms of patients to walk around and to look at their anatomy and pathology individually, or in groups of clinicians.

'One of the advantages of using MR is that the clinicians are more accessible and not bound by the physical location of the hardware. With a head-mounted mixed reality device, one can see a model with depth as if it were in real life and can point and interact using one's hands. You can toggle the visibility of the virtual elements or peek inside to better understand the spatial distribution of the anatomy and pathology.'

Challenges to XR implementation in surgery

'It's crucial to remember that patients are in three dimensions, but medical professionals still focus on flat images for decision-making. For education and case reporting, documentation is commonly limited to text or annotations on medical images. It is constrained and needs a lot of imagination to understand where all these locations are inside the patient. By creating 3D volume renderings and holograms, you can point and show virtual models and combine all these mediums and information for more detailed documentation.

'However, one major challenge is the preparation of XR, the data that needs to be processed into 3D models and holograms. Hospitals are sitting on a lot of unprocessed data they still use for the traditional way of examining.

'I believe that doctors, surgeons, and even patients should start asking for 3D representations of their anatomy and pathology.

'Then again, to create 3D models of every patient, you need to have sufficient evidence that it will help, that you cannot make the best decision for the patient without it. Hospitals are sitting on this resource, but too few are processing it; too few are bold enough to invest without solid evidence that having that data processed will be important in the future. But the proof can only be established if someone spends enough time on this and publishes the research results.'

Different navigation and visualisation methods in XR

'Medical images can be used, for example, to create virtual 3D models to lay over the patient during surgery. Once patient-specific 3D models are created, physical and virtual spaces can be combined with tracking technology. You can, for example, have an optical tracking system with cameras in the OR that detect spheres placed on various objects to be tracked. This enables real-time tracking of objects and the ability to place virtual elements in the OR. These fused scenes and images can be presented either on screens, in augmented reality, or in mixed reality.

'This process can need some navigation system set-up and a certain amount of input from the users. HoloLens offers eye-gaze control so that some functions can be controlled by looking at them. For example, when the surgeon's hands are occupied during surgery, he can look at and activate certain buttons for interaction to reduce the physical clicking of buttons.'

Pelanis: A 'perfect' future OR

'Today, we miss a complete solution for integration. Existing and new technologies in the OR are mostly independent; they have different systems and standards.

'I see a bright future where all systems talk to each other, where images and information are synergistically flowing between devices; I see decision-support mechanisms using AI that provide automatic patient- and user-specific workflow in which next steps are predicted and shown.

'Maybe the patient lies on a table and complete patient data is shown holographically in the surroundings.

Egidijus Pelanis a PhD candidate working at The Intervention Centre, Oslo University Hospital in Norway. He works with technologies in healthcare and is part of both the Section of Clinical Research, led by Professor Bjørn Edwin, and the Section of Medical Cybernetics and Image Processing, led by Professor Ole Jakob Elle.

Then treatment is performed by a robot-assisted surgical system with current and accurate visual controls that support surgeons in their intra-operative decision-making and surgery.

'Whatever new gadgets or technologies are brought into the OR, I hope these will seamlessly integrate into the whole imaging, diagnostic and treatment workflow.'

Could XR become the new standard for surgery?

'First, we should remain focused on the patient by improving patient care from a value-based healthcare perspective and not get distracted by all futuristic emerging technologies – which resonate with our Sci-Fi fantasies from childhood.

'Secondly, various modalities will find their place in healthcare systems. 'Surgeons, and clinicians in general, will use what they have available and what works best. We are always looking for solutions to solve problems, to treat the patient. XR is one potential candidate for solving particular communication, visualisation and navigation challenges.'

Augmented reality in the OR

AR helps to see, feel and understand

X-ray vision, context-sensitive guidance, coordinator, training assistant and more: augmented reality (AR) has hit the OR. While still in its infancy AR does grow rapidly and has already shown enormous potential. University Professor Dr Rüdiger von Eisenhart-Rothe, Chair of Orthopaedics and Sports Orthopaedics at the Technical University Munich, explains the advantages of different AR applications. Interface between the engineers and the surgeons, it is Professor von Eisenhart-Rothe's task to provide feedback from the physician's perspective whenever new technology is about to be implemented in his OR, so that the engineers can tailor solutions to the actual needs and requirements of the OR staff

Report: Wolfgang Behrends

Virtual reality (VR) has become an important element of the training for joint replacement surgery. Using head-mounted displays OR processes are simulated in an entirely computer-generated environment. Augmented reality in contrast merges reality and virtual reality: virtual content is shown in the surgeon's field of view to supplement the visible information on the real-world OR table. Thus the physician's eyes can return to the patient rather than having to focus on the screen.

AR is useful for training purposes since a further dimension is added. 'In VR there is usually no haptic feedback. The user doesn't get the physical sensation for example when a saw or a biopsy needle hits a harder object,' Professor von Eisenhart-Rothe reports.

In AR different devices can provide haptic feedback on the interaction with the patient thus, he says,

'the additional reaction significantly improves the learning effect.'

Interface between engineer and surgeons

Any AR solution requires a lot of fine-tuning of the hardware and the software before it can be used in the OR. The goggles, for example, need to be lightweight so they don't become a nuisance during long interventions. Important questions need to be answered in extensive tests such as the kind of data that is important and the location of the data on the surgeon's display. 'Often enough the engineers don't know what the surgeons really need in the OR – and the surgeons don't know what's technically feasible. Therefore, it's crucial to have an interface between these two worlds,' Professor von Eisenhart-Rothe points out.

In orthopaedic surgery implants from different manufacturers are used and fixed with special tools. Here, AR can help: detailed instructions can be shown in the head-mounted display and even a product specialist can be brought in who sees the current situation via a camera and can virtually show the steps or devices needed. But the entire OR team benefits he points out: 'The OR nurse will also receive this information and can prepare all necessary instruments.'

X-ray vision for smaller incision

Superimposing image data from CT or MRI is still being tested and not yet used in the real-world OR. A major obstacle is the fact that current hardware does not offer the required computing power. 'Obviously, it depends which kind of data needs to be displayed in the surgeon's field of view,' says the orthopaedist. Showing vital signs or the tilt of an instrument is not a problem. If however a live CT scan has to be displayed that shows the exact site of a fracture – that's an entirely different ball game. Immense computing power is required since complex data has to be displayed in real-time with millimetre precision on the patient body. 'This would give the surgeon X-ray vision. Such functionality is still in the experimental stage since precise matching is a major challenge,' he underlines. In addition to high-performance computers, specific markers are required. They are placed on the patient's body to tell the camera where certain parts of the anatomy are located when the patient is moved or when the surgeon changes her viewing angle.

Von Eisenhart-Rothe is sure that the effort will be worthwhile particularly for tumour surgery: 'Patients with abdominal tumours often require large incisions for the surgeon to get a good overview of complex anatomy. If the exact site of the pelvis and the tumour were shown in the head-mounted display, much smaller incision could be made.' Combined with intelligent navigation systems 'collateral damage' during surgery could be further reduced.

Through the eyes of the surgeon

Another very promising idea according to the professor is 'remote sitting-in' which is already being applied in select cases: a surgeon performs an intervention in his/her field of expertise. The data goggles allow less experienced colleagues to join. 'Particularly now – during the pandemic – this has many advantages', von Eisenhart-Rothe points out.

