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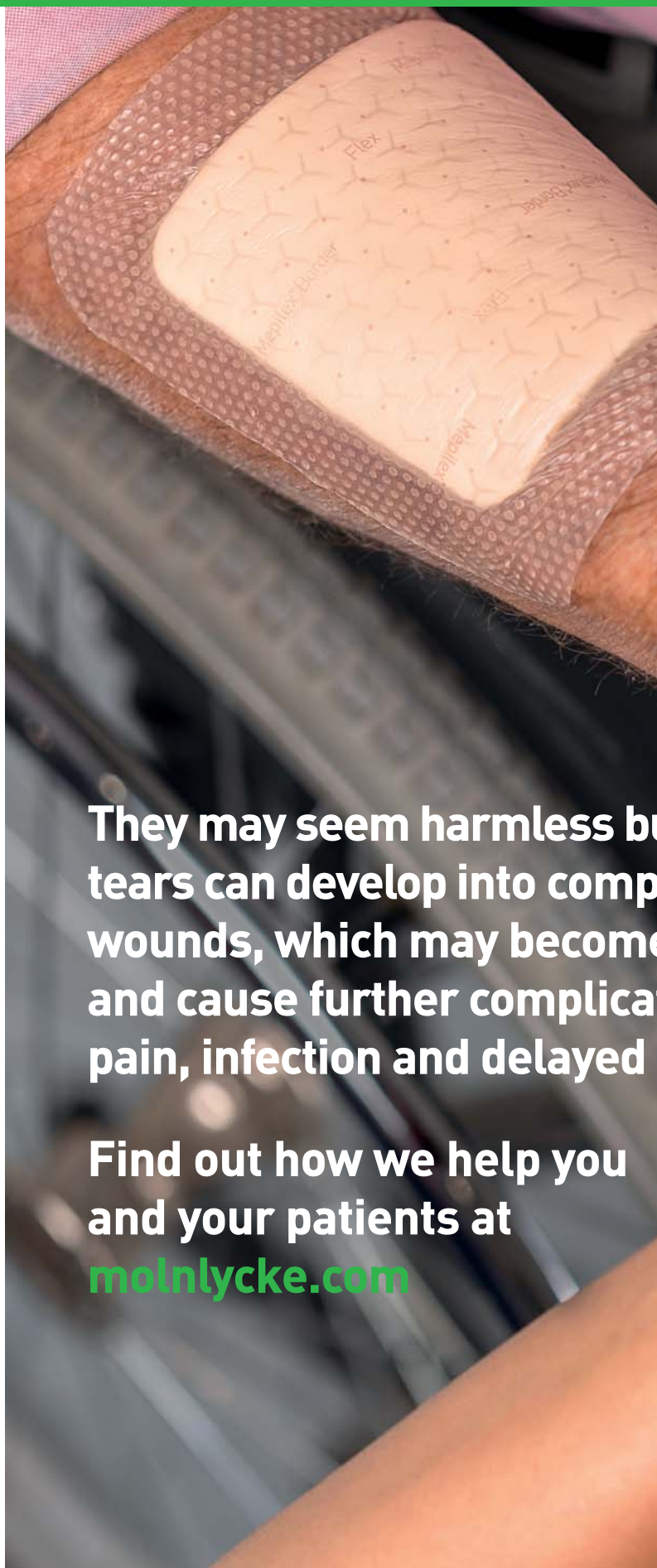

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*ISTAP skin tear classification· LeBlanc K, Baronoski S, Christensen D, Langemo D, Williams A, Edwards K, et al. International skin tear advisory panel: A tool kit to aid in prevention, assessment, and treatment of skin tears using a simplified skin tear classification system. Advances in Skin and Wound Care. 2013:26(10):459-476.

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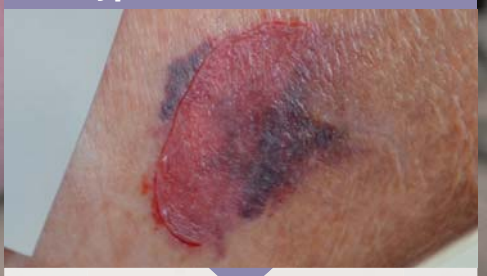

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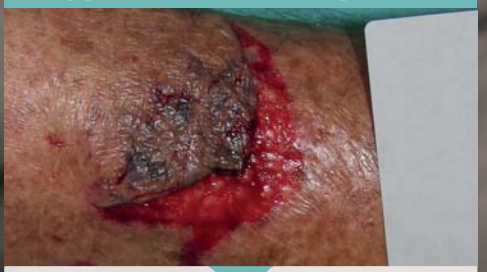

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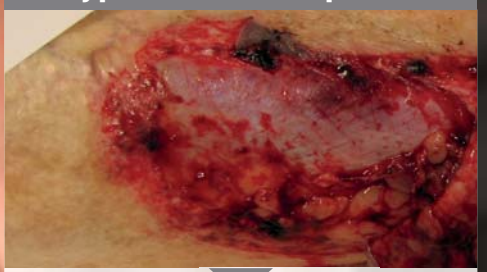

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Issue 23 2019

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Ready to engage

People and technology have traditionally been positioned as incompatible. As Albert Einstein stated, "It has become appallingly obvious that our technology has exceeded our humanity." However, there are numerous examples throughout history where technological developments have provided a platform to improve humanity.

Nowhere is this truer than within healthcare, where the latest advancements are constantly drawn upon to enhance patient care. In genomics, which we explore in this issue with Professor Clare Turnbull from the Royal Marsden Hospital, dramatic technological evolution has enabled genetic sequencing to be conducted on a much larger scale than was previously possible. The insights from this work has helped to not only provide faster and more cost-effective diagnoses to patients, but also to predict which treatments patients are most likely to respond to.

Within chronic wound care, a problem that can be traced back over three millennia, recent advances within biomechanics and microtechnology have led to the creation of smart bandages. These allow healthcare professionals to respond to the complicated and heterogeneous environment of an individual wound, tailoring treatment appropriately. In this issue, we find out more about the US Defence Advanced Research Projects Agency (DARPA), which is working on improving outcomes for the victims of blast injuries and chronic wound sufferers thereafter.

Technology can also provide the ability to give a stronger voice to patients so that they are able to play a more active role in decisions about treatment. In this edition we speak with Kristina Sheridan from MITRE, and her daughter Kate, about the patient toolkit they've developed to help those with chronic illnesses better manage their care, in and out of the hospital. Bearing all these applications in mind, it is clear that people and technology are not only compatible, but even complementary.

Emma Green, editor

On the front lines – how chronic wounds are being tackled by military-funded smart bandages (page 69).

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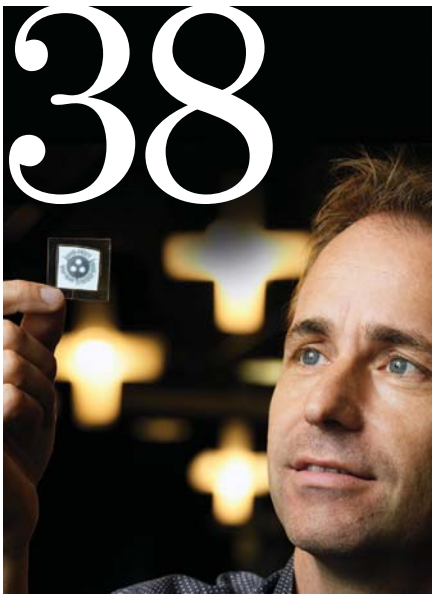

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BIOMÉRIEUX

DIAGNOSTICS IS POWER

The power to sustain antibiotic efficacy for future generations

#pioneeringdiagnostics

44% Amount of users citing the monitoring of physical activity as the main reason for wearables use, down from 54% in 2017.

Rock Health

Heavy smoking can damage vision

Smoking more than 20 cigarettes a day can damage your vision, according to a new paper published in *Psychiatry Research*.

The Center for Disease Control and Prevention estimates that 34.3 million adults in the US currently smoke cigarettes and that more than 16 million are living with a smoking-related disease, mainly those relating to the cardiovascular system.

The study included 71 healthy people who smoked fewer than 15 cigarettes in their lives and 63 who smoked more than 20 cigarettes a day, were diagnosed with tobacco addiction and reported no attempts to stop smoking. The participants were between the ages of 25 and 45, and had normal or corrected-to-normal vision as measured by standard visual acuity charts.

The researchers looked at how participants discriminated subtle differences in shading and colours while seated 59in from a 19in cathode-ray tube monitor that displayed stimuli and monitored their eyes.

The findings demonstrated significant changes in the smokers' red-green and blue-yellow colour vision, suggesting that the consumption of substances with neurotoxic chemicals, such as those in cigarettes, may cause a loss of colour vision. Scientists also found that the heavy smokers had a reduced ability to discriminate contrasts and colours when compared with the non-smokers.

"Cigarette smoke consists of numerous compounds that are harmful to health, and it has been linked to a reduction in the thickness of layers in the brain, and to brain lesions, involving areas such as the frontal lobe, which plays a role in voluntary movement and control of thinking, and a decrease in activity in the area of the brain that processes vision," said co-author Steven Silverstein, director of research at Rutgers University Behavioural Health Care. "Our results indicate that excessive use of cigarettes, or chronic exposure to their compounds, affects visual discrimination, supporting the existence of overall deficits in visual processing with tobacco addiction."

Silverstein said the findings also suggest that research into visual processing impairments in other groups of people should take into account their smoking rate or independently examine smokers versus non-smokers.

Breast cancer survival rates rise

Recent estimates from the US indicate that, since 1989, hundreds of thousands of women's lives have been saved by mammography and improvements in breast cancer treatment. Published in *CANCER*, a peer-reviewed journal of the American Cancer Society, the findings point to progress made in early detection and management of breast cancer.

Mammography screening became widely available in the mid-1980s, and a number of effective therapies have been developed since that time. To estimate the number of breast cancer deaths averted since 1989 as a result of these, Edward Hendrick from the University Of Colorado School Of Medicine, together with Jay Baker from Duke University Medical Centre and Mark Helvie from the University of Michigan Health System, analysed mortality data in females in the US aged between 40 to 84.

Cumulative breast cancer deaths averted from 1990 to 2015 ranged from 305,000 to more than 483,000 women, depending on different background mortality assumptions. When extrapolating results to 2018, cumulative breast cancer deaths averted since 1989 ranged between 384,000 and 614,500. In 2018 alone, an estimated 27,083 to 45,726 breast cancer deaths were prevented.

"Recent reviews of mammography screening have focused media attention on some of the risks, such as callbacks for additional imaging and breast biopsies, downplaying the most important aspect of screening – that finding and treating breast cancer early saves women's lives," said Hendrick. "Our study provides evidence of just how effective early detection and modern breast cancer treatment have been in averting breast cancer deaths."

Electronic tool may improve asthma care

A new electronic decision support tool for managing asthma has the potential to improve the quality of asthma care in primary care settings, as the result of a new study led by St. Michael's Hospital in Toronto, Canada, suggests.

The research, published in the *European Respiratory Journal*, aimed to determine whether the Electronic Asthma Management System (eAMS) could help close existing gaps in asthma care. The system is a first-of-its-kind, evidence-based computerised decision support tool.

59% The increase in asthma control assessment from 14% of patients thanks to the Electronic Asthma Management System (eAMS).

European Respiratory Journal

"We have excellent therapies for this disease, yet most patients do not receive the best care," said Dr Samir Gupta, lead researcher and associate scientist at the Li Ka Shing Knowledge Institute of St. Michael's Hospital. "There are many barriers facing busy primary care physicians in providing the best care, including lack of time, knowledge, training and local resources. We sought to overcome these barriers through the power of technology."

Researchers followed 23 physicians for two years across three large family health teams, assessing care provided to 1,272 unique patients with asthma. They analysed baseline care for one year, then integrated the eAMS into practices and monitored care for another year to identify quality changes.

With the eAMS, asthma control assessment increased from 14 to 59% of patients. The system also increased the proportion of patients who received an asthma action plan from 0 to 18%.

Gupta and his team aim to integrate the system across the different electronic medical record systems in use across Canada, conduct further studies on the system, and add additional tool features.

Healthcare innovations

Money spent:

$742 billion

The total spent by the US National Institutes of Health (NIH) on R&D since 1938.

$100 billion

The cost of just 16 of the 210 new drug approved by the FDA since 2010 that received NIH funding for basic research.

£814.1 million

The UK's Medical Research Council's (MRC) gross research expenditure in 2017–18, funded primarily through the public purse.

£1 billion

The total the UK's National Health Service (NHS) spent purchasing medicines that had received public investment covering between one to two thirds of upfront drug R&D costs.

Lack of value for patients:

<0.01 in 10,000

Compounds that reach the market approval phase in the R&D process, a success rate of less than 1%.

4%

Amount of newly approved products in 2010–15 that were for neglected diseases that affect middle and low-income countries.

Problems with health innovation:

- R&D priorities are not determined by public health needs
- Lack of transparency and stifled collaboration
- Out-of-reach drug prices
- Short-termism and finalisation

Priorities for improved health innovation:

- Directed innovation and 'mission' setting
- Collaboration and transparency
- Affordability and access
- Long-term horizons and patient finance

Potential solutions:

$92billion

Could have been saved by the US in 2016 if it had used a delinked R&D model.

75–99.6%

The possible reduction in price for some cancer medicines in the UK if they were procured as generics in a competitive market.

Source: UCL Centre for Innovation and Purpose

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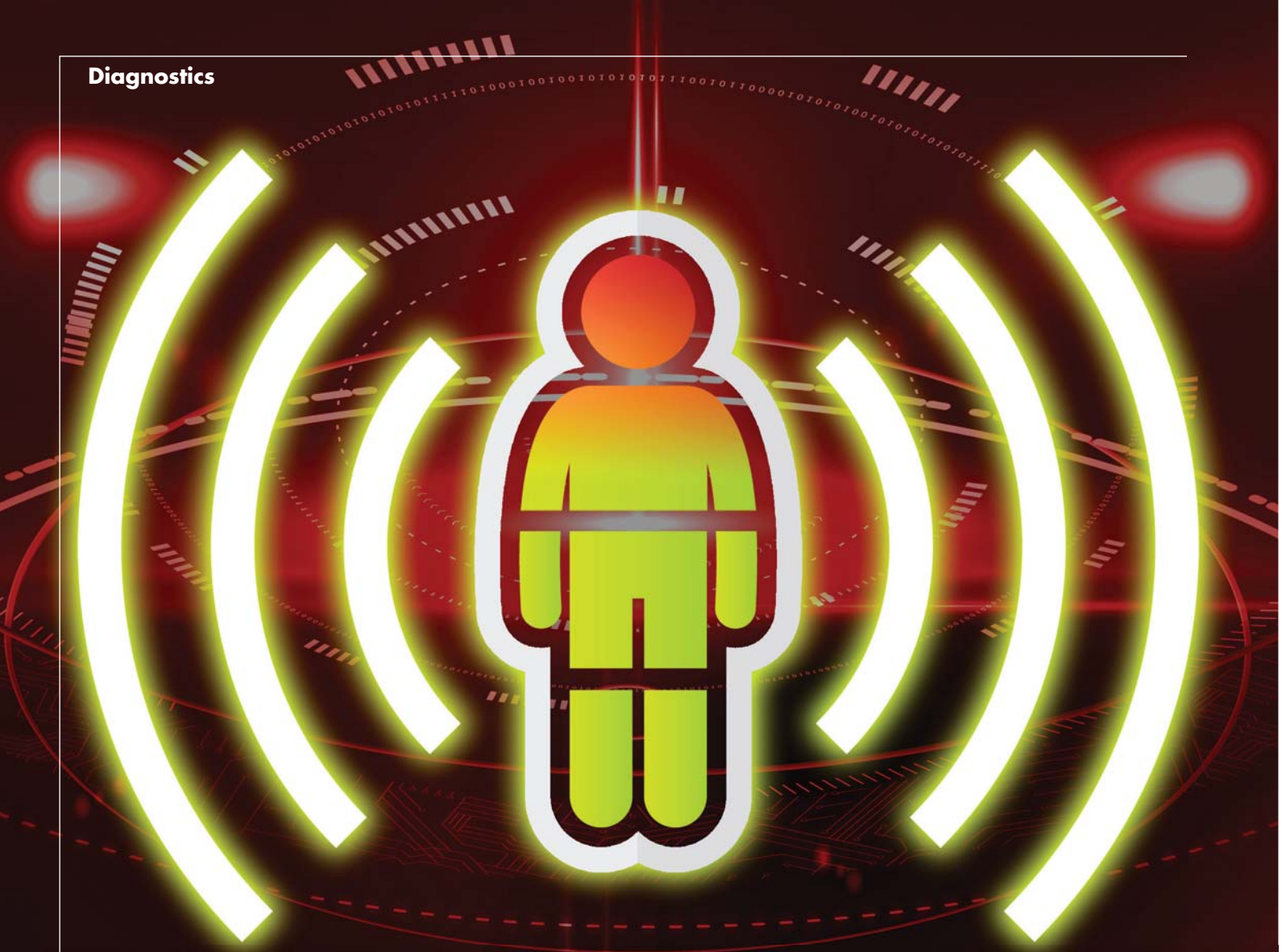
ECCMID, as the world's premier Clinical Microbiology & Infectious Diseases event, brings together experts from many fields to present their latest findings, guidelines and experiences to an expected audience of 13,000 colleagues. This year, the Programme Committee has developed a multi-faceted program incorporating keynote lectures and oral sessions, as well as interactive workshops, meet-the-expert sessions, and a wide range of symposia.



Better connected

Patients' access to treatment and advice is already dramatically improving, as a result of mobile health, or 'mHealth'. Now, when combined with internet-connected diagnostic devices, it offers novel ways to diagnose, track and control infectious diseases, and to improve the efficiency of the health system. A research team led by Imperial College London has investigated the opportunities and challenges of these technologies. Louise Thomas considers the implications for healthcare worldwide.

Rapid advances in technology have dramatically improved the speed and efficiency with which data can be processed and exchanged. The advent of smartphones, in particular, and the networks needed to support them are rapidly reducing the costs of data gathering and transfer worldwide. This is particularly advantageous to resource-limited settings where there are often high barriers to care.

The ways in which disease is detected and responded to are also continually improving. The development of more sensitive, and specific, immunological and molecular-based diagnostics, and genetic sequencing, has facilitated the ability to diagnose an increasing number of diseases. This in turn has enhanced the understanding of the burden and transmission of infectious agents as well as informing clinical decision-making, especially in the field of infectious diseases.

Potential for infectious disease response

Of course, the diagnosis and monitoring of diseases are key to clinical management. Infectious diseases, however, represent a unique challenge because these can be transmitted to others and thus early detection and treatment are key to prevent outbreaks. In order to limit the spread of infection, mHealth tools must

therefore be integrated with effective surveillance and control measures.

A 2019 paper published in *Nature* identified two main mechanisms that would allow these technologies to improve the efficiency, speed and interconnectedness of an integrated clinical and public health response – increased access to healthcare outside care settings and the real-time, or nearly real-time, reporting of diagnostic results to elicit rapid, and appropriate, clinical and public health responses to endemic infections and outbreaks of epidemic potential.

Most mHealth interventions have focused on the use of established mobile technologies to connect healthcare professionals with patients with each other and/or with test results. The use of portable diagnostic tools thus have huge potential to streamline these processes.

The current global risk of antimicrobial-resistant infections is huge and demands improved diagnostics to guide antimicrobial therapy. Connected diagnostics that can simultaneously detect a pathogen, and identify antimicrobial sensitivity and resistance, are thus hugely valuable because they are able to select appropriate treatments while reporting results to surveillance centres.

Resources and benefits

In resource-limited settings, where health services are often already overwhelmed, mHealth approaches can also be hugely beneficial. Taking diagnostics outside formal health facilities and into the community in these situations could provide a cost-effective and user-friendly solution. These interventions could improve patient access to precision medicine. In resource-rich settings, connected healthcare systems are already starting to stratify patients into remote-treatment and response-monitoring programmes.

The use of connected diagnostics and symptom-reporting apps, along with the electronic collection of epidemiological and clinical data, has huge potential to enhance the efficiency and speed of managing epidemic and endemic infections. The real-time reporting of diagnostic test results can enable this surveillance through the geospatial mapping of infections via geotagged test results, social network and internet search analysis, providing new tools for effective outbreak control.

Despite the potential benefits and increasing number of diagnostic devices, it is still early days in terms of implementation of these technologies. For example, there is not yet an mHealth intervention featuring a connected diagnostic linked to a clinical care pathway and/or surveillance system for an infectious disease.

To achieve successful integration, systems need to be established for the secure transfer, analysis and storage of the data generated. Any conclusions made on the basis of this information must be reported to and acted upon by either the patient, healthcare professional or relevant institution, along with linkage to a suitable care pathway. Of course, for this to run smoothly, measures must be in place to protect against the misuse of confidential health and personal data.

Connected point of care

The World Health Organisation (WHO)'s ASSURED criteria outlines the key features for point-of-care diagnostics. Connected devices have additional requirements whereby the signal generated must be transduced into digital information ready for transmission. Systems meeting these needs have already been developed and these technologies are being increasingly used to create connected point-of-care diagnostics. These devices tend to either use the sensors already in the phone, or use those external to the phone, and take advantage of its computational and connective power to create a diagnostic.

A smartphone camera could potentially take the place of advanced laboratory-based spectrometers, matching their quantitation and multiplexing capability via innovative engineering. Such developments would permit access to otherwise costly laboratory equipment and reduce the training required to interpret test results.

An example of this is smartphone-based microscopy, which is becoming increasingly used within parasitic infections. It is fast approaching the standard of laboratory-based microscopes but with a substantially lower upfront cost. Smartphone-based microscopy is even yielding portable, handheld options for fluorescent imaging of viruses and DNA molecules.

Sensors in smartphones have also been explored in a broader context, including the accelerometer for monitoring the body's motion, changes of which can be linked with diseases such as Parkinson's, and the microphone, which can be used to monitor lung function. As new capabilities continue to be added to smartphones, the full diagnostic applications of these technologies is yet to be seen.

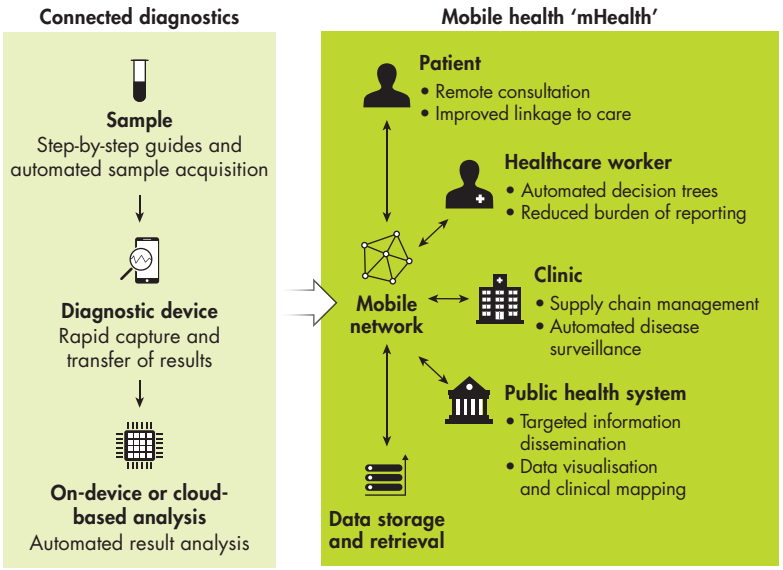
External sensors are particularly valuable overcoming the issue of interoperability within healthcare, which hampers approval by regulators.

These can be engineered around any suitable biosensor or signal transduction system and connected to share data via mobile networks. Many manufacturers have started to integrate internet connectivity directly into their laboratory-based diagnostic equipment, providing faster access to results and enhanced integration into laboratory information management systems. As these devices

94%

The amount of people aged 18–35 who own a smartphone.

Nature



Source: 'Taking connected mobile-health diagnostics of infectious diseases to the field'

decrease in size, they are being increasingly deployed at or near to the point of care and have recently been applied in response to the recent Ebola epidemics.

Automated result analysis has the potential to dramatically reduce user error when interpreting, recording and transmitting results of diagnostic tests. Currently there are a number of methods to automate the visual interpretation of images, with suitability dependent on the type of data and resources available within a particular setting.

Cloud-based methods, for example, work best for more computationally expensive analysis, such as high-resolution image or video data, in situations where there is sufficient connectivity. If connectivity is low, on-phone feature extraction to reduce the size of the images before their transmission and cloud-based interpretation can overcome this issue. Cloud-based systems are highly advantageous, as they allow connectivity to databases and algorithms to be updated centrally. They also remove the processing burden from mobile devices, thereby increasing the range of compatible devices.

Challenges in mHealth

On-phone analysis is most suited when less complex analysis is required or in remote settings with limited mobile network connectivity and bandwidth. These methods can reduce the amount of data that needs to be transmitted and allow results to be stored on-phone and subsequently uploaded once in range of mobile networks. These capabilities are further enhanced by the continual improvements in mobile processing hardware. The use of dedicated neural-processing units and software frameworks for on-phone machine learning facilitate increasingly efficient and nuanced image classification, and could also improve automated inference when using defective equipment, or in poor lighting conditions.

Despite the huge potential of mHealth tools as a valuable source of data, they are associated with a number of challenges. Regulation is a key issue because it has not kept pace with the rate of technological advancement. Authorities, such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare Products Regulatory Agency (MRHA), have adopted a tentative approach to legislation around these applications. In order to address this issue, there is a need for regulatory frameworks that are able to be applied to the wide range of technologies available, as well as harmonisation among different regulatory bodies so that legislation does not become a barrier to future innovation.

The devices themselves also pose issues. If a diagnostic test is designed to be used with a range of smartphones, then their variability in hardware and software makes it difficult to assess risk in the regulatory review process. This is causing companies to either develop individual devices with defined components or ship a standardised smartphone with the test while carefully monitoring the software environment, both of which increase cost.

The clinical governance of mHealth-based care pathways also demands consideration. In instances where patients provide data remotely, it is essential that there is escalation capability to a range of healthcare professionals and to face-to-face services when required. This requires quality assurance of clinical decision trees, care pathways and remote prescribing decisions, as well as a secure and user-friendly interface for remote use.

Cost and clinical effectiveness must also be comprehensively assessed on a large scale for the successful implementation of these tools into healthcare. Although these parameters have been assessed in point-of-care diagnostics and some mHealth strategies, connected diagnostics with associated mHealth interventions have yet to be analysed. This is because of the inherent complexity in evaluating individual components of these devices, which consist of mutually dependent interactions.

While mHealth technologies provide the opportunity to broaden access to diagnosis for a range of health conditions, it is important to consider those who may be left behind. It is estimated that 35% of the world's population do not have access to mobile technologies. This is primarily because of the lack of access to these tools in low and middle-income countries, although those of lower socio-economic status in resource-rich settings are also affected.

Evidence suggests the gaps are narrowing but more needs to be done to ensure that these technologies are available to all, particularly those most in need and with the largest barriers to overcome.

A new test to measure 3GC hydrolysis activity

Coris BioConcept, a Belgian company specialising in rapid antimicrobial-resistance diagnostic kits, is now releasing a new solution to accelerate the detection of cephalosporin-resistant strains.

The rate of resistance to third-generation cephalosporins (3GC) in Gram-negative nosocomial infections is increasing worldwide, forcing clinicians to adopt alternative treatments to face resistant strains. Rapid confirmation of 3GC resistance remains a priority for microbiologists. Today, microbiological susceptibility cultures are largely used because of their simplicity and low cost. However, the average time-to-results of cultures are too long, providing resistance profiles within 24 to 48 hours.

New diagnostic advancements

Although presented as interesting alternatives, biochemical colorimetric tests could be in some case difficult to interpret because they are based on a subjective reading of a colour change. To circumvent that issue, Coris BioConcept is currently developing a new diagnostic tool to measure 3GC hydrolysis activity from bacterial broths. This new assay is based on a recently patented electrochemical method, which uses an electroactive cephalosporin analogue to measure the hydrolysis profile of Enterobacteriaceae.

The BL-RED (Beta-Lactamase Rapid-Electrochemical-Detection) test delivers a fast and objective result on the 3GC hydrolysis profile of Enterobacteriaceae strains. Used as a front-line test, BL-RED is seen as the ideal tool to accelerate decision-making on the antimicrobial prescription. Coris BioConcept develops and manufactures in vitro diagnostic tests. With this new product in the pipeline, Coris BioConcept is offering an additional solution to its already existing RESIST products – immunochromatographic tests for the precise determination of carbapenemase-expressing organisms – and tightening its position as a main actor in the field of antimicrobial resistance diagnosis. ●

For further information

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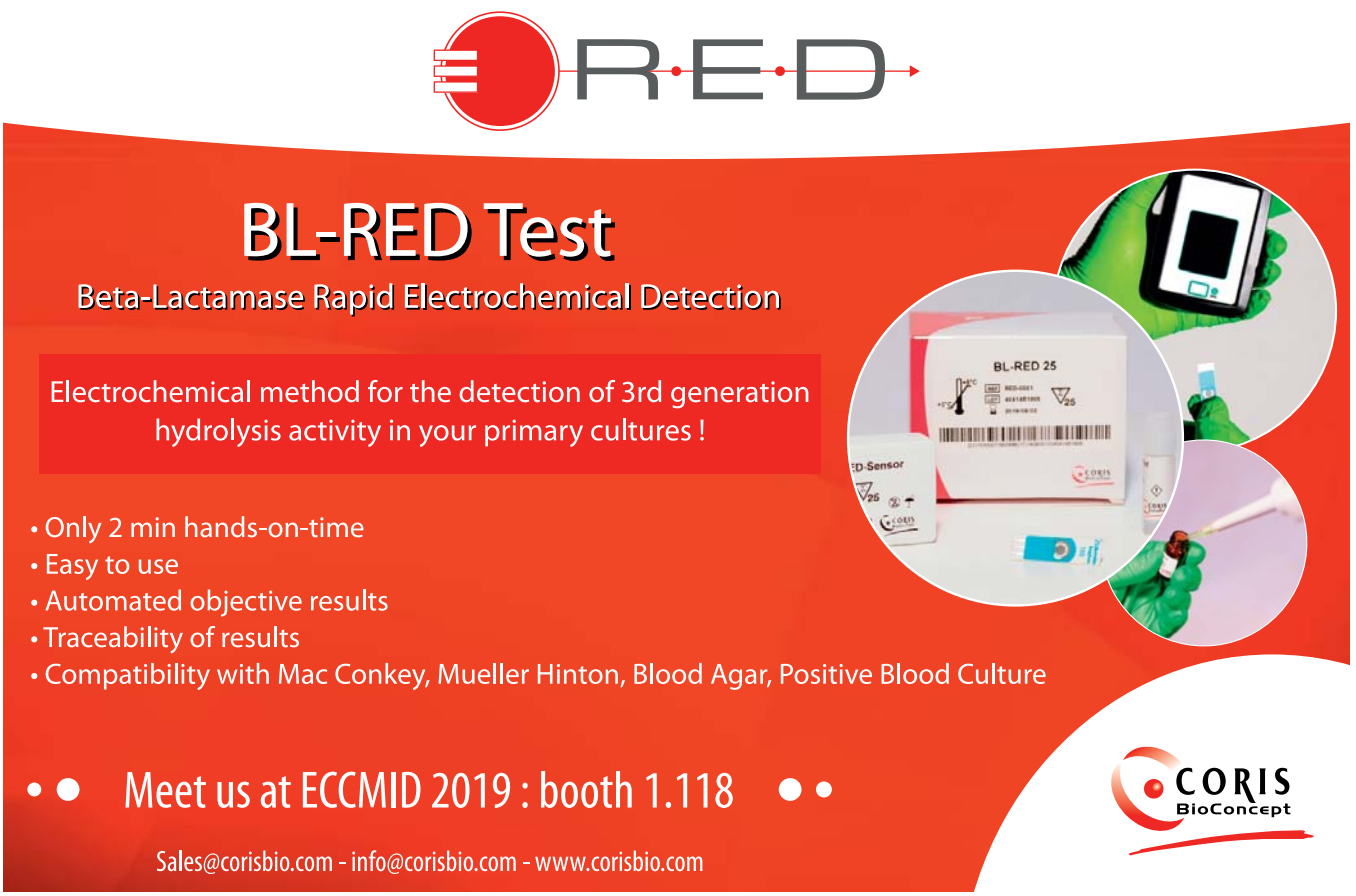

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Fast and accurate identification of CPOs

Dr Ken Thomson of the University of Louisville and Bill Folkerts, head of ID/AST global marketing at **BD Life Sciences – Diagnostic Systems**, discuss the new BD Phoenix automated identification and susceptibility testing system's potential for combatting the emerging global pandemic of antibiotic resistance.

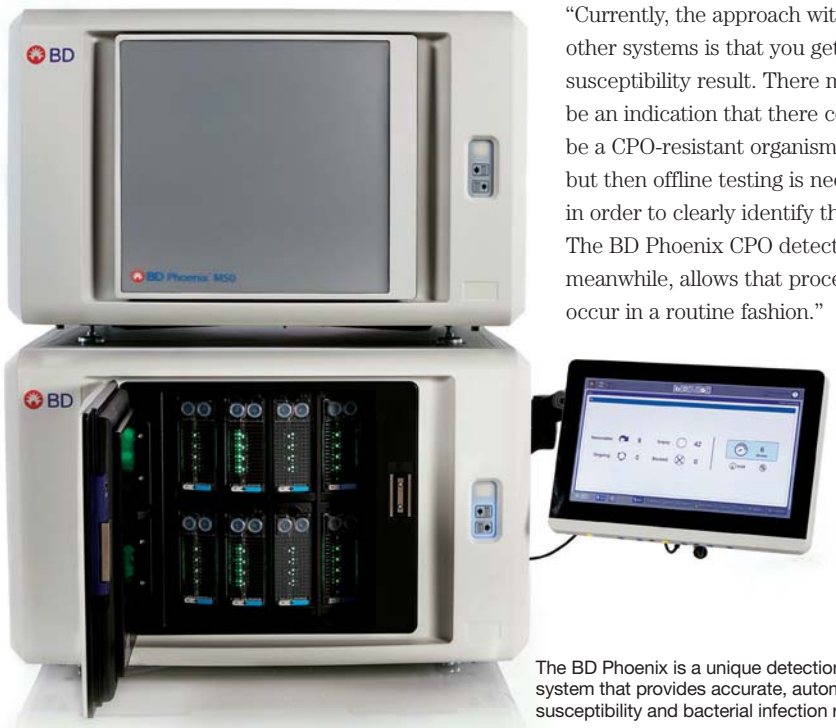
Dr Ken Thomson has been involved in the field of antibiotic research for over 25 years. As a clinical professor at the University of Louisville's Department of Pathology and Laboratory Medicine, he has seen antimicrobial resistance in carbapenamase-producing organisms (CPOs) – so named for their ability to produce an enzyme that counteracts the effects of powerful carbapenem antibiotics – turn from a rare evolutionary quirk into an ever-present threat to the effective treatment of an infection. "We're running out of antibiotics," says Thomson. "And we're running out of time."

The result has been a high-mortality global pandemic of infections by CPOs, and without the development of new antibiotics, microbiology labs have been left to hold the line. "If labs cannot detect CPOs, patients are going to receive inappropriate therapy," explains Thomson, resulting in an enormous, uncontrollable resistance problem. "Labs therefore require rapid, accurate systems capable of identifying CPOs."