However, even in non-Corona times this technology could make long and expensive travel obsolete. Moreover: In minimally invasive interventions the incisions are only a few centimetres.

Even colleagues right at the OR table scarcely see anything. When the steps can be observed from the point of view of the surgeon that is much more instructive,' von Eisenhart-Rothe explains, adding that, vice versa – an experienced surgeon can be called upon to follow the surgery and support the colleague when needed.

(© Nicki Schäfer)

University Professor **Dr Rüdiger von Eisenhart-Rothe** is Chair for Orthopaedics at the Medical Faculty of the Technical University Munich and Director of the Clinic and Polyclinic for Orthopaedics and Sports Orthopaedics at the Rechts der Isar Hospital of the Technical University Munich. He is Vice President of the German Knee Society, Founding President of the German Hip Society and Member of the Board of the German Society for Joint Replacement (Deutsche Gesellschaft für Endoprothetik). Von Eisenhart-Rothe publishes the journal 'Der Orthopäde' and has co-authored more than 300 scientific books and papers.

Robot-supporte simplifies every

Robot-based assistance in medicine and in everyday hospital life relieves staff and improves patient care. This is demonstrated in many examples from different areas, such as radiotherapy, diagnostics or rehabilitation. The robotics specialist KUKA aims to be a driving force in the development of further applications and expand its leading role as a technology supplier for customers in medical technology. The company presents, among other things, various collaborative applications based on the lightweight robot 'LBR Med', the world's first robotic component to be certified according to the 'CB Scheme' for integration into a medical device. What can be possible with the support of the lightweight robot will be demonstrated by means of a feature demo cell, which illustrates several possible applications of the 'LBR Med'. In the ultrasound demo, for example, an ultrasound probe attached to the flange is guided over the body. The robot records the path and can then repeat the learned path independently and with constant pressure. The robot can also take into account a change in the surface and continues the path

Neuro and spine surgery in a networked OR

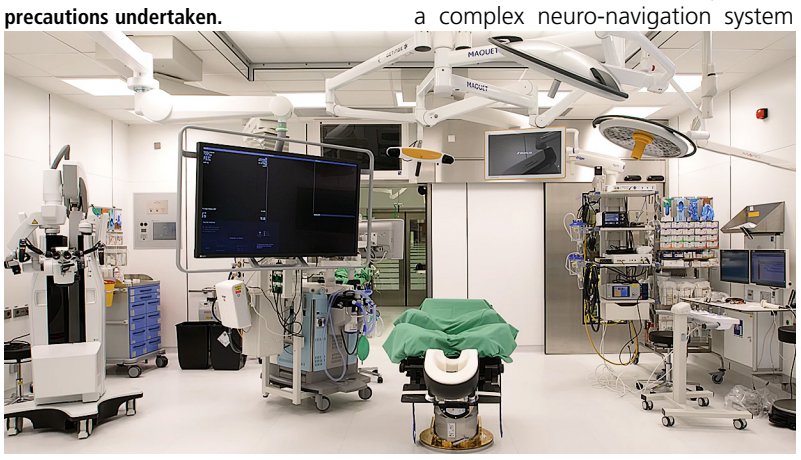
A robot, neuro-navigation and VR headsets

Neurosurgeons must often make compromises because most ORs were not designed for the specific needs of their discipline. Addressing this issue, the University Hospital in Essen, Germany, equipped an OR specially for neuro and spine surgery. The aim is nothing less than revolutionising the field with the help of digitisation and cutting-edge technology.

Report: Sonja Buske

'For some time, we had been planning to integrate intraoperative imaging in the OR but there was no device on the market that met our requirements,' says Professor Karsten Wrede MD, Deputy Director of the Department of Neurosurgery and Spine Surgery at the University Hospital Essen. While previously, as Professor Wrede explains, the surgeons had to make a choice for their intraoperative imaging modality – either MRI or CT – now 'The robot-guided angio system Artis pheno by Siemens Healthineers provides CT images thanks to 3-D acquisition technology in top quality and which allows us to perform angio at the same time. Thus we have a single system with which we can perform almost all interventions and which makes the choice between CT and MRI obsolete.'

The new operating room is only used exclusively by the Department of Neurosurgery and Spine Surgery. To accommodate all the technology, a wall had to be moved and significant safety precautions undertaken.



Installation with no shut-down

To be able to install this innovative technology in the OR the space had to be expanded. 'Not a trivial task without a shut-down,' Wrede remembers. Moreover, Siemens requirements, such as lead-enforced walls and adequate safety distances, had to be met. 'In this particular case the Corona pandemic turned out to be an advantage. Since we had to reduce the number of surgeries we could entirely close one OR for five months,' Wrede explained.

In addition to the x-ray robot a complex neuro-navigation system and a robotic arm by Brainlab were installed. After almost three years of prep work, the big day came: right after Easter 2021 the new operating room was opened.

The systems combination is unique

'The systems by themselves are nothing spectacular – they are used in many hospitals. What's unique in Germany is the combination and the networking as well as the fact that this OR is specifically set up for neuro and spine surgery,' Professor Wrede proudly reports. At the same time he concedes that not all technology is fully used in each intervention: 'When we are dealing with an aneurysm, we do use the entire set-up but when we fixate screws in the spine, that's not necessary.' The surgeon is particularly impressed by the many advantages of the networked robotic unit: 'Before, we made X-rays while fixating the screws in order to check their position. This means high radiation exposure for the patient and the team. Later, we used a 3-D X-ray system, which was rather cumbersome. Now we can take a 3-D image in the OR within 10 seconds without the staff having to leave the room. The image is sent right to the navigation software and we can then guide the robot to the sites in question.'

Before the patient leaves the OR a final image is acquired, to check the screws. With this technology, Wrede explains, 'Screw positions that need to be corrected are a thing of the past.'

VR headsets are used in preoperative planning at the Essen hospital

In brain surgery the combination of neuro-navigation and ultrasound is crucial. When for example a tumour has been partially removed a 3-D ultrasound image can be acquired intraoperatively that shows the remaining tumour tissue live. 'That's much faster than a time-consuming intra-operative MRI,' Wrede points out. Moreover, the ultrasound data can be transmitted to the microscope. Thus the surgeon does not have to interrupt the workflow to review the images on-screen.

Virtual anatomy becomes reality

Aneurysm patients also benefit from the checks in the OR. Whilst before, an angio had to be performed three to four days after the surgery without anaesthesia, it can now be done on the open skull. Thus remaining damaged vessels are instantly detected and treated.

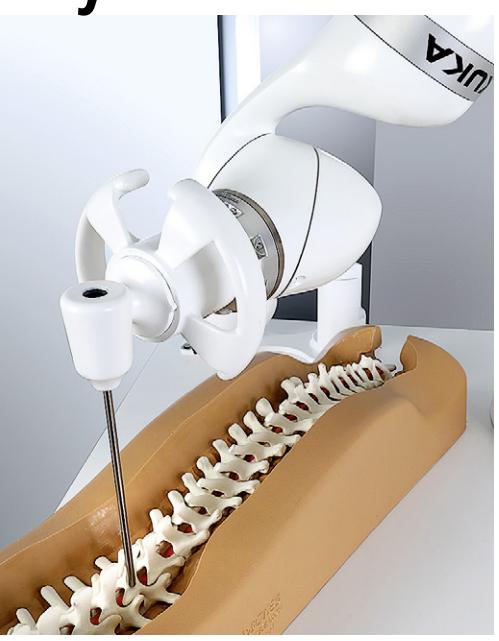
With aneurysms another new technology is used: VR headsets. Although not yet approved for intraoperative use, they are a helpful tool for preoperative planning: 'Particularly for junior physicians it is quite a challenge to fully understand the complex anatomy of the brain and the spinal cord. Thus our young physicians and students love this technology because the VR headset shows them the patient's vessel structures on-site. They don't have to imagine where exactly the aneurysm is located in the head. They see it right in front of them.'

Professor Wrede can well imagine that, in the future, stand-alone navigation systems will be replaced by VR headsets with integrated navigation.

With all these benefits, we must not forget that the complex technology requires a longer learning curve and a well-attuned team. 'We had one week of training, but still only scratched the surface,' Wrede admits. 'No manual tells you how to position a patient for a certain intervention. That's something we learn with practice.

'Additionally, it's not sufficient for a few physicians to master the technology; the entire team must be familiarised with their tasks and that takes time,' Wrede emphasises. Nevertheless, Wrede is convinced that the approach of the University Hospital Essen is the future. 'The technology – particularly VR and AR – will revolutionise healthcare.'

d technology day medical life



with the appropriate adjustment. The spinal application is used to assist with operations. Here, the robot is either guided by hand to the location on the spine to be operated on or – with appropriate imaging or connection of an external camera – can automatically move to the desired position. At the site to be treated, the 'LBR Med' holds its defined position and supports the doctor during the procedure.

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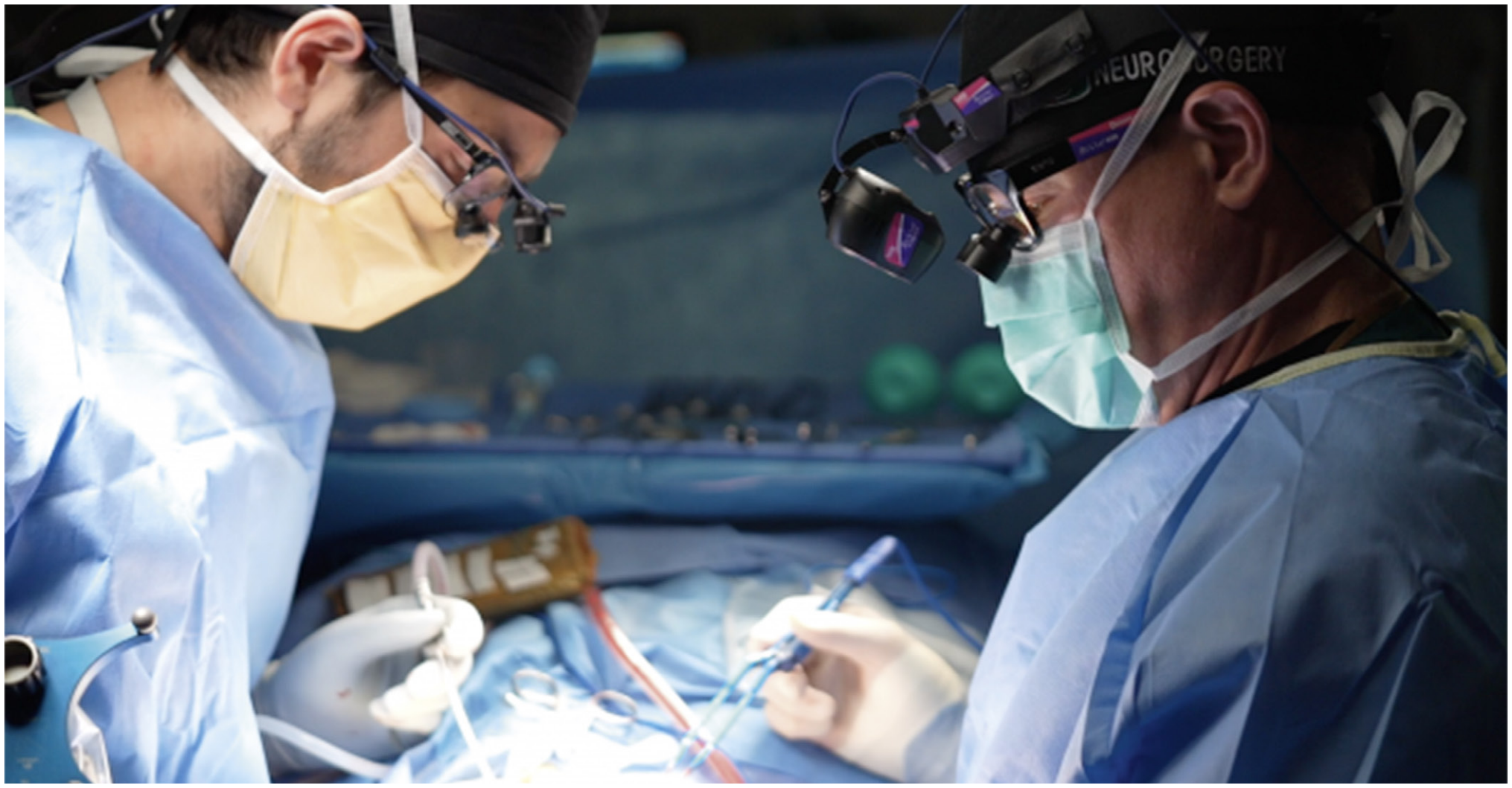


Wearable devices in the surgical environment

Wearable technology has become an important part of medicine, from tracking vital signs to disease diagnosis. In surgery, wearable technologies can now assist, augment, and provide a means of patient assessment before, during and after surgical procedures.

Report: Sascha Keutel

Wearable technologies are applied before the patient even reaches the operating room, for example in prehabilitation, i.e. pre-treatment rehabilitation. In a current study, researchers used smartwatches and mobile applications to deliver prehabilitation before major abdominal cancer surgery. Results provided early indicative evidence that such technologies can improve functional capacity prior to surgery.[1]

In trauma care, first responders can transmit real-time data to the hospital to provide data for the staff to prepare for the patient. This allows the hospital team to plan staff and equipment for the incoming patient.

In addition, wearables are used in surgical training to track the physiologic response of learners and educators to better assess and understand stressors in real and simulated surgical environments.

Intraoperative

Wearables can replace physical tasks, e.g. in a sterile environment. For example, surgeons use arm-mounted devices for gesture control of a PACS to review imaging data without breaking sterility.

Surgeons use smart glasses or heads-up displays to receive clinical or biometric data in real-time or superimpose diagnostic imaging, such as a CT scan, onto the operative field at the patient.

Neurosurgeons in the Sylvester Comprehensive Cancer Center, part of the University of Miami Health System, adopted the Reveal fluorescence-guided system. This head-worn device provides better illumination, giving surgeons more precise guidance to differentiate between brain tumours and healthy tissue. The system is essentially a super high-tech headlamp that shines light wherever the surgeon is looking. The system magnifies the surgical area and offers different light options to light up tumor cells.

Checking for fatigue among surgical staff

Wearables and sensors are also used to monitor staff in the operating room to avoid fatigue and resulting errors. They could also be used to analyze data in order to provide assistance, e.g. nurses can be shown the instruments to be used in the next phase of surgery.