"The BD Phoenix system is based on a unique detection technology that provides accurate, automated susceptibility and bacterial infection results," explains Bill Folkerts, head of ID/AST global marketing at BD Life Sciences – Diagnostic Systems. "The BD Phoenix CPO detect test has been incorporated into the routine panels that are used for testing. It is the only automated phenotypic-based, rapid approach towards carbapenamase detection in the market."

Reduced uncertainty

The incorporation of the BD Phoenix CPO detect test into a routine panel is in response to the seriousness of the problem confronting microbiologists – it's also unique in the marketplace when it comes to detection technology. "It's a clear differentiator," says Folkerts. "Currently, the approach with other systems is that you get a susceptibility result. There may be an indication that there could be a CPO-resistant organism, but then offline testing is needed in order to clearly identify that. The BD Phoenix CPO detect test, meanwhile, allows that process to occur in a routine fashion."



The BD Phoenix is a unique detection system that provides accurate, automated susceptibility and bacterial infection results.

The fact that the presence of a CPO is determined by the BD Phoenix on an automated system, and not individual microbiologists, also serves to diminish uncertainty and increase sample throughput. "Manual tests rely on someone at the bench to interpret them and when a borderline result occurs, it is difficult, sometimes impossible, for microbiologists to interpret them accurately," Thomson explains. "The BD Phoenix CPO detect test does a carbapenamase test on a Gram-negative isolate that has an antibiotic susceptibility test. The machine reads the test, so you don't have any problems with laboratory staff not knowing whether a borderline test is really positive or negative."

In addition, the BD Phoenix instrument is capable of automatically classifying the type of CPO present in the sample. "That, again, is unique," says Folkerts. "The ability to not only determine the presence of a CPO, but also to identify its Ambler classification, drastically impacts the appropriate therapeutic choice for the patient."

New agents have now been developed that are effective against CPOs that produce Class A carbapenamase. "These new agents should only be used on infections with Class A carbapenamases," affirms Thomson. "If there's a Class B carbapenamase, these organisms are intrinsically resistant. The BD Phoenix system can let you know when to use these new agents."

Above all, the BD Phoenix is practical. "You just inoculate a panel to put into the machine, and walk away," says Thomson. "It will incubate for six to eleven hours and then it'll give you a result. So, there's not much hands-on time, especially compared with other state-of-the-art rapid tests that require manual use." ●

For further information

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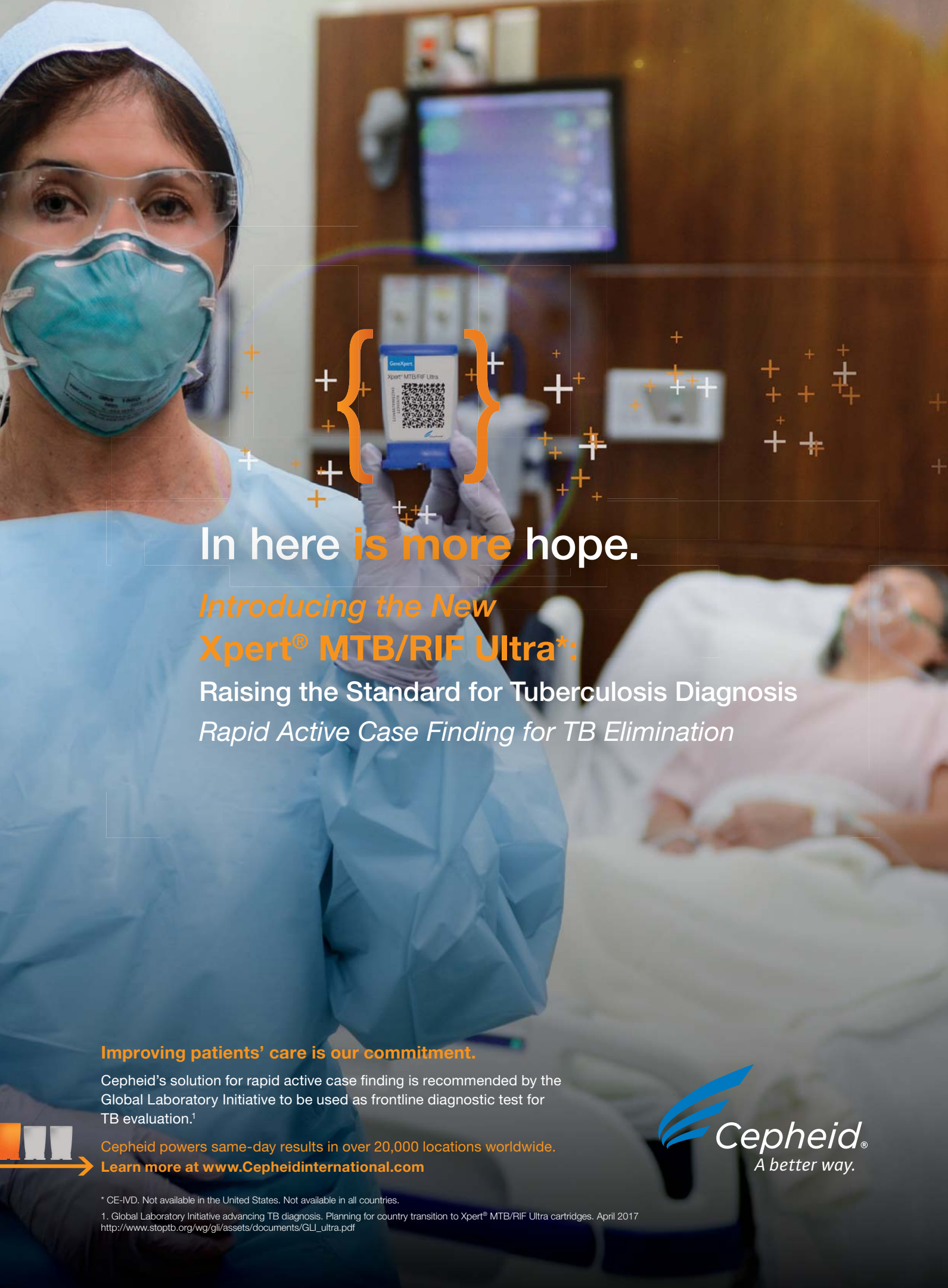

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* CE-IVD. Not available in the United States. Not available in all countries.

1. Global Laboratory Initiative advancing TB diagnosis. Planning for country transition to Xpert® MTB/RIF Ultra cartridges. April 2017 http://www.stoptb.org/wg/gli/assets/documents/GLI_ultra.pdf

Eliminate TB through rapid active case finding

Tuberculosis (TB) is a pressing health problem, with England having one of the highest TB rates in Western Europe. Dr Pranab Haldar, respiratory physician and training director, and Hemu Patel, senior biomedical scientist at the University Hospitals of Leicester NHS Trust in the UK, share their experiences of how **Cepheid** and the GeneXpert (GS) System has revolutionised the TB testing process by enabling rapid active case finding.

Can you provide us with an update about the situation of TB in the UK?

Dr Pranab Haldar and Hemu Patel: TB continues to be an important health problem. Over 5,000 cases were reported in 2017, with England continuing to have one of the highest rates of TB in Western Europe. Migrants arriving from countries with a high burden of TB account for approximately 70% of all cases.

TB is typically concentrated in densely populated urban areas that have high numbers of migrants. In this context, TB services are needed to provide a robust model of care to help with early diagnosis to limit onward transmission of the infection, ultimately to help achieve national TB program goals of TB elimination. In Leicester, for example, we see almost 200 new cases of TB each year, at a rate that is almost four times the national average.

Can you share some details about your TB network and testing model?

Over the past decade, we have developed and established a centralised rapid access pathway for the early assessment and management of TB, particularly infectious pulmonary TB, for the whole county of Leicestershire.

The model provides an alternative and speedier route into specialist secondary care that bypasses delays imposed by conventional referral processes. The pathway provides direct access to primary care referrals and incorporates TB codes attached to radiology and microbiology reports that suggest possible TB cases.

Coded results are flagged and copied to the service, which is administered by a rapid-access TB coordinator, who works closely with the clinical TB lead. Referrals are triaged for their likelihood of TB, based upon the results of tests that have already been performed, the patient's clinical history and any risk factors they may have.

What has been key for the implementation of your rapid access pathway and what recommendations would you make to others considering a similar approach?

Our network began with an agreement between stakeholders across multiple disciplines to work collaboratively to deliver a coordinated strategy for early diagnosis, treatment initiation and TB prevention in at-risk groups. TB networks form part of the national TB strategy and the key to their effectiveness is engagement, enthusiasm and innovative thinking by these different stakeholders. The inclusion and working together of stakeholders from both radiology and microbiology, and being supported by the TB leads in these specialities to establish the current pathway, has been vital to the success of the network. We also perform regular audits to identify areas that need to be improved. The results are fed back to the TB network, where appropriate changes to the pathway are agreed.

In addition to alignment between stakeholders, the implementation of rapid molecular testing for rapid active case finding has been integral for our success. The GeneXpert® model as a first-line diagnostic for suspected TB has evolved with the introduction of Xpert® MTB/RIF Ultra, which offers a significant improvement in sensitivity compared with the previous assay, avoiding unnecessary screening of people with a low clinical risk of TB.

Could you explain the importance of rapid active case finding for suspected patients and how your model supports this?

Early diagnosis and treatment are essential for TB control to limit the risk of the infection being transmitted – our rapid access pathway aims to meet this goal. It has been supported by developing a multifaceted model of referral. Our focus on developing coded alerts on X-rays has allowed us to identify possible TB before a GP is able to act.

Our team contact the patient directly and arrange for a sputum collection immediately. Our microbiology services offer rapid Xpert MTB/RIF Ultra testing to all samples that are submitted by patients on the rapid access pathway. Results of these tests are available within 24 hours and help greatly with triaging patients for further care. All Xpert-positive patients are seen and start treatment in an outpatient clinic the same week.

Since using Xpert MTB/RIF Ultra, we have confidently discharged over 60% of referrals with suspected pulmonary TB without the need for additional investigation, allowing us to focus on patients who are more at risk.

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How NGS helps in the fight against drug-resistant TB

Tuberculosis is one of the top 10 causes of death globally, killing nearly two million people per year. Philip Supply, senior scientist at the French National Centre for Scientific Research, explains how Genoscreen is combatting drug-resistant TB with **Illumina**'s next-generation sequencing.

How did you get involved with Genoscreen? And is your research applied by the company?

Philip Supply: My research group developed and internationally standardised a portable 24-marker genotyping method for the molecular tracing of the TB-causing pathogens. I worked with Genoscreen to develop genotyping kits, which facilitated the adoption of these markers for global surveillance of the disease. The knowledge acquired through our research on the strong clonality and other biological peculiarities of the organism are now used within the company to develop new molecular tools for the rapid detection of bacterial drug resistance.

Can you tell us about Genoscreen and its involvement in 'eradicating tuberculosis (TB)'?

Genoscreen is a biotech company that offers a large range of next-generation sequencing (NGS) including Illumina instruments, genome and metagenome analysis services. The company prioritises developing innovative tools for microbial research and applications. TB is one of the top causes of human death and the first contributor to mortality due to antimicrobial resistance. A large part of the company's R&D is devoted to fighting it.

How do you incorporate NGS in your workflow? And what are the benefits?

In our research, we use NGS as a molecular approach to study factors underlying the high or low-epidemiological success of different strain lineages worldwide, and to track the evolution of drug resistance. Whole genome sequencing (WGS) provides us with a comprehensive view on the molecular mechanisms involved. At a basic scientific level, we can thereby identify early branches and key mutational events involved in the evolution of the organism towards pathogenicity. We can also track the epidemic spread of major multidrug-resistant clones, and understand their origins. We now use targeted deep sequencing to better detect the emergence of resistance, especially to recent anti-TB drugs. That recently helped us to identify an outbreak of drug-resistant TB in South Africa, undetected by WHO-endorsed tests. These TB strains unexpectedly presented mutational signs of emerging resistance to bedaquiline, the newest antibiotic used to treat multidrug-resistant TB.

What improvements do you see now that NGS has been incorporated in TB genotyping?

TB genotyping is widely used for molecular-guided outbreak control and prevention. TB is typically concentrated in vulnerable and hard-to-reach risk groups. This complicates contact investigation around TB cases, which represents a central component of outbreak control and prevention. WGS offers ultimate resolution at strain level, and its use allows for more precisely guided investigations of probable transmission links among patients.

You were chosen in WHO's technical guide on the use of NGS for detecting mutations associated with drug resistance in *Mycobacterium TB*. How did this come about?

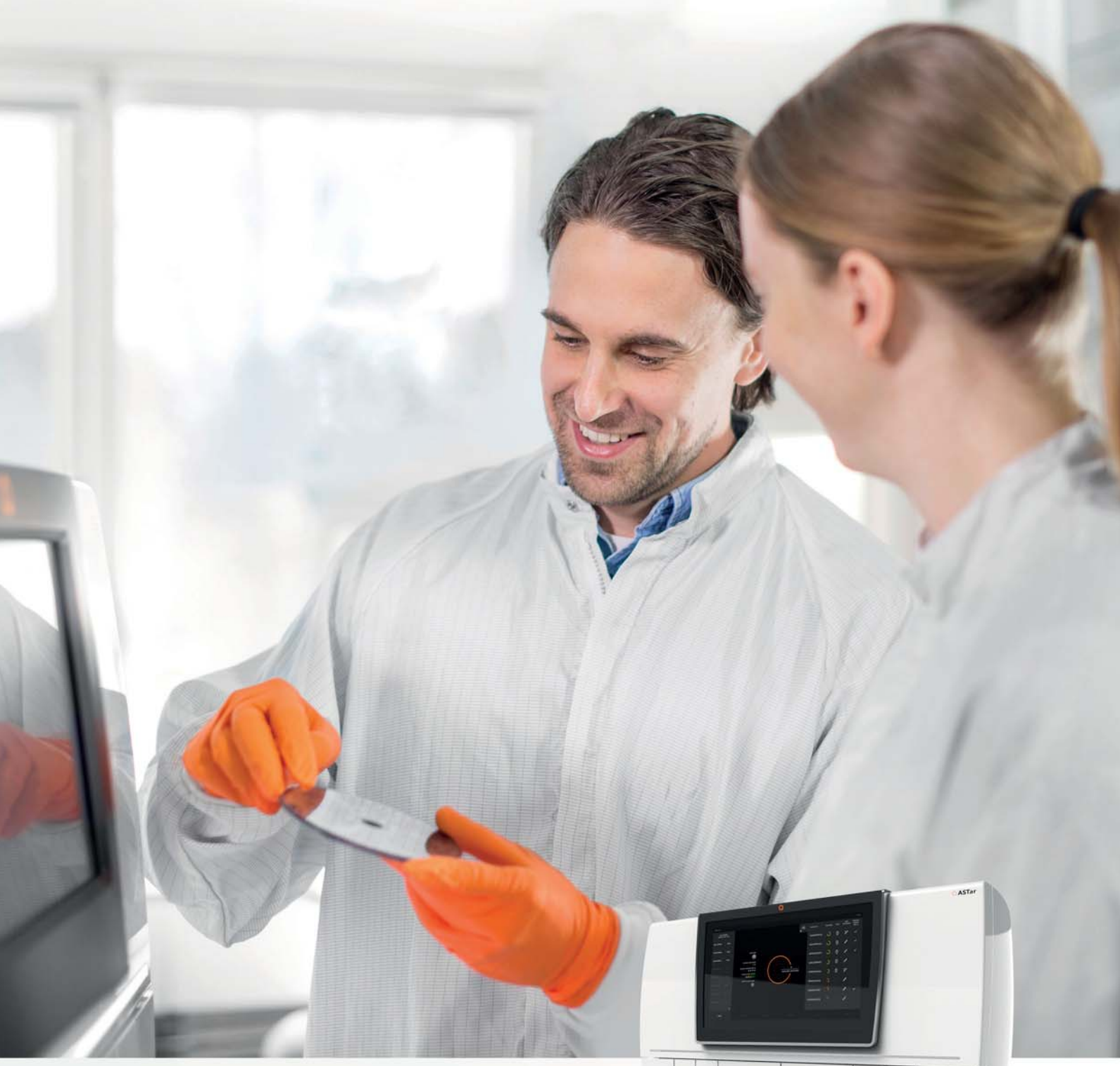
This is the result of the meticulous development with Genoscreen of a novel targeted deep sequencing solution, called Deeplex-MycTB, for culture-free detection of drug-resistant *M. tuberculosis*. In contrast to WGS, this amplicon-based test can be directly applied on clinical specimens. This authorises diagnostics and patient treatments at least one week faster than WGS, and weeks faster than phenotypic tests. The assay consists of a single 24-plex amplification of 18 drug resistance-associated gene targets, plus mycobacterial identification and *M. tuberculosis* genotyping targets. This molecular compartment is coupled to a fully parameterised and automated web application for quick, efficient analysis, making the test a unique end-to-end solution.

How do you see NGS being used in detection of multidrug-resistant TB?

The use of NGS, either targeted or even more so by WGS, permits more comprehensive detection of drug resistance-associated mutations than existing molecular tests. Especially with a targeted format, deep sequencing of the resulting amplicons provides a highly accurate analysis of drug resistance mutations, including in minority populations causing heteroresistance. Moreover, the already extensive catalogue of known drug resistance mutations is expected to be almost comprehensively covered soon, thanks to international collaborative efforts by the CRyPTIC and ReSeqTB consortia, involving WHO. These collaborations are causing several countries to transition to NGS-based TB diagnostics. As a result of lighter infrastructures needed for molecular tests rather than for culture-based assays, NGS also has a great potential to help closing diagnostic gaps existing in high-multidrug-resistant TB incidence settings. ●

For further information

www.illumina.com



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Q-LINEA

Antibiotic susceptibility tests delivered with speed

Increasing levels of antimicrobial resistance globally demand antibiotic susceptibility tests that are easy to use and deliver actionable results quickly. We talk to Dr Marijo Parcina of the University of Bonn, and Dr Jonas Jarvius, CEO and president of **Q-linea**, about how the latter's ASTar technology promises both.

Can you give us an indication of the scale of the problem surrounding microbial resistance around the world?

Dr Marijo Parcina: Antibiotics are widely used in hospitals and medical practices, and make an enormous contribution in reducing loss of life. Growing concern over emerging antibiotic resistance, therefore, is justified. Indeed, it should be considered a global health issue. Bacterial resistance itself is a genetic feature in bacteria, acquired in their evolutionary development long before the arrival of humans. Even so, the exposure of the organisms to antibiotic agents has sped up this previously gradual evolutionary development. In particular, Gram-negative (GN) MDR bacteria – with or without carbapenemases – create challenges in everyday hospital work, and their incidence in epidemiological reports is steadily rising.

What demands exists within the analytical labs for new technologies and methods within antibiotic susceptibility testing (AST) analysis?

MP: AST results deeply inform calculated antibiotic treatment. This is based on the positive identification of the pathogen, which contributes towards the shaping of epidemiological data and natural resistances for the given pathogen. The real calculational therapy should be based on the phenotypical AST, especially for the GN pathogens. New technologies and methods in AST should be able to deliver an accurate minimum inhibitory concentration (MIC) in a shorter time span than other, more conventional techniques. Furthermore, new technologies should, preferably, implicate not just MIC but also additional information over what end-point measurement can provide, such as bacterial morphology and response over time, which could provide deeper insights in some critical bug-drug combinations. Hopefully, the development of more practical tools to divine new combination therapies, giving us actionable proofs through different measurements of in vitro efficiency of certain antibiotic combinations.

The ASTar system uses true broth dilution to automatically deliver a true MIC-value with speed and accuracy.

A rapid AST result can be delivered one to two days faster than conventional methods. What else do clinicians need to know in order to confidently change an initial empirical antibiotic treatment to more suitable and effective antibiotic(s)?

Dr Jonas Jarvius: Clinicians are faced with two key decisions in this case when confronted with an infection resistant to antibiotic treatment either to increase the dosage of the drug already prescribed, or de-escalate the current treatment. Since all septic patients are placed on broad-spectrum antibiotics, a de-escalation decision is extremely important in reducing the development of antimicrobial resistance in the patient, hospital and, in the long run, society. In order to make actionable decisions for escalation and de-escalation, the diagnostic test needs to support a sufficiently large panel of antibiotics, which is offered by Q-linea's ASTar panel.

ASTar technology uses true broth dilution to deliver a true MIC value and not an estimated MIC value that is also common. We feel that this has been important for the understanding and legitimacy of our chosen strategy, since this is based on the reference technology for AST. Of course, with the difference that ASTar can provide the answer faster and fully automatically. Also, in contrast with established technologies for AST, our image-based technology has the potential to detect other features of susceptibility such as heteroresistance.

What lessons did Q-linea learn from the development of its ASTrID project that were applied to its latest rapid diagnostics instrument, the ASTar?

JJ: ASTrID was developed with the intention of delivering same-day results for patients with sepsis. The ASTrID program itself gave us a much deeper understanding of workflow in the lab and what was currently lacking. It also enabled us to develop state-of-the-art sample preparation technology for complex blood samples. This technology could then be used for the ASTar system and, since it was developed to handle large volumes of complex samples, we think it will enable us to grow the ASTar menu expansion in the future. We also learned that the path to market is more straightforward when clinical guidelines are in place for the upcoming clinical studies, and that it can be beneficial to be second to market if you think your product has competitive advantages over what is currently out there. ●

For further information

www.qlinea.com

Dr Matt Inada-Kim

National Clinical Sepsis Lead,

NHS Improvement

Over the last five years we have made terrific strides in improving the awareness, recognition and treatment of patients with suspected sepsis. When I say 'we', I am talking about patients, their families, and health and care professionals who have all become more vigilant in 'thinking sepsis' and have worked together to advance the sepsis agenda. This collaboration has enabled a sustained, national improvement in screening and treatment from 50%, to 90% within one hour of deterioration.

But, we must be relentless in our ambition – the work must continue. Infections that can lead to sepsis are responsible for 40% of emergency admissions and are the admission reason for two thirds of hospital deaths. As the population ages and lives with ever increasing comorbidities, the threat of sepsis also grows. This, coupled with the growing threat of antibiotic resistance means we must carefully balance expedient treatment with antibiotic stewardship.

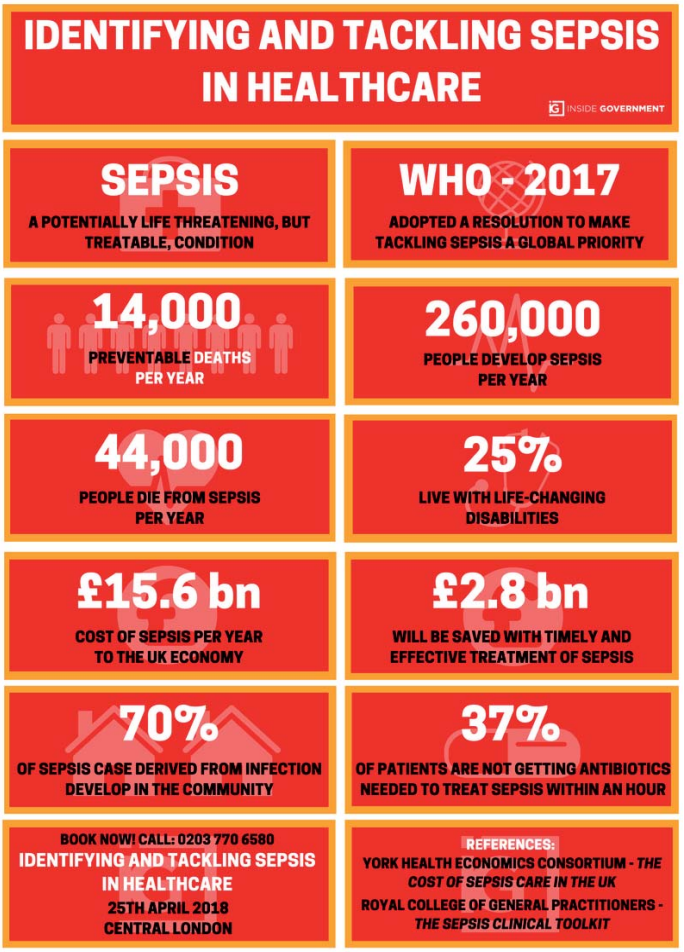
Whilst we still strive for a 'sepsis test' and standard definition, we must acknowledge the progress we have made in both measuring response, and crucially, outcomes through the Suspicion of Sepsis Insight Dashboard. The Dashboard has enabled clinicians, for the first time, to assess the impact of sepsis improvement programmes and determine the interventions that are working, and disseminate them everywhere. It's also an example of what can be achieved through cross-system collaboration.

Sepsis remains a challenging diagnosis to make, particularly in the urgent care setting, and for us to make further inroads into its improvement, we must be consistent and reliable at spotting a sick and deteriorating patient and then considering if sepsis might be present.

Enter the National Early Warning Score, or NEWS2. We must support the implementation of NEWS2 in our workplaces and across the system. It provides us with a standardised language of sickness that healthcare professionals at every level can use and recognise to identify those at risk of sepsis.

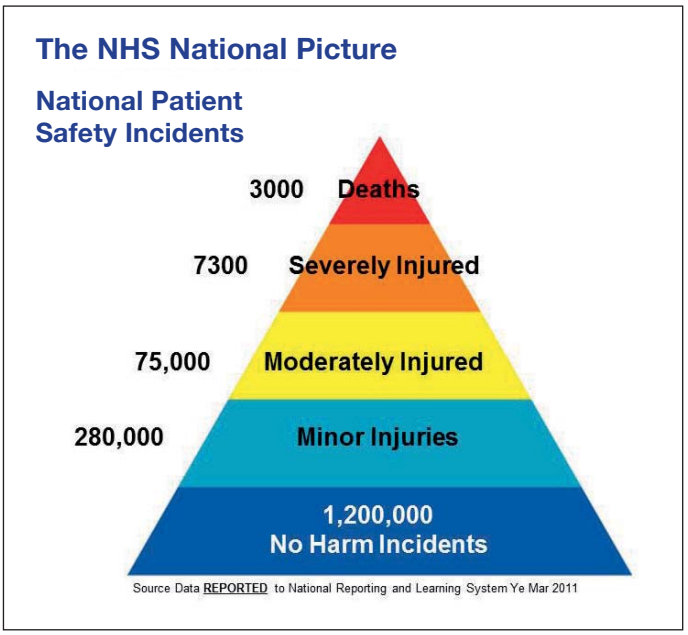
The efforts and progress made in sepsis improvement through our collaborations is terrific but there is still a lot more work to do. At the conference you will hear more from colleagues and partners from across the system on the points I have touched on here. We are united in our ambition to improve outcomes and save lives – a joined up approach will help all of us realise this goal!

For more details please go to www.sepsis2019.co.uk



In December 2018 NHSI announced a consultation on Patient Safety as part of the Long Term Plan.

In the Spring of 2019, NHSI will publish the consultations taken for a new national Patient Safety Strategy Plan. In June in Birmingham, we will announce the plans for local delivery and steps for implementation.



In healthcare systems all over the world there are times when things go tragically wrong. We all understand that healthcare is a people business, and that with the very best intentions anything involving people is liable to human error.

Improving safety is about reducing risk, minimising mistakes and establishing the necessary checks and balances. It is also the evolution of a 70year old free of charge at the point of access national service to a 24/7 seamless provision.

The NHS has embarked on a journey to become one of the safest healthcare systems in the world. In England over the last 4 years improvements have been achieved. We have had a complete overhaul of CQC standards, and comprehensive inspections of all trusts, as well as primary care providers.

Patient safety is also a main driver in achieving cost savings and efficiencies across the whole health economy.

We have seen the introduction of the new protections for those who raise concern and whistleblow, which means that the NHS is now more transparent. There are now Patient Safety collaboratives, each established and led locally delivering stakeholder owned improvement programmes.

The NHS approach to patient safety is widely recognised as world-leading and their continuous work with national and international partners ensures continued improvement which will benefit patients.

The “Patient Safety 2019” conference with the input of leading quality and safety experts will look at what needs to be done over the coming years to improve even further with a particular focus on operating theatres.

Topics covered on the day will include, Leadership, Change Management, Preventing HAI’s, Never Events and Reducing Medication Error. There will also be a progress report on the Patient Safety Incident Management system (PSIMS) which in April 2018 completed the Alpha phase and is about to move into the Beta stage of development.

For more details please go to www.patientsafety2019.co.uk

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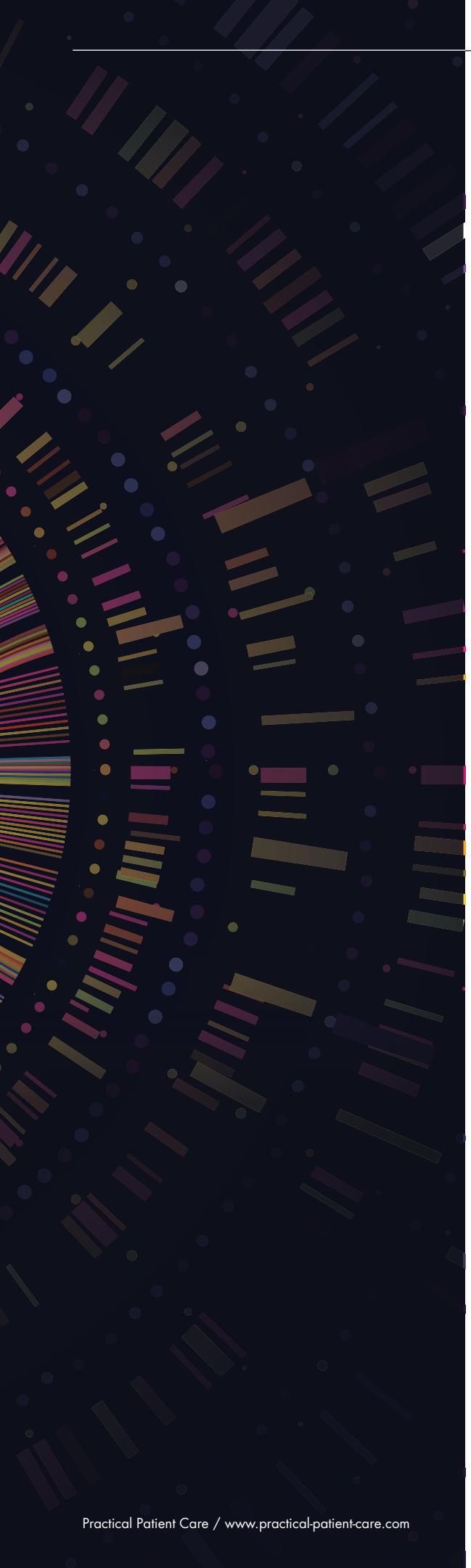
Map the future

Hot on the heels of the success of the NHS's 100,000 Genomes Project, which finished at the end of 2018, the NHS Genomic Medicine Service is due to be launched later this year. It aims to bring equitable access to genetic and genomic testing to patients in the UK to improve the diagnosis and treatment of cancer and rare diseases. **Professor Clare Turnbull**, researcher and consultant at the Royal Marsden Hospital, speaks to Emma Green about how this technology can enhance diagnostic strategies.

Over the past decade, we have witnessed dramatic technological evolution, transforming a number of industries. In October 2018, the UK health and social care secretary released a policy paper outlining his tech-vision for the UK NHS to modernise both its practices and services delivered. As part of this strategy, there has been pressure for the NHS workforce to expand their skills and knowledge to be able to take advantage of these advances.

One of the areas most affected is genomics, the branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes. Professor Clare Turnbull, a senior researcher at The Institute of Cancer Research, fuses genetic sequencing technologies to identify and characterise genetic predispositions to a number of different cancers. Her team investigate ways to optimise next-generation sequencing (NGS) and analyse the resulting data to identify novel cancer predisposition genes.

Turnbull has been heavily involved in the NHS's 100,000 Genomes Project, which aimed to capitalise on these recent improvements in technology. One of



the key advantages of NGS is that researchers do not have to know the question they are asking before carrying out the sequencing. “Until next-generation sequencing, if we wanted to look at a gene, we could only look at one chunk at a time,” says Turnbull. “This meant you had to know which gene or part of the genome you were interested in before being able to amplify and sequence it.”

The capabilities of NGS not only allow the use of different sequencing techniques but also to carry these out at a much larger scale than was previously possible. “The technology shift completely changed what we were able to do,” explains Turnbull. “It allows you to sequence an entire genome in one experiment. If there are a few genes you are interested in, you could sequence them all in a way that wasn’t possible before.”

Within genomics, the speed of technological advancement and reduction in costs has massively outpaced predictions. “Before the human genome project, it was shotgun sequencing, so they were having to sequence each chunk separately. Each would be sent to a different lab for sequencing, and it took 10 years to get the first draft assembly and cost $2.7 billion dollars,” explains Turnbull. “Now, in a very high-throughput laboratory, they can do a test for a tiny fraction of the price.”

Up the ante

NGS, although well established as a technology, has only recently been implemented into the NHS due to a lack of infrastructure, tools, skills and funding. In late 2012, then UK Prime Minister David Cameron announced the provision of financial support for several important projects, as part of the Olympic Legacy Funding.

One of these was the 100,000 Genomes Project. Following consultation, it was decided that rare disease and cancer research would stand to gain the most from the technology and thus became the focus. In order to deliver the project, a new sequencing site, the Genome Campus in Hinxton, near Cambridge, was built and funded by the Wellcome Trust.

An upgrade of software was also needed to deal with the huge amount of information generated by the research. A major element was building the informatics infrastructure to process, analyse and interpret the sequencing data and to distribute the results out to NHS centres. This also enabled UK researchers and partners from the industry to access the genome data in a secure research environment, where it was held in a de-identified format.

Clinical staff received special training to ensure that this data could be accurately and ethically interpreted. “There was a lot of work to create a knowledge base to ensure that we could make the best clinical inferences from the genomic data,” explains Turnbull. ▶

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The 100,000 Genomes Project was completed at the end of 2018. Researchers even managed to overreach their target number of samples and are currently finalising the analysis of the data. The next stage involves rolling out the first UK genomic medicine service, which is due to go live in 2019.

One of the key aims of the project was to make a significant impact within rare disease, which has been the mainstay of clinical genetics since its inception. Rare diseases are defined as those affecting less than one in 2,000 people. Roughly 75% of these conditions are diagnosed in children before the age of five and most are life threatening or involve serious disability.

As the majority of rare diseases are due to a single gene defect, genomics offers huge potential to diagnose these conditions more efficiently. "Our work has tried to identify genetic causes for children with congenital anomalies, intellectual disabilities or unusual dysmorphic facial features, and then involves using testing to identify that genetic cause," says Turnbull.

Conducting genomic sequencing allows clinicians to make better predictions about which treatments are likely to be most effective. "Sometimes, that will point to a treatment, especially if it's an enzyme deficiency," says Turnbull. "If it's a particular pathway, there will be a drug to treat, and if it's a metabolic disorder, there are certain dietary approaches where the patient will respond favourably." Even if a suitable treatment is not available, genomics allows for the identification of additional symptoms that may be experienced by the patient and pre-empt complications.

A genetic diagnosis can also provide the family with information about the probability of reoccurrence in subsequent pregnancies. "It may be important reproductively for the couple, particularly if the condition is recessive; they will have a one in four chance of a subsequent pregnancy being affected."

The major advantage of NGS is not only the value of the insights themselves but also the speed at which they can be delivered to patients and families. "It's a big step forward that we'll be doing whole genome sequencing in these children and doing it while they are young," says Turnbull. "This means that if there's an identifiable genetic cause, you will get that quickly, while you can still treat the patient."

Put it into practice

The other key impact of the 100,000 Genomes Project has been upon cancer diagnostics and treatment. Although not always conceptualised as such, cancer essentially is a genomic disease.

"Tumours have very disordered genomes because the first mutation will trigger a process in the cancer that gradually releases it from the 'policemen' that control the division of cells," says Turnbull. "Once those policemen are knocked out by gene mutations, cells reproduce in an increasingly uncontrolled fashion, and so the tumour grows and eventually metastasises."

There are two key ways that NGS can positively influence cancer, by sequencing the tumour and the blood. "Sequencing the tumour itself is informative because, as well as giving us a blueprint of how it developed, the changes can tell us which drugs will be effective," explains Turnbull.

The ability to conduct this sequencing has not only informed predictions about treatments but also changed the terminology used for these diseases. "We used to classify tumours by what the cells look like, on histology, whereas now we make a molecular classification," says Turnbull. "Increasingly, rather than describing cancer as a 'non-small cell lung cancer', you'll see it's called an 'EGFR-positive lung cancer' because that lets you know that it will respond to an EGFR inhibitor, which is important."

In conducting NGS in the blood, specific genes can be identified, which is valuable even if the person does not have cancer. "BRCA1 and BRCA2 [brought to public attention by Angelina Jolie when she found she had a genetic mutation in these genes] can tell you that you're at high risk of particular types of cancer," says Turnbull. "They can be identified when the person is completely well, particularly if it runs in the family, and then you can offer high-risk screening." Additional action can be taken to prevent specific cancers, such as surgery to remove of the ovaries or a mastectomy.

As a result of improving diagnosis and treatment, the prognosis for a number of cancers has been significantly improved in recent years. "Previously, the prognosis for someone presenting with non-operable lung cancer was a few months and now it is two, three or four years," explains Turnbull.

Look to the future

In light of the rapid, ongoing changes in technology and the parallel reduction in costs, there is huge potential for NGS to have a positive impact beyond rare diseases and cancer. To facilitate this, it will be necessary to become less reliant on clinicians and instead make greater use of online resources.

"I've just put in a grant with other researchers to do BRCA testing end-to-end on a saliva sample, with the patient and the workflow managed by an app, rather than serial appointments with a clinical geneticist or genetic counsellor," says Turnbull. "The information and consent would be given via the app and the results, if negative, would be delivered by the app, and if they were positive, would ask patients to attend a clinic."

With the increased drive for person-centred approaches, including the desire for patients to take greater ownership of their healthcare, it is only a matter of time before genetic testing for a range of conditions is a normal part of life. ●

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A key tool to fight against antimicrobial resistance

Mobidiag offers a comprehensive range of fast, reliable and cost-effective molecular diagnostic solutions to screen for the most common infectious bacteria and resistance markers.

Since its inception in 2000, Mobidiag has been engaged in the fight against antibiotic resistance and has tackled the issue with two product lines. It has been developing solutions for all sizes of laboratories. The Amplidiag product line is tailored to large hospital laboratories, which require systems capable of handling large numbers of samples efficiently and in an automated manner. Thanks to its on-demand capacity, the fully automated Novodiag solution offers easy handling of samples and quick analysis, and allows the user to interpret samples without the need for extensive expertise.

An urgent need for tools to prevent and control infection

The excessive use of antibiotics has given rise to multidrug-resistant organisms, also called 'super bacteria', making antibiotics less and less effective. A simple routine case of bacterial infection can then result in a medical emergency, with no efficient drugs available for treatment. The most common antibiotics used worldwide are known as beta-lactams and include a class of highly effective antibacterials called carbapenems. These were always regarded as the most effective treatments against Gram-positive and Gram-negative bacteria.

However, over the past decade, bacteria that are less susceptible to carbapenems have been increasingly reported worldwide – most notably, the bacterial family *Enterobacteriaceae*, which includes *salmonella*. As a result, carbapenemase-producing *Enterobacteriaceae* (CPE) are considered 'critical' targets in the WHO priority pathogen list. New diagnostic tools are therefore needed to support early decision-making prior to the delivery of any treatment.

Solutions to fight antimicrobial resistance

Through its Amplidiag and Novodiag solutions, Mobidiag offers a comprehensive range of fast, reliable and cost-effective molecular diagnostic solutions to detect the most common infectious bacteria and resistance markers, including CPE.

These involve single tests to screen for:

- 'high-risk' patients (Amplidiag CarbaR+VRE, Amplidiag CarbaR+MCR)
- 'contact' patients (Novodiag CarbaR+).

Their benefits have not gone unnoticed. "Amplidiag CarbaR+MCR efficiently detects the most relevant carbapenemase-producing Gram-negative bacilli (*Enterobacteriaceae*, *Pseudomonas* and *Acinetobacter*) from swabs and culture, with performances of 99.57% for CPEs, 100% for CP-Abaumannii and 100% for CP-Paeruginosa, isolated over the period 2012–16 in France," says Dr Thierry Naas, director of the National Reference Center for Antibiotic Resistances at the Bicêtre Hospital, France.

"Amplidiag CarbaR+MCR efficiently detects the most relevant carbapenemase-producing Gram-negative bacilli from swabs and culture, with performances of 99.57% for CPEs, 100% for CP-Abaumannii and 100% for CP-Paeruginosa, isolated over the period 2012–16 in France."

Dr Thierry Naas, National Reference Center for Antibiotic Resistances

The new Novodiag CarbaR+ cartridge offers easy handling for on-demand testing.

The fast turnaround time, and the comprehensive screening panels in these assays, assist in the rapid detection of organisms containing genetic markers of antibiotic resistance. This enables faster infection control implementation, decreasing the risk of infection spreading, and accordingly guide patient treatment and reduce unnecessary costs. Molecular diagnostics are poised to replace standard culture-based tests, and act as an adjunct to supplementary and confirmatory tests for antimicrobial resistance (AMR).

Focus on new on-demand tests

Novodiag CarbaR+ combines multiplex qPCR and microarray testing in a single product allowing cost-effective and fast analysis of more than 200 variants of most common CPE and colistin-resistance markers. These bacteria may cause multiple antibiotics to perform inefficiently, which in turn can lead to serious infections, particularly in healthcare settings. The test is designed to run on-demand using the automated Novodiag system, producing results in 80 minutes with less than five minutes hands-on time by an operator. ●

For further information

www.mobidiag.com

Detect latent TB infection

Latent tuberculosis infection is present in over a quarter of the world's population. Measures to detect it, therefore, could improve the quality of life for millions of people. Dr Pranab Haldar, a senior clinical lecturer at the University of Leicester, talks about how an ambitious new study has revealed the benefits of using **Oxford Immunotec**'s T-SPOT.*TB* test over more traditional methods of detecting this infection.

In the UK, tuberculosis (TB) is widely considered to be a Victorian disease, its symptomatic cough more likely to signal the untimely demise of a character in a period drama than to appear among our neighbours or extended family. This, however, is a fallacy – over 25% of the world's population harbours latent TB infection. While incidence of the disease is fairly low in the UK, the presence of the latent form of the infection in high-risk groups, particularly among those that have recently been exposed to the disease, presents a reservoir for future disease that is preventable if identified and treated.

Diagnosing and treating TB early in a patient is one thing. Even so, says Dr Pranab Haldar, a senior lecturer and consultant in respiratory medicine at the University of Leicester, that won't help drive down overall rates of infection. Nor can you test everyone for latent tuberculosis and treat them. "What we need are tests that can give us more information about who is and isn't at risk of developing TB in the future," Haldar explains. And as a major new study on latent tuberculosis carriers in England has shown, Oxford Immunotec's T-SPOT.*TB* test may just be the diagnostic tool required.

The T-SPOT.*TB* test detects the presence of activated T cells producing gamma interferon in blood samples.

Tried and tested

Commissioned to compare the risk of TB with latent infection between three diagnostic tests – the traditional tuberculin skin test and two Interferon Gamma Release Assay tests (IGRAs), QuantiFERON and the T-SPOT.*TB* test – the PREDICT Study was the largest of its kind, including data from over 9,500 participants. Although the latter two tests were IGRAs, the way they measured the release of gamma interferon in blood samples – a telltale sign of latent TB – was subtly different, with QuantiFERON using an ELISA that measures the total amount produced in whole blood, and the T-SPOT.*TB* test using an ELISPOT that measures the amount produced specifically from reactive T cells after washing and standardisation, making it the more sensitive assay.

"The T-SPOT.*TB* test actually performed the best, out of all three tests," explains Haldar. This was determined through two metrics – the positive predictive value of the test, which indicates what proportion of people with a positive result for latent TB will actually go on to develop full-blown tuberculosis, and the incidence rate ratio, which measures the ratio for the rate of TB in people with a positive test compared with those that have a negative test. This ratio offers a measure of how well the test can discriminate future TB risk.

"The T-SPOT.*TB* test had an overall positive predictive value of just over 4%," says Haldar. "Knowing that, I can tell a patient who has undergone the test that they've got a similar risk in developing tuberculosis over the next two years. It allows me to have an informed discussion with them about whether or not they wish to have ameliorative treatment."

The higher incidence rate ratios found in the T-SPOT.*TB* test compared with QuantiFERON and the skin test also suggests that the former is a more effective tool in predicting those at a high risk of progressing to active disease in the most at-risk populations. "The incidence rate ratio in migrants is particularly important because they're a very large community," Haldar explains. "What you really need is a test that provides the best accuracy, if you like, between those who are at risk and those who are not at risk. And the significantly higher incidence rate ratio that we saw with the T-SPOT.*TB* test in this population supports, I would say, the use of the T-SPOT.*TB* test in migrants over the other tests."

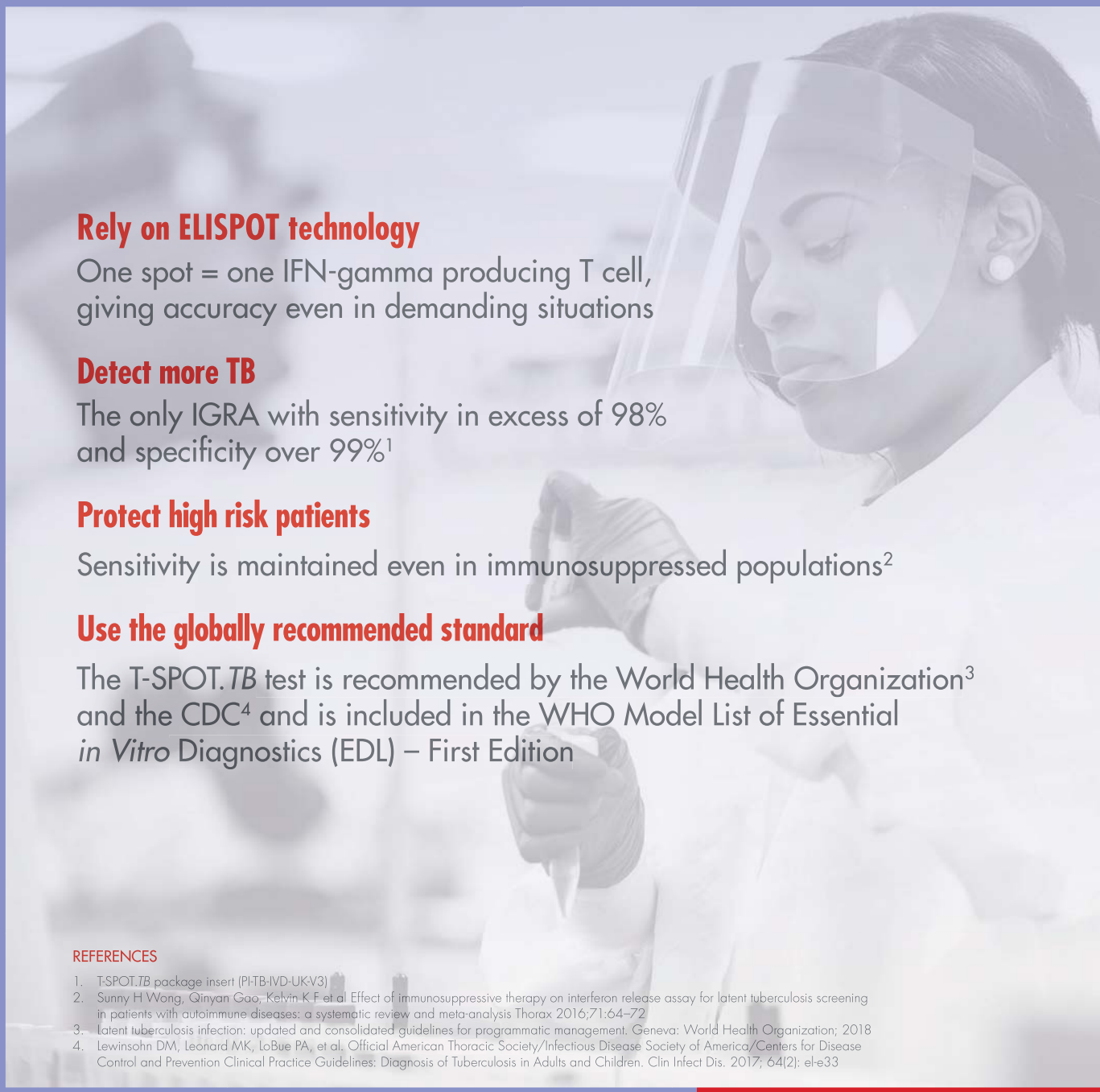
Crucially, the performance of the T-SPOT.*TB* test during the PREDICT Study has underscored just how useful an alternative it would be to the relatively impractical skin test. "While it might be the cheapest diagnostic tool, it is actually the most inconvenient to perform in practice," explains Halder. "The patients need to have the test performed by someone who is trained, and are required to return to have the size of the skin reaction produced after two to three days measured by another professional. Certainly the repeatability is not as good as for a test that is laboratory based, like IGRAs." ●

For further information

www.oxfordimmunotec.com/international

T-SPOT.*TB*

Use the T-SPOT.*TB* test to detect TB infection



Rely on ELISPOT technology

One spot = one IFN-gamma producing T cell, giving accuracy even in demanding situations

Detect more TB

The only IGRA with sensitivity in excess of 98% and specificity over 99%[1]

Protect high risk patients

Sensitivity is maintained even in immunosuppressed populations[2]

Use the globally recommended standard

The T-SPOT.*TB* test is recommended by the World Health Organization[3] and the CDC[4] and is included in the WHO Model List of Essential *in Vitro* Diagnostics (EDL) – First Edition

REFERENCES

1. T-SPOT.*TB* package insert (PI-TB-IVD-UK-V3)
2. Sunny H Wong, Qinyan Gao, Kelvin K F et al Effect of immunosuppressive therapy on interferon release assay for latent tuberculosis screening in patients with autoimmune diseases: a systematic review and meta-analysis Thorax 2016;71:64–72
3. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018
4. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Disease Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin Infect Dis. 2017; 64(2): el-e33

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TB-UK-AD-MPN141-0001 V1

Procedure boxes for better patient care

For hospitals striving to reduce waste, improve efficiency and provide better patient care, procedure boxes offer an innovative solution. Laura Marquez, procedural solutions manager at **Medtronic**, discusses their benefits for inventory management, operational efficiency and standardisation in surgery.

As funding becomes stretched and patient numbers rise, hospitals come under pressure to reduce costs and improve efficiency – but this is not always an easy task, and the provision of instruments for surgery is no exception. Inventory management is complex and takes time, while the need to have the right equipment on hand results in overstocking. The selection and assembly of individual items are time-consuming, slow up surgeries and are an area open to possible errors.

Improved operational efficiency

Tailored procedure boxes by the healthcare solutions company Medtronic provide answers to these issues. Each box contains all the instruments required for specific surgical procedures, streamlining the process of ordering stock and managing invoices. This is supported by a survey conducted by Medtronic on the use of procedure boxes at a number of European hospitals: Great Western Hospital in Swindon, UK, found the time spent investigating invoices reduced by 91% when ordering boxes.

An easy ordering process also helps hospitals with financial efficiency. Each procedure box – and therefore each surgery – has one unique code for reorder. "Hospitals have to manage budgets, and kits are the perfect tools to control the specific expenditure per procedure," says Laura Marquez, procedural solutions manager at Medtronic. The use of procedure boxes allowed University Hospital Limerick in Ireland, Clinical Institute Beato Matteo in Vigevano, Italy, and Great Western Hospital in Swindon, UK, to reduce inventory volume by 30% and inventory value by 50%.

Tailored boxes mean inventory management is simplified and storage optimised. "You know exactly which products to use for every surgery, so you get rid of all the extra stock that may not be needed," Marquez explains. Improved efficiency in this area frees up space; furthermore, Medtronic reports that waste can be reduced by up to 50%, as extensive packaging for individual items is eliminated.

Each procedure box contains all the required instruments for a surgery, improving operational efficiency.

Enhanced surgical experience

The benefits of using procedure boxes extend into the operating room itself. Having all the required instruments together in one box cuts the time it takes to prepare for surgery, as nurses do not have to select instruments from a variety of locations. This is borne out in Medtronic's survey results: University Hospital Limerick reduced its set-up time by 63%.

This has knock-on effects on the overall efficiency of the hospital. "Because there's a reduction of time in several processes in the operating room, there is more time to treat more patients," Marquez says.

Having all instruments packaged together in a kit removes the chance of mistakes when picking products for theatre. Medtronic's survey found that error rates in this area were lowered by 16–20%, reducing the likelihood that nurses would have to leave the theatre to retrieve missing items and allowing a smoother surgical experience. Furthermore, the use of prepared kits is a significant step towards the goal of standardisation in surgery, with identical items used in each specific procedure. Standardisation reduces clinical variants, which is then associated with better clinical outcomes.

Medtronic's procedure boxes are customisable, allowing surgeons to specify the equipment they require for procedures. "They can choose whatever product they want to be included in this box, and so it's tailored to the customer's needs," Marquez says. The inherent efficiency of procedure boxes offers hospitals a tool to improve in numerous spheres at once: budget and inventory, waste reduction, procedure times and standardisation in surgery. ●

References available upon request.

For further information

www.medtronic.com

Medtronic Procedural Kits support **Healthcare professionals** become **more efficient** in managing daily duties while improving **quality of patient care.**

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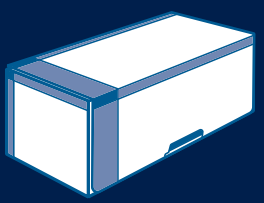
Maximising Efficiencies

Delivering Patient Care



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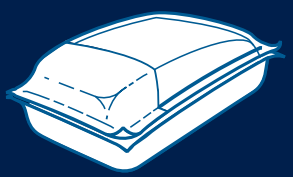

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From Flu Season to Fusion Season

Last flu season, molecular diagnostic labs across Europe switched their diagnostic instruments to Hologic's Panther Fusion™ system. The scientists who made the change tell their stories.

Meeting the Challenge

A long flu season with multiple strains of influenza heightens pressures and increases specimen numbers for virology labs. Ease of diagnostic use is crucial for dealing with a busy flu season, and the Panther Fusion system has proven capacity to deliver, with fast turnaround times as well as random and continuous access to samples and reagents.

Dr Albert Heim, from the Institute of Virology at the Hannover Medical University, started using the Panther Fusion system in December 2017, explains his reasons for switching to using the Panther Fusion system as their sole instrument for respiratory virus testing: **"We wanted a random access machine because it greatly reduces turnaround time between sampling and report of the result compared to batch testing. Currently the Panther Fusion system is one of the very few machines that has this option."**

Also in December 2017, the Medical Microbiology laboratory at Jeroen Bosch Ziekenhuis, Netherlands, adopted the Panther Fusion system in place of their previous molecular diagnostics instrument. Jeroen Schellekens BSc. wanted high throughput and random access capabilities after a limiting capacity of only 24 samples proved unproductive. **"It was very welcome to our lab. Random access and hands-on times of only 2 minutes per sample are great advantages,"** Mr Schellekens, a key user of the Panther Fusion system in the Jeroen Bosch Hospital, observes.

In October 2017, labopart - Medizinische Laboratorien in Dresden, Germany, made the decision to change their molecular platform from r-BioPharm-Assays to the Panther Fusion system with the Panther Fusion Influenza A/B/RSV assay by Hologic. **"The switching process was relatively easy, and it's very convenient to use,"** describes Dr Thomas Zimmermann, Head of Molecular Biology at the Medizinische Laboratorien Dresden.

Anne Kailow, Department Biomedical Laboratory Scientist at Herlev and Gentofte Hospital, Denmark, and her team analysed 11,000 respiratory samples from October 2017 to April 2018 using the Panther Fusion Influenza A/B/RSV assay on the Panther Fusion system. **"It was very easy to learn and use. Our technicians new to the Panther® system had five days training and after that they were capable, whilst our experienced Panther users had just two days training,"** Mrs Kailow says on adopting the Panther Fusion system for last year's flu season.

> *Dr Heim recalls his experience with testing growing sample numbers with the Panther Fusion system:*
>
> **We had a very rough influenza B season last year and we tested about 4,000 specimens for Flu and RSV, which is roughly twice the number we had to test the year before. It was easily achievable with the Panther Fusion system; without extra personnel and without stress."**

Excellent Assay Performance

Performance is key to any molecular diagnostics assay and instrument to ensure reliability of every result. Regarding the Panther Fusion Influenza A/B/RSV assay performance on the Panther Fusion system, Dr Zimmermann states: **"It is, in my opinion, very good. We can trust the results."** Dr Heim also praises the performance of the Panther Fusion Influenza A/B/RSV assay on the Panther Fusion system. After comparing 1,500 samples from the 2016/2017 flu season with an assay developed in-house by the Robert Koch Institute, he concludes: **"The performance of the Flu/Respiratory assay on the Panther Fusion system is excellent. Concordance was 98.4% after initial testing, and 99.4% after re-testing."**

In the Herlev laboratory, the Flu/Respiratory assay was validated to have an improved performance on their previous method. **"We will need further testing by sequencing before we can say for sure, but our initial testing found improved sensitivity and specificity compared with the method we used before, so that's really great,"** says Mrs Kailow.

Be Ready

With a broad Flu/Respiratory menu on a single molecular instrument, the Panther Fusion system has the capability to run increasing specimen numbers for a wide range of respiratory viruses, with no addition to workload. Dr Heim believes the Panther Fusion system managed the influx of respiratory samples during the 2017/2018 flu season, without needing additional technician support: **"In spite of growing numbers of specimens, we can use the same number of personnel."**

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RSV, respiratory syncytial virus.

On the paper trail

Researchers from Eindhoven University of Technology in the Netherlands and Japan's Keio University have developed a glow-in-the-dark paper strip for quick detection of infectious diseases. **Maarten Merkx**, a researcher from Eindhoven University of Technology, talks to Abi Millar about the potential of this technology to provide cost-effective and efficient diagnosis.

Testing for infectious diseases is often a drawn-out process. Generally speaking, it involves an expensive laboratory test, which may have a relatively slow turnaround time and require sophisticated equipment.

Clearly this isn't ideal for patients who want a quick diagnosis, or for the doctors seeking to treat them. To use just one example, a doctor may prescribe antibiotics to a patient with a suspected bacterial infection. If, further down the line, it transpires the infection was actually viral, that antibiotic prescription will have been useless or even harmful. It would be helpful to get a diagnosis on the spot.

Then there's the fact that lab tests aren't always feasible in low-resource settings. Particularly in developing countries, there is a need for cheap point-of-care testing that can diagnose infections quickly and help control their spread.

"In the developing world, the infrastructure is not in place, so there's a general need to develop cheap and quick assays," says Professor Maarten Merkx of the

Department of Biomedical Engineering at the Eindhoven University of Technology (TU/e). "In the area of point-of-care diagnostic assays, there have obviously been a number of developments, the most well-known being glucose testing and pregnancy tests. Commercially, glucose testing is very successful, but the principle behind glucose sensing is not suitable for infectious diseases. The laminar flow immunoassay used in pregnancy tests can be used to detect antibodies, but is not very sensitive and ill-suited for quantitative measurements."

As leader of the Protein Engineering research group at TU/e, Merkx is interested in developing new techniques for point-of-care diagnostics. His lab focuses predominantly on protein-based switches, some of which are designed for detecting antibodies.

Most recently, his team announced they had developed a radically new way of testing for infectious diseases. Together with a group led by Professor Daniel Citterio at Keio University in Japan, they have created a quick, cheap technology that can diagnose an infection within 20 minutes.

"We developed a sensor protein here in Eindhoven, and then together with our collaborators in Japan; we integrated the sensor protein into a paper-based device," says Merkx. "All you need to do is apply a drop of blood, and then everything happens within the paper strip."

Wait and see

The device is striking in its simplicity. After the blood has been applied, you wait 20 minutes before turning the paper over. Its underside will emit a blue-green light, which will be bluer or greener depending on how many antibodies are present in the blood.

"The device is basically like a traffic light that produces either green light or blue light," says Merkx. "It produces green light in the absence of a specific antibody, but if the sensor protein recognises that antibody, it changes its structure and emits blue light."

The test, then, is not only capable of determining the presence of a given antibody – it's capable of determining the concentration of those antibodies. A digital camera (for example, from a smartphone) can be used to determine the exact colour.

"Since our sensor always produces green and blue light, we don't look at the intensity of the signal, or how much light is produced, but rather the ratio between those two colours," says Merkx. "The ratio is a measure of the antibody concentration, meaning it's much easier to measure quantitatively."

As he explains, the sensor within the device is a 'bioluminescence protein' – a protein that can generate photons and essentially makes the device glow in the dark. It relies on an enzyme known as luciferase, which is also the enzyme responsible for lighting up fireflies.

"In the presence of a substrate molecule, the enzyme catalyses a chemical reaction and in the process generates light," says Merkx. "In this case, the luciferase itself generates blue light."

In the absence of an antibody, a second step takes place in which the energy of the blue light is transferred to a green fluorescent domain, and green light is produced. However, if there are antibodies in the blood, they will bind to the sensor protein and block that second step, meaning the light stays blue.

"Our technology is very generic, so it could be used to develop sensor proteins for any antibody and therefore, in principle, also any infectious disease."

As for the paper strip itself, this consists of three layers. On the bottom layer, there are three different compartments, patterned out with wax.

"In each of these compartments we can introduce a sensor protein, so it can be three sensor proteins for three antibodies," says Merkx. "Then on top of that there's a second layer of paper – it's just ordinary filter paper – that contains the substrate. This is the organic molecule that our sensor will oxidise to generate light."

The top layer, he says, is a filter used to separate the blood. It retains the red and white blood cells, allowing the plasma (including any antibodies) to flow through into the layers below.

"The bottom has a plastic lamination, and on the top there's a hole," says Merkx. "So if you apply a drop of blood, the blood will be sucked into the paper. The blood cells will be retained because they cannot go through the first layer, but the rest of the plasma will go to the second layer where it dissolves the substrate molecules. Finally, it will end up in the bottom where the sensor proteins are." ▶

Left: Maarten Merkx holds up the glow-in-the-dark strip.

Below: The rapid paper test gets under way.

20 minutes

The time it takes to diagnose patients using the new paper strip test.
TU/e

The bottom layer now contains a substrate, the bioluminescent sensor proteins, and the antibody (if present). After 10 to 20 minutes, you flip the device over and take a photo of the light that's produced.

"What is important here is you don't have to do any of the handling steps that you would typically do with other assays," says Merkx. "A drop of blood is sufficient, as the exact amount of blood you apply does not affect the assay. All the other steps – the separation of the cells, the mixing of the substrate molecule – happen automatically in this paper."

It's important to mention that the technologies being applied here aren't entirely new. Devices of this kind – microfluidic paper-based analytical devices – have received increasing attention in the past 10–15 years. However, Merkx' prototype has several important advantages over its predecessors.

For starters, many of these earlier assays gave a simple yes/no answer – they were able to determine the presence of antibodies or other analytics, but not their concentration. They also required an external light source.

"What's attractive about the combination we have here is that our sensor is based on bioluminescence, so the sensor itself produces photons and you don't need to illuminate it," says Merkx.

From the beginning

In their prototype, Merkx's team successfully tested for three antibodies at the same time. Beginning with blood serum from a pig, and then with whole blood, they spiked the sample with antibodies against HIV, flu and dengue fever. The test worked well, in that the blueness or greenness of the light corresponded with the concentration of antibodies.

"In this proof of principle, we demonstrated that we've developed sensors that are specific for three different antibodies," says Merkx. "Our technology is very generic, so it could be used to develop sensor proteins for any antibody and therefore, in principle, also any infectious disease."

In order to do so, you would need information about what kind of antibodies are produced in response to an infection, along with a peptide sequence that can be used for antibody recognition.

"If you have that, you can generate a specific sensor," says Merkx. "But there is another caveat, which is the heterogeneity in the kinds of antibodies the immune system will produce in different people in response to a specific infection. You probably need to develop a panel of sensors that target slightly different antibodies, so that you're covered."

A device of this nature would be invaluable within the developing world, particularly when it comes to detecting tropical diseases. You could take it into a community setting, and diagnose patients within 20 minutes. Currently, the researchers are focusing on making the device more stable and reliable, so that it's suitable for use in these conditions.

"Ideally we'd like to have devices you can keep for months and they would still work, and so we make sure that all the components are stable," says Merkx. "If you have a device that's only stable where you store it frozen or in the fridge, that makes it less suitable for point-of-care diagnostics."

The potential, however, does not end there. As Merkx explains, the technology might also be used to monitor the dosage of therapeutic antibodies that patients receive; for example, within oncology or inflammatory diseases. "Many of the drugs that are being developed today are not small molecule drugs but antibodies," he says. "All patients basically get the same dose of these therapeutic antibodies even though it's known that different patients respond differently to them. In some patients, they are cleared very quickly and in others they stick around for a longer time. It would be useful if there were a test to ensure everyone received the right dose."

In fact, he thinks this application might be the first to be commercialised. While the device has many potential uses, it really comes down to finding a gap in the market – something for which either no equivalent technology exists, or for which current technologies are too expensive and aren't being applied. Currently, his team is looking to create a start-up company, which will work on developing the technology outside the academic labs.

"I don't think this technology will replace all the immunoassays that are being used in clinical chemistry laboratories," says Merkx. "These laboratories are highly automated, and can do multiple tests all using the same technologies. So I think it'll be most successful being used in applications where assays are not currently being done."

Although he thinks it will take a number of years before the device is fully commercialised, his team are making real strides in that direction. They are working to create different sensor proteins for different antibodies, and ultimately want to measure other types of biomarkers too.

The next step will be to take real patient samples and compare the performance of the assay to the current gold standard (laboratory assays, for example). They are hoping the device will provide a similar level of accuracy to what's out there already, helping pave the path towards commercialisation.

"These technologies are quite novel and different from classical immunoassays," says Merkx. "We think they will be suitable for use in resource-limited areas, or for monitoring therapeutic antibodies on a patient-specific basis – those are where the best chances are."

Molecular techniques to detect pathogens

CerTest Biotec is dedicated to the identification of infection-causing pathogens, and has embraced molecular techniques to efficiently and accurately detect multiple pathogens in a single sample.

Respiratory and gastrointestinal infections are among the top 10 causes of death in the world and have remained one of the leading causes of death globally in the past 15 years.

Respiratory infections caused three million deaths worldwide in 2016. The number of deaths from diarrhoeal diseases was 1.4 million in 2016. Similarly, tuberculosis is still among the top 10 causes of death, with a death toll of 1.3 million.

Identifying the pathogens causing the infections is one of the most important means for treatment and for the reduction of preventable deaths. Additionally, it enables a country's health system to be assessed and the focus of its public health actions to be determined.

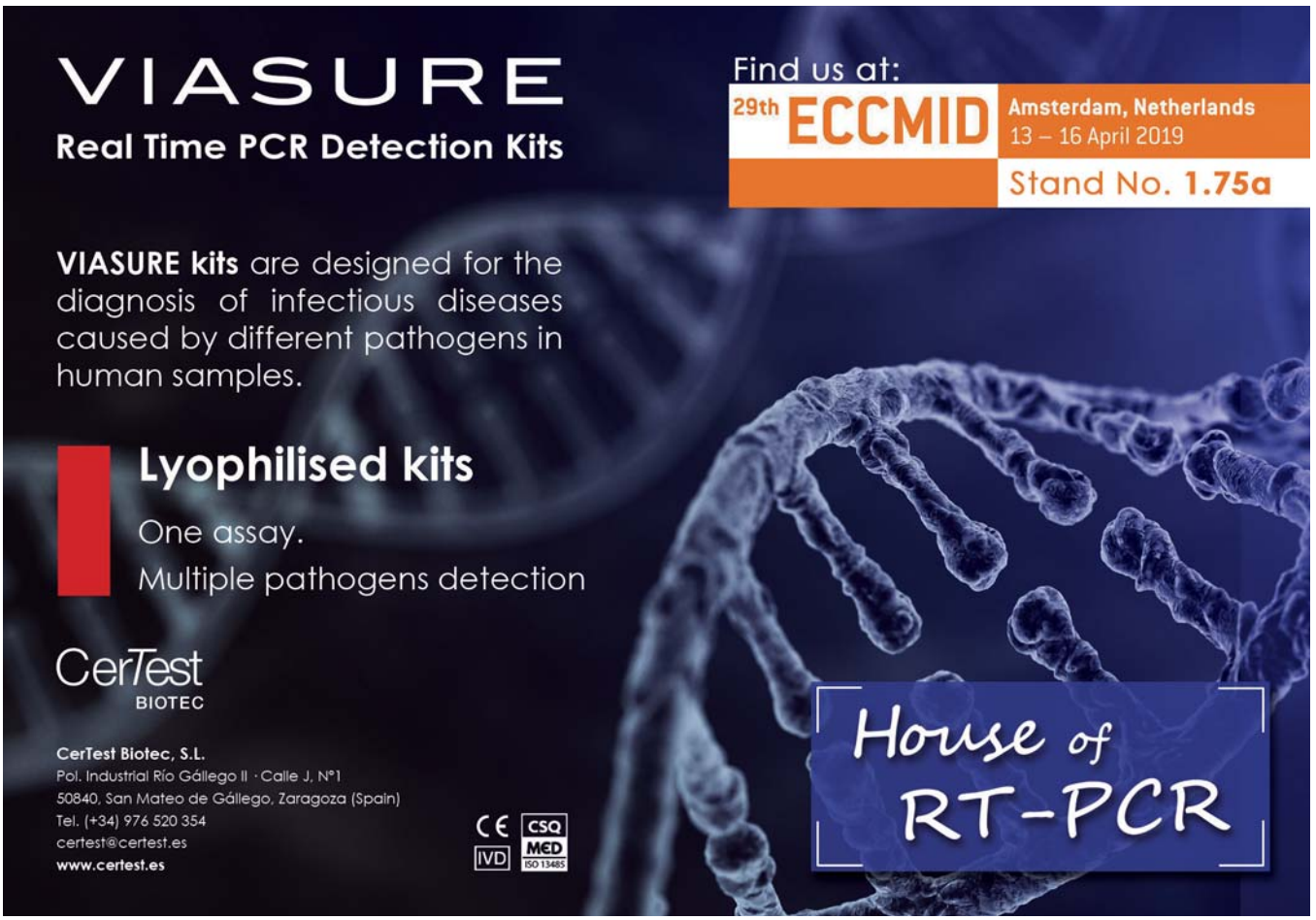
Identification techniques

Molecular techniques such as Real Time PCR are high-sensitivity and specificity techniques that enable identification of the etiological agent in a short period of time. The VIASURE Real Time PCR kit is in a lyophilised format that is ready for use. Its high stability and resistance to high temperatures allows transport and storage at room temperature for a long time, avoiding the use of a network set-up and ensuring the maintenance of the cold chain, as well as high reproducibility of the results due to the absence of extra pipetting.