Carla Pugh MD PhD, Professor of Surgery at the Stanford School of Medicine, participated in a multi-institutional collaboration called the Surgical Metrics Project. The project harvested data from audio and video recordings of surgeons and wearable sensors that measured motion, brain waves and tactile pressure. Instead of parsing every dataset of a surgery, Pugh and her team looked for overarching trends. The motion-tracking sensors fed visual data back to a computer, allowing the researchers to see movement patterns of a surgeon's hands, including where they paused and where they spent more time. The aim was to understand how specific motions and decisions correlated with the quality of the surgeon's work. 'To me, collecting surgical data is less about evaluating the skill of a surgeon and far more about quantifying what it took to take care of a specific patient,' Pugh said.[2]

Patients vulnerable to unoticed detrioration

Wearable sensors are used to measure disease severity and clinical outcomes. They also enhance patient safety. Current standard of care in surgical wards leaves the patients mostly unmonitored during their stay, leaving them vulnerable to unnoticed deterioration.

Continuous monitoring of a wide range of parameters can indicate early signs of deterioration, lowering risks of complications and potentially helping patients recover faster.

Postoperative

Scientists at Lawson Health Research Institute found out that a simple device can reduce swelling after a kidney transplant. The geko device is a non-invasive, self-adhering, battery-powered and recyclable muscle pump activator which significantly improves blood flow by stimulating the body's 'muscle pumps'. Patients who used the device following kidney transplants experienced shorter hospital stays and reduced surgical site infections by nearly 60%.

Researchers at Johns Hopkins Neurosurgical Spine Center are developing wearable devices to be implemented during surgery to allow continuous, postoperative treatment of acute, subacute, and chronic spinal cord injury.

The team's goal is to build and test three implantable devices and three wireless wearables that work together to monitor perfusion pressure, oxygenation, temperature and other biomarkers, as well as deliver interventions.

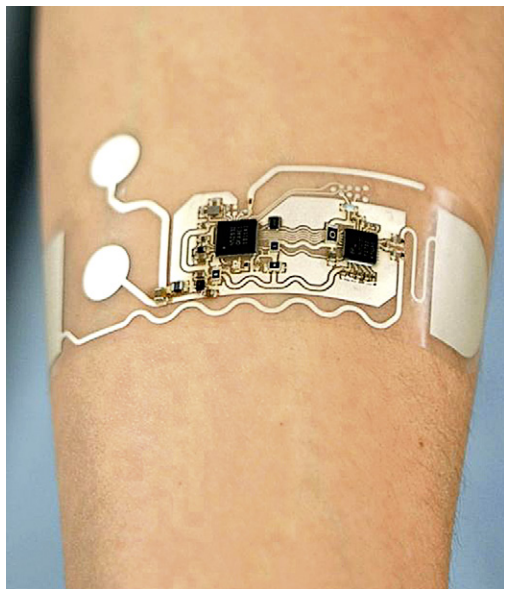
The wireless wearables include a blood pressure imaging sensor, a bladder volume imaging and pressure sensor, and an electromyography tracking sensor. These technologies would deliver real-time data to one software application that will help inform treatment decisions.

Finally, GE Healthcare and VTT are jointly developing lightweight wireless sensors to ensure patient safety in recovery and freedom after surgery.

Benefits and risks to the OR

Wearable and sensor technology brings both benefits and risks to the OR. Properly used, it has the potential to greatly improve efficiency and accuracy of surgical care. Wearables can assist staff and provide a means for an objective and real-time assessment of the patient.

However, staff needs to be trained properly in their use and policies need to be put in place to ensure that the generated data is used appropriately.



1 https://link.springer.com/article/10.1007/s00464-021-08365-6

2 https://med.stanford.edu/news/all-news/2019/12/tracking-the-movements-minds-of-surgeons-to-improve-performance.html

Body-on-a-chip technology

A boost for drug development

Integrating laboratory functions on a microchip circuit is helping to improve the cost-effectiveness of drug development.

Report: Mark Nicholls

So-called 'lab-on-a-chip' or 'human-on-a-chip' technology can highlight which treatments may, or may not, work before advancing along the clinical trial process. It can also have benefits for chronic and rare diseases, as well as helping shape personalised medicine.

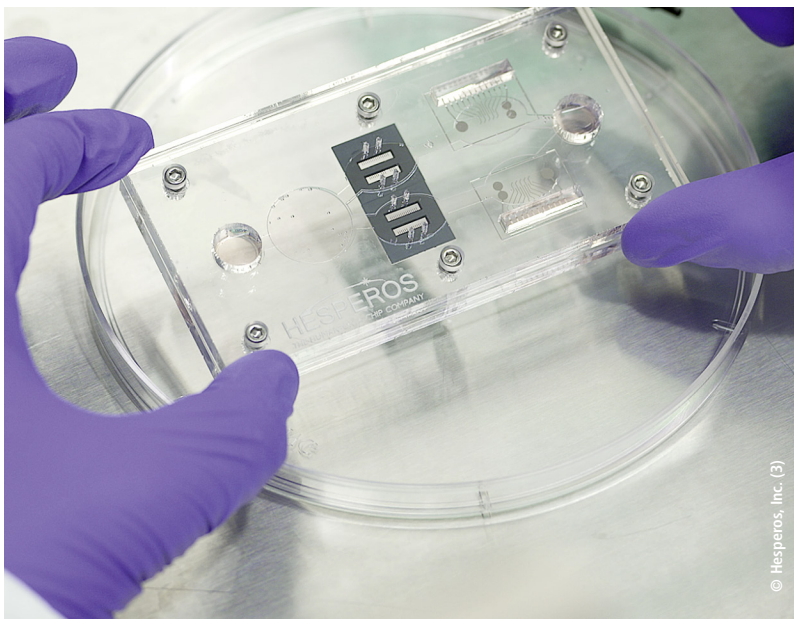
Professor Michael Shuler, who is one of the pioneers of this technology, outlined how it has evolved. Over the past two decades his group at Cornell University in New York has applied chemical reaction engineering principles to biological systems to develop conceptual tools to test hypotheses about cellular mechanisms. This work combines mathematical models of subcellular and cellular mechanisms with models of the whole body as a means to relate the rapidly increasing insight from molecular toxicology and pharmacology with human and animal physiology via body-on-a-chip devices constructed on a microscale using the techniques of nanotechnology. 'My work has focused primarily on micro-physiological systems, or body-on-a-chip, where we try to emulate what happens in the body and use it in terms of drug development to determine which drugs may most likely be successful in clinical trials,' said Professor Shuler, who is Professor Emeritus of Engineering at Cornell and CEO & president of Hesperos, Inc. in Orlando, Florida. The technology integrates multiple analytic steps (such as measuring the time-dependent concentrations of drug and metabolites as well as cellular activities) on a single chip with the physiological-based pharmacokinetic models mimicking the integrated responses of organs such as the liver, colon, heart or lung to predict outcomes and reactions of proposed new therapeutical approaches.