VIASURE Real Time PCR kits are designed to detect multiple pathogens in a single sample, depending on the area and public health situation. Their high portfolio of products and flexibility of use allow the kits to be adapted for the diagnosis of different infectious diseases, helping to monitor the effectiveness of the therapeutic treatment and assisting in clinical decision-making.

For further information

www.certest.es



Improved diagnostics

Designed for the patient and optimised for the lab, **GenMark Diagnostics**' new ePlex system is the first truly integrated sample-to-answer solution for clinical diagnostics. Dr Julie A Ribes and Dr Vaneet Arora, directors of clinical microbiology at University of Kentucky HealthCare, an associated hospital system in Lexington, have recently tested the system, and they share their conclusions with us.

What benefits have you found from using ePlex blood culture identification panels over traditional diagnostic methods?

Dr Julie A Ribes: The ePlex panels have superior inclusivity compared with the panel we are currently phasing out. The Gram-negative (GN) coverage is particularly outstanding. During our head-to-head comparison of ePlex to our current blood culture identification (BCID) system, there was more than a 30% increase in pathogen detection. The ePlex detected 43 true positive results compared to only 29 by our other method. For the Gram-positive (GP) panel, ePlex detected an additional 13 true positive results above our current method, for an increase of 9% in rapid detection.

UK Healthcare caters to a large intravenous drug-using population, and we have a relatively large number of patients with unusual organisms in their blood as a result. During our evaluation, we had three *Serratia* spp, three *Stenotrophomonas maltophilia*, one *Morganella morganii*, and even a *Fusobacterium necrophorum* detected by the ePlex and culture, but not by the rapid microarray method. Historically, our pharmacy doctors (PharmDs) have requested more rapid identification for *Serratia* spp and have asked us to perform additional molecular testing if a Gram-negative organism was seen on Gram stain, but not identified by our primary BCID. The ePlex will take away this redundant testing and delay in turn-around-time for detection.

The ePlex pan-Gram-negative and pan-Gram-positive analyses are also helpful. We had several instances where these were positive, but the Gram-stain morphology had not been recognised initially, particularly with mixed cultures.

GenMark's new ePlex system offers notably greater Gram-negative and positive detection than previous panels.

Can you describe the ePlex user experience? How does it help to prevent errors and ensure patient safety?

Dr Vaneet Arora: The ePlex system is true walk-away technology with an intuitive process. First, the positive blood culture bottle is processed under the biological safety cabinet to remove an aliquot to a labelled tube, prepare the Gram stain and plate the cultures. The appropriate ePlex panel is then selected based on the Gram-stain characteristics of the organisms seen. Patient and specimen identification are barcode driven, so the test results are linked to the specific patient being tested. The cartridge is scanned for definitive patient and panel identification, and is then inserted into the instrument, and the tech walks away as testing proceeds. The instrument's interface allows for the test results to be uploaded directly for reporting into the electronic medical record.

Our current instrument has several phases of testing, and resulting is all manual. This has been a significant cause of error over time and is another major reason why we are replacing the current platform.

How does ePlex compare with or fit in with your organisation's standard of care methodologies? Has it impacted how you think about standard of care for blood sampling and diagnosis?

VA: Our PharmDs are clamouring for a more comprehensive panel for reporting blood culture results. Our current panel was brought in with the understanding that all molecular blood culture results would be reported to a PharmD 24/7 so that antimicrobial administration could be optimised to better support patient care. The ePlex system with its more extensive coverage will allow for a more robust intervention, especially for GNs like *Serratia* and *Stenotrophomonas*, which we see so commonly in our patients. The Fungal Panel – which we are still evaluating – also promises to be an excellent addition to our current testing platform, which is quite limited in comparison.

How has ePlex improved or aided your antimicrobial stewardship efforts?

VA: UK HealthCare is already at the cutting edge of antimicrobial stewardship. Having the ePlex panels will better allow our PharmDs and the clinical care teams to manage patients, and to either escalate or de-escalate antimicrobials more efficiently. This is the ultimate goal in switching platforms.

In our evaluation, the ePlex results would have decreased turnaround times by 24 hours for antimicrobial optimisation in at least eight patients using the Gram-negative panel. We are anxious to make this switch to ePlex for rapid BCID testing. ●

For further information

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Integrated microbiology for better patient care

The success of any clinical microbiology laboratory is defined by its ability to accurately and rapidly test samples and report results to the medical team. Dr Danielle Brabant-Kirwan, a clinical microbiologist at Health Sciences North (HSN), talks about how **bioMérieux**'s integrated solutions are helping the lab make a greater positive impact on antimicrobial stewardship and patient care.

Microbiology labs are an integral part of healthcare systems faced with challenges including bloodstream infections, sepsis and multidrug-resistant organisms. Providing reliable results in the minimum amount of time is crucial. Like many labs today, Health Sciences North (HSN), in Sudbury, Canada, needed a means to refine its approach in this ever-more challenging healthcare environment.

Dr Danielle Brabant-Kirwan, clinical microbiologist at Health Sciences North (HSN), explains that to improve efficiency and workflow for identification (ID) and antimicrobial susceptibility testing (AST), and blood culture, HSN selected an integrated solution from bioMérieux, based on three platforms: BACT/ALERT VIRTUO for blood culture microbial detection; VITEK MS for microbial identification based on mass spectrometry; and VITEK 2 for antimicrobial susceptibility testing. These are complemented with powerful middleware, MYLA.

"We've considerably reduced the time it takes to report ID and AST as well as negative blood cultures. We have been able to reallocate our resources, increase productivity and extend our in-house testing menu."

"We've considerably reduced the time it takes to report ID and AST, as well as negative blood cultures," says Brabant-Kirwan. "We have been able to reallocate our resources, increase productivity and extend our in-house testing menu."

Lab efficiency improves care

"Our average time to detection from the VIRTUO is 19.28 hours," says Brabant-Kirwan, an improvement of 4.8 hours over the previous system. "As a fully automated system, VIRTUO has also reduced labour-intensive hands-on steps and facilitated high-quality reports."

Brabant-Kirwan says the lab now relies heavily on VITEK MS for identification. With a much more extensive database than the previous solution, covering most routine clinical isolates, it has greatlt decreased the number of additional tests needed. For the most difficult organisms, she notes, that can mean two to four days faster identification.

AST workflow is also significantly improved with VITEK 2. "VITEK 2's validation and reporting software programs are well designed and user-friendly," says Brabant-Kirwan. "And quality is enhanced. Technicians really appreciate the extra layer of comfort using the validation software to recognise inconsistent antibiotic profiles."

The flexible middleware solution, MYLA, is designed specifically for microbiology labs. "I have all the information from multiple instruments flowing into one intuitive, web-accessible software. I can customise and generate reports in minutes, or have them on a schedule. This is key to being more efficient. It saves time and improves quality," says Brabant-Kirwan.

"The overall integrated system has improved our turnaround time (TAT) metrics," she adds. Total time savings for identification of an organism in a blood culture is, on average, 24 hours faster and susceptibility reporting is approximately 10 hours faster.

"This is very significant when considering the importance of time to appropriate antibiotics for surviving sepsis," explains Brabant-Kirwan. "Alerting the physician that their patient's blood cultures are positive several hours earlier than what could previously be achieved can greatly improve patient care outcomes. Proper antibiotics can be administered in a timely fashion and then appropriately de-escalated."

Actionable information for antimicrobial stewardship

HSN's Antimicrobial Stewardship Program (ASP) has antibiotic cascades with very limited antibiotics being released as a first line to ensure responsible antibiotic use. The VITEK 2 software enables custom rules to help technicians confidently report appropriate antibiotics. "Strategic and selective culture and AST reporting, along with interpretative comments, helps clinicians better understand the culture results for proper antimicrobial prescribing," says Brabant-Kirwan.

As a member of HSN's ASP committee, Brabant-Kirwan recognises MYLA's impact for these needs as well. "We do a lot of data mining to be proactive in identifying trends and resistance patterns in bacteria," she says. "We need to provide feedback to antibiotic stewardship committees, infection prevention and control, and our physicians, and epidemiology reports to provincial and national surveillance programmes."

The services, training and consultancy by bioMérieux have further enhanced HSN's capabilities and workflow. For Brabant-Kirwan, it is about relationships, "With a single company and integrated solution, you work very closely and develop a good working relationship. There's a level of trust that develops."

For further information

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Break down carbapenem-resistant Enterobacterales

Carbapenem-resistant Enterobacterales are a major global health risk, as they are becoming increasingly immune to a wide variety of antibiotics. We talk to Dr Axel Hamprecht, from the Institute for Medical Microbiology, Immunology and Hygiene at Cologne University Hospital, about combatting the problem with **GenePOC** and their innovative revogene system.

Could you briefly tell us about the carbapenem-resistant Enterobacterales (CRE)?

Dr Axel Hamprecht: Enterobacterales are common Gram-negative bacteria, such as *E. coli* or *Klebsiella pneumonia*. Although they are typically found in the gut, they can cause serious infections, such as sepsis, urinary tract infection or pneumonia.

Enterobacterales can usually be treated with beta-lactam antibiotics, such as penicillins or cephalosporins. Last resort antibiotics are called carbapenems, but increasingly carbapenem-resistant strains are growing. These strains are called carbapenem-resistant Enterobacterales (CRE) and most commonly, the carbapenems are inactivated by enzymes called carbapenemases, or carbapenemase-producing Enterobacterales (CPE).

The most common carbapenemases are OXA-48, KPC, NDM, VIM and IMP. They are prevalent in places such as India, China, Greece, Italy and some parts of the US, but less active in Northern Europe. Infections with CPE are difficult to treat, and with few – if any – antibiotics remaining active, fatalities in severe infections are high. Because of the increasing numbers of CPE and other resistant organisms, the worrying possibility of a post-antibiotic era has been postulated.

Who are the patients at risk of carriage and/or infection with CRE?

There are different guidelines by the CDC, ECDC and WHO on the prevention of CRE dissemination.

Patients who have stayed in healthcare facilities in the past 12 months are most at risk, especially in high-prevalence regions. Additionally, other risk factors are previous antibiotic therapy, travel to high-risk countries, previous carriage of CRE in the past 12 months and epidemiological linkage to a known carrier of a CRE.

How can you test or detect for CRE carriage or infection?

There are many different ways to detect CREs – most rely on bacterial cultures. Usually, isolates with resistance or elevated minimal inhibitory concentrations for carbapenems are further analysed for carbapenemases. This can be done through different methods – for example, phenotypic disk tests, colorimetric tests, PCR, MALDI-TOF or immunochromatographic tests. Not all tests work equally well and some carbapenemases (such as OXA-48) are more difficult to detect than others.

PCR is considered the gold standard for the confirmation of carbapenemases, but it is expensive and not always readily available. The relatively new immunochromatographic assays work very well for confirmation of carbapenemase production and are very fast.

The reservoir for CRE is the gastrointestinal tract. For screening of patients, stool samples or rectal swabs are therefore used, which are inoculated on special agar plates for CRE detection. If any CRE is detected, this is usually investigated further (for the type of carbapenemase, using the previously mentioned tests, for example).

Why choose to use molecular testing to identify CRE carriage and/or infection?

The problem with bacterial culture is that it takes a relatively long time to detect – usually 24–72 hours. Molecular tests can be done directly from clinical specimens and most CRE can be detected in less than two hours. Additionally, the different types of carbapenemases can be differentiated, which is helpful especially in outbreak situations. Furthermore, strains that produce more than one carbapenemase can be detected more reliably.

How was your experience with GenePOC and its revogene system?

We have tested a large collection of 176 clinical isolates, including 133 CPE isolates, which produced 139 carbapenemases of 40 different types. All carbapenemases were correctly detected, even some rare variants belonging to the IMP type, which are missed with most other systems currently available. The revogene system was fast and easy to use, with results available within 70–80 minutes.

Do you think it is time to fight against CRE globally?

Absolutely – the need to fight CRE has been recognised by most health organisations. WHO recommends further research on antibiotics especially against CRE. Recently, the topic of increased antibiotic resistance has made it to the top of global political agenda. Shortly after the G7 summit, the Berlin Declaration on Antimicrobial Resistance was agreed in 2015. The declaration recognises antimicrobial resistance (AMR) as a serious global threat to public health that requires immediate concerted global action. Nevertheless, the knowledge of healthcare professionals on CRE needs to be improved and further research on detection, prevention and treatment of CRE infections is needed. ●

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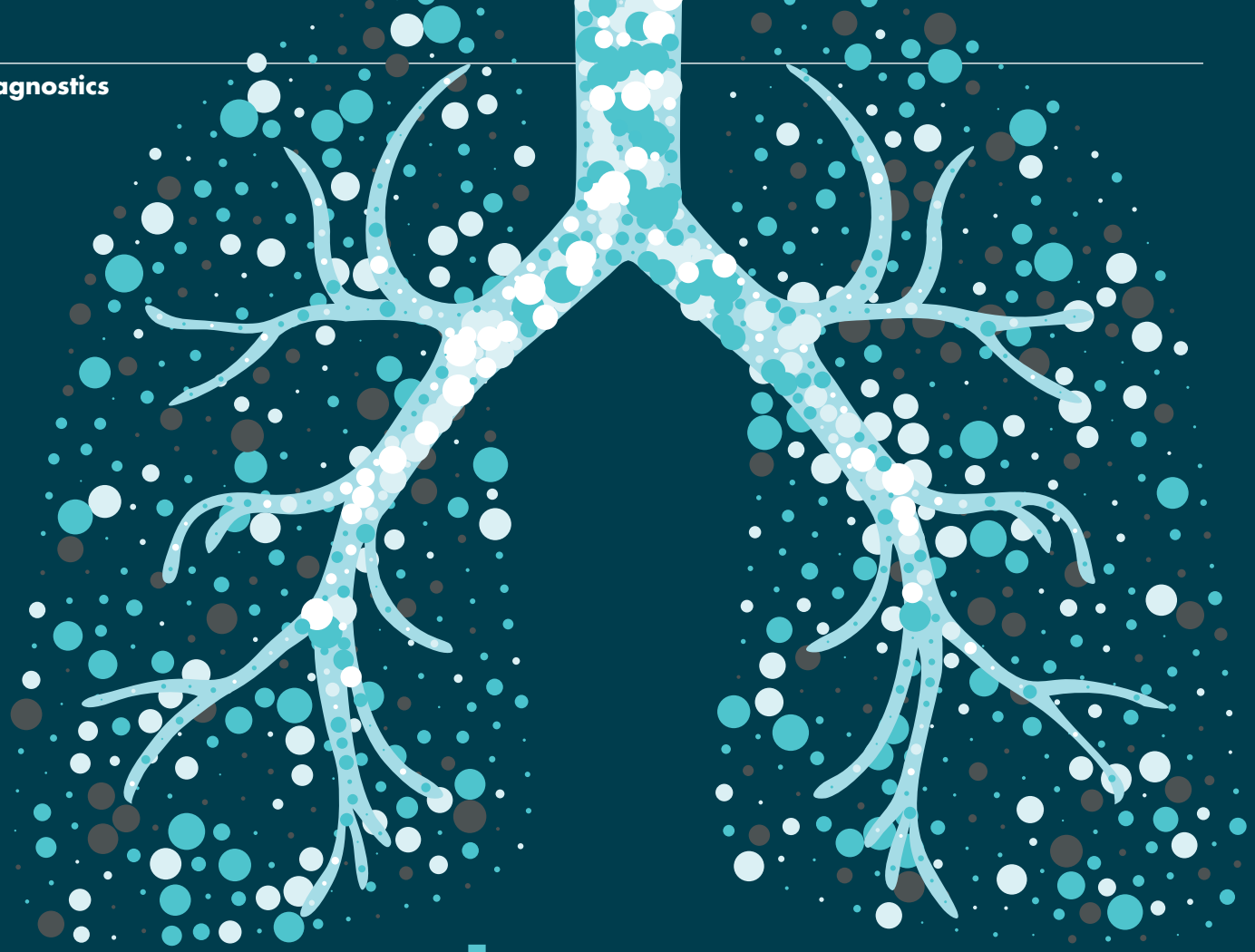


The TB balancing act

TB remains a public health issue in developing nations, partly due to the lack of adequate diagnostic testing facilities. Is molecular detection – faster and simpler than conventional tests – the answer? Kim Thomas speaks to health economist **Hassan Haghparast-Bidgoli** about the benefits and challenges.

An infectious disease caused by *Mycobacterium tuberculosis* (MTB), TB still claims the lives of 1.6 million people every year worldwide, while approximately 10 million people in total become ill with the disease. Symptoms include coughing with sputum and blood, chest pains, weight loss and fever.

Most infections occur in developing countries in Asia and Africa: in 2017, 87% of new TB cases occurred in the 30 high-burden TB countries, while eight countries (India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa) accounted for two thirds of new cases. India alone is home to 27% of all TB cases worldwide. It's a disease that poses a particular risk to people infected with HIV; about 300,000 of TB deaths are in people who are HIV-positive. Most of these HIV-positive deaths take place in sub-Saharan Africa.

Hassan Haghparast-Bidgoli is a principal research fellow at the Institute for Global Health, University College London. His main area of work involves analysing inequalities in health and healthcare, and in the economic evaluation of

healthcare interventions. One of the areas he has looked at is the question of the most cost-effective approaches to diagnosing and treating TB.

Drug resistance is hampering progress

There are three strains of TB, says Haghparast-Bidgoli – TB that is not resistant to any drugs, multiple-drug-resistant (MDR) TB (which is resistant to both rifampin and isoniazid, the two first-line antibiotic drugs) and extensively drug-resistant (XDR) TB, which is resistant, not only to the first-line drugs, but to Fluoroquinolone antibiotics and at least one of the injectable second-line drugs. While the XDR strain is still quite rare, the emergence of the MDR strain has hampered progress in treating the disease. In 2017, there were 558,000 new TB cases resistant to rifampin, the most effective first-line drug.

Drug resistance is a major cause for concern, according to Haghparast-Bidgoli. "The drug-resistant strain is increasing in a lot of countries," he says. "Because of this it's very important to develop new technologies for faster and more accurate diagnosis, and also better treatment."

Worldwide, only 55% of MDR-TB patients are treated successfully. One of the causes of drug-resistant varieties of TB is patients with drug-responsive TB failing to complete the course – a problem that arises because treatment for TB is usually lengthy and involves more than one drug. The problem of drug resistance is greater in high-burden countries.

There have long been efforts to stamp out the disease. The 1970s saw the development of the directly observed treatment, short-course (DOTS) strategy, which aimed to standardise treatment, and record and measure outcomes. A major step forward came in 2014 with the publication by the World Health Organisation (WHO) of its End TB Strategy, which set a target of reducing deaths from TB by 95%, and incidence of TB by 90%, between 2015 and 2035. A third target stated that no TB-affected households should experience catastrophic costs due to the disease by 2020.

These are ambitious goals, and so the strategy takes a three-pronged approach to meeting them: integrated patient-centred care and prevention; bold policies and supportive systems; and intensified research and innovation. Currently the incidence of TB is falling at about 2% a year, but that needs to accelerate if the targets are to be met. That will involve improving patients' access to diagnosis, and the quality of diagnosis, as well as scaling up interventions to reduce some of the risk factors for TB (such as smoking, alcohol consumption and diabetes), and integrating control programmes for TB and HIV.

Traditional diagnostic techniques are far from perfect

When it comes to making a diagnosis, as with any disease, there are two important factors. One is the sensitivity of the test – how good it is at accurately diagnosing who has the disease. The other is the specificity – the ability of the test to identify those without the disease. If a patient is diagnosed by a test with low sensitivity, they might be wrongly identified as having the disease. "You give them incorrect treatment and it is not effective for them," Haghparast-Bidgoli says. "That can change the outcome and there can be side effects for the patients."

Traditionally, TB has been diagnosed by two separate methods, both far from perfect. One involves culturing the bacteria from sputum samples – this is highly accurate, but involves waiting several weeks before a diagnosis is reached. The other, more widely used method, smear microscopy, is to take sputum samples and look at them under a microscope to see if TB bacteria are present. Although this is a relatively speedy method of diagnosis, it is effective at detecting only half the number of cases, and it cannot identify whether the sample is from a drug-resistant strain. (Sometimes chest X-rays are used to confirm the diagnosis.)

More recently, however, molecular detection methods have been developed. These include the nucleic acid amplification test (NAAT) and whole-genome sequencing (WGS). An NAAT works by looking for the TB bacterium's DNA markers in a sputum sample, while WGS involves sequencing the whole genome of the TB bacterium. In both cases, diagnosis is rapid, and both tests can diagnose rifampin resistance. WGS is too expensive for use in most high-burden countries, however.

Lengthy treatment affects a patient's livelihood; typically, treatment for TB that is receptive to drugs involves a six-month course of medication (usually a combination of four antimicrobial drugs), and the patient doesn't need to be in hospital. Treatment for MDR-TB, however, is expensive and usually involves hospitalisation – in some countries, for up to 24 months. Because of the loss of income from work, the economic impact for the patient and their family can be substantial.

Governments are working all the time to improve treatment modalities. "Some countries are very good – they have substantially improved their treatment and the control of TB," explains Haghparast-Bidgoli.

The advantage of using NAAT and WGS detection is that faster diagnosis means faster treatment, Haghparast-Bidgoli explains. "If the patient is infectious they transmit the disease to other people," he says. "A rapid diagnosis test means you can put

Hassan Haghparast-Bidgoli

1.6 million

The number of people who die of tuberculosis each year globally.
WHO

$2,621
The average cost of installing Xpert in Nigeria.

$7,000
The cost for sites requiring additional space for installation.
The Pan African Medical Journal

them in isolation, and reduce the risk of others becoming infected." It also makes it easier to achieve successful contact tracing. The test's ability to identify the MDR strain means that patients can be given appropriate treatment immediately, reducing the likelihood of transmission and also reducing the amount of treatment needed. "All this can be translated into cost saving," he says.

Haghparast-Bidgoli has examined the research into whether using Xpert (also known as GeneXpert), a cartridge-based NAAT, for diagnosis is cost-effective. Xpert, which has been endorsed by WHO for use in TB-endemic countries, is an automated system – the chemicals needed to interact with the sputum sample are contained in a cartridge, which is then inserted into a machine that provides an accurate result within two hours. Xpert also identifies whether the strain of TB is resistant to rifampin. A study of 29 high-burden countries by the Stop TB partnership in 2017, however, found that only 15 had adopted a policy of 'Xpert for all' and of them only seven had widely implemented the test.

Is the gain worth the cost?

Evidence on cost, cost-effectiveness and affordability are important for decision-makers, says Haghparast-Bidgoli. It is not simply a question of whether a particular method of diagnosis achieves better results but whether the health gain is worth the additional cost – or, alternatively, whether a cost saving is worth the additional health loss. In the case of Xpert, the question was whether incorporating it as a diagnostic method would be cost-effective compared with the traditional methods of sputum microscopy and culture.

Cost-effective analysis (CEA) models had predicted that Xpert would be cost-effective, either through a reduction in TB-related mortality, or a reduction in overtreatment, or both, in a wide range of settings.

The cost-effectiveness of a treatment is highly affected by context, Haghparast-Bidgoli points out. That context includes deployment capacity, the performance of current diagnostic algorithms, the cost of treatment regimens for TB and MDR-TB, the mode of implementation and the modelling approach used to assess cost-effectiveness. For example, in some countries the poor healthcare infrastructure means that the quality of the sputum sample is low. "You have to have high-quality sampling to use it for molecular testing," Haghparast-Bidgoli says. In order to improve diagnosis and treatment, it's important to regularly adapt diagnostic algorithms according to context.

Faster diagnosis is not always cost-effective

The major downside of using Xpert is that it is highly expensive. The machine to hold the cartridges costs thousands of dollars, and the individual cartridges, which are discarded after a single use, cost $10. It also requires a constant power supply and a cool environment – something that can be a problem in some rural clinics in developing countries.

In 2013, research was carried out into the use of the system in TB clinics in South Africa, Zimbabwe, Zambia and Tanzania, with patients randomly assigned to either Xpert or conventional testing. Surprisingly, the difference in outcomes for the two groups was negligible. This seems to have been because, rather than wait for the results in the group who were tested by conventional means, the clinic started treatment quite soon after admission. So the conclusion from the research was that Xpert was not a cost-effective solution – at least in those particular settings. In other settings, Haghparast-Bidgoli notes, the conclusion might be different.

In Nigeria, a high-burden country, research published in *The Pan African Medical Journal* in 2014 into the cost of installing Xpert found that the basic cost for installation was $2,621.98 per machine, rising to nearly $7,000 for sites that required additional space. The research concluded that space and power requirements have a "significant effect on installation costs" and that countries should carefully consider the placement of Xpert machines based on the quality and size of the available infrastructure.

Further research in Nigeria by Public Health Action in 2018 looked at the reliability of Xpert machines. It analysed 52,219 test results and found that 4.7% of the total number of results were invalid, 4.2% had error results and 2.1% had no result outcomes. The most frequent errors were technical, often as a result of poor adherence to standard operating procedures. There were also temperature-related errors in some parts of the country.

Generally, says Haghparast-Bidgoli, Xpert is being used in the high-burden countries, such as South Africa, India and China, because it is in those countries that it is most cost-effective. The test is also used in some low-burden countries, such as the UK. In those countries, it is less cost-effective, but in a well-resourced health system, the cost is less of an issue. In medium-burden countries, however, the cost of setting up the infrastructure for diagnosis means that use of Xpert is not cost-effective.

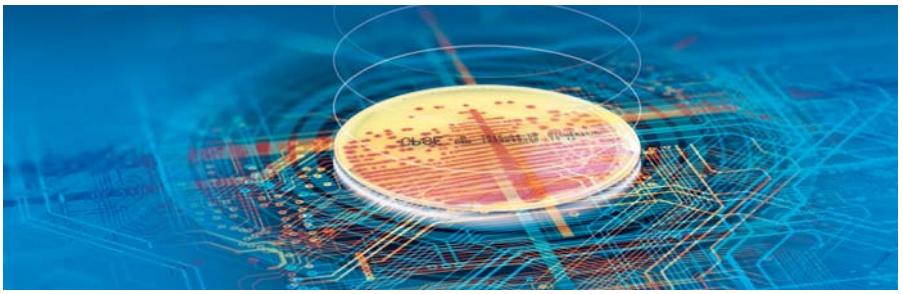
Therefore, it's important, he points out, that future investments in diagnostics by healthcare systems should reflect the uncertainty and additional costs of implementation constraints. Counter-intuitively, it's not necessarily the case that the speedier, more accurate method of diagnosis is the most appropriate choice in a particular setting. ●

Empowered through AI

In response to the technological advances transforming the medical industry, **bioMérieux** has launched PhenoMATRIX – an artificial intelligence processing solution that has made the total workflow of the microbiological sample faster, more accurate and more efficient, revolutionising the microlab in its wake.

Identifying and processing up to thousands of patient samples quickly and accurately is a pressing concern for microbiologists worldwide. In today's healthcare system, a speedy and accurate diagnosis is essential to patients waiting for results, while lab technicians are overworked and in short supply. Microbiologists, therefore, need assistance when it comes to juggling a heavy workload with the constant pressure to deliver accurate sample results.

Recently, diagnostic solutions providers have sought to address this problem by harnessing automation in microbiology, with the implementation of digital microbiology and sophisticated algorithms that can quantify and interpret organisms. This software gives microbiologists the ability to segregate and analyse bacterial cultures with the click of a button.



Diagnostic solutions providers like bioMérieux are harnessing automation in microbiology.

A productive partnership

Through the unique PhenoMATRIX software, which was developed by Copan, bioMérieux has successfully partnered with LaboSud, a clinical laboratory based on Montpellier, to implement WASPLab microbiology processing system.

Founded in 2009 as an influential part of the INOVIE group, LaboSud comprises more than 70 neighbourhood sites connected through specialised technical platforms. The structure continues to evolve by introducing innovative technologies that harness the latest scientific advances.

Empowered by bioMérieux, the state-of-the-art WASPLab processing solution was taken up by LaboSud in 2017, making it the first laboratory worldwide to have sophisticated artificial intelligence embedded in its microbiology processing solutions.

This advanced form of microbiological processing addresses all aspects of automated specimen processing – from planting and streaking to automated slide smear preparation and enrichment broth inoculation. It also automates incubation with one or more smart incubators, while plate reading is done with a high-quality image acquisition system and the easy-to-use WASPLab computer interface.

The introduction of PhenoMATRIX software in 2018 ushered in the next level of innovation. The software consolidates algorithm results with demographic patient data from the central lab information system (LIS), based on the lab's specified rules, which are entirely customisable. Plates are automatically discharged and sorted according to user-defined rules, meaning no plate handling is necessary. PhenoMATRIX also enables specific pathogen detection in chromogenic media such as CHROMID CPS Elite, as well as automatic enumeration.

Keeping track of images is easy, as they can be traced through the bidirectional connection with the central LIS and archived images on the main server. Reproducibility is improved through standardised streaking, enabling a good level of isolation for further testing needs. All negative plates are directly disposed of, and positives are automatically sorted and placed on racks designated for further tasks (such as identification or AST).

One of the main benefits that the PhenoMATRIX software system has had on LaboSud is that time spent reading plates and quantifying positive and negative results is significantly reduced. This means more samples can be processed through the laboratory – currently, LaboSud handles 1,400 samples a day, and are expecting to increase that figure to 1,750 before the end of the year, without additional staffing.

Over 80% of the laboratories routine urine test results can be reported with the click of a button. Overall safety has increased as there has been a significant reduction in plates or sample handling, lowering risk to technicians.

The accuracy of the laboratory has been greatly enhanced as the system quantifies and analyses data efficiently and impartially, eliminating the potential variability that can occur through human error.

"PhenoMATRIX software has had an immediate, positive impact on LaboSud. One of the main benefits of the system is that time spent reading plates and quantifying positive and negative results is significantly reduced."

PhenoMATRIX also allows technicians to narrow their focus on areas of clinical interest and prioritise certain samples over others, allowing staff to be used more efficiently and producing faster results for at-risk patients. The use of PhenoMATRIX software in laboratories will enable practitioners to be quicker, more accurate and more efficient. It could shape the future of microbiology in the coming years. ●

Copan is the legal manufacturer of PhenoMATRIX.

For further information

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The quality of treatment starts with diagnosis

DiaSorin Molecular manufactures and distributes molecular diagnostic products worldwide, helping laboratories to streamline workflow and improve patient management. The company is a vendor partner to hospitals and reference laboratories that provides value through high-quality products, service and support solutions. It believes that quality patient treatment begins with effective diagnosis of their illness and its products are designed to provide the most accurate diagnosis as quickly as possible.

DiaSorin Molecular is part of the DiaSorin Group, which is an Italian multinational company and a global leader in the market of in vitro diagnostics. For over 40 years, the group has been developing, producing and commercialising diagnostics tests for a wide range of clinical areas including paediatrics, oncology, women's health and infectious diseases.

Molecular detection kits for infectious diseases

In 2016, DiaSorin acquired the molecular business of Focus Diagnostics to expand into the molecular diagnostics market. The DiaSorin Molecular portfolio includes Simplexa kits for infectious disease, and more than 55 primer pairs and general purpose reagents. Most Simplexa kits are developed as direct assays, requiring no sample extraction and providing results in about an hour.

Simplexa products are designed for use on the LIAISON MDX, a real-time PCR instrument that has the capability of running either an 8-well or 96-well disc, providing an ideal platform to accommodate low and high-volume testing needs. This allows users to leverage the system's flexibility and scalability to handle most laboratory challenges.

The latest DiaSorin Molecular product to launch is the Simplexa Bordetella Direct kit, receiving CE marking and FDA clearance in 2017 and 2018 respectively. The assay allows for the detection and discrimination of *Bordetella pertussis* and *Bordetella parapertussis* directly from nasopharyngeal swabs in a range of sample transport media. It is a CLIA moderate complexity assay that improves efficiency with a true sample-to-answer workflow without DNA extraction in about an hour.

The importance of an accurate whooping cough diagnosis

Pertussis, commonly called whooping cough, is a highly contagious disease of the respiratory system caused by small Gram-negative bacteria, mainly *B. pertussis* and *B. parapertussis*. Clinically, it presents with a prolonged cough illness and patients often have episodes of violent coughing that may be followed by an inspiratory whoop.

"Pertussis can be detected among all age groups – neonates, children, adolescents and adults, and so on. However, it primarily affects children less than six months old with severe clinical symptoms that typically result in admission to intensive care units."

The World Health Organisation estimates that there are 50 million whooping cough cases worldwide each year, resulting in 350,000 deaths. Pertussis can be detected among all age groups – neonates, children, adolescents and adults, and so on. However, it primarily affects children less than six months old with severe clinical symptoms that typically result in admission to intensive care units. A great majority of these cases are caused by *B. pertussis* – however, up to 20% of cases are caused by *B. parapertussis*.

The LIAISON MDX with disc options – the 96-well Universal Disc and 8-well Direct Amplification Disc.

Molecular testing for *Bordetella* detection speeds up diagnosis by up to seven days after symptoms occur compared with culture testing, due to its faster turnaround time and higher sensitivity. Timely diagnosis guides antibiotic treatment that can mitigate symptoms and prevent transmission. This is especially critical for early diagnosis and treatment in patients less than three months old.

The Simplexa Bordetella Direct assay provides a quick and reliable result for early decision-making, treatment and improvement of patient care. DiaSorin Molecular also provides a comprehensive list of molecular diagnostic assays, including HSV, VZV, respiratory syncytial virus (RSV), influenza A&B, Group A *Streptococcus*, and Group B *Streptococcus*. ●

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New solution to increase sample throughput

Visual analysis of microbial samples is a crucial and time-intensive part of the work performed by medical microbiology laboratories around the world. Theo Liebregts, head of bacteriology at the PAMM laboratory in the Netherlands, talks about how its use of **Copan**'s WASPLab sample-processing solution, in combination with the PhenoMATRIX image recognition algorithm, promises to drastically increase sample throughput at the institution without compromising on accuracy.

PAMM is small but mighty. Short for the Laboratory for Pathology and Medical Microbiology in Dutch and located in Veldhoven in the Netherlands, the institution performs diagnostics on cassette samples for five hospitals and 500 general practitioners in the country. "In the world, that isn't so significant," says PAMM's head of bacteriology, Theo Liebregts. "In Holland, though, it's quite big."

With so many hospitals and doctor's surgeries across the southern part of the Netherlands relying on PAMM to process samples, the laboratory has made a conscious effort over the past decade to invest in lab automation to boost the accuracy of its reports and increase overall sample throughput. In this regard, its partnership with Copan Italia and MLS, the distributors in Benelux, has been crucial, with the company supplying PAMM with its WASPLab automated sample-processing solution, supported by the PhenoMATRIX system module. The reason why Liebregts chose the company over its rivals in the marketplace is clear.

"At the time, its competitors could all deliver very big systems that were very, very expensive," he explains. "Meanwhile Copan could deliver, as it still does, a solution tailor-made for your lab size and procedures. It understood what our needs were a lot more than its competitors did." The positive fruitfull and continuing collaboration between Copan and PAMM has served to improve Copan's solutions, and has helped PAMM to remain efficient and competitive in an increasingly challenging market.

Copan's WASPLab technology, powered by PhenoMatrix, has helped PAMM increase its sample throughput.

The mother of invention

PAMM installed WASPLab in 2014, says Liebregts. "We needed a way of increasing the speed of diagnostics with the same number of people, but we didn't want to do so at the expense of accuracy," he says. "That made us decide on an automated solution."

WASPLab works by producing high definition pictures of the plates before and during the incubation period, delivering them to lab technicians without the need to physically handle them for examination. This serves to drastically reduce the capacity for human error during the interpretation phase, and increases sample throughput. When PAMM's technicians began working with the WASPLab, the lab was processing around 3,000 samples per week. Two years later, that throughput has increased to 5,000. Its staff numbers, meanwhile, have only grown by 10%. "We could only have achieved this gain in capacity by embracing automation," says Liebregts.

The addition of the PhenoMATRIX algorithm, meanwhile, allows for more sophisticated image analysis by evaluating the growth present on an individual sample plate. Rules on the sorting of negative and positive plates can be tweaked by the user. This reduces the time it takes for lab technicians to read individual samples, freeing them for other duties within the lab and enables them to apply a constant quality refinement with deep learning techniques.

The impact of these technologies on the patient is obvious to PAMM's head of bacteriology – as automation increases sample throughput and allows staffing costs to be redistributed, diagnostics will become even cheaper and faster. Liebregts believes that his lab can help realise this ambition, at least in the area it covers, very soon indeed.

"Six months ago, we were using the PhenoMATRIX module to automate image analysis of chromogenic agars," explains Liebregts. "I believe that within one year, the software should be able to handle the reading of more than 50% of our plates. That's a target that I really want to set, and I believe we will be able to reach that." ●

For further information

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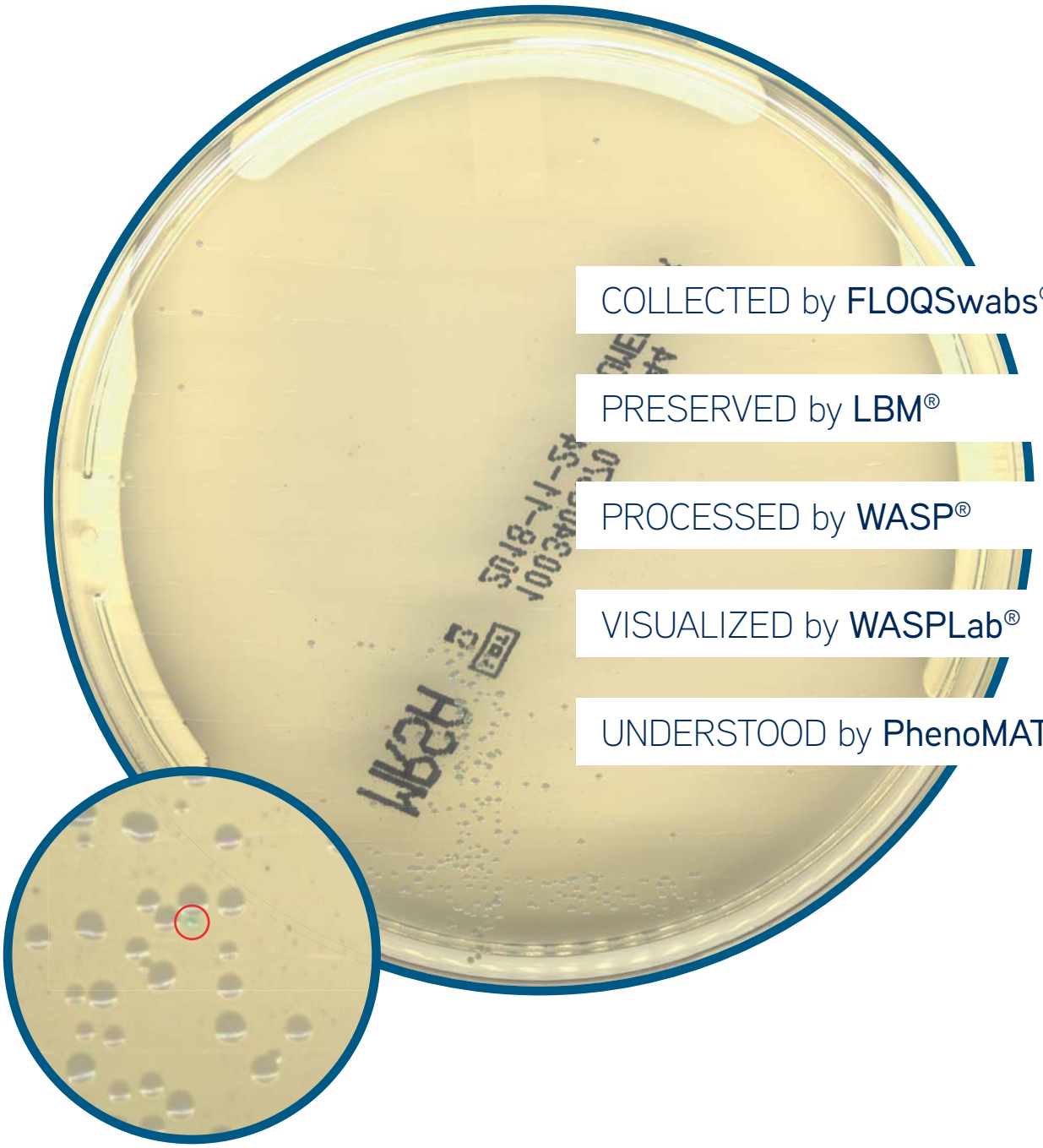

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Break down barriers

To reach its full potential, the diagnostic laboratory of the future needs to become more than a mere data factory. Professor Ana-Maria Simundic, laboratory director of the University Hospital Sveti Duh in Zagreb, Croatia, and president-elect of the European Federation of Laboratory Medicine, talks about how the 'lab of the future' can overcome present-day obstacles and generate results, and how IT solutions from companies like **Abbott Diagnostics** can help.

What are the biggest challenges in today's clinical practice that keep laboratories from adding more value to their institutions and the patients' pathway?

Professor Ana-Maria Simundic: In the past, laboratories have been sample-oriented and too focused on analytical quality. These days, labs are still seen as 'factories' that produce a great amount of data. We need to become a patient-oriented partner in healthcare that is providing high-quality information. In addition to our focus on high analytical quality, we need to also focus on patient outcome. We should practice laboratory medicine as a clinical speciality rather than a number-generating system.

"We have to eliminate silos and work together with clinicians on joint guidelines, respecting their clinical autonomy and contributing our valuable knowledge about the testing process."

Such a change requires a paradigm shift inside and outside the lab. Our primary focus should be on the areas of demand management and test interpretation. We should stand up and show that we are knowledgeable and competent to serve as consultants in test ordering and test interpretation. To do this, we need to go out of our laboratories and take a responsible role within the total testing process, engaging in the pre-analytical phases as well as the post-analytical one. We have to eliminate silos and work together with clinicians on joint guidelines, respecting their clinical autonomy and contributing our valuable knowledge about the testing process.

What role can IT play in improving demand management and test interpretation?

Test algorithms, panels and various gate-keeping strategies can be implemented into hospital information systems (HIS) and laboratory information systems (LIS) not only to automate test ordering and test interpretation, but also to complement the laboratory and clinicians' skills, and enhance the quality of care provided.

Such systems can effectively support the diagnostic process, ensuring that patients are always receiving a standard level of care, while allowing for exceptions and respecting the autonomy of each clinician. Furthermore, laboratories are a kind of gold mine for data. The amount of data in healthcare doubles every three to five years and the role of IT is to analyse big data and use it to improve laboratory medicine.

As such, IT should be offering much more in the future. For example, the LIS should be able to capture, store and analyse various lab-related data, and even act upon it. Artificial intelligence will certainly play a role as well. We can use information to increase our productivity, optimise efficiency and improve the quality of our service. Though many argue that our jobs might become redundant if we allow IT to take over tasks that were traditionally done by humans, I suggest we redefine our roles to make the most of it and focus on areas where cognitively challenging actions are required.

What were the first relevant steps you took in your working environment to overcome barriers and move towards value-added testing?

Since my arrival at Sveti Duh three years ago, we have agreed on some successful gate-keeping strategies to reduce the overuse of thyroid, D-dimer and tumour marker testing. Recently, we created a joint interdisciplinary team to implement algorithms for some most common emergency pathological conditions. It was hard work but there was a great enthusiasm and mutual respect, which was very important and motivating. Now the algorithms have been created and the next step is to implement it into the HIS.

Of course, none of this is simple, but the key is to take little steps. I'm lucky to have a supportive hospital manager who saw how this work could improve the quality of the patient care or reduce overall costs. In institutions with less support and interest from management side, laboratories should step up and document implementation outcomes. Once the first objectives are reached, it's important to present results like savings, improvement of the patient safety and prestige to hospital management.

I also served as the president of the Croatian society for medical biochemistry and laboratory medicine during 2012–18. In June 2018, we launched a joint project with the Croatian medical society for emergency medicine. We have agreed on a project to produce diagnostic algorithms for the most common emergency conditions and provide assistance for nationwide implementation. Again, IT solutions will play an important role here. ●

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Challenges for tuberculosis diagnostic tests in Europe

The rise of drug-resistant tuberculosis in Europe in the past few years has highlighted the importance of isoniazid resistance testing in the eyes of **BD**, which is one of the largest global medical technology companies in the world and is advancing the world of health by improving medical discovery, diagnostics and the delivery of care. BD helps customers enhance outcomes, lower costs, increase efficiencies, improve safety and expand access to healthcare. The company outlines and discusses the top five challenges to tuberculosis diagnostic testing in Europe.

Isoniazid (INH) resistance is not always known at the beginning of the tuberculosis (TB) diagnostic pathway. INH status (susceptible or resistant) is only known once samples have been cultured and tested for drug susceptibility, which can take several weeks. This is different from rifampicin (RIF) status (susceptible or resistant), which can be ascertained right from the beginning with rapid molecular assays. The main challenges to knowing the full diagnostic profile for patients suspected of having TB include INH monoresistance, assigning the right patient to the right diagnostic pathway, diagnostic testing setting, cost containment and reimbursement, and implementing next-generation sequencing.

INH monoresistance

The TB epidemic is a major threat to global health. *Mycobacterium tuberculosis* complex (MTBc) is the leading cause of death from a single infectious agent. RIF and INH are the two most effective drugs against TB and part of the TB first-line treatment regimen. However, not all patients respond to these treatments, because they can be infected by rifampicin-resistant (RR) TB or multidrug-resistant (MDR) TB.

If patients are only tested for RIF resistance, INH monoresistance can go undetected at this stage of the diagnostic pathway. TB strains with undetected INH monoresistance could also acquire resistance to other drugs while subjected to inappropriate treatment, leading to MDR-TB or extensively drug-resistant (XDR) TB – for example, MDR-TB plus resistance to any fluoroquinolone antibiotic and at least one of three injectable second-line drugs.

A recent systematic review and meta-analysis carried out by Gegia showed that the standard World Health Organisation (WHO) regimen may be suboptimal when treating INH-resistant TB and may lead to treatment failure, relapse and acquired MDR-TB. Molecular tests including both RIF and INH allow for a more rapid and efficient way to determine the most appropriate treatment.

Assign the right patient to the right diagnostic pathway

There seems to be a lack of consensus among clinicians across Europe on which patient profile should undergo molecular testing for drug-resistant TB. Diagnostic strategies vary between European countries and medical institutions, and it is not clear which diagnostic pathway should be used.

There may be a gap between WHO recommendations and what is feasible or practiced by healthcare providers. Good communication between microbiologists and clinicians is also important.

The right expertise is needed by laboratory personnel to interpret the results and help clinicians make informed decisions on diagnosis and treatment regimens.

Where molecular testing should be carried out

The setting depends on how the laboratory system is organised, which varies from country to country. In some countries, the clinical laboratory system is centralised – as it is in the UK – and in others, it is regional. In France and Italy, molecular testing is carried out in public hospitals and results are then sent to TB reference laboratories.

Looking at cost containment and reimbursement

It has been shown that MDR-TB results in a higher financial cost to healthcare systems. Healthcare facilities are under increasing pressure from governments to control costs. Isolating patients in hospitals is costly and it is important to have suspected TB confirmed as soon as possible. The earlier the clinician receives the preliminary report, the easier it is to optimise healthcare costs.

Implement next-gen sequencing

Over the next 5–10 years, next-generation sequencing (NGS) has the potential to change TB diagnostic testing by delivering more targeted results for individualised treatment regimens. It is already being used in Germany and Italy on MDR-TB cases that have been detected using molecular and culture testing. NGS has the ability to detect INH resistance mutations outside of the commonly targeted regions of the inhA and katG genes. As costs decrease and genotyping and phenotyping data become linked, this testing method is gaining momentum for TB diagnostics and surveillance.

In spite of these major challenges, rapid molecular TB testing can provide the following benefits to laboratories and clinicians: greater predictive value, shorter time to results to detect INH monoresistance, RIF monoresistance or MDR-TB, rapid communication to the clinician, faster clinical decisions, improved cost-effectiveness and improved laboratory efficiency. ●

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Move healthcare forward.

The benefits of automated microbiology solutions

With decreasing reimbursement, staffing issues and antimicrobial resistance, working in microbiology laboratories is an increasingly challenging task. Renee LeMaire-Adkins, PhD, senior director of marketing at **Beckman Coulter Diagnostics**, talks about how automated microbiology solutions can significantly improve productivity.

What does full automation bring to a microbiology laboratory?

Renee LeMaire-Adkins: Patient care is a 24/7 process, but in many microbiology laboratories that is not the case. Often, culture reading is performed in one shift, sometimes two. Culture reading performed outside of the day shift is typically limited, with STAT testing and specimen processing being the primary focus. Microbiology labs often have a bench-centric mindset, and it has been that way for decades.

Microbiology automation, while still relatively new, completely changes that perspective. It facilitates 24/7 testing and reporting of results, which provides a greater impact to patient care decisions. After their initial introduction to the pre-analytical processing area, instruments such as the DxM Autoplak increase productivity, providing automated flexibility that adapts to the lab's current processes and ensures quality of streaking for accurate results. The addition of full automation in microbiology supports increased productivity in all processes in the lab and an improvement in quality, all of which have a direct impact on time to result and thus patient care.

Why would a pre-analytical microbiology processor be needed in a micro lab?

Every laboratory environment faces the same challenges, and microbiology is no different. Challenges include decreasing reimbursement, retirements and staffing shortages, increasing antimicrobial resistance and constant fear of consolidation. Microbiology automation addresses a significant portion of these challenges by automating manual processes, minimising errors and increasing productivity through streamlined workflow and support.

For example, staffing shortages are one of the biggest challenges for any lab, meaning microbiologists often have to perform manual tasks such as processing samples. With instruments like the DxM Autoplak the microbiologist is freed up to perform those more complex tasks such as reading and reporting cultures, performing molecular testing, and potentially increasing culture-reading capabilities in multiple shifts

How does workflow change with automating a micro lab?

The introduction of automation to a microbiology lab has many benefits, directly impacting on workflow and productivity. The addition of a pre-analytical processing instrument could potentially automate the manual workload of two to three FTE's, often decreasing manual labour related to processing by close to 74%. The redeployment of FTE resources provides additional support to the laboratory staff, improves productivity to manage increasing volumes. It also allows the lab to prepare for staff reductions or retirements, and increases testing capacity on multiple shifts. There is often a marked decrease in overtime after implementing automation due to the staff being able to better manage the workload. A significant benefit to the automated plating is the decreased need for subculturing bacterial isolates, which leads to a faster turnaround time (TAT) when reporting culture results.

How does the DxM Autoplak system perform compare with other systems on the market?

The DxM Autoplak has the smallest footprint of pre-analytical analysers available for streaking media plate and allows for a lean placement in the microbiology lab. The system is reliable, and has an open platform for several types of containers. Its barcode scanning allows for full traceability of the specimen all the way through the microbiology process.

What types of specimens and specimen containers can be used with the DxM Autoplak?

About 95–98% of all specimen types can be processed. With the variety of transport mediums and enrichment broths, almost every sample type, including tissue, stool and sputum, can be transformed into a liquid format for easy processing.

The DxM Autoplak has an open system for simultaneous container processing, so batching is not based on container dimensions. The system has a wide range for minimum or maximum dimensions, allowing any lab, with or without outreach clinics, to maintain most of their sample containers.

How complex is installation and what is connectivity like between the DxM Autoplak and a LIS?

The DxM Autoplak is extremely user-friendly and most installations involve almost a simple plug-and-play process. The design and footprint result in a lean installation in the lab, as it can be placed against a wall with minimal clearance on the sides. With the support of dedicated applications specialists, configuration and training is simple, allowing current processes to be defined in the instrument and processing samples to begin quickly and efficiently.

The DxM Autoplak has a standard HL7 format to allow connectivity to any LIS. The system works off a bidirectional query to 'request' the specimen information from the LIS for processing. ●

For further information

www.beckmancoulter.com

In safe hands

Understanding the beliefs of healthcare professionals regarding glove use and associated hand hygiene is imperative in order to improve practices. However, research in this area is limited. Louise Thomas explores the research on the perceptions and behaviours of healthcare professionals as well as the most effective strategies to improve adherence.

Healthcare-associated infections are a considerable social and economic burden for patients, relatives and the health services, lengthening duration of hospital stay and increasing resistance to antimicrobial agents. Hands are acknowledged as a major vehicle for the transmission of infection between patients and have been responsible for outbreaks of infection reported in the literature.

Adherence to hand hygiene practices is strongly recommended as the primary infection prevention measure. The risk of transmission of infection to patients can be minimised by hand decontamination immediately prior to contact with a patient or a susceptible site such as a wound or invasive device. The World Health Organisation (WHO) developed a framework for infection prevention and control education on hand hygiene in 2009, which has since been adopted worldwide. Interestingly, WHO guidance does not explicitly integrate the use of gloves within its framework. However, the incorrect use of gloves, such as failure to change them between patients or between different sites on the same patient, combined with inadequate hand hygiene after use, can result in the transmission of micro-organisms.

The introduction of universal precautions, as well as the concept of body substance isolation, was an important development as this triggered the introduction of latex and vinyl gloves into routine clinical activity. National guidelines subsequently advised the use of gloves as part of standard infection-control procedures to prevent exposure to blood and bodily fluids, based on a risk assessment. However, compliance rates among healthcare professionals are relatively low, in the range of 40–60%, particularly at entry to patient rooms or before patient contact. Hand hygiene is also subject to a Hawthorne effect, where behaviour is modified under observation.

The factors of non-compliance

A 2015 paper, published in the *American Journal of Infection Control*, identified a number of factors associated with non-compliance, which were

categorised as being motivational factors or related to perceptions of the work environment.

With regard to the former, social influences, acuity of patient care, self-protection and use of cues were all significant. Healthcare worker compliance with hand hygiene guidelines was influenced by the behaviours of others from a peer or organisational perspective. Junior doctors and medical students were mainly affected by the actions of senior medical staff. Similarly, student nurses were influenced by the practices of qualified staff. This could increase and decrease adherence, depending on what was modelled.

Patient care activities vary in acuity, and this has been linked to the judgements made by healthcare professionals with regard to hand hygiene. For example, in emergency situations, staff acknowledged that they did not stop to wash their hands.

Although self-protection has been identified as a key driver of hand hygiene behaviour, there is significant variation among individuals in their perception of risk. In some cases this extends to concern about the impact on family members, which can serve to enhance motivation for adherence.

The use of cues has also been cited as being important. This includes carrying out practices before and after examinations, using visual prompts, such as alcohol and hand gels. These have been shown to consistently boost adherence to hand hygiene practices, but to varying degrees. The most effective types of cues thus require further testing.

In terms of the workplace environment, resources, knowledge, information and organisational culture were all identified as being influential. The time required to complete a task and the facilities available to healthcare workers impacted their compliance, with workload and staff shortages being particularly problematic. Understaffing was linked with lower compliance and an associated increase in healthcare-associated infections.

Readily available hand hygiene products also supported compliance. Conversely, a lack of these negatively impacted adherence as staff admitted they did not often seek out alternatives. When healthcare workers were provided with electronic hand hygiene monitors, these were viewed positively, which suggests that this is a useful strategy to boost engagement in hygiene practices. The adequacy of supplies and time to perform hand hygiene are clearly both essential to compliance. Convenient access at the point of care is therefore highly recommended.

The knowledge of healthcare professionals about when to carry out hand hygiene practices was unsurprisingly associated with subsequent adherence. Some healthcare workers were found to be unaware of the importance of the behaviour and the use of gloves was often perceived as a proxy measure. In addition, the provision of information was well received by staff, highlighting the importance of education in strategies to boost compliance and reduce infection risk.

Visual prompts, such as alcohol and hand gel dispensers, consistently boost adherence to hand hygiene practices.

Organisational culture was highlighted as being significant across all disciplines. Cultural factors, such as a lack of openness and a fear of negative consequences, were also apparent. The value the organisation placed on hand hygiene was also cited as important by healthcare professionals.

Although hospital culture is difficult to measure and the instruments used are relatively unreliable, it is a topic frequently discussed because it is significantly associated with infection control. When there was a supportive culture, compliance with hand hygiene guidelines was improved. Where there was a lack of organisational commitment, healthcare workers felt disempowered to correct poor adherence.

Fits like a glove

Interestingly, the literature on glove use specifically is more limited, but is growing. Two broad categories of influences have been identified – emotions and socialisation. Emotions include the positive feelings of healthcare professionals associated with protecting themselves, patients and their family members. Disgust was also significant, among those healthcare professionals who felt that some patients were unclean and, as a result, were more likely to use gloves when caring for them.

In terms of socialisation, perceptions of professional, organisational and patient expectations influenced practices. When asked about what they used gloves for, healthcare professionals highlighted their professional duty to protect patients from harm and described appropriate clinical indications such as anticipating contact with blood or bodily fluids. Observing other staff members using gloves was also a key driver.

Healthcare professionals also indicated that features of the clinical setting, especially the desire to save time

Failing to adhere to proper hand cleaning was a common issue when workload was at a high level, and often only gloves were used.

and work efficiently, also influenced their decisions about glove use. However, some suggested that changing gloves wasted time.

Organisational dimensions of socialisation included issues relating to rules formalised in hospital policy, as well as unwritten rules. However, these were not always consistent. For example, some healthcare professionals indicated that wearing gloves was part of the hospital law, but that this conflicted with infection control policy.

Being challenged about glove use was also a feature of organisational socialisation. These tended to be directed at enforcing glove use, although there were examples where this was related to glove removal.

The decisions of healthcare professionals were also based on perceived expectations of patients that glove use would indicate more professionality and respect. Although most staff felt that patients would want them to wear gloves, some felt that it made their interaction with them too clinical.

Bring it all together

Although the literature on hand hygiene and glove use highlights some potential overlap in the influences of the two practices, research examining both together is limited. Interestingly, only a small amount of research has explored beliefs about these practices. Understanding the perceptions, beliefs and attitudes of the healthcare professionals is imperative in order to improve practice, thereby maximising patient safety.

A 2019 study, led by Jure Baloh from the Carver College of Medicine, University of Iowa, explored this in three academic hospitals in the US. Researchers conducted observations and interviews over a six-month period, and found that average compliance rates were around 70%. This was considerably lower than the rate of almost 90% that was reported to hospital prevention programmes over the same time period.

Surprisingly, the discrepancy between the two figures decreased over the course of the study, which researchers hypothesised was due to staff becoming aware of being observed and changing their behaviour accordingly, which characterises the Hawthorne effect. These results highlight the importance of re-evaluating how adherence to hand hygiene practices is measured.

In terms of reasons for using gloves, healthcare professionals indicated that this was mainly related to their own protection and, secondarily, for patient safety. In terms of hand hygiene more generally, patient safety was regarded as being of greatest importance, particularly in preventing cross-contamination. Some raised doubts about the need for hand cleaning before applying gloves, although it was unclear whether this was related to their own or the patient's protection. Habits were also cited as a key driver, which required no conscious effort to maintain.

A number of barriers were also described by healthcare professionals. This included observing their colleagues not adhering to hand hygiene guidance. Workload was another influential factor, with non-compliance reported when this was at a high level in general or when they were particularly busy. In such instances, some hand hygiene practices were omitted and only gloves were used. This was not always cited as being conscious, healthcare staff said that they would sometimes forget because of being preoccupied with patient care tasks.

Specific activities were associated with lower adherence. For example, if staff were making a short visit to a patient's room or if they did not anticipate they would be making direct contact with them. Certain tasks also served as a barrier, such as carrying a tray of food or if they started talking to the patient before they had undertaken hand hygiene practices.

The context, physical and cultural, also played a key role. Sanitisers were sometimes unavailable due to being empty, hard to find or covered. However, the presence of these products outside a patient's room could prompt healthcare professionals to use these before placing gloves on. In addition, it was most helpful if gloves were inside the room as otherwise staff would sometimes use these in place of other hygiene practices. Role models could serve to promote or decrease adherence, and individual level factors were influential as several hospital staff members did not perceive hand hygiene as being important if they were wearing gloves. Some also experienced skin issues from engaging in these practices.

It is clear that a comprehensive approach to infection control involves addressing glove use and sanitisation behaviours in healthcare professionals. Although education about the importance of the issue is required, work targeting beliefs and habits is another key strategy to ensure that adherence is optimised. Furthermore, new approaches to measuring compliance need to be explored to ensure that an accurate picture of staff behaviour is gathered.

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Reprocessing finances

A huge number of medical devices used by hospitals are labelled as 'single-use'. As a cost-saving measure, many hospitals rely upon 'reprocessed' single-use devices as a cheap, yet safe, alternative to buying expensive new equipment, but recent manufacturer efforts to halt reprocessing could lead to hiked hospital costs. **Nancy Chobin**, sterile processing educator and consultant at Sterile Processing University, talks about best practices when using this technique.

Following concerns regarding the safety of multiple-use devices in the 1980s, original equipment manufacturers (OEMs) began labelling their medical devices as 'single-use' rather than 'reusable'. However, they didn't make any structural changes to these medical devices, and amid escalating costs, healthcare providers realised that rather than simply discard them, the equipment could be reprocessed and made safe for use again, and again, and again.

During the subsequent 30 years, numerous medical devices have been taken apart, rigorously cleaned, thoroughly tested and resterilised before being returned to the medical market. The environmental impact of single-use devices (SUDs) was not given a second thought back in the '80s, but with soaring costs for healthcare providers and landfill overflowing, repurposing them is now considered the responsible thing to do. In developing countries and those with limited resources, reprocessing SUDs is incredibly common; it can make healthcare affordable for those who would otherwise find the cost prohibitive and ensures there is a supply of necessary medical devices where access to them is not always guaranteed.

Reprocessing is not a new idea; historically most items in a hospital were designated as 'reusable'. Some medical devices were made of glass, rubber and metal and were simply cleaned with a cleaning solution and wiped down before being reused; others were steam sterilised where applicable.

Some SUDs really are intended to be used only once and are therefore disposed of through hospital waste systems; others are just labelled so by the OEMs and can be safely reprocessed. A reprocessed SUD is an original device that has been used previously, and has been subjected to additional processing and manufacturing for the purpose of an additional single-use on a patient.

Disposable SUDs were introduced when the healthcare industry became concerned about devices that were used multiple times. Newly designed medical devices were also becoming increasingly complex and therefore more difficult to clean, and so SUDs became popular thanks to their convenience and ability to reduce the risk of contamination.

However, SUDs are wasteful and it can be expensive to dispose of such hospital waste, so healthcare providers felt a need to return to reusable items and to reprocess certain devices. After all, if an instrument has been properly cleaned, tested and considered functional,

repackaged and sterilised, then why shouldn't it be used again and again?

Reprocessing would originally have taken place at an in-hospital centre, but since the late 1990s, it is carried out by a registered third-party reprocessor, or occasionally the OEM. Outsourcing is advantageous to many hospitals and healthcare providers that would not otherwise be able to reprocess items adequately, or that may have downsized their own sterilisation department with the advent of SUDs. The Association of Medical Device Reprocessors (AMDR), a global trade association consisting of members of the commercial SUD reprocessing and remanufacturing industry, has described the practice as "a celebrated supply chain cost-reduction strategy for hospitals" that it says can help increase quality, reduce costs and improve patient care.

One rule for some

Not every device labelled as single-use should be reprocessed; in fact, only a small percentage actually are. Approximately 2% of all SUDs on the US market are thought to be eligible for reprocessing by a qualified third-party reprocessor, with the most popular being sequential compression device sleeves – drill bits, saws, blades and burrs; and biopsy forceps. Such medical devices are made of materials that can withstand repeated cleaning, high-level disinfection and sterilisation.

There are three categories of reprocessed SUDs, as detailed by the US FDA:

- **Class III:** a high-risk reprocessed SUD, intended to contact normally sterile tissue or body spaces during use; for example, surgical forceps.
- **Class II:** a medium-risk reprocessed SUD, intended to contact intact mucous membranes and not penetrate normally sterile areas of the body, such as endoscopes.
- **Class I:** a low-risk reprocessed SUD, intended to make topical contact and not penetrate intact skin – it includes devices such as stethoscopes.

The vast majority of reprocessed SUDs are in Class II and include pulse oximeter sensors, ultrasound catheters, drills, compression sleeves and most laparoscopic equipment, for example. Other devices that are typically reprocessed include electrophysiological and ablative cardiac catheters, orthopaedic devices made of steel and titanium, and non-invasive devices like tourniquet cuffs, bed alarms and blood pressure cuffs.

Commercial reprocessing is essentially a remanufacture of the product; the device is disassembled, cleaned and tested for functionality, before being repackaged and resterilised. Only certain devices can be reprocessed, and only those submitted by a reprocessing company to the FDA may be remanufactured. A device may only be reprocessed if, once it had been remanufactured, it meets the specifications of the OEM. Reprocessed devices should be safe and reliable, otherwise they should be retired.

"The third-party companies develop proprietary protocols for each device," explains Nancy Chobin of Sterile Processing University. "They also barcode each device and, through their testing, know how many times they can safely reprocess the device."

These unique barcodes provide a history of the device, allowing healthcare providers to determine how many times a device has been reprocessed and where. It is important to know how many times a device can be safely reprocessed to avoid failure. Any failure is the responsibility of the reprocessor, not the hospital/institution that has used a faulty device.

"If a facility sends back a device and it has exceeded the number of reprocessings, it is not reprocessed," continues Chobin. "If the device fails the inspection/testing during the reprocessing, it will not be reprocessed. For example, a sequential compression sleeve might be able to be reprocessed five times but if on the third reprocessing it fails, the company will not reprocess it and the facility is not charged for it."

$1 million

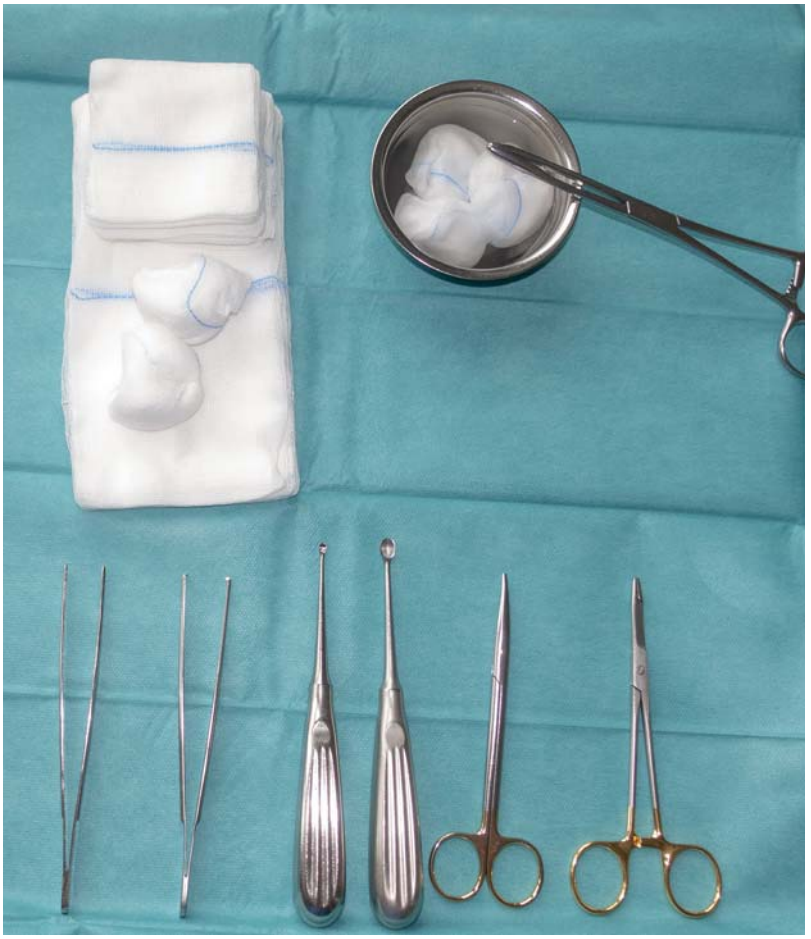
The average amount that could be saved, per hospital, on device costs annually with reprocessing.

Association of Medical Device Reprocessors

"Manufacturers are losing money. So much so that two of the major manufactures who tried everything in the book to stop third-party reprocessing now own reprocessing companies."

It is believed by some commentators that using reprocessed devices represents a lower standard of care, rather than a sensible reuse of costly and otherwise wasteful materials. Reprocessing might carry a significant risk to the patient and questions could be asked about the effectiveness of the cleaning efforts and whether product performance is compromised the more it is used, they argue.

The reprocessing industry is subject to a stringent and comprehensive regulatory scheme, says the Association of Medical Device Reprocessors, which played a key role in establishing the reprocessing industry. Providing all guidelines have been adhered to, the medical device should be as safe as a brand-new device. When submitting a pre-market submission, the third-party reprocessor will often have to include extra data that OEMs do not, validation data on cleaning, sterilisation and functional performance, for example, to prove that the reprocessed device is 'substantially equivalent' to the original. "By law, a reprocessed device must be the equivalent of a new device," states Chobin. ▶



Reprocessing devices can help to significantly reduce hospital costs.

Devices therefore must meet, or exceed, the requirements of the original manufacturer, and their unique barcode means they are 100% traceable, ensuring quality control and accountability. In some cases, reprocessed SUDs perform better than a new device.

A 2013 study by Banner Health, a non-profit health system in the US, found that OEM SUDs were defective 4.9 times more frequently than comparable reprocessed devices. They took 3,112 devices, 55% of which were reprocessed and 45% were new; they were considered defective if surgeons determined they did not function in a manner consistent with their intended purpose.

Between August 1996 and December 1999, the FDA's Medical Device Reporting system chronicled 245 adverse events linked to the reuse of SUDs: seven deaths, 72 injuries, 147 malfunctions and 19 other incidents as reported by manufacturers. But there was no pattern of failures that differed in any way than those observed with their initial use. In February 2000, the FDA estimated that 464 of three million reported adverse events might be associated with reuse of an SUD, meaning 99.8% of reported adverse events may have occurred with new OEM devices.

Not only is reprocessing SUDs often safer thanks to strict guidelines imposed on those preparing the devices for reuse, it allows healthcare providers to maintain patient care quality while also saving vast amounts of money. A reprocessed device can cost almost half the price of a new device – estimates suggest on average, $1 million per hospital can be saved on device costs annually – and it is as safe as the original product. It is also more environmentally friendly as 50,000lb less medical waste is going to landfill annually per hospital in the US.

"In addition to saving 50% of the cost of a new device, facilities also save on medical waste because the companies remove it from the facility," says Chobin. "It's a win-win."

For or against

But if reprocessing SUDs is so beneficial in terms of reducing the skyrocketing costs healthcare providers are faced with while also preventing completely unnecessary waste ending up in landfill, why are manufacturers trying to stop the practice?