Weeding out the drug candidates

The body-on-a-chip technology can also be used for rapid analysis or screening, and while Professor Shuler believes the main application is within pharmacology, the technology can be applied to toxicology and even to determine the safety of cosmetics. Professor Shuler said: 'At present, it is generally associated with pharmaceuticals and developing new drugs in clinical trials. A key question is how to decide which drug is best to take into clinical trials. About 10% of drugs in clinical trials are approved as useful. The rest are not, but it still costs a lot of money to go into clinical trials, particularly with those candidates that get to Phase III trials. So, if you could have a device which tells you which drugs in the human body are likely to fail and which are likely to succeed, there could be savings of hundreds of millions of dollars.

'The idea is to divide the body into different organ compartments and use the physiologically based pharmacokinetic model, in conjunction with a physical microscale model with organs represented by living cell constructs, to predict the efficacy of a drug (i.e.: 'does it work on a critical organ?') and determine the potential side effects. A whole-body model is needed because many drugs fail due to side effects even if they work on the primary target. The ultimate idea would be to have a system to improve the success rate of drugs in clinical trials.'

He said it is a fast-evolving field with major opportunities to improve the success rate for pharmaceutical companies in clinical trials. Professor Shuler, who was the first to demonstrate the feasibility of such body-on-a-chip systems, explained that while he focussed on the whole body on a chip looking at multiple organ systems and their behaviour, others have developed more specific systems for a single organ-on-a-chip, such as a detailed liver model for liver response, for example. 'Our model is a physiological model which predicts what will happen in the human, and is being applied to different diseases – some chronic and rare diseases, although cancer is a big area of application,' he added.



Finding the right diseases and target groups

With drug development, the technology can examine complications from drugs and how they may be affected by other medications patients are taking, before they are advanced to the clinical trial stage. 'It may be helpful for some chronic diseases where it could take the cells from a body and expand or use them directly to test multiple potential treatments and see which of those treatments work best,' he continued.

While a drug may work well in the majority of the population, there may be a proportion of the population in which they do not, so a clinical trial can be designed to select a subpopulation in which the drug should be tested. 'You can also build a system where you have representation of different types of phenotypes, people from different backgrounds and groups and see how the treatments will work,' he added.

Future applications

Professor Shuler suggests an additional area where the technology may be applied is the support of regulatory approval. In the future, he believes a strong application for the technology will be in personalised medicine, rare diseases, and immunological disorders where there are no robust animal models at present. 'Having a human-based model is better for predictions than animal models. In some cases, for example for rare disease where there are no animal models, it becomes essential,' said Professor Shuler. 'This kind of technology will have a major, or more immediate, impact because there is not a good alternative.'

Michael Shuler is Professor Emeritus of Engineering at Cornell University in New York and former Samuel B. Eckert Professor of Chemical Engineering at the Meinig School of Biomedical Engineering. He maintains a funded research program at Cornell, which focuses on applying chemical reaction engineering principles to biological systems.

Lab tests

Watch out! Conflict ahead

In May 2022 a shortage of several lab tests may come as many manufacturers struggle to comply with EU regulation requirements covering in vitro diagnostic medical devices (IVDR, Regulation (EU) 2017/746). Even modified tests and laboratory-developed tests will present a problem for hospitals and labs as explained by Dr Thomas Streichert, Private Docent and Director of the Institute of Clinical Chemistry at the University Hospital Cologne, Germany.

Interview: Daniela Zimmermann.
Text: Michael Krassnitzer

In about six months, the EU regulation on in vitro diagnostic medical devices (IVDR) will apply. Lab managers, as well as experts in laboratory medicine, severely criticised the regulation. What are the problems?

Streichert: 'In the worst case scenario next year many tests with CE mark that are currently used in labs and hospitals will no longer be available. We are facing a difficult situation and a major challenge for the healthcare system.'

What are the critical issues in IVDR?

'IVDR contains many aspects that I consider important and correct: increased patient safety, classification of products according to risk, harmonisation of the conformity assessment procedure, supervision of the so-called notified bodies, harmonisation of the EU regulatory framework, or quality standards for products manufactured outside the EU. Another issue I find very positive: In the future, clinical tests will be reviewed for clinical performance. That means each new test that's launched has to demonstrate its clinical value in performance evaluation studies, for example enhancement of a therapy.'

Where's the hitch?

'First, the time frame for implementation is rather short. The regulation came into force in 2017 and will apply as of 26 May 2022. While this transition period might sound long, it has turned out to be very ambitious, in view of the infrastructure that must be established for the future approval of in vitro diagnostic devices. Moreover, a precondition for the regulation, the central data base EUDAMED, is not yet fully operational. 'In addition, there's a problem with the notified bodies that need to be involved in the conformity assessment of critical products: after Brexit there were only six rather than 18 notified bodies left in the EU. This creates a bottleneck that slows down the process.'

According to a recent study under IVDR, a notified body has to be involved in about 78% of the approval procedure for in vitro diagnostic medical devices – up from previously 8%.

'You are referring to a MedTech Europe study which is quite enlightening in many aspects: it shows the substantial risk that, next year, many tests will no longer be available. Particularly for rare diseases there are tests which are distributed by very small enterprises, often university spin-offs. For them, continuing to offer these tests might financially not be viable due to the high costs. If a manufacturer can no longer sell his tests as a CE-marked product, the test is still available on the market but the lab manager who purchased it has to validate the test and can be held liable. But validating a purchased test is pretty close to impossible.'

We understand that tests developed by the labs themselves will also face difficulties. Can you explain the problems?

'A university hospital uses on average 700 to 800 laboratory-developed tests – so-called LDTs. In the future, all these in-house tests will have to comply with IVDR standards. This means a lot of work for hospitals and labs.

'The most problematic assays, in my opinion, are modified tests – i.e. commercially available assays where the labs deviate from the manufacturer's protocol, for example by using the test with a different matrix.

'At the University Hospital Cologne we measure a certain tumour marker in CSF, not in serum or plasma as the manufacturer prescribes. Strictly speaking this is a significant modification, which means we are considered the manufacturer of this product. Consequently, we have to validate this test ourselves. However, to do so we'd need the technical details of the assay, for example where the antibody binds, and we'd need access to the relevant performance tests.

'This is not only a time-consuming task but also requires the manufacturer to disclose this information. It might well happen that we have to discontinue using this test even though it is useful for the patients.'

Could manufacturers adapt the intended purpose of their tests?

'Manufacturers are not keen to do that. They are currently busy making their tests IVDR-compliant by the deadline. If they modified the intended purpose they would also have to go through the conformity assessment procedure again.'

There are also concerns that, in the future, labs will have to pay for tests that they themselves developed, but that are being distributed by an external company. Are these concerns justified?

'At the University Hospital Cologne we use a number of mass spectrometry assays which we developed ourselves to measure medication levels. Today, a company is offering one of these tests in its product portfolio.

'If we want to comply with IVDR requirements with regard to the so-called industry privilege, we have to clinically and technically validate the assay that we developed ourselves against the commercially available test. If the latter is as good as or better than our own test, then we have to discontinue using our test and purchase the commercial assay. But why should we use scarce resources to develop a test which two years down the road will be offered by a company and we will be forced to buy it?'

How can this problem be solved?

'By defining the intended purpose for the patient groups very narrowly and, at the same time, highlighting the benefits, e.g. useability in other matrices such as CSF. Even when we use a smaller sample than indicated by the manufacturer, our test is still better because it's better for the patient – less blood has to be drawn. 'Thus I'm not too worried about the industry privilege. I think it will be rather unlikely that a manufacturer will insist on us using his test and threatening litigation. In order to do so he would have to show that his assay fully complies with the quality requirements of our in-house assay. That means he would have to disclose his development processes – which he rather wants to avoid.

'The pressure is not applied by the manufacturer but by the regulatory body. In general, the number of LDTs used will be much smaller.'

Will this have financial consequences?

'In-house developments are often sig-

Dr Thomas Streichert is Director of the Institute for Clinical Chemistry, Medical Director of the Centre for Laboratory Diagnostics (Clinical Chemistry, Microbiology, Virology, Pharmacology, Endocrinology) and Interim Director of the Institute of Pharmacology, Therapeutic Drug Monitoring, at the University Hospital Cologne.
Born in South Africa, Streichert studied medicine in Hamburg where he also worked as junior physician and consultant. In 2013, the specialist physician for laboratory medicine joined the University Hospital Cologne.
He is chair of the E-Learning Commission at the University Hospital Cologne and member of the German Society for Clinical Chemistry and Laboratory Medicine (Deutsche Gesellschaft für Klinische Chemie und Laboratoriumsmedizin e.V.).

Steps toward IVDR conformity

Which lab-developed tests are in use?

Assessment of the LDT

Are there commercially available alternatives?

Assessment has to be documented!

Are the requirements for an LDT met?

(QM & RM)

Production:

- Intended purposes
- Classification
- IVDR Annex I, analytical and clinical performance assessment and technical documentation
- Documentation of process, production and validation

Putting into service

Conformity declaration (publicly accessible)

nificantly cheaper for labs. However, the comments on IVDR point out that economic considerations must not be the reason for the use of LDTs. Thus, the hospitals have no incentive any more to develop their own tests. In the long run this will impair the ability of hospitals and labs to react in acute situations. During the pandemic, imagine if we would have had to wait for commercial manufacturers to offer Covid-19 tests.'

What other difficulties will labs and hospitals have to face in the wake of IVDR?

'The term *in vitro* diagnostic device was expanded to include software. While this is only one line in the regulation, it has immense consequences: software developers have to meet the same requirements as the manufacturers of lab products.

'In Next Generation Sequencing, human genetics or molecular tumour diagnostics labs use complex software solutions that integrate several test results. All these software solutions must be reviewed to make sure they are not lab-developed items under IVDR. Hardly anybody has ever validated software – much less validated for IVDR conformity.'

Product monitoring / vigilance

How can this issue be navigated?

'I am chair of a sub-group in the Working Group of Scientific Medical Societies (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften – AWMF), which deals exclusively with software issues in the context of IVDR.

'We compiled a guidance document for all those who develop such software solutions. After all, IVDR is not overly specific with regard to software, which gives us some room to manoeuver. But the requirements exist and must be complied with. At the end of the day we will have to jump through that hoop.'

Body-on-a-chip technology

Emerging technologies in POCT

Considerable advances in point-of-care testing (POCT) devices are emerging from lab-on-a-chip platforms, innovations in smartphone-based technology and wearable technology. Cloud-based deep learning systems herald a future revolution, writes Bernard Banga.

The World Health Organisation (WHO) has endorsed bedside diagnostics as the top research priority in response to the so-far two-year long epidemic without let-up. The aim is to improve turnaround time and ease of use compared to the gold standard lab-based PCR test. These have included rapid antigen tests, alternate nucleic amplification methods and novel sensors in proximity to the patients.

POCT deployed in multiple clinical contexts in 2021

POCT is being rolled out in various healthcare settings in 2021. The most obvious applications are blood-glucose monitoring and pregnancy testing. 'Widespread POC testing and diagnostic devices are available, including, but not limited to, glucose monitoring, pregnancy and infertility testing, infectious disease testing, cholesterol testing and cardiac markers,' said Amit Saha from the Stanford Genome Technology Center in California. Today, blood gas analysis along with haemoglobin, prothrombin time and infectious disease testing are the dominant applications in the POCT market.

Looking to the future, tumour markers, flow cytometry (mainly for chemotherapy monitoring), endocrine function tests and therapeutic drug monitoring will all benefit from recent technology advances in the POCT field.

Technology advances change POCT applications

Miniaturisation in chip technology, microfluidics and new biosensors have heralded the design of new systems for POCT. Lab-on-a-chip technology is one of the main drivers of POCT, especially in infectious disease diagnosis. This technology means various bioassays, such as microbiological culture, polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA), can now be used at the point of care.

Similarly, emerging microfluidic technologies include a set of miniaturised components allowing chemical or biological samples to be analysed at the microscopic level. Microfluidic-based POCT devices are widely used in molecular biology as well as in chemical and biochemical analysis. They enable detection and fluid regulation in a single unit. 'Greater sensitivity and specificity when detecting target analytes in small volumes overcomes several challenges encountered when using traditional POCT techniques,' Saha said. POCT currently centres around two technologies: lateral flow assay (LFA) and nucleic acid amplification. The first is used in pregnancy testing; testing for HIV, herpes simplex virus, hepatitis, infectious diseases (Ebola, dengue, malaria, Zika virus) and respiratory infections; and also for diagnosis and prognosis in conditions such as cancer, by identifying specific biomarkers.

The second, which is much more sensitive and specific, is based on polymerase chain reactions (PCR) on a chip and isothermal amplification. Nucleic acid amplification can be used to detect a whole array of infectious diseases, such as Mycoplasma pneumonia, Bordetella pertussis, Legionella pneumonia, Influenza A virus, SARS, Legionella, Aspergillus, West Nile Virus and, now, SARS-CoV-2.

A seventh format joins POCT

POC device manufacturers are continually looking for ways to design products that deliver greater user comfort in a cost-effective manner. POCT relies on six main formats: bench-top, monitoring, transportable, portable, handheld and disposable. In recent years, the latest advances have seen the launch of a seventh: smart devices with smartphones and wearable devices. Mobile POCT uses sensors to detect signals from samples in vitro, whereas wearable POCT detects signals directly on the body. Both systems then send quantified results to the clinic via wireless communication. Various body fluids such as tears, urine, blood, sweat and saliva can be used to analyse metabolites, hormones, proteins, viruses and bacteria.

Smartphones act as minicomputers for sensitive and specific data quantification with built-in sensors, high resolution cameras, rapid wireless connectivity and the ability to use various software and apps. This means they can function as standalone sensors and detectors in mobile POCT,' Saha pointed out.

Similarly, wearable POCT devices can be physical sensors used to acquire samples from the skin, eye or mouth with minimal invasion. They come in various forms, such as tattoos, patches, bands, watches, spectacles and contact lenses, and can be integrated with smartphones for data capture. This type of testing is especially important for patients suffering from critical conditions, as they can monitor their health constantly without the need to go to hospital, or for trained personnel.

Artificial intelligence and machine learning

Artificial intelligence (AI), machine learning (ML) and neural networks are now starting to be integrated into POCT. These AI modules have demonstrated their value in diagnostics studies. However, the accuracy of test apps varies greatly and relying on these apps is cautioned against. The future is bright. Since samples can be digitised directly at the point of care, advanced digital diagnostic techniques, such as sample analysis using medical AI algorithms, can be deployed outside high-end laboratories. 'Hence POC digital microscopy, supported by automated digital image analysis and AI, might be deployed for routine microscopy diagnostics on samples harvested during cancer surgery, or on parasitology samples with an emphasis on potential areas of application in low-resource settings,' added Oscar Holmström from the Faculty of Medicine at the University of Helsinki.