"Manufacturers are losing money," states Chobin, who has been in the sterile processing profession for 37 years. "So much so that two of the major manufactures who tried everything in the book to stop third-party reprocessing now own reprocessing companies."

Many OEMs now reprocess their own devices; the Association of Medical Device Reprocessors lists companies such as Stryker and Cardinal Health as members who offer remanufactured SUDs as part of their overall business model. There are also several third-party reprocessors such as Vanguard and Medline ReNewal that offer the same services. But what steps should be taken when choosing who to reprocess devices?

"Verify the company is registered with the FDA and how long they have been in business," suggests Chobin. "Have they had any citations from the FDA during the FDA inspections? Ask for a listing of their customers and contact them to see if they are satisfied with the service."

The benefits of reprocessing are obvious; not only does it save hospitals and healthcare providers a vast amount of money, is it also more environmentally friendly than simply discarding a product that could be reused following a remanufacturing process. It is clear that the decision to reprocess SUDs is complex and contentious, with many commentators believing the practice is unsafe or offers a lower standard of care. It is important that hospitals and healthcare providers understand the risks and limitations of the process and choose a third-party reprocessor who adheres to the strict regulations set out by the FDA. ●

The war on wounds

The interest in using smart systems that can monitor, report on and possibly even influence the healing process is intensifying by the year. Now that the US Department of Defense is launching a project to support wounded soldiers with the technology, Tim Gunn talks to programme lead **Paul Sheehan**, wound care expert **Professor Michael Clark** and smart bandage engineer **Hossein Derakhshandeh** about the world's prospects for tackling the 'silent epidemic' of wounds.

We don't like to think about chronic wounds. It's a long-standing trait. On their way to Troy, the Greeks marooned the snake-bitten Philoctetes, "burning flux oozing from the heel of his louse-ridden foot", on a deserted island because he was putting them off their prayers and sacrifices. The infection his only companion, he remained there for a decade.

An odd three millennia and a few different models of reality later, chronic wounds affect 2–3% of the population of the developed world. They cost the UK NHS about as much as obesity-related diseases but attract scarcely a fraction of the media coverage. Evidently, no one much enjoys being reminded of the unsightly, unpredictable ways their skin can expose and let them down.

We are all, however, suckers for things we can prefix with the word 'smart'. Over the past 15 years, TVs, phones, kettles, tables, boilers, mirrors and more have all felt our passion for integrating information technology into everyday objects. Now one of the oldest human innovations of all, the humble wound dressing, is taking its turn in the smartlight. Soon, wounds may well be managed with dressings that automatically convey their condition to clinicians, or even intervene to facilitate the healing process.

It's easy to see why we might want to smarten our approach to chronic wound care. According to the UK's National Institute for Health and Care Excellence's (NICE) guidance on leg and foot ulcers, a Doppler ultrasound is the necessary first test for reaching a diagnosis and determining the right treatment. A study published in the *BMJ* in 2015 showed that only 16% of patients suffering from these conditions received one. Almost twice as many patients were unable to get a differential diagnosis as were given the right test. ▶

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"For many GPs, it's an area where they have minimal experience, so it becomes an issue for their practice nurses," explains Professor Michael Clark of the Welsh Wound Innovation Centre, the first of its kind in the world. Any patient who spends a long time in hospital could well develop a non-healing wound. "There just isn't a label on a door that says this is the right route for difficult cases," says Clark.

As such, Clark believes that the 'silent epidemic' of non-healing wounds won't be tackled without parallel work across three areas. The first task is communicating the basics of wound care to busy clinicians; then researchers need to devise diagnostic tests that can indicate the likely outcome of any wound; and finally engineers need to integrate those tests into sophisticated technologies that can both monitor and intervene in the wound-healing process.

Hossein Derakhshandeh, a researcher and engineer at the Laboratory for Innovative Microtechnologies and Biomechanics, University of Nebraska, is doing just that. In his view, the impact smart bandages and wound dressings can have on non-healing wounds comes down to the fact that "for many reasons, chronic wounds become trapped in the inflammation phase of healing". To use his patient simplification, in these cases a range of factors result in the body's "smart" response being interrupted, which means "closed-loop smart dressings have the potential to manage the healing process instead".

This is the truly revolutionary promise of the smart dressing. It's a way to move from a more passive model of wound management, where clinicians put the body in the best position to heal, past static, healing-enhancing scaffolds like hydrogels and bioglasses, to a dynamic and active paradigm, where the healing process can be directed by precise interventions.

Battle scars

Philoctetes had long since given up hope of his foot healing when his comrades finally came back. They identified his cave by the pus-infused rags he'd left to dry outside. It wasn't a charitable visit. The Greeks had discovered that the war could only be won with the bow and poisoned arrows bestowed on Philoctetes by Hercules, and they planned to steal them. In one telling, Neoptolemus, the son of Achilles, called up after his father was slain by an arrow to the heel, was entrusted with the task.

It all came far too late for Achilles, but over the past 250 years, medical advances spanning everything from modern nursing and antisepsis to the concept of triage have been spurred by warfare. Now, the US Defense Advanced Research Projects Agency (DARPA) is launching a Bioelectronics for Tissue Regeneration (BETR) programme that it believes will put closed-loop smart bandages on that list, improving outcomes for the victims of blast injuries in the process, and chronic wound sufferers thereafter.

As Paul Sheehan, programme lead for BETR, puts it, "There's no evolutionary precedent for a blast injury." No Homeric character had their legs amputated above the knee; their pelvis fractured; their hands and genitals mutilated; and soil driven deep into soft tissue wounds all across their body by an improvised explosive device.

"We don't exactly know why," continues Sheehan, "but blast injuries tend to scramble the physiological processes." This results in complications like heterotopic ossification, where bone grows through the soft tissue – which takes place after more than two thirds of blast injury amputations – or wounds from amputations that give the impression of healing well until, in Sheehan's words, "they just start to fall apart".

The BETR programme is designed to integrate the disparate technologies and types of expertise required to tackle the challenges presented by such an injury. Not only does it need to implement advances in biosensors, actuators, artificial intelligence and machine learning, it needs to account for the fact that each individual wound is a complicated and heterogeneous environment, and areas that may respond well to a particular treatment are often crosshatched with others that might not.

Derakhshandeh puts it in terms of chronic wounds. "The biggest problem is that there are many reasons and many factors preventing healing, and we need to take care of each at a specific time with a specific material."

"We don't exactly know why, but blast injuries tend to scramble the physiological processes."

Paul Sheehan

For Clark, making sense of that heterogeneity across both time and space is one of the main challenges intelligent dressings will have to face. Before then, it would help to work out which of the signals we can get from a wound are worth our attention. "You're almost limited by your imagination in terms of what you think you can measure at the wound surface," he explains. "The challenge comes in identifying which parameters are actually providing useful information"

"Ultimately," sighs Clark, "if you're looking for the missing piece in much of wound healing, it's our lack of diagnostic tools." Both he and Sheehan agree that experienced clinicians can intuitively identify roughly where a particular wound is in the healing process, but there is presently no clear way to identify which wounds will heal easily, which ones require extra effort, and which are likely to get stuck along the way. ▶

16%

The percentage of patients with chronic leg ulcers in one UK study who were given the Doppler ultrasound that is stipulated by the country's guidelines.
British Medical Journal

30%

The amount of chronic wound sufferers that experience symptoms of depression and anxiety.

University Hospital Erlangen

For Sheehan, this is what makes smart bandages a perfect project for DARPA, which prides itself on its ability to bring together several fields on the cusp of major breakthroughs and help them push towards a specific capability. One of the key fields here is machine learning. Sheehan believes facilitating and advancing wound experts' intuitive understanding by sorting and identifying the most critical pieces of data resembles "a classic machine-learning programme, taking in many different signals and merging them into a more robust quantitative one".

"What we discovered when researching to set up this programme was that many of the efforts to date have been stovepiped," he continues. "Everyone was doing great research in their small mechanistic worlds, but we wanted to step back and say, 'If you could do anything, if you were to pick the most critical processes, what would they be? How would you control them? And how would you put it all into a system?'"

Being a mythical character, Philoctetes was already part of a system. What's more, in the ancient play that bears his name, his salvation actually comes courtesy of a machine. Just when it seems there can be no solution to the onstage drama, a crane whirs into life, bringing Hercules down from the heavens, deus ex machina. The deified hero quickly convinces Philoctetes to go with his countrymen to Troy, where he will be healed by the sons of Asclepius, god of medicine, and help win the war. The rest is well-known, if not quite history.

Health from the machine

However fervent the hype might get, machine learning and artificial intelligence do not exist to bring us closer to the gods. They are, however, central to making a closed-loop intelligent dressing possible. Take heterotopic ossification, for instance. "That would be an example of an abnormal system," says Sheehan. "Our goal is to be able to monitor it and use machine learning to develop a vision of what normal healing should look like and then try to steer the wound back onto that pathway."

"That also fits into a classic machine-learning programme," he continues. "You do not have to specify every process that is going into healing – AI can take the signals that are there and indicate that there's a missing process we don't know about, and sometimes even provide control without knowing every single piece of information."

Nevertheless, BETR will need to build up this capability with a far sparser data set than a typical machine-learning programme. Sheehan's team also have to consider the method of drug delivery. The answers there are still to be determined, though Derakhshandeh speaks cryptically about an upcoming breakthrough. "We're about to publish some results that I think will open a new door, not just for chronic wound healing, but for burns and cosmetic issues," he says carefully, weighing every word. "It's possible that our method of delivery has changed that. We have changed the hypothesis and tried to bypass some barriers in the wound."

Similarly, Clark sees a lot of potential for a smart bandage that works to facilitate wound management by regulating the amount of pressure applied in the vicinity of a leg ulcer. It's a more traditional method that doesn't rely on administering treatments to the wound surface, but it's still a long way from today's bandage.

Whatever technology might be installed in the bandages of the future, and however impressive it might prove, it will not be a panacea. As Clark puts it, "We need to get clinicians to do the right things, the simple things, consistently." If we can't do that, costly smart bandages are likely to be misused, and patients will continue to suffer. Indeed, Philoctetes' ordeal came to an end because Neoptolemus paid attention to him. With more than 30% of today's chronic wound sufferers also experiencing depression and anxiety, we would do well to follow that example. ●

The Welsh Wound Innovation Centre, the first of its kind globally.

Slice of the action – the latest in wound care

Sue Bale, president of the **European Wound Management Association (EWMA)**, explains why wound care professionals should not miss the EWMA conference during 5–7 June 2019, which will be held in Gothenburg, Sweden.

Why attend the EWMA 2019 conference?

Sue Bale: The conference offers a wide variety of sessions, ranging from prevention and management of wounds to epidemiology, pathology and diagnosis. This makes it easy for delegates to tailor their own programme based on their interests and professional background. EWMA conferences have a very welcoming and friendly atmosphere, enabling easy contact with other delegates for effective networking. I would highlight four reasons to attend EWMA 2019:

- First of all, the delegates will be able to get a unique overview of the latest research in wound management. This year, 740 abstract submissions came from 57 countries around the world, with Sweden among those countries with the highest number of contributions.
- Secondly, you will be able to look at the recent innovations in wound healing – equipment, devices, dressings and so on. The conference will feature more than 125 industry exhibitors from leading companies in wound management.
- Thirdly, the delegates will get the chance to learn and acquire hands-on experience in the latest techniques in wound care during numerous workshops and interactive sessions.
- The last but most important reason would be networking. The conference is an opportunity to meet many delegates from other countries and cultures, and the friendly conference atmosphere facilitates knowledge and expertise exchange between the delegates. I want to give a piece of advice to those of you who are considering attending the conference – when you stand in a queue for a coffee or lunch, take these moments to speak to people around you about who they are and what they do. These informal conversations are one of the best settings for exchanging your expertise and hopefully making new friends, colleagues and contacts.

The theme of EWMA 2019 conference is 'Person-Centred Wound Care. Who is in Charge of the Wound?' Why did you decide to choose this topic in 2019?

This theme has been chosen because there is an increasing awareness of how important the person/patient is in wound care and that we need to work in a collaborative partnership with our patients. It is crucial that we understand the patients' needs and wishes.

Without cooperation and trust between the two, patients may not be able to tolerate the care that is suggested by the professionals. The patients may be more willing to accept the less-effective treatment, and the wounds will take longer to heal if it means that he or she can go on a holiday or do whatever they would like to do. The conference question, "Who is in charge of the wound?" implies that wound care professionals are willing to refrain more and more from the patriarchal viewpoint when caring for their patients.

"Nurses play a very special role in wound management, and EWMA is committed to strengthening this message. For patients with wounds, nurses are the healthcare professionals they spend the most time with, providing most of the wound care."

Can you highlight a couple of reasons why nurses should attend the EWMA conference 2019?

Nurse delegates at EWMA 2019 will have the chance to network and exchange expertise with other nurses from across the world. They will also have exposure to experiences and knowledge of other clinical staff and professionals in wound management.

Moreover, nurses play a very special role in wound management, and EWMA is committed to strengthening this message. For patients with wounds, nurses are the healthcare professionals they spend the most time with, providing most of the wound care. As a result, nurses are one of the most important elements of wound care, and their presence is crucial at one of the biggest wound management conferences in the world, which will take place in Gothenburg this year. ●

EWMA Secretariat has the authorship for this interview. The full version of the interview was initially published in Sårmagasinet No 1:2019.

For further information

www.ewma2019.org

Rapid exudate absorption, even under compression

Kliniderm Superabsorbent dressings by **Medeco** are a market leader in terms of cost, clinical effectiveness and patient preference. The four-layer superabsorbent dressings are held together by a unique patented seal, are indicated for moderate-to-highly exuding chronic and acute wounds, and can be used under compression. Susan Mason, a tissue viability nurse and senior clinical adviser for NHS Shared Business Services, explains why she favours the dressing.

Although exudate is a vital part of wound healing, chronic-wound patients often think of it in terms of disgust, channelling it into feelings of self-loathing and low self-esteem. If mismanaged, it can also lead to further physical damage, increased pain and a greater risk of already debilitating wounds becoming infected. As care providers assess, find causes for and act to manage exuding wounds, they need to keep all of this in mind.

Kliniderm Superabsorbent dressing can absorb 33 times its weight.

"We look at the whole of the patient, not the hole in the patient," says UK wound care expert Susan Mason. A former manager for tissue viability in a large NHS primary care trust, she now spends two days a week as a tissue viability nurse and the other three as a senior clinical adviser for NHS Shared Business Services. With her range of experience and responsibilities, she's as well placed as anyone to practice what she preaches.

Patient first

It's because of patients that Mason wants to speak about Kliniderm Superabsorbent, which she is quick to recommend for managing foot, leg and pressure ulcers, lymphoedema and more. Comprising of a hydrophilic wound contact layer, an absorbent core that can absorb 33 times its own weight, a fluid-repellent backing layer and an ultrasonic seal that removes the risk of reactions to the glue used, all of which are held together with a patented seal. The product is indicated for moderate-to-highly exuding wounds and is designed to rapidly absorb exudate even under compression, locking exudate and MMP's into the dressing core. The product is comfortable for the patient over a long wear time, conformable, and easy to apply and remove. In addition, Kliniderm Superabsorbent dressings are 34–79% cheaper than other superabsorbents.

"It's all about quality of life for the patient and you can't equate that with cost because everybody's so different. It's about ensuring that the patient's quality of life is enhanced. To make sure products are of a standard you would accept, you involve patients."

"It's all about quality of life for the patient," Mason continues, "and you can't equate that with cost because everybody's so different. It's about ensuring that the patient's quality of life is enhanced. To make sure products are of a standard you would accept, you involve patients."

In her previous management role, Mason tested Kliniderm's product against the exudate management dressings already in the trust's formulary. "The product we were using at the time was quite costly, and we were still having issues with suppuration," she explains. "We did an evaluation with that product and the Kliniderm range and saved a phenomenal amount of money with no detriment to the patient."

In fact, patient feedback about Kliniderm dressings' wearability, conformability and comfort was extremely positive. Clinicians praised the ease with which the product could be applied and removed, as well as how beneficial it was for patients. "It was a no-brainer for us," Mason laughs. "I wish all our decisions were like that."

Equally, the Humber Foundation Trust's 2015 study into superabsorbent dressing reviewed use in the three months before and after the implementation of Kliniderm products, and found costs fell from £61,372.06 to £21,366.77 and 26% fewer dressings needed to be applied. Apparent cost savings can prove to be a false economy if the suitability of wound care products isn't considered, but, as Mason stresses, these savings were not achieved at the patient's expense. Indeed, in Humber's product evaluation, 27 of 30 clinicians rated Kliniderm superabsorbent's ability to manage exudate as 'very good' or 'excellent', and 18 rated the improvement

in the wound bed in the same terms. As a result of the study, the Kliniderm dressing was added to the Humber Trust Formulary as the first-line superabsorbent product. Since then, the organisation has been able to reconsider the number of nursing visits required to provide care.

Kliniderm Superabsorbent dressings' best feature is their ease of use.

"One size doesn't fit all," notes Mason. "I'm patient-led, not product-led. That's how I work with companies. I will never be product-led because I'm going to be a patient one day. So if it's a dressing that the patient warrants and it's beneficial to them, then I will use it, and we've had no issues with this product. It's been used very successfully and effectively."

Patient throughout

Kliniderm Superabsorbent dressings are also tailored to address the precise problems that impair healing in highly exuding wounds. The product is a powerful protease modulator, restricting matrix metalloproteinases (MMPs) that remove damaging extracellular matrices during normal wound healing, but are often too abundant in chronic wounds, creating a highly destructive wound environment that struggles to repair itself. In fact, in vitro studies have shown that Kliniderm superabsorbent dressings can completely remove MMP-2 within 24 hours and are 74% more effective at restricting MMP-9 activity versus control dressings.

Still, a chronic wound is much more than its biology. "Not all wounds heal," says Mason grimly. "Some patients don't want them to." When she talks about looking at the whole of the patient, this is what she wants to be taken into account. "Everybody thinks that if you had a wound, you'd want it to heal, but some people don't because they don't see anybody apart from their nurses. They just love that connection – love sharing a cup of tea."

It's in this context that Mason calls Kliniderm superabsorbent dressings' ease of application "the biggest plus ever". It means patients can sometimes change their dressings themselves, reducing their reliance on nurses and allowing them to achieve a greater degree of autonomy.

"They can take control over their wounds," Mason explains. "They can go shopping more easily and feel more comfortable. We're getting younger patients with leg ulcers and this really matters to them. From their perspective, the dressing means they're in control of the ulcer more than the ulcer is controlling them. In each respect it's a win-win." ●

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The benefits of single-use negative pressure wound therapy

Negative pressure wound therapy (NPWT) is widely recognised to advance wound healing and support surgical incision closure. Heli Kallio, authorised wound care nurse at the Trauma Department and Outpatient Clinic, Turku University Hospital, Finland, discusses her clinical experiences and the benefits with **ConvaTec**'s Avelle NPWT System.

What factors do you consider before using the Avelle NPWT System?

Heli Kallio: Before starting treatment, I consider the aetiology and position of the wound, if it will it be beneficial for the patient and how long negative pressure wound therapy will be needed if I decide to apply it.

The patient must be concordant with the treatment to progress wound healing. The challenges associated with dressing changes in a home care setting or healthcare centre are important as the treatment continues when the patient returns home with the device.

Heli Kallio, authorised wound care nurse, Turku University Hospital

Comorbidities and associated medications must be considered; for example, arterial insufficiency in diabetic foot ulcers means the wound needs to be closely monitored and dressing changes made more frequently. Possible anticoagulant and antiplatelet therapy impacts the treatment decision due to the increased risk of bleeding.

Heavy exudate levels can also be an obstacle to commencing treatment with a canisterless NPWT system like Avelle, which is indicated for low to moderate exudate levels. The peri-wound skin condition must be considered; for example, if the patient's skin is fragile and will not tolerate an adhesive dressing or adhesive sealing strips. If it is irritated and red, I would not commence NPWT. Due to the anatomical location of the wound it is sometimes challenging to establish a seal and maintain negative pressure, in areas such as around fingers, toes and genitals.

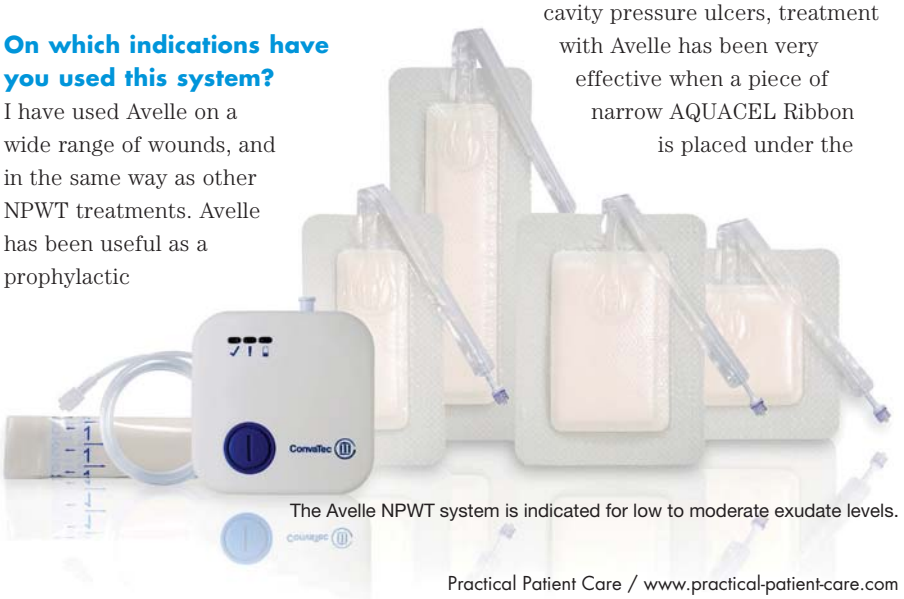
"The challenges associated with dressing changes in a home care setting or healthcare centre are important as the treatment continues when the patient returns home with the device."

On which indications have you used this system?

I have used Avelle on a wide range of wounds, and in the same way as other NPWT treatments. Avelle has been useful as a prophylactic treatment for high-risk patients immediately after surgery or after surgical site infection (SSI) revision surgery. I have used Avelle when surgical incisions have not healed through primary intention and led to partial dehiscence after removal of staples or stitches.

These types of wounds have been in breast, gastro or the perineum area cavity, which typically require a long healing time. I have also used Avelle on chronic wounds, such as diabetic foot ulcers and sacral pressure ulcers. It is important that the patient's wound is not infected or heavily exudating when the treatment is applied, as NPWT usually increases the volume of wound exudate.

Avelle allows for the use of absorbent filler dressings in the wound bed, including AQUACEL Extra. In sacral cavity pressure ulcers, treatment with Avelle has been very effective when a piece of narrow AQUACEL Ribbon is placed under the



The Avelle NPWT system is indicated for low to moderate exudate levels.

Avelle dressing at the beginning of treatment for one to two weeks and then continued with Avelle on its own.

"I have used Avelle on a wide range of different wounds, and in the same way as other NPWT treatments. Avelle has been useful as a prophylactic treatment for high-risk patients immediately after surgery or after surgical site infection revision surgery."

What clinical benefits does the Avelle NPWT System deliver?

The Hydrofiber Technology wound contact layer of the dressing is suitable for most wound patients and does not cause hypersensitivity reactions. The advantage of the Avelle dressing is that it is also suitable for use with cavity wounds when a AQUACEL Ribbon is placed in the cavity.

It also has the benefit of being a device that is easy to use and the patient may shower with the Avelle dressing in place. The duration of use of the device is up to 30 days, which is good, because often a week or two weeks of treatment does not provide sufficient response to stimulate wound healing.

Treatment with Avelle results in fewer dressing changes when used on the right patient at the right time. Negative pressure wound therapy stimulates new blood vessel growth and develops new granulation tissue at the wound base. It also reduces the oedema around the wound environment, thereby promoting wound healing. It has also been possible to use Avelle in conjunction with compression therapy.

How has Avelle benefitted your patients?

We have seen positive wound healing progression from the start of treatment, leading to very good wound healing outcomes. Treatment with Avelle has reduced the number of dressing changes. Patients only have to visit the healthcare centre once a week instead of two to three times a week for a dressing change. They have been particularly pleased with the advancement of wound healing, although some patients have said that the device and tubing slightly disturbed daily activities. However, a small device without a canister has been viewed by patients as a rather easy and discreet form of wound treatment. ●

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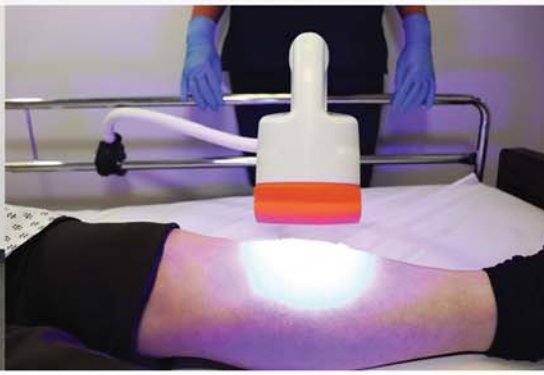

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Fluorescence Biomodulation for the Management of Wounds:
Acting at a Cellular Level to Control Inflammation and Improve Healing
Wednesday, June 5th | 15h30 to 16h30 | Room: A1

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Heal through fluorescence

There's nothing like the feeling of sun on your skin. Light can do just as much for a chronic wound. **FB Wound**, a Klox Technologies company, offers the LumiHeal System that uses the principles of fluorescence biomodulation to impact the three critical phases of healing – inflammation, proliferation and remodeling. Jason Gugliuzza, a senior vice-president at the company, explains what makes fluorescence energy a pain-free, non-invasive and cost-effective way to stimulate and enhance the healing process.

Sometimes, interminable problems disappear in an instant. After years without any progress, a sudden flash of insight can change everything. But that's a psychological phenomenon. Light-bulb moments solve frustrating riddles, they don't heal chronic wounds.

Then again, our skin is speckled with photoreceptors. It uses sunlight to create Vitamin D, and can detect light bulbs at the very least. Working out what this mean for wound healing is a riddle of its own. Klox Technologies' fluorescence biomodulation technology was born from solving it. A recent study into the effectiveness of FB Wound's unique LumiHeal phototherapy – conducted across 99 chronic patients with a mean wound age of 35.5 months – found that 47.5% of wounds totally closed after an average of 70.3 days.

"These were really tough, really recalcitrant wounds that had a lot of therapy for a number of years, and they just weren't healing," explains Jason Gugliuzza, senior vice-president at Klox Technologies. "Over that time there are issues with patient quality of life and patient morale; then there's nursing time, physician time, hospital time, and a hell of a lot of money spent. The majority of these wounds had at least one prognosis of poor healing, and our results were impressive." The study was called EUREKA.

Let there be light

Along with photoreceptor cells, human tissues contain photoacceptors, molecules with secondary-light-absorbing capabilities. These, it turns out, can be stimulated by certain wavelengths of light to enhance biological processes. By shining an LED on a wound coated in LumiHeal gel, which contains chromophores that convert light into low-energy fluorescence, it's possible to instigate mitochondrial biogenesis, even in elderly patients, stimulating and enhancing all phases of wound healing.

"Our work on mitochondrial biogenesis has been a real breakthrough," says Gugliuzza. "That primary mechanism of action, interacting with mitochondria to create [the energy-storing molecule] ATP, kick-starts healing and facilitates it across the inflammation, proliferation and remodelling stages. It brings about a cellular response in the wound, so it's an active therapy rather than a passive one."

Fluorescence biomodulation works through a mechanism known as the Stokes shift. Chromophores in the LumiHeal gel absorb photons from the LED and emit fluorescence energy at elongated wavelengths tailored for the unique light-absorbing characteristics of different cell and tissue types in the body. Longer wavelengths within the visible spectrum penetrate into the hypodermis, the deepest layer of the skin, while shorter wavelengths are localised nearer the wound surface and the underlying dermis.

The upshot of this is that in the inflammation phase, LumiHeal reduces the presence of IL6 and TNF alpha – the two main inflammatory markers in a chronic wound. Thereafter, the therapy heightens the proliferative phase by increasing blood flow and angiogenesis, which improves the availability of growth factors and brings about a significant increase in collagen production. In the remodelling phase, the collagen stimulated from within the wound, rather than through its contraction, is optimally aligned and extremely high quality – mimicking the collagen found in healthy human tissue, rather than that which produces hypertrophic scars."It's not one product that fixes one problem," stresses Gugliuzza. "It's looking at the holistic issue of wound healing and stimulating all of those three phases at the same time."

Increased quality of life

Traditional moist wound healing doesn't feel like a therapy so much as a wound-cleaning, dressing-changing, clinic-visiting chore. By contrast, fluorescence biomodulation requires physician and patient alike to don bright orange-tinted glasses. Then, while the gel is illuminated, it fluoresces through the whole colour spectrum.

"We have excellent patient engagement and compliance with this technology," beams Gugliuzza. "By down-regulating the inflammatory markers we immediately lessen any pain, but, more than that, patients actually feel like they're having a therapy, which keeps them very engaged and very invested."

After the last treatment visit in the EUREKA study, 94.9% of doctors said they would recommend the treatment, which is flexible enough to be combined effectively with moist wound dressing, negative-pressure wound therapy, and to improve outcomes after split-thickness skin grafts. "It's a five-minute procedure," says Gugliuzza, "but it's a very different way of managing a wound." ●

For further information

www.fbwound.com

A challenging landscape

Atypical wounds include a broad spectrum of conditions caused by inflammation, infection, malignancy, chronic illnesses or genetic disorders. An atypical wound may be suspected if the wound has an abnormal presentation or location and does not heal following a good treatment plan. The European Wound Management Association (EWMA) discusses its work to increase awareness about the clinical picture, diagnosis and treatment of these wounds.

An author group, chaired by document editor Dr Kirsi Isoherranen, is currently working on a new EWMA document that will be published and launched at the EWMA 2019 conference in Gothenburg, Sweden. The document focuses on atypical wounds – those wounds that create the most challenging situations for clinicians and/or patients from prevention, treatment and organisational perspectives. The author group includes prominent and well-respected clinicians who have all volunteered to use their expertise to describe the aetiologies and treatment strategies of different types of atypical wounds.

The prevalence of atypical wounds can be as high as 10% of all wounds, and it is probable that many of these wounds are underdiagnosed. Typical challenges include considerable diagnostic delays and prolonged healing times – for example, inflammatory and vasculopathy wounds (such as pyoderma gangrenosum, an inflammatory neutrophilic disorder, and cutaneous vasculitis). In addition, many atypical wounds have an enormous impact on the quality of life in the affected individuals, and a multidisciplinary team approach is necessary to ensure patients receive high-quality treatment in a timely fashion.

Risk factors and diagnosis

The risk for atypical wounds is usually higher in elderly people with weaker immune systems and is associated with pre-existing chronic medical illness, infections, inflammations or tumours. Taking a number of prescribed medications and leading an unhealthy lifestyle can also increase the risk for developing these wounds.

Managing any type of wound successfully demands an accurate patient assessment using a multidisciplinary approach that moves beyond standard care. Comorbidities, medical history and social support networks should all be evaluated during this process. It is essential that the clinician

is able to recognise common wound types a well as atypical characteristics in order to identify the best course of treatment. Problems with the assessment can result in failing to recognise the early signs of infection or wound deterioration, which can result in more expensive treatment, the use of antibiotics or hospital readmissions.

A systematic approach needs to be taken to determine wound aetiology and underlying causes, and thus obtain an accurate diagnosis. This often entails multiple steps, including a biopsy, which provides a histopathologic diagnosis and identifies a skin disorder that is not responding to current treatment.

Research published in *Wounds* recommends a biopsy for diagnosing inflammatory, microthrombotic and bullous disorders such as non-atherosclerotic ischemic ulcers, inflammatory conditions, malignancies, infections, autoimmune bullous disorders, venous ulcers, neuropathic ulcers, medication-induced wounds, pressure ulcers and traumatic wounds.

If a punch biopsy performed in an outpatient setting cannot confirm a suspected diagnosis in a wound that has failed other treatment measures, a surgical biopsy that can sample a larger area of tissue may be needed. In cases where the biopsy does not help diagnose the wound aetiology, the clinician should review the patient's medical history again.

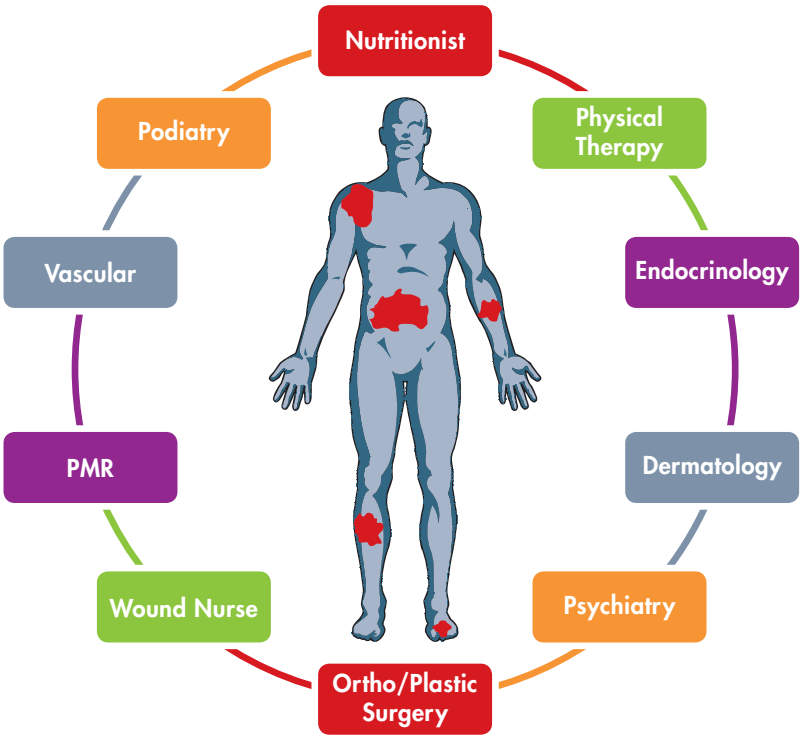
Some newer oncology drugs can also trigger skin reactions. Tracking the timing of chemotherapy is therefore essential, as it can be the cycle of the medication, not just the medication itself, causing the wound.

Atypical wound treatment

Normal wound care therapies tend not to be effective and when treating atypical wounds it is also essential to control the underlying disease process. This includes evaluating and managing wound tunnels. During treatment, it is important to understand proteases and inflammatory processes. Proteases are enzymes that break down proteins into peptides and amino acids. In wound healing, the major proteases are the matrix metalloproteinases (MMPs) and the serine proteases, such as elastase.

Types of atypical wounds

There are six main types of atypical wounds – inflammatory, vasculopathy, infection, malignancy, hereditary and genetic, and wounds of external cause. In terms of inflammatory wounds, pyoderma gangernosum is a condition characterised by skin cell death and destruction resulting from an unknown cause. It causes large painful ulcers to form, mainly on the legs, but they can also occur anywhere on the body as a secondary complication of any skin cut or trauma. An example is Bullous pemphigoid, a rare autoimmune inflammatory condition of unknown cause. This is where the immune system creates antibodies against its own tissue.



Atypical wounds, as with other types of wounds, also require treatment by clinicians from a range of disciplines.

"Many atypical wounds have an enormous impact on the quality of life in the affected individuals, and a multidisciplinary team approach is necessary to ensure patients receive high-quality treatment in a timely fashion."

These are formed against the junction between the upper and lower skin layers, leading to large clear fluid-filled blisters formation that are difficult to rupture. If this does occur, the blisters can become painful and sensitive. These are most frequent on the abdomen, groin, inner thighs and arms.

The two key vasculopathy wounds are cryoglobulinemia and vasculitis. Cryoglobulinemia is a systemic inflammation primarily affecting the kidneys, joints and skin and is caused by deposits of immune complexes containing cryoglobulin. The condition leads to itchy, small red skin lesions and ulcers, particularly on the legs, and causes joint pain in fingers, hands, knees and ankles, bloody urine, general weakness, and decreased

10%

The amount of all wounds that can be classified as atypical wounds.

European Wound Management Association

Kirsi Isoherranen speaks at the Atypical Wounds Session at EWMA2018.

sensation in the extremities, as well as abdominal pain. Vasculitis is an inflammatory condition of the blood vessels due to unknown origin. It can be occurred throughout the body (known as systemic) or in one area (referred to as localised) and can impact all types of blood vessels. The presentation varies from mild redness and irritation to occlusion of blood vessels and ischemia of the affected area.

"Managing any type of wound successfully demands an accurate patient assessment using a multidisciplinary approach that moves beyond standard care. Comorbidities, medical history and social support networks should all be evaluated during this process."

Infected wounds are where bacteria or other microorganisms have colonised, causing either a delay in wound healing or deterioration of the wound. These occur when the body's immune defences are overwhelmed or cannot cope with normal bacterial growth. Most infected wounds are caused by bacteria, originating either from the skin, other parts of the body or the outside environment. Infection of wounds can also be caused by surgery, which represents a serious health risk. The vast majority of deaths of patients who have undergone surgery are caused by surgical site infections.

A malignant wound is also known as tumour necrosis, a fungating wound, ulcerating cancerous wound, or malignant cutaneous wound. These occur when cancerous cells invade the epithelium, infiltrate the supporting blood and lymph vessels, and penetrate the epidermis. This results in a loss of vascularity and nourishment to the skin, leading to tissue death and necrosis. Malignant wounds may take the form of a cavity, an open area on the surface of the skin, skin nodules or a nodular growth extending from the surface of the skin. They can present with odour, exudate, bleeding, pruritus and pain.

Genetic or hereditary wounds can be the result of single or multiple causes, including psychological factors. Examples include Dermatitis artefacta, a condition that presents with multiple superficial, self-inflicted skin lesions of variable shape, size and depth on accessible areas like the face, arms and abdomen. In such cases the patient tends to have a history of chronic skin conditions and either a personal or familial history of psychiatric conditions.

Wounds of external cause can be either primary or secondary. An example of the former is brown recluse spider wounds, which can initially go unnoticed but within a few hours progress to severe pain, itchiness and a clear fluid-filled cyst with a red surrounding border. The wound can also be accompanied by a number of other symptoms, such as nausea, vomiting, diarrhoea, fever and even seizures. Conditions such as radiation necrosis are usually secondary to treatment for existing central nervous system tumours, which are being treated using radiotherapy. The existing tumour makes the surrounding tissue more vulnerable to radiation, leading to the destruction of cells, causing further damage.

It is clearly highly challenging to treat atypical wounds, as they have diverse causes and do not respond to conventional wound therapies. The EWMA document will thus provide a hugely valuable resource in helping to optimise care for patients with these wounds. ●

Reduce the risks of suprapubic catheterisation

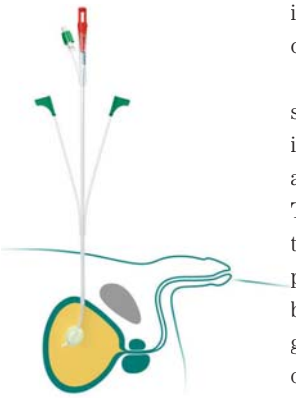
The use of the Seldinger placement technique with **B. Braun Medical**'s new Cystofix SG puncture sets make suprapubic catheterisation safer for both the practitioner and the patient.

Suprapubic catheter placement is not without risks for both the patient and the user – when done inappropriately the cannula may perforate the bowel, or cut the operator's gloves and fingers. Moreover, the catheter itself may also be damaged during placement. Taking these risks into account, it is common practice to call the most skilled urologist and ask them to do the job.

The metal splittable cannula has so far been the most popular suprapubic catheter placement tool, but at some point you need to split it and you end up with a very long and sharp piece of metal. This clearly conveys a risk, particularly when there is an element of time pressure present.

In addition, the splittable metal cannula was not designed to fit into the guide of an ultrasound probe, making it complicated for it to benefit from ultrasound guidance.

A solution exists – the Cystofix SG puncture sets use the standardised and safe Seldinger placement technique, with ultrasound guidance, and comes in a complete set. The Seldinger technique is well known by urologists who use it during percutaneous nephrostomy (PCN), and by emergency specialists who use it for central venous catheters (CVCs).



Cystofix SG puncture sets use the Seldinger placement technique.

There is no more splittable metal cannula, but instead a long 18G needle, a guide wire and a dilator. The 18G needle fits into the guide of an ultrasound probe and allows the user to benefit from the ultrasound guidance. This allows direct visual control of the puncture track in order to avoid bowel loops. ●

For further information

www.bbraun.com/cystofix-sg

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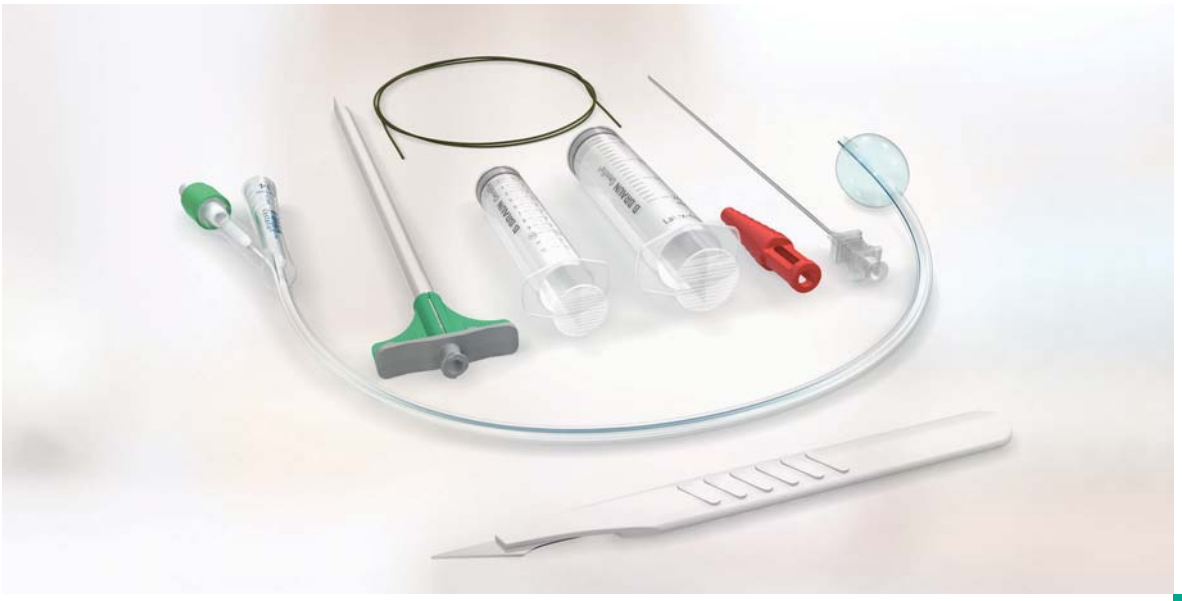

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Debridement made easy

Debridement is the process by which unhealthy tissue is removed from a wound site, and as such is crucial in the safe and healthy treatment of everything from deep cuts to chronic wounds. Liezl Naude, an independent wound management consultant, talks about how her use of **B. Braun Medical**'s Prontosan Debridement Pad complements and even in some cases replaces the traditional versions of this healing technique, where the main outcome is to deliver better outcomes for the patient.

What is debridement, and why is it important in the wound-healing process?

Liezl Naude: Debridement is one of the cornerstones of wound bed preparation and wound management in general. Since the introduction of wound bed preparation (WBP) in 2002, several authors have turned WBP into an art form. Probably the most well-known teaching on debridement is the use of the principles of the TIME model published by Caroline Dowsett and Heather Newton in 2005. Standing for tissue, infection/inflammation, moisture imbalance and edge of wound, the focus of this technique is on managing the wound bed by removing non-viable or deficient tissue.

Can you explain how the Prontosan Debridement Pad by B. Braun Medical complements more traditional wound debridement methods?

The Prontosan Debridement Pad is ideal for treating chronic wounds, including pressure ulcers, venous leg ulcers and diabetic foot ulcers. The microfibre technology within the pad is what makes all the difference. The hydrophilic structure of the dressing is a microfibre fibrous structure that picks up particles and debris without causing pain.

Additionally, the pad's microfibers use microscopic electrostatic forces to bind to particles, further increasing their ability to lift and retain particles of slough and debris. It almost works like a hoover, sucking up all the non-viable and deficient tissue. The pad is also very effective in removing senescent cells around the wound bed in chronic venous leg ulcers.

"The hydrophilic structure of the dressing is a microfibre fibrous structure that is able to pick up particles and debris without hurting the patient."

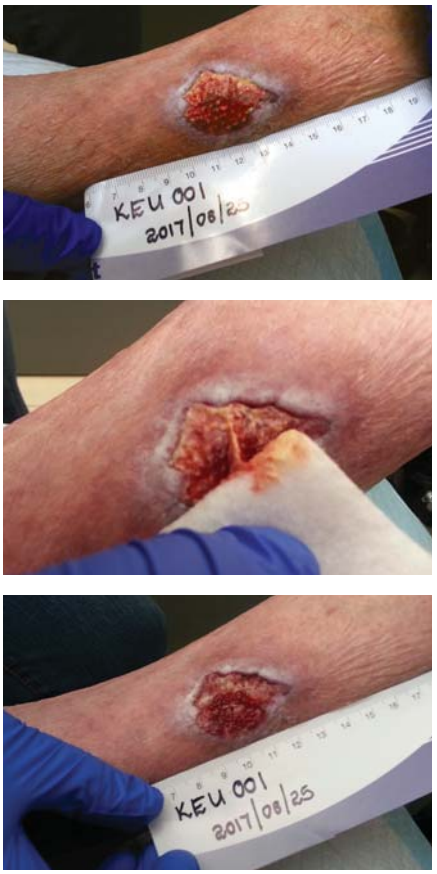
Why are chronic wounds uniquely difficult to treat through debridement?

Chronic wounds are, by their very nature, contaminated wounds. The degree of contamination present is often dependent on a variety of factors, including the nature of the host's immune response, the wound site, the type of tissue involved and co-morbidities. This means that biofilm formation is inevitable, and that good wound bed preparation or cleansing techniques are essential in managing and preventing infection. Another factor that cannot be disregarded in the treatment of chronic wounds is pain. Special attention must be paid by the attending physician or nurse to procedural pain when it comes to local debridement in the community or out-of-hospital setting. Chronic wounds also often require regular debridement to deal with the build-up of fibrin and biofilm formation.

How easy have you found it to use the pad, and how have patients you've treated with it benefitted?

We've been using the Prontosan Debridement Pad on a variety of different patients and wounds, and the shape of the pad makes it easy to get to that difficult-to-reach areas. Crucially, it doesn't require specialist training, and can be used as much in the community as in home nursing settings. In terms of improvements, the most significant has been the noticeable decrease in procedural pain, but also pain in general.

The wound bed is also cleaned easily without invasive debridement techniques.



©Liezl Naude

From the top: Chronic wound before cleansing, during cleansing and after cleansing.

Healthy granulation of the tissue at the wound site was often visible with one application in combination with a Prontosan irrigation solution soaking.

How have patients reacted to the treatment?

Patients requested the use of the Prontosan Debridement Pad rather than the use of a curette or sharp debridement. Quality of life improved and, overall, patients were able to cope better with procedures, and wound healing occurred faster. ●

For further information

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Prontosan®

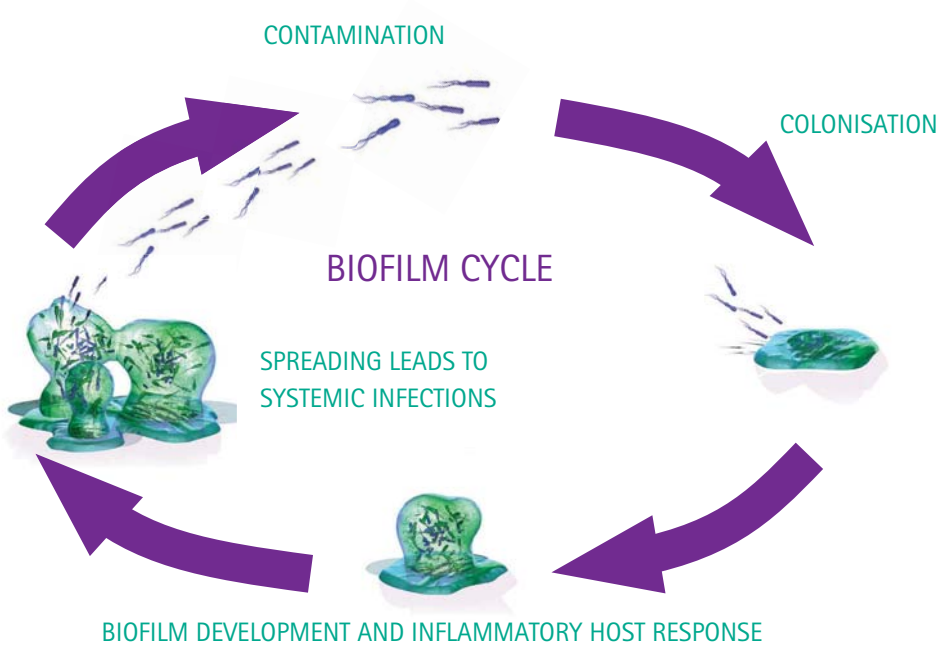
BREAKS THE BIOFILM CYCLE

THE PROBLEM

Traditional wound cleansing with saline and water is ineffective at removing coatings and debris in many wounds, especially complex biofilms.

FACT: Over 90% of chronic wounds have a biofilm present which is a major barrier to wound healing[1].

OVER
90%
OF WOUNDS HAVE A BIOFILM[1]



SOLUTION

Prontosan® with it's unique combination of Betaine surfactant and Polyhexanide antimicrobial is proven to disturb biofilms in wounds.[1,2]

Over 10 years of clinical practice demonstrate that by routinely introducing a Prontosan® regime as part of your patient pathway you will achieve better results, incl.:

- Improved patient outcomes, including time to heal[3]
- Prevention of complications[4]

B. Braun Medical AG | Infection Control | www.bbraun.com

1) Cutting K, (2010), Addressing the challenge of wound cleansing in the modern era, British Journal of Nursing, 2010 (Tissue Viability Supplement), Vol 19, No 11.
2) Davis SC, Harding A, Gil J, Parajon F, Valdes J, Solis M & Higa A "Effectiveness of a polyhexanide irrigation solution on MRSA biofilms in a porcine wound model" IWJ 1742-4801, 2017, 1-8.
3) Bellingeri, A. et al. "Effect Of A Wound Cleansing Solution On Wound Bed Preparation And Inflammation In Chronic Wounds: A Single-Blind RCT". Journal of Wound Care 25.3 (2016): 160-168. Web.
4) Moore, M 0.1% Polyhexanide-Betaine Solution as an Adjuvant in a Case-Series of Chronic Wounds, Surg Technology International, 2016.

IC2720_3047_01.0218

From past to present

Surgical site infections are the most common healthcare-associated infections, resulting in widespread suffering and economic loss. **Adrian Gombart**, author and professor of biochemistry and biophysics in Oregon State University's College of Science, and **Jingwei Xie**, assistant professor at the University of Nebraska Medical Centre, discuss the opportunities of nanofibre-based dressings for wound care.

Infections occur in wounds from both traumatic injuries and surgical sites. The latter accounts for approximately 300,000–500,000 infections every year in the US, equivalent to 2–5% of surgical patients. The subsequent increase in hospital stays results in up to $10 billion annually in additional healthcare costs. It is thus imperative to address this issue to reduce infections, save lives and lower healthcare costs. Although wound treatment may seem to be a relatively recent phenomenon, it can be traced back to prehistory. Different herbal remedies for wounds were developed depending on the trees, shrubs, or any other type of plants located within their environment. Knowledge about effective treatments was passed down through generations by tribal healers.

Wound dressing through the ages

Within ancient Greece, as these healers developed into doctors, it evolved into a primitive pharmaceutical industry where traders would travel overseas bringing

herbs that would be used for specific wounds. As with most industries, patients began to avoid the doctors altogether and instead purchased the herbs directly from traders, who would provide advise on the effects and quantities that should be taken. The Greeks also acknowledged the importance of wound closure, and were the first to differentiate between acute and chronic wounds, referring to them as 'fresh' and 'non-healing', respectively. Galen of Pergamum, a Greek surgeon who served Roman gladiators circa AD120–201, made a number of significant contributions to the field of wound care. The most important was the recognition of the importance of maintaining wound site moisture to ensure successful wound closure.

The clinical history of wound care can also be traced back to ancient Egypt. The Ebers Papyrus, circa 1,500 BC, details the use of a number of materials for topical treatments for wounds, including lint, animal grease and honey. The lint provided its natural absorbency, the animal grease provided a barrier to environmental pathogens, and the honey served as an antibiotic agent, all of which are important properties in wound treatment today.

The first major advances in the field occurred with the work of Ignaz Philipp Semmelweis, a Hungarian obstetrician who discovered how cleanliness prevented maternal deaths. This work was further developed by an English surgeon, Joseph Lister, in the 1860s, who treated his surgical gauze with phenol and was able to significantly reduce his surgical team's mortality rate.

Building on Lister's success with pre-treated surgical gauze, Robert Wood Johnson, co-founder of Johnson & Johnson, began producing gauze and wound dressings sterilized with dry heat, steam, and pressure in the 1890s. These innovations in wound site dressings marked the first major steps forward in the field since the previous advances of the Egyptians and Greeks.

During the First World War, chemist Henry Drysdale Dakin was consulted and invented Dakin's Solution, sodium hypochlorate and boric acid, to wash the wounds of British soldiers fighting in France. In the 1950s, the advent of fibrous synthetics such as nylon, polyethylene, polypropylene, and polyvinyls provided new materials that could be used for not only treating wounds but accelerating the natural healing process, in line with the aims of modern treatment approaches.

Rethink regeneration

When a wound occurs, it is imperative to quickly establish the skin's structure and functions to maintain homeostasis in the body. Although the skin possesses self-regenerative abilities, many types of wounds do not heal by themselves. Wound dressings are thus necessary to enhance healing while being able to cope with microbes, specifically antibiotic resistant bacteria that could interfere with the process.

Types of wound dressings

There are a number of different wound dressings available, which are dependent on the particular injury sustained:

- **Dry dressings:** these dressings are usually comprised of a gauze material and used for wounds with a small amount of drainage. These dressings are useful for keeping the wound covered after cleaning and to promote healing, as well as taking out small amounts of infection.
- **Wet-to-dry dressings:** these are mostly used for post-surgical wound care as well as debridement of wounds. In this type of dressing, the gauze is soaked in saline, placed lightly inside of the wound and covered with a dry dressing. The gauze can be removed once it has dried.
- **Foam dressings:** dressings that require additional padding use foam pads to help absorb and provide a moist healing environment. They also act as a shield to the wound and prevent any damage from occurring.
- **Alginate dressings:** these dressings are comprised of calcium and sodium salts, and provide a moist environment for the healing process. They are most suited to larger wounds, such as ulcers or donor sites.
- **Hydro-fibre dressings:** these are similar to alginate dressings in terms of absorption but they do not affect haemostasis. They are composed in sheets which contain polymer carboxymethylcellulose and can be cut according to the size and severity of the wound. A secondary dressing is always required.
- **Hydrogel dressings:** this type of dressing is designed for infected areas and those in need of a moist environment to sufficiently heal. It helps promote the body's own natural functions of removing necrotic tissue and is not advised to be used on dry wounds.
- **Self-adaptive dressings:** these are highly absorbent and rely on the properties of smart polymers, which are sensitive to humidity levels. The material responds to changes in wound moisture in real time and can switch between absorption and hydration. They can be used on most open wounds.

Source: *Biomedicine*

To overcome this issue, new bioactive dressings have been developed to mimic the skin's native structure and are compatible with cell loading (keratinocytes, fibroblasts and stem cells). Depending on their ability to replace the epidermis, they are grouped as epidermal, dermal and epidermal-dermal substitutes respectively. However, the production costs of these are high and often the dressings are unable to fully re-establish all native skin features.

Adrian Gombart and Jingwei Xie have been keen to approach this issue from a new perspective. "My group discovered that vitamin D induces the expression of an antimicrobial peptide gene (cathelicidin antimicrobial peptide or CAMP gene) in immune cells and skin cells," explains Gombart. "We proposed that we could use this knowledge to improve immune responses in wounds to reduce infection." Researchers published their findings in *Nanomedicine*.

In addition to boosting the immune system, vitamin D plays an important role in reducing inflammation and improving wound healing, making it ideally suited for this purpose. However, it cannot simply be used topically because it is rapidly absorbed and requires repeated application. ▶

$10 billion

The annual cost in increased hospital stays due to post-surgical infections.

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To address this problem, researchers used a different method to encapsulate drugs and other molecules in nanofibre materials that could be used to produce bandages, sutures and coatings for surgical materials. "By encapsulating vitamin D, we can provide a sustained release over time that obviates the need for repeated applications to wounds, thus stimulating the production of the antimicrobial peptide, reducing inflammation and promoting wound healing over time," says Xie. "These nanofibre materials provide a scaffold for wound healing, and are safe and biodegradable."

A novel aspect of this research was the use of the active form of vitamin D. Previous research with nanofibre-based sutures has used the inactive form, 25-hydroxyvitamin D3. In the current study, the dressings were capable of delivering vitamin D on a sustained basis over four weeks. These significantly induced production of a peptide, hCAP18/LL37, which kills microbes by disrupting their membranes.

The dressings work by enhancing innate immune responses rather than by containing conventional, single-target antimicrobial compounds. This means they are less likely to contribute to drug resistance. In the study, they were tested on human skin (in vitro) in a culture dish, as well as in vitro with keratinocyte and monocyte cell lines, and in a mouse model (in vivo).

A new tale is spun

Nanofibres can be prepared by a series of techniques, including self-assembly, phase separation and electrospinning. The latter is most common and has been applied in a number of biomedical contexts, including drug delivery systems, 3D constructs for tissue regeneration of cartilage, bone, heart valves, muscle, neural tissue as well as skin.

Electrospinning is not new. It has been widely used since the late 20th centuries but has since dramatically improved in terms of instrument design, material used, and nanomaterials produced. Since its inception, it has gathered increased attention in the scientific community and in industry, and is now considered to be a vital scientific and commercial venture with global economic benefits. Gombart and Xie used electrospinning to prepare the dressings containing the bioactive form of vitamin D. This fibre production method uses electric force to draw charged threads of polymer solutions or polymer melts up to fibre diameters in the order of several hundred nanometres.

"Electrospinning is a versatile, simple, cost-effective, and reproducible technique for generating long fibres with nanoscale diameters," explains Xie. "It is difficult to encapsulate hydrophobic molecules inside hydrogels. In sponges, hydrophobic drug molecules usually crystalise after encapsulation, which slows down the dissolution rate and is unfavourable." As a result, electrospun nanofibre wound dressings offer

Nanofibre-based wound dressings induce the production of antimicrobial peptides.

significant benefits over hydrogels or sponges for local drug delivery. "They offer ease of incorporation of drugs, particularly hydrophobic molecules, inside nanofibres, ease of control of release profiles by controlling the porosity of nanofibres and their degradation profiles, and exhibit an amorphous state for hydrophobic drug molecules, thus enhancing the solubility of drugs," explains Xie. "The architecture of electrospun nanofibres mimics the collagen structure of the extracellular matrix (ECM) – a 3D network of collagen fibres 50–500nm in diameter; therefore, compared with traditional wound dressings, nanofibre-based wound dressings provide several functional and structural advantages including haemostasis, high filtration, semi-permeability, conformability and scar-free healing."

Xie's and Gombart's groups have demonstrated that these nanofibres induce the expression of the antimicrobial peptide in vitro and in vivo, representing proof of concept. Researchers are now keen to build upon these findings in their future work. "With funding from the NIH, our collaborators, Dr Arup Indra and Dr Gitali Indra at Oregon State University, we are now testing the ability of nanofibre bandages to induce the antimicrobial peptide gene and improve wound healing in the mouse," explains Gombart. "We are also exploring the potential of these bandages to reduce bacterial infections in the mouse. Xie is working on co-encapsulation of other molecules with vitamin D that could improve the function of these wound dressings."

Aside from taking this particular research forward, researchers are looking to explore possibilities outside wound care. "The Gombart lab is looking for additional molecules; in particular, natural products that regulate expression of the CAMP gene," says Gombart. "We hope to develop safe therapies for treating a number of conditions that involve immunity and inflammation, from infections to obesity and metabolic syndrome."

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Prevent pressure ulcers

The skin is the body's largest organ, making it vulnerable to friction, moisture and shear – factors that create painful pressure injuries or pressure ulcers, which can cost up to $70,000 to treat per patient and can increase mortality rates by 350% over persons with the same risk factors but without pressure injuries. Jessica Pehrson, senior technical service engineer at **3M Health Care**, discusses the best strategies for preventing the injuries that can develop during hospital stays.

Whether we refer to them as pressure injuries or pressure ulcers, their impacts can't be disputed. In the UK, which calls them 'ulcers', they cost the NHS £2.1 billion a year. In the US, where the term 'injury' is now preferred, the total figure is $11 billion. What's more, the Centers for Medicare and Medicaid Services will no longer reimburse stage 3 and 4 pressure injuries that are hospital acquired. And those expensively elongated hospital stays are far from figures and formalities – each pressure injury contributes to greater patient suffering, and some can lead to premature mortality. Approximately 60,000 people die from complications arising from pressure injuries every year.

"Pressure injuries can affect every aspect of your life," says Jessica Pehrson, senior technical service engineer and nursing expert at 3M Health Care. "It's time away from your family as well as increased pain and suffering. Pressure injuries can also leave scars or deformities. Chronic pressure injuries that cause long term pain can affect your psychological well-being as well. People can or may feel isolated and alone."

Prevention starts the moment a patient enters the care setting and/or has a medical device installed. Care providers need to be aware of the issues that can arise from the patient's location and the patient themselves. This is about more than regular repositioning, though that is vital, it also means routine skin and risk assessments that that take into account age, health, blood flow, mobility, diet and more. "It's not just about where a patient is positioned and what dressings we put on them," explains Pehrson, "it's also about them."

Typically, an injury will start on an area of the skin overlaying a bony prominence. Indeed, more than 50% of these injuries start in the innocuous-seeming regions of the sacrum and the heels, areas that are subject to large amounts of pressure, moisture, friction and shear, particularly in bed-bound patients. Unhelpfully, those are not neatly partitioned causes, and need to be managed with a holistic approach. This is not simple. Moisture on the skin can increase the risk of pressure injuries by as much as 22 times, but many of the creams and ointments long used to combat it can actually increase the friction coefficient at the skin surface. By contrast, the 3M Cavilon Advanced Skin Protectant creates a film over the patient's skin, minimising friction, shear and moisture all at once.

3M Health Care's products are refined until they are as functional and user-friendly as possible.

The whole patient

By her own account, Pehrson dreams of pressure injuries. As part of her work, she monitors best practice guidelines around the world and educates caregivers about how to implement them. Previously a nurse in trauma and burn units, at 3M she uses her practical knowledge and experience to shed "clinical light" on the company's wound care innovations. It's about achieving the same goals on a far larger scale. "In the hospital setting I could affect several patients every day," she explains, "but what I do now can affect thousands."

The value of her work is clear with the 3M Tegaderm Foam. The 3M patented spoke delivery system, holding the dressing firm so it can be applied easily with one hand – even while wearing gloves. They're a technical service innovation. It's part of a five-layer dressing that effectively distributes pressure while outlasting other dressings. Equally, although the product is designed to re-adhere so clinicians can access and assess the wound, the low-profile edge doesn't roll up in high-shear situations.

By focusing on how 3M's products fit into practical healthcare situations and day-to-day clinical requirements, Pehrson and her colleagues are able to help refine them until they're as functional and user-friendly as possible. "We really just have an honest look at each product," she explains. "Sometimes we point out something that isn't going to work for a nurse: perhaps the dressing isn't shaped right for them; or, on the other hand, it might be too small for patients with different body types, for instance." 3M's silicone foam dressings, are designed to be thin, comfortable and patient-friendly while being easy to apply correctly. As such, 3M supports its best practice education initiatives with products that meet and exceed best practice guidelines.

"We're really looking at the whole picture, our whole patient," explains Pehrson. "It's our job to protect the patient from beginning to end." There's no better way to tackle pressure injuries. Or pressure ulcers, for that matter. ●

For further information

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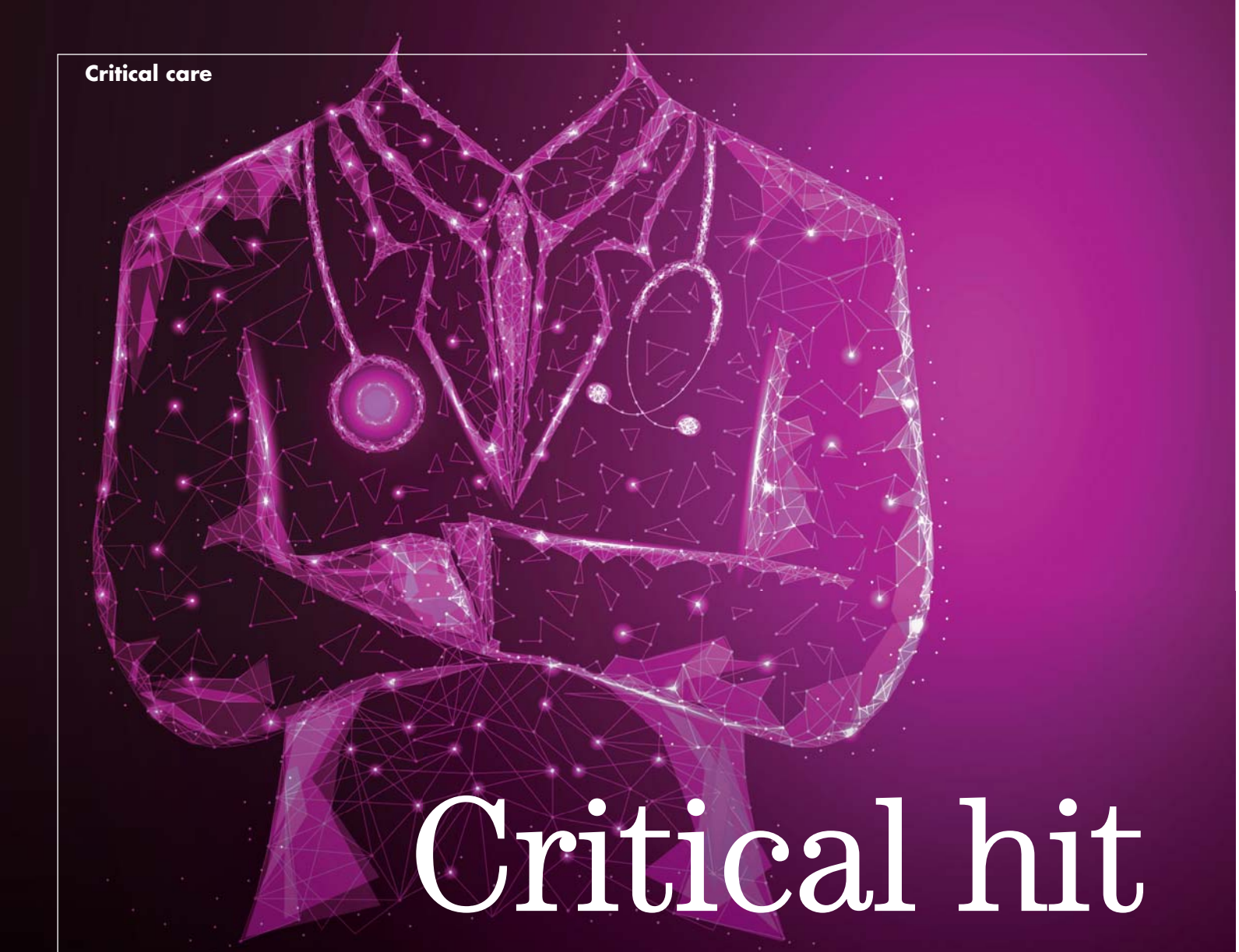


Critical hit

In the past few decades, we have witnessed a particularly rapid period of technological advancement in the area of critical care, with data and the need to interpret it now an integral part of the field. Emma Green explores these developments and considers the implications for optimising patient care.

It is clear that 21st-century healthcare requires intensive use of technology to acquire, analyse, manage and disseminate data. Nowhere is this more critical than in the intensive care unit. While there have been major improvements, the medical industry, for the most part, has not yet fully incorporated many of the advances in computer science, biomedical engineering, signal processing and mathematics that many other industries have embraced.

Despite the growth of critical care, the basic approach of data collection and management has remained largely stagnant over the past 40 years. Large volumes of information are collected from disparate sources and reviewed retrospectively. This is highly challenging in itself as providers are required to navigate through a jungle of monitors, screens, software and often paper.

Data from patient monitors and medical devices, although sometimes visible at bedside, is difficult to acquire and store in digital format. Currently, there is limited medical device interoperability and integration with the electronic medical record (EMR) remains incomplete and cumbersome.

In addition to these limitations, standard analytical approaches provide little insight into a patient's pathophysiologic state, which is imperative to understand the dynamics of critical illness. In order to optimise care in this context, healthcare professionals need precisely time-stamped data, integrated with clinical context and processed with a range of analytical tools. These demands are often beyond the capability of typical commercial monitoring systems.

A comprehensive understanding from advanced data analytics can aid physicians in making timely and informed decisions, and improving patient outcomes. Ultimately, an integrated critical care informatics architecture will be required, which

includes acquisition, synchronisation, integration and storage of all relevant patient information into a single, searchable database, as well as the ability to gain practical insights from this data.

Computers in the ICU

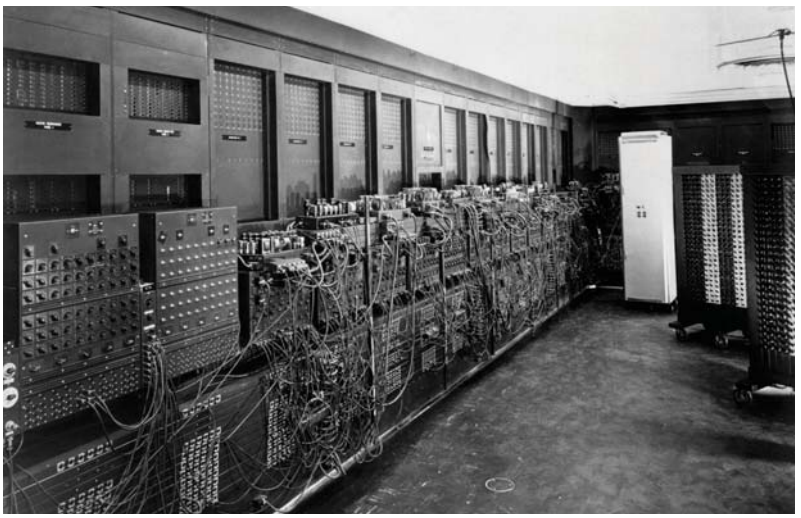
The Electronic Numerical Integrator and Computer (ENIAC) was the first general-purpose computer and was introduced in 1946. It was developed to calculate missile trajectories for the US Army and was the size of a room, weighing 27t. A few years later, commercially available computers hit the market, but due to their high cost their use was limited to large corporations to manage their accounting.