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Surging POCT demand

POCT systems account for 30% of in-vitro diagnostics. According to Reportlinker, the global POCT market is anticipated to experience rapid growth in a few years – estimated to reach USD 50.6 billion by 2025, from USD 29.5 billion in 2020 – a CAGR of 11.4%.

Fifteen key market players: Abbott Laboratories (US), Roche Holding AG (Switzerland), Siemens Healthineers AG (Germany), Danaher Corporation (US), Becton Dickinson and Company (US), Johnson & Johnson (US), Instrumentation Laboratory Company (US), PTS Diagnostics Inc (US), Quidel Corporation (US), Chembio Diagnostic Systems Inc (US), Sekisui Diagnostics LLC (US), Nova Biomedical Corporation (US), EKF Diagnostics Holdings plc (UK), AccuBioTech Co., Ltd (China) and Trinity Biotech Plc (Ireland).

Anticipated 2022 revenues by product in the POCT market: glucose monitoring (39%), blood gas analysis (15%), cardiac markers (13%), infectious diseases (8%), pregnancy & fertility testing (5%), alcohol & drug abuse (5%), haemoglobin testing (4%), cholesterol testing (3%), urine chemistry (3%), tumour markers (3%), others (2%).

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POCT and Covid-19

Most promising SARS-CoV-2 POCT methods: immunoassays for antibody and antigen detection, RT-PCR as the gold standard, isothermal amplification and CRISPR/Cas9 genome editing technology as an emerging technique. Due to growing confirmed Covid-19 cases globally, rapid and reliable POCT is needed urgently for early detection. A reliable POCT device could reduce transportation, risk of spreading infection, strain on healthcare, and cost of care.

Despite outbreaks caused by infectious viral diseases such as MERS, SARS, and Ebola, existing POCT platforms were not sufficiently ready to address the Covid-19 viral threat. However, in 2020 great efforts were made in POCT to improve Covid-19 detection.

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An overview

COMPAMED 2021

Consequences of the pandemic, supply bottlenecks, and a multitude of innovations all result in an agenda full of exciting topics

Since COMPAMED could only be held digitally last year, due to the pandemic, the event now takes place publicly again. Almost 500 registrations from exhibitors prove that there is a high level of interest from medical technology suppliers – a huge step towards reaching normality again.

Both the omnipresent Covid-19 pandemic and its consequences provide much food for thought: 'Due to the impact of the corona crisis, supply bottlenecks have occurred: flight and seaborne transportation cancellations have led to huge supply bottlenecks, particularly for electronic products. During the crisis, this was exacerbated by unnecessary stockpiling. Companies bought and stored more components than they needed to ensure they were safe, because they were scared of experiencing a shortfall in supply,' explains

Dr Thomas R Dietrich, CEO of the IVAM International Microtechnology Business Network.

Raw materials and individual components were also scarce, because the industry recovered more quickly than many suppliers expected it to. However, this will return to normal within a short period of time.

Computer chips also became in short supply during the crisis because medical technology suppliers in particular suddenly needed far more of them. Dr Meinrad Lugan, CEO of BVMed, recently put the situation into perspective: In many sectors, the issue was not shortages in terms of quantity but, instead, distribution issues. Lugan notes that there was a 'trend to make huge excess orders or multiple orders'. The resulting supply bottlenecks should be combated using 'smart digital solutions based on existing e-standards'.

According to IVAM, internationalisation of the economy would still be expedient, as the global supply chains could not be maintained, which is the opposite of constructive. European manufacturers need the option to carry out production at a lower cost in other countries in order to remain competitive. These producing countries, in turn, need European customers in order to keep their own economies running. However, according to IVAM, there should still be local supply chains for critical components – particularly for sensitive products that are important for basic care of the entire population, for example in the healthcare sector.

Current developments throughout the entire process chain

The CompaMed Suppliers' Forum has even more to offer in terms of content. Current developments throughout the entire process chain are presented in a hands-on way: mechanical and electronic components have their moment in the spotlight in the expert talks, along with innovative basic materials, manufacturing processes, all types of contract manufacturing, design and useability aspects and quality assurance. Keynote speeches on new markets complete this diverse programme. Further focal themes include the added manufacturing, electronic and regulatory affairs sectors.

Thus, Dr Benedikt Janny, who is the Managing Director of USE-Ing. and Head of the User Research and Usability Engineering Division there, reports on human-centred development of medical technology products, better known as useability engineering: This is not only a regulatory obligation for medical device approval, but also offers medical device manufacturers the opportunity to differentiate themselves in the market by taking relevant user wishes into account early on in the product development process and implementing them in innovations.

The keynote speech (15 November) explores which regulatory requirements are applicable for useability engineering and the opportunities that exist to establish human-centred development processes and to create actual added value for the product user by increasing useability within the scope of user-centred innovations.

The useability engineering process is closely linked with quality management and the requirements of the engineering process. In addition, Dr Janny, as an expert, will indicate which types of use-based risks exist and are to be analysed within the course of product development. Additionally, the question is also explored regarding which prototypes companies can generate without great cost and effort in order to validate their medical products early on with real users.

Additive manufacturing for customised implants

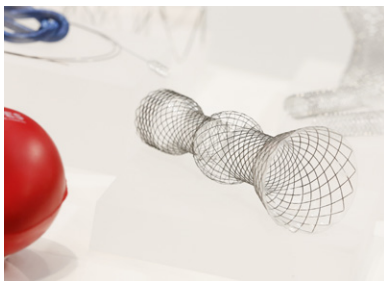
Additive manufacturing and robotics remain exciting themes in medical technology. Toolcraft AG sees itself as a pioneer of future-oriented technology such as additive manufacturing and in the construction of individual robot cells. As a partner for complete solutions, the company offers the entire process chain, from the concept to manufacturing to qualified precision components using additive manufacturing, machining and injection moulding, electrical discharge machining and mould making. Within the scope of robotics, customised, fully programmed integrated solutions are implemented. Daniel Distler and Patrick Meyer (Head of the Robotics Division and Head of Technical Sales and Distribution at Toolcraft) put their knowledge gained over 30 years of experience in the industry to good use in their talk at the CompaMed Suppliers' Forum and detail the advantages of additive manufacturing using a wide variety of application cases for medical technology.

For example, Toolcraft AG uses additive manufacturing to make custom implants for individual patients. Furthermore, this mid-sized company has developed an automated complete solution for manufacturing and packaging a cerumen filter for hearing aids (which protects against contamination with ear wax and moisture).

Holger Frank, CEO of Mechatronic, talks about 'The potential of the IoT in medical technology – using the

example of the AED. An AED is an automated external defibrillator, a portable medical device that can also be used by people without medical training. 'In terms of the future development of important IT technology, 80% of all those surveyed assume that the Internet of Things will play an important role, according to a study by PwC', Frank explains.