In the 1960s, hospitals began to develop EMR systems including the Problem Oriented Medical Record (POMR) at the University of Vermont, Health Evaluation through Logical Processing (HELP) at the University of Utah, The Medical Record (TMR) at Duke University and the Computer Stored Ambulatory Record (COSTAR) at Harvard. Although these early systems were capable of processing medical information, they were rarely connected to the real-time data-intense environment of the ICU and thus has limited applicability in this context.

The first computer to be introduced into critical care was in 1966 and was used to collect vital signs from the bedside monitor automatically. Through connecting this device, it was possible to obtain arterial and venous pressure, heart rate, temperature and urinary output. This had been previously attempted in 1934 with a mechanical contraption but was not entirely successful.

Basic analytical tools, such as trend analysis, were later added to the automated data collection system to improve functionality. Other early applications of computers in healthcare included clinical decision support systems to assist in the diagnosis of haematologic disorders, tools for respiratory monitoring and automation of blood transfusion after cardiac surgery. For example, the computer-based Clinical Assessment, Research and Education System (CARE) was a clinical decision support system designed to help with the treatment of critically ill surgical patients. This continuously monitored physiologic and metabolic markers and managed data about fluid and electrolytes as well as cardiac and respiratory functioning.

In the 1980s, automatic collection of heart rate and blood pressure became increasingly advanced with data being presented in graphical displays instead of bedside flow sheets. The architecture also improved from the locally contained model to the client/server model in which a workstation in the ICU interacted with a central computer housing patient data via a local area network. Links to the hospital EMR systems were also being made, such as computers systems that handled admissions, discharges and transfers so that patient demographic data could be readily accessed by healthcare professionals. Physician and nursing notes were later able to be entered electronically into problem-oriented medical records.



The Electronic Numerical Integrator and Computer (ENIAC) was the first general-purpose computer, introduced in 1946.

Computers were also being introduced into the operating room, with computerised anaesthesia records allowing for more reliable collection, storage and presentation of data during the perioperative period, in addition to providing basic record-keeping functions. However, data from medical devices were rarely integrated with the other physiological information.

Clinical information systems

Today, there are a number of commercially available clinical information systems for the ICU. These have continued to evolve over the years, with various acquisitions resulting in the creation of broad end-to-end platforms. While these represent a significant improvement compared with past technology, there are several existing limitations.

Currently these systems are restricted in terms of functionality and the acquisition of high-resolution physiologic data. This is due to a trade-off between the memory requirements of capturing high-resolution physiological data versus capturing data snapshots that may be sufficient for some clinical decisions. Standards have yet to be set about where that balance lies.

Despite the increasing amount of information collected, visual displays in the ICU have remained largely unchanged for the past several decades. Clinicians can be confronted with more than 200 variables when caring for critically ill patients, yet most people cannot judge the degree of relatedness between more than two, which can contribute to medical errors. In order to prevent this from occurring, graphical displays must be mindfully designed by applying a human systems integration approach. It is important to understand not only how information should be optimally presented to promote a better

27 tonnes

The weight of the very first general-purpose computer in 1946.

British Broadcasting Corporation

The increase in monitoring technology and stand-alone medical devices has been central to the growth of critical care.

understanding of the patient's pathophysiologic state and support decision-making, but also to facilitate collaboration and optimal work-flow among the whole healthcare team.

The promise of critical care informatics lies in the potential to use these advanced analytical techniques on high-resolution multimodal physiological data to obtain more knowledge of the complex relationships between physiological parameters, improve the ability to predict future events and thus provide targets for individualised treatment in real time. Future systems will go beyond simply reporting streams of raw data, but will synthesise it to generate hypotheses that best explain the observed data, providing situational awareness to the clinician.

Medical device interoperability and data integration

Central to the growth of critical care has been the increase in monitoring technology and stand-alone medical devices. A wealth of information is generated by reflecting dynamic and complex physiology, which can only be understood through integrating data with the clinical context. However, the vast majority of these variables are generated from individual devices that are not readily compatible with each other.

Some connect directly into the bedside monitor but many only do this partially, if at all, which means that not all data is captured electronically. The lack of interoperability is one of the most significant limitations not only within critical care but within healthcare more generally. This is in stark contrast with the 'plug and play' capabilities of consumer electronics.

Many groups are tackling the problem of interoperability on their own by developing the hardware and software interfaces that facilitate device connectivity. Connecting with analogue data ports demands appropriate hardware interfaces, analogue-to-digital (A/D) converters, and filters to eliminate aliasing due to a mismatch between sampling rate and the frequency content of the signal being acquired. It also requires that the data be properly scaled to the voltage range of the A/D converter (microvolts to millivolts) to maximise the resolution. Although such approaches provide the opportunity to individually interface with a variety of devices in the ICU, a system that provides comprehensive, cross-manufacturer medical device integration for the care of a single critically ill patient at the bedside is not yet available.

When data is being acquired from different devices, each with its own internal clock, the time stamps of data acquired simultaneously can all be different. In order to align these, time synchronisation of the information is critical. Furthermore, even when acquiring data from a single patient monitor, time drifting from natural degradation, daylight savings time or incorrect adjustments made by the clinical staff need to be rectified. Without a universal clock ensuring that all the values are in sync, interpreting the information is highly challenging, if not impossible.

Data acquisition and integration systems

Commercial off-the-shelf products do typically not support high-resolution physiologic data acquisition, archiving, or annotation with bedside observations for clinical applications. This is largely because such systems have been developed in academic settings largely for clinical research. As they are not open source, most of these are not readily available, which has resulted in substantial duplication of effort in software development for acquiring and archiving physiological data. There has been considerable effort to address this issue, ranging from developing and testing of new mathematical and analytical tools, to hardware and software solutions for patient data acquisition, archiving and visualisation. Some have also focused on multimodal data collection linked with clinical annotation.

While there have been significant improvements in intensive care monitoring, there remains a lot of untapped potential to capitalise on recent advances in computer science, biomedical engineering, signal processing and mathematics. Acquiring, synchronising, integrating and analysing patient data remains highly challenging due to the lack of sufficient computational power and a lack of specialised software, incompatibility between monitoring equipment and limited data storage within current hospital systems.

As a result of recent developments in technology, all of these technical problems are now surmountable. Today, we are fortunate to be living within a data-intensive science era in which there is a wealth of information available to generate insights that can be used to optimise the speed and accuracy of clinical decision-making, improving the lives of patients. ●

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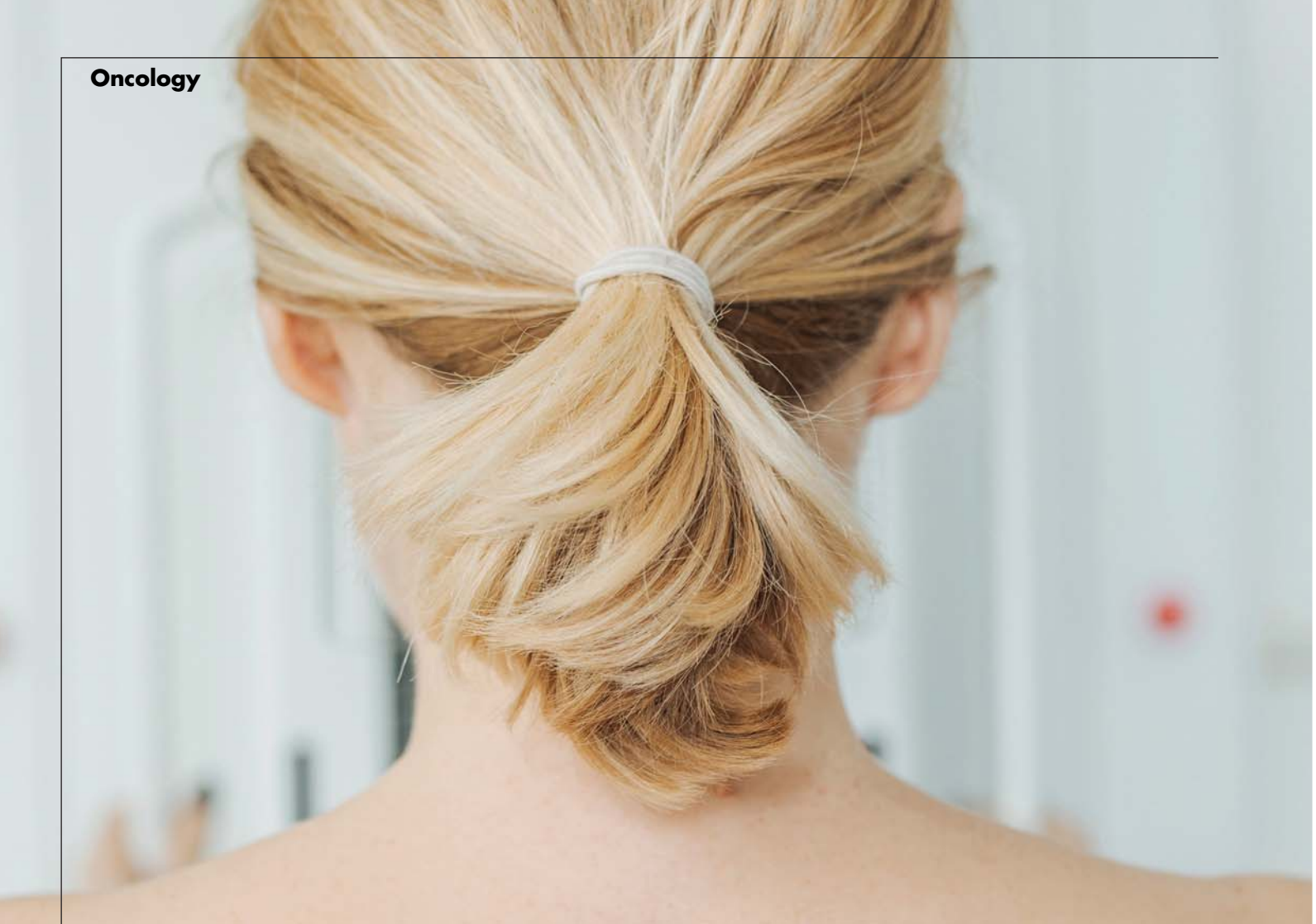

Back and forth

A team of international researchers has developed a new methodology that can better determine the mortality risk associated with the combination of early detection through screening and stage specific therapy. **Sally Turner** talks to the project's leaders about the important findings and implications of the study.

Despite a substantial volume of strong evidence supporting the value of mammography screening, in 2011 a report in the *British Medical Journal* claimed there was no evidence that nationwide mammography screening played a direct role in breast cancer mortality reductions. The piece triggered fierce debate, with some critics of screening even suggesting that mammography may do more harm than good. Since then, hardly a year has gone by without a new mammography controversy.

The team behind the recent 2018 study believes the 2011 conclusions were incorrect and at odds with most of the global evidence on the efficacy of mammography.

The new research was funded by the American Cancer Society; Professor Robert Smith is the organisation's vice-president of cancer screening and is a member of the Swedish Organised Service Screening Evaluation Group (SOSSEG) that initiated the study; he also holds an adjunct professorship at Queen Mary University of London. "The conclusion from this study was made on the basis of a deeply flawed analysis comparing trends in registry data in six European countries," he contests. "The research team broke elementary epidemiological rules for an analysis like this – most importantly having no data on whether women had been screened or not, and by not isolating deaths from breast cancer in the evaluation period that had been diagnosed before screening was available."

Now, eight years on, conjecture surrounding the issue may finally be put to rest by new methodology

developed by the SOSSEG – the team of scientists gathered in Sweden to produce a new report on the benefits of mammography screening during an era when breast cancer treatment has been improving. The study of more than 50,000 women, published in November 2018, has determined that those who participate in breast screening have a significantly greater benefit from modern treatments than those who are not screened.

A groundbreaking study

The research revealed that women who chose to take part in an organised breast cancer screening programme had a 60% lower risk of dying from breast cancer within 10 years after diagnosis, and a 47% lower risk of dying from the disease within 20 years after diagnosis. This vast difference in outcomes was observed despite the fact that each woman with breast cancer had access to the same state-of-the-art therapy that was appropriate for her disease stage at diagnosis.

The study involved 52,438 women aged 40–69 years in the Dalarna region of Sweden, screened over a 58-year period. Those diagnosed with breast cancer received stage-specific treatment in line with the latest national guidelines.

Led by Dr Laszlo Tabar, of Falun Central Hospital in Sweden, researchers used an innovative method to fully evaluate the impact of mammography screening on death from breast cancer.

"Our novel method is based on the date of diagnosis, not on the date of death," explains Tabar. "We developed the method for examining the incidence of breast cancers each year that eventually were fatal within 10 and 20 years with women's participation, or lack thereof, in mammography screening."

Essentially, for every year over the 58-year period, the team measured two variants – attendance to screening and diagnosis of breast cancer in that year.

Smith offers further insight into the methodology used. "We then measured the incidence of breast cancer death at 1–10 years and 11–20 years after that year of diagnosis," he explains. "We know that there have been advances in treatment, and conventional approaches to evaluating long-term outcomes associated with breast cancer screening have been challenged to disentangle the effects of screening and treatment. In this case, in any given year, women will receive the standard therapy for their stage of diagnosis, regardless of whether their breast cancer was diagnosed by screening or not."

Global teamwork

Developing this new methodology was a demanding process. Assembling such a large and unwieldly dataset was complicated, as data had to be drawn from hospital records and vital statistics, and then carefully scrutinised for accuracy and continuity. "Determining the correct population denominator was a key challenge," comments Tabar, "but successful cooperation between the programmers of the hospital information systems and our biostatisticians solved this complex problem using our prospectively collected and stored data."

A diverse group of experts from Europe, Asia and the US collaborated on the study and all agree that the benefits it reveals are down to the fact that screening detects cancers at an earlier stage – this makes for a far better prognosis, as the earlier cancer is diagnosed the easier it is to administer effective treatment.

The team have worked together for more than 20 years, evaluating the effectiveness of mammography screening, participating in ongoing debates about its effectiveness and identifying strategies that produce better outcomes.

There are many approaches to measuring the benefits of mammography screening, but with this new methodology, the team saw an opportunity to answer a very simple question: 'If I participate in mammography screening, how much will I reduce my risk of dying from breast cancer compared with not attending?'

The 'unique and very complete data' from the Swedish study offered an opportunity to apply a new methodology with the potential to offer greater clarity on screening statistics for clinicians, patients and the public.

Smith is keen to explain why the new methodology is so important. "The findings clearly and simply compare the outcome of participating in mammography screening compared with not participating," he says, "and they show that no matter what advances have been made in breast cancer treatment, women who attend breast cancer screening have a substantially reduced risk of dying from breast cancer compared with women who do not attend."

Countering the critics

The new methodology comes in the wake of years of anti-mammography campaigning, and supports other strong evidence regarding the importance of organised nationwide breast screening.

Since the contentious 2011 study, the UK independent review of breast screening has concluded that the process has indeed reduced mortality from breast cancer, and the International Agency for Research on Cancer's comprehensive report draws the same conclusion.

Professor Stephen Duffy, a senior author of the new methodology, confirms this point. "Most organisations conclude that the benefits of screening outweigh the harms," he says. "The 'harm' that has the highest public profile is overdiagnosis, and estimates of this vary widely. However, those

60%

The lowered risk of dying from breast cancer within 10 years of diagnosis for women who chose to take part in breast cancer screening.
SOSSEG

estimates that fully take into account complexities such as changes in underlying incidence of breast cancer, and lead time from screening, find at best modest levels of overdiagnosis."

A vital service

After many years of emphasis on the alleged 'harms of screening', the international team is keen to dispel misconceptions and extol the many benefits of screening.

"'Harms' represent a spectrum of adverse outcomes that range from minor to more serious," say Duffy. "The most common 'harm' is being recalled for further evaluation. Most women say that this is not a serious concern, although short-term anxiety is common and not surprising. A much smaller proportion of women undergoing screening will need to undergo a biopsy to rule out the presence of cancer."

"Of all the 'harms' associated with breast cancer screening, the greatest harm comes from non-attendance," adds Tabar. "There is a need for educating women about the very real benefits of early breast cancer detection through mammography screening, which results in a significant decrease in advanced breast cancers." He cites the key benefits as a significantly lower risk of dying from breast cancer, fewer mastectomies and a higher frequency of breast conserving surgery, and fewer patients requiring more severe forms of adjuvant therapy.

"The list of the benefits of breast cancer screening is much longer," he continues. "My personal opinion is that the complex issues surrounding breast cancer screening require subspecialisation by the professionals – including radiologists, pathologists and surgeons. Keep in mind that screening radiology is not for every radiologist. Likewise, the use of large format histopathology should be a must for optimum imaging-histopathologic correlation interpreted by pathologists with special training and interest in diagnosing breast diseases. The detection of an unprecedented number of non-palpable breast cancers challenges the diagnostic and therapeutic teams, offering multiple avenues for high-quality research."

Breast cancer screening is recommended by many countries and the SOSSEG researchers hope their findings will instil greater confidence in regular screening, and demonstrate that regular attendance is more advantageous than many people appreciated.

The way forward

In the UK, the NHS Breast Screening Programme offers all women aged 50–70 a regular mammogram. However, although participation rates average more than 70% nationally, they vary dramatically across the regions, with lower rates in economically deprived, inner-city areas. There is a need to improve participation in breast screening programmes, particularly in socio-economically deprived areas.

Another 2018 study at Queen Mary's, funded by Bart's Charity, also indicated that breast cancer is still seen as 'a white women's disease'. While breast cancer incidence is lower among black women in the UK, survival rates are also lower, which may correlate with a reduced level of awareness about the prevalence of breast cancer among black women. The report references 'the whiteness of the media coverage of breast cancer'.

"Screening recommendations are designed to apply to most of the target population of women in a specific age group," explains Smith. "Mammography is less sensitive in women who have such significant mammographic breast density that a breast cancer cannot be seen, and for these women supplemental imaging with ultrasound or MRI can overcome the mammography's limitations in imaging very dense breast tissue." The same limitation applies to women with an inherited predisposition to developing breast cancer because their risk is higher at an earlier age, when breast tissue is dense, but also mammography is less sensitive than MRI in these women when they are older. This is why most recommendations for women who carry a known or suspected mutation on a breast cancer susceptibility gene call for regular exams with MRI. "We need to make sure these women receive personalised approaches to screening in order to ensure they have the same chance of benefitting from breast cancer screening as average risk women," adds Smith.

Breast cancer and benign breast disease are both extremely complex, so no single imaging modality is capable of imaging tissue changes with optimal precision. "In recent years, in addition to substantial improvements of mammography, there have also been significant developments in handheld and automated breast ultrasound, magnetic resonance imaging and interventional methods for more accurate multimodality diagnosis of breast diseases," says Tabar. "Since the prerequisite for decreasing mortality from breast cancer is detecting the tumours in their early, asymptomatic stages, it would be hoped that high-quality mammography screening programmes could be offered in all countries."

There is no doubt that introduction of multimodality imaging to breast cancer screening would improve the detection of even more cancers at an early stage. However, as with most aspects of healthcare it all comes done to cost, and with the NHS in dire need of a funding injection it seems unlikely we will see this level of precision screening in the UK any time soon.

"The single greatest priority we have is to improve upon the system of women getting regular high-quality mammography," concludes Smith.

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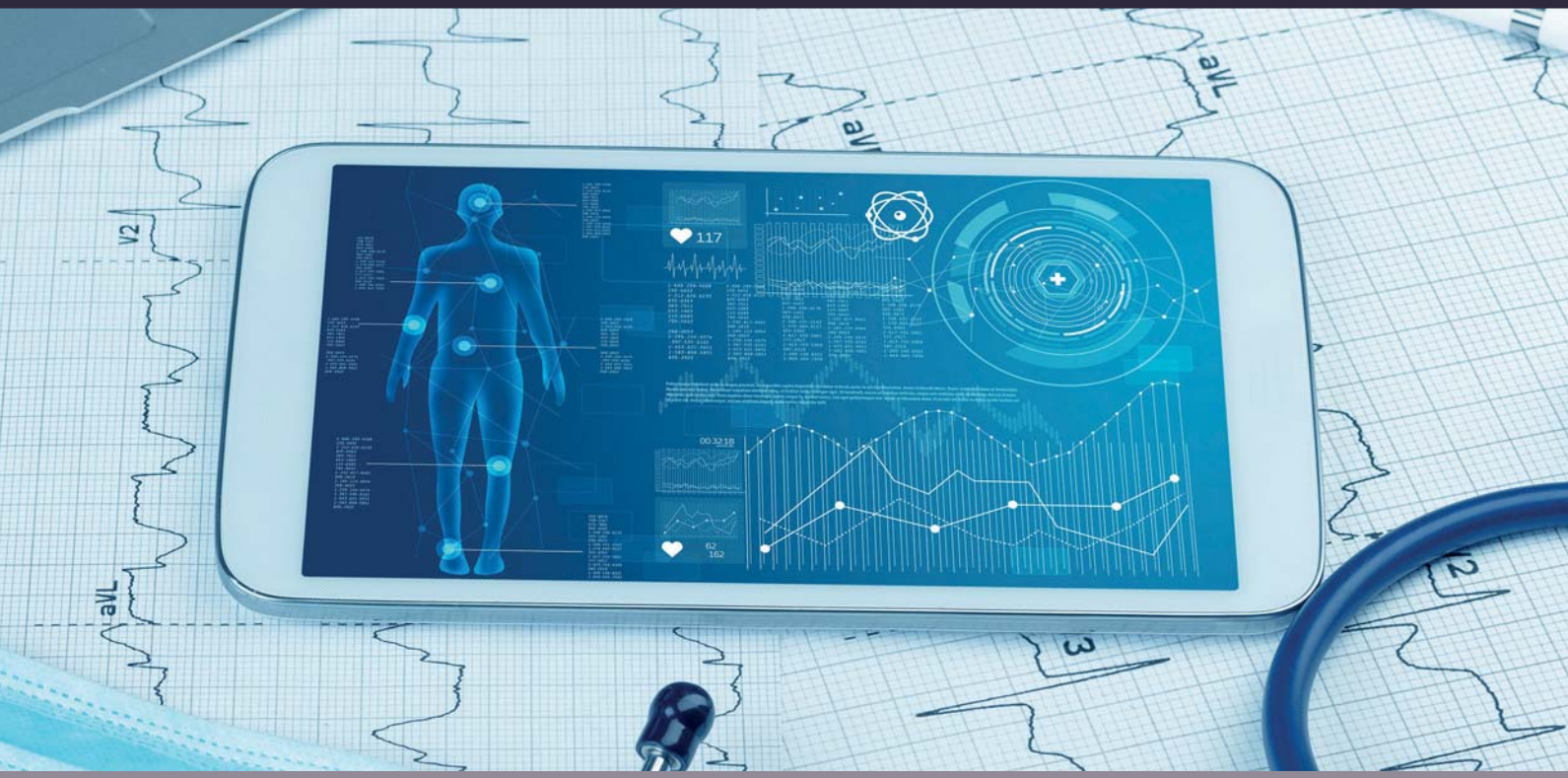

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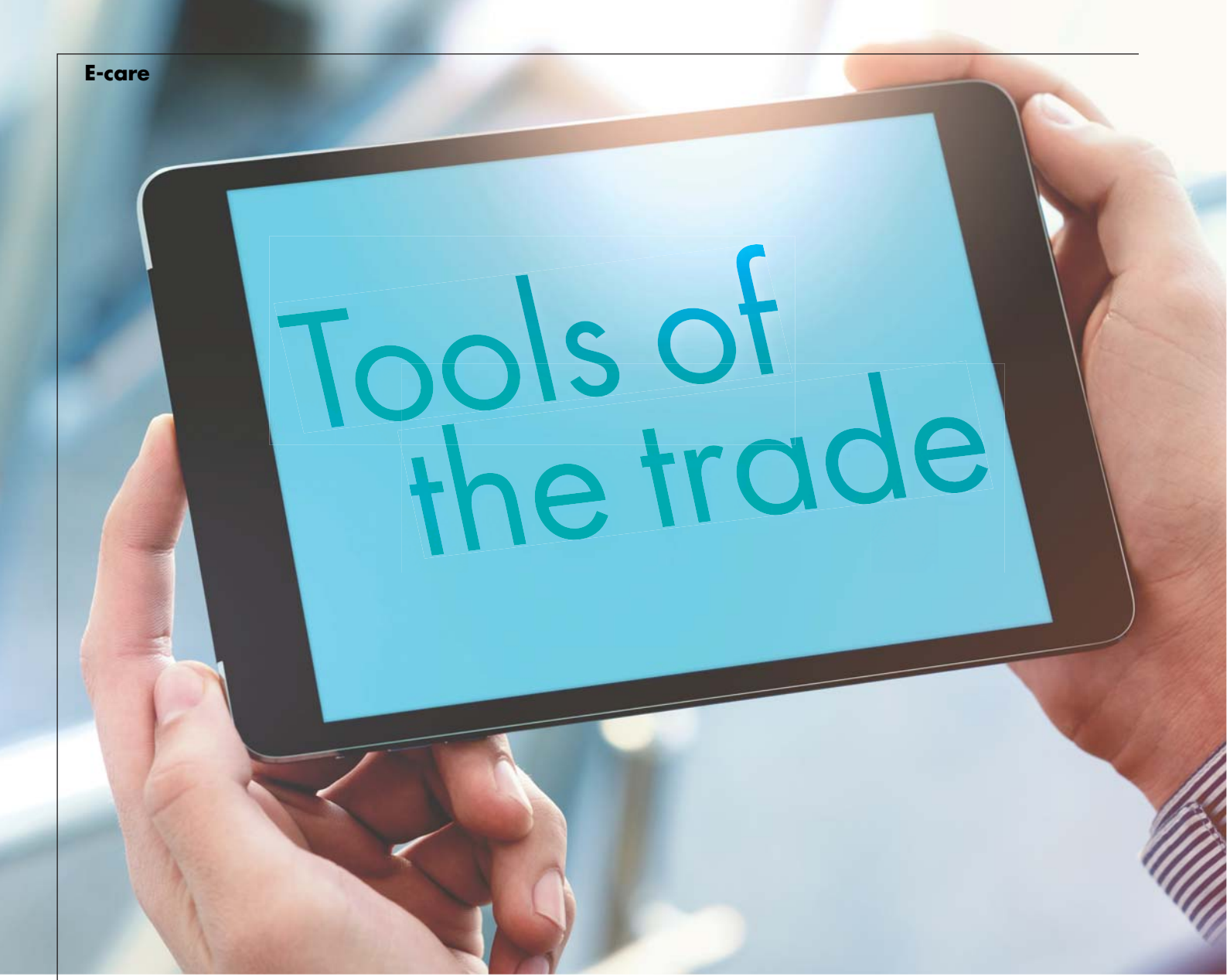

The Patient Toolkit, developed by the non-profit MITRE Corporation, allows patients to digitally record symptoms, treatments and medications, as well as communicate with providers. It also addresses the needs of healthcare professionals, by generating longitudinal severity and compliance data. **Kristina Sheridan**, head of the enterprise strategy and transformation department at the MITRE Corporation, and her daughter, **Kate Sheridan**, discuss how this technology can be used to optimise the care provided to patients.

Both the clinician and the patient hold an important piece to the care puzzle. The physician has expertise in treating illness, whereas the patient is the authority on living with the condition. However, transferring the patient's experience into a usable data set can pose challenges. Attempts at tools to facilitate strong collaboration tend to track a narrow range of symptoms and are often not able to be easily incorporated into the daily lives of patients.

These issues became apparent to Kristina Sheridan, head of the enterprise strategy and transformation department at MITRE, when her daughter Kate was diagnosed with Lyme disease. Prior to working at the non-profit, her career had a completely different focus. "Initially, I was in space engineering and astronautics," says Kristina. "But the experience that my family went through finally gave me an understanding of what it takes and how hard it is for complex chronic patients to manage their health and for their caregivers to support them. That was why I shifted careers and joined MITRE."

For MITRE, serving the public interest means being forward-focused while also trying to solve existing problems across the US through both technological and scientific innovation. "At MITRE, we work with government healthcare public health agencies to focus on complex problems," explains Kristina. "We help and empower patients with chronic conditions, which is not currently focused on as much as it should be," she continues.

Although seemingly unrelated to her work at MITRE, Kristina 's background in space engineering and astronautics allowed her to approach the care of her daughter's condition in a novel way. "Approaching this problem from a systems perspective, coming at it from a patient's and a provider's lens, allowed us to come up with a solution that would enable better information-sharing and improve outcomes," she says.

With roughly four out of five healthcare dollars in the US being currently spent on chronic conditions, such a tool is greatly needed. The difficulty in managing these illnesses is that they demand coordination between multiple healthcare providers, which is challenging for patients, caregivers and clinicians alike. All too often, healthcare professionals are required to make decisions based on limited patient-provided data, resulting in duplication of tests, uncoordinated treatment plans, extended illness, and higher costs. "This is a national challenge," says Kristina. "We've got 117 million people with one or more chronic conditions and between 34–52 million caregivers."

Lack of support

Despite the large chronic illness population, Kristina was disappointed to find a lack of adequate resources to help manage her daughter's care. "What we found is that there were different tools spread out across multiple different areas but there was nowhere we could go that had things in one place that were designed for us," she explains. "A lot of tools are designed from a clinical perspective, built around one disease, one condition or trying to track only one type of information."

Despite increasing discussion of 'patient centricity', this concept is rarely translated into clinical practice, which the toolkit aimed to address. "Patients are at home managing their own chronic condition the majority of the time, and they are in the clinic for a small amount of time," says Kristina. "Life can get in the way."

Outside the clinic, patients have their normal daily activities to maintain and accommodating care of a chronic condition into this daily routine can be highly challenging. Combined with attempting to pay attention to symptoms and then relaying this to healthcare professionals, this can become hugely overwhelming for both the patient and their caregiver. "All these things add up to this huge burden," says Kristina.

Her experiences led to the development of the patient toolkit, an interactive resource to track a range of chronic condition symptoms, which could be easily integrated into the individual's daily life. "We had to design it around the whole person," says Kristina. "Our experience with Kate was that, it was not just about one diagnosis, or one set of symptoms, it was the holistic picture of what was going on that was needed so we could understand the best way to manage her care and treat her condition that allowed her to have a fuller life."

The toolkit was designed to achieve three key aims for patients – to manage their care, collect the relevant information about their chronic condition and use that to inform decisions about their care on a daily basis. For Kate, the toolkit allowed her to experience more autonomy over her condition. "It's an element of control," she says. "It made it easier for me to clarify it in my own head and make plans around it. I could also develop coping skills for specific scenarios."

The Patient Toolkit is an iPad application developed in modules to maximise the reuse of code. Its relational database is HL7-compliant to ensure future interoperability with other electronic healthcare systems and the potential for translation into other languages. Although currently only being

Features of the Patient Toolkit

My Day
The user interface was designed to be easy to use and help patients get through the administrative aspects of their days. From this one location, patients can update how they are feeling, the severity of their symptoms, special journal entries and their schedule.

My Journal
The journal feature helps patients capture unusual events or things they want to tell their doctors such as odd symptoms, what they have been eating, or details on how they are feeling. This helps them track these events over time and see how these events affect their overall health. It also helps patients remember the things they wanted to share during provider visits.

My Medications
Patients can easily add their prescription information by selecting the medication that matches their prescription label, and request reminders for taking medication. When patients are not able to take their medications the data is captured to support a conversation with their providers to develop a plan they are able to comply with.

My Symptoms
Patients can explore, input, and edit their health data, including symptom severity, on an easy-to-use mobile platform. They can identify a full set of symptoms by choosing from a pick list, then capture the severity in a few touches using a tailored list. This data is mapped to the source standards used by EHRs.

My Appointments
Patients can track their appointments, set up goals and questions pre-appointment, and enter notes in real time during or after their appointment for maximum retention. Integrating the capture of information into a patient's day removes a significant amount of stress and enhances appointment quality.

My Reports
Once historical symptom and medication data is captured, patients can view visual reports to discover changes in their symptoms, see how they responded to medications, and track their overall state of health over time. These reports help patients decide when they need to contact a provider, and provide new patient-generated data to help providers with clinical decision-making.

Source: MITRE Corporation

117 million
Number of people with one or more chronic conditions in the US.
MITRE Corporation

Kate and Kristina Sheridan speaking at CHIME CIO Forum in February 2019.

used within the US, it was designed with the ability to be rolled out on a wider scale and eventually used by patients with chronic conditions worldwide.

The tool takes advantage of mobile technology and provides meaningful ways for patients and caregivers to visualise and understand illness data. It addresses both the financial and personal burden of chronic illness by increasing a patient's awareness of their health status, enabling them to participate more fully with their healthcare team and improve their treatment compliance.

Central to achieving these capabilities was the collection of what Kristina calls 'active patient-generated data'. In contrast to information obtained by technologies like wearables and monitoring devices, which collects passive data from users, the key idea of the toolkit is that it uses data that is created by the patient.

Rather than needing to remember the often huge list of symptoms at clinic appointments, which can result in an incomplete picture being given, this information is gathered ahead of time, resulting in patients and caregivers being "more prepared and able to have a richer conversation" with healthcare providers. For example, rather than focusing on adherence in a binary way, patients can more easily identify and relay if a treatment is causing difficulties. "Sometimes I would end up missing medications for a specific reason," says Kate.

This is beneficial for both clinicians and patients as no extra time is required for appointments because the communication is more efficient. The toolkit can also reduce healthcare costs as patients can more readily determine whether their symptoms require medical attention or not.

The Patient Toolkit is intuitive to use and offers invaluable services.

Obstacles to be overcome

With her scientific background, Kristina went to great lengths to ensure that the tool was evidence-based and validated by patients, caregivers and healthcare professionals. To assist in the development of the toolkit, the MITRE team collaborated with academia. This included conducting research in more rural areas. "It was very important to us that we didn't increase disparities," says Kristina. "We did usability testing in a hospital in Montana and the majority of patients found it easy and intuitive to use."

Particularly popular was the journal feature, which allows for notes and photos to be taken. In chronic conditions a lot can change in a short space of time, so the ability to track symptoms in a variety of different ways ensures that nothing is missed. In addition to improving healthcare interactions, this enables patients to better understand their own health status, which can be hugely empowering.

Despite the positive feedback received about the toolkit so far, implementing it into clinical practice is an ongoing challenge. This is because it demands making a dramatic shift in the role that patients play in their care. Rather than being passive recipients, they become active members of the team. This requires acknowledgement of the value that patients offer by healthcare professionals. "It's not an easy problem," Kristina acknowledges.

Despite these issues, Kristina remains optimistic that decisions within the industry are moving in the right direction and that in time it will be a "common and normal tool given to patients to help them reduce the burden and better manage their own care, leading to more engagement and improved outcomes". With more and more discussion about patient centricity and the increasing appreciation for the role of technology, this is only a matter of time.

A fresh perspective

Over the past decade, we have witnessed a dramatic evolution of consumer electronics, including the emergence of wearable technology. Typically referring to electronic devices with sensing and computational capabilities that are worn by or attached to the body, these have the potential to be a disruptive force in healthcare, particularly within the operating room. Emma Green considers the potential of these technologies to enhance surgical education, intraoperative documentation and patient care.

While interest among medical professionals surrounding consumer wearable devices has precipitated widespread