Mechatronic delivers important devices for IoT developments in the medical field, which enable communication between the device and the cloud. In essence, two solutions are possible: the device and communication are either integrated into one system or into separate units. An important factor for all versions is the question of which radiocommunication standard they need to be certified with. These vary throughout Europe and the USA and also differ based on the country in which one is based. Large countries such as China, Russia and Canada also have their own standards. Mechatronic emphatically pleads the case for AEDs that execute an automatic test every day and has developed the relevant hardware to enable the test state to be monitored via a cloud solution. Background: 30% of the devices that are available in public space do not work because the maintenance and servicing have not been performed correctly.



Measuring blood pressure via an optical sensor

Highlights on the IVAM stand include new sensory developments. Conditions involving the cardiovascular system are among those which are most frequently cited as a cause of death in the industrialised nations. An important indicator for this is high blood pressure, which is currently still diagnosed and monitored by regularly taking blood pressure mechanically using an upper arm cuff.

This method is uncomfortable and limits the patient in their daily activities, and, in comparison to other methods, only delivers a few selective measured values. An optical sensor can provide help here. This sensor, which works using the basic principle of photoplethysmography (PPG), records the fill level of the blood vessels in the skin over time. Using the contour curve (pulse waves) recorded in this manner, a patented procedure is used to identify relevant points in time to determine the cycle of the pressure wave in the aorta, which enables conclusions to be drawn on changes in central blood pressure. In addition to offering an alternative to classic cuff measurement, the process also gives a blood pressure result for each individual heartbeat. With this analysis of short-term and mid-term fluctuations, doctors expect to achieve a novel diagnostic approach for early detection of a variety of conditions in multiple different patient groups (e.g. pre-eclempsia). The sensor developed at the CiS Forschungsinstitut für Mikrosensorik (CiS Research Institute for Microsensors) can be worn in the ear, which, in addition to numerous physiological advantages for signal quality and signal stability, means that it is comfortable to wear throughout the day. In addition to blood pressure, it can record many other vital signs, such as heart rate, heart rate variability as well as the blood oxygen levels.Within the scope of the CompaMed High-Tech Forum, Dr Martin Schädel, Head of the MOEMS Division at the CiS Forschungsinstitut für Mikrosensorik, gives a lecture on this development

High-tech communication between the body and modern IT

With its next-generation electrode design, CorTec creates new pathways for communication between the body's own electric signals and modern information technology. This young medical technology company specialises in developing efficient technology for active implants for recording over long periods of time and stimulation of neuronal activity. The technology comprises customised components such as electrodes for derivation and stimulation within the central and peripheral nervous systems. Its patented AirRay electrode technology has enabled CorTec to overcome the current limitations when working with electrodes with mechanical properties that can be adapted flexibly and highly precise manufacturing conditions. The manufacturing process, using ultrashort pulse lasers, makes the technology highly reproducible even at very small dimensions as little as 25 µm, and with a high density of electrical contacts. The flexibility of the technology enables a wide variety of product properties, such as thickness, the number of contacts, contact spacing and contact shape, and the total size of the electrode, to be modified.

The components can, for example, help localise the epileptogenic focus that needs to be removed using surgery in patients with certain types of epilepsy . CorTec's aim is to be a leading partner in developing innovative therapies. In particular, the design flexibility of the AirRay electrode technology makes it an important building block for the approach of communicating with the human nervous system and connecting it with AI.

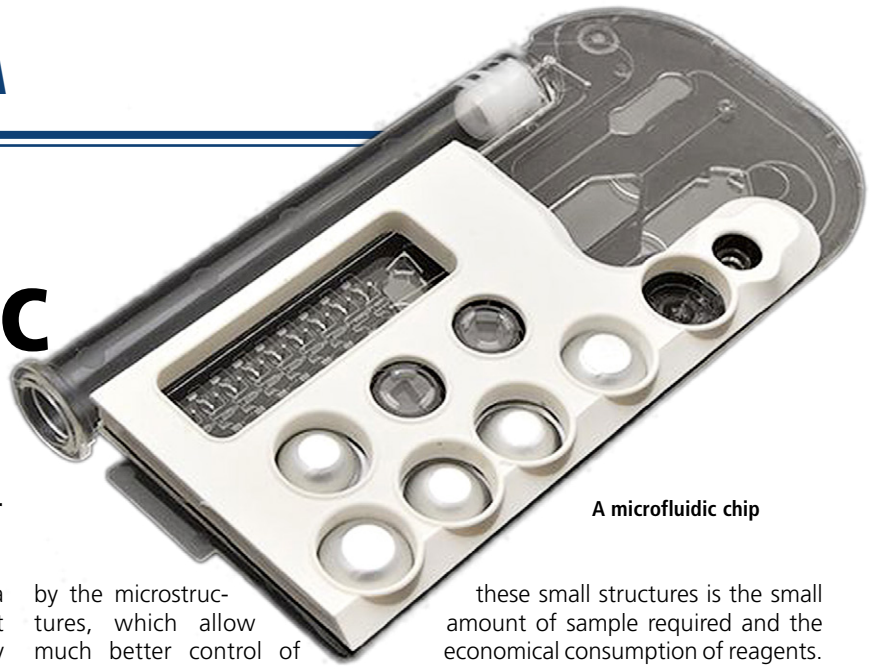
This special electrode technology is, like the ceramics-based hermetic encapsulated casing, part of the CorTec Brain Interchange, a technology platform for innovative neurotherapy in a variety of fields of application, such as epilepsy, Parkinson's disease, or bioelectronic medicine.

*** More information from COMPAMED 2021: https://www.compamed-tradefair.com.**

Accelerating the pace of development

Fighting the pandemic with microfluidic

The Corona pandemic has a major impact on all areas of life. Nearly everyone is affected in some way – in their health, in their jobs, in their entire lives. But there are also notable bright spots.



A microfluidic chip

Chief among these effects is the rapid development of vaccines, test kits and, in the future, medicines that are making a significant contribution to overcoming the crisis. Microfluidic components in particular are capable of significantly accelerating the pace of development.

Microfluidic components allow a large number of experiments to be performed rapidly in what is known as high-throughput screening (HTS). This makes it possible to realise a large number of tests in a very short time, for example to test the efficacy of drugs or vaccines on living cells. The speed and accuracy of the tests is achieved, among other things, by the microstructures, which allow much better control of the physical and chemical parameters (e.g. temperature, pressure, reaction time). Another advantage of these small structures is the small amount of sample required and the economical consumption of reagents. In recent months, new products and drugs have been developed in a very short time. This would not have been possible without microfluidic devices. Devices and components such as lab-on-a-chip, mobile diagnostic devices or chemical microreactors are already helping to fight the pandemic.

Covid-19 and the very rapid development of effective vaccines have put the focus on microfluidics and affiliated topics. It is now impossible to imagine medical technology without microsystems that can safely handle the smallest quantities of liquids and gases.

Legal now:

Internally-coated pharmaceutical gas cylinders

Medicinal gas bottles are pharmaceutical packaging. Therefore, according to the Medicinal Products Act, they must not interact with the filled medicinal product.

Medicinal products currently in use, such as gas cylinders made of steel or other metals may interact with their contents in an unwanted way. Gas bottles like these emit particles, for example rust, into the pharmaceutical gas. The pharmaceutical gas cylinders currently in use do not meet the pharmaceutical law requirements.

Over recent years, the Austrian company Oxytop has developed an inner coating for pharmaceutical gas cylinders. Having worked with recognised testing institutes, the company reports that it can satisfy the pharmaceutical legal requirements and offer complete patient safety with its product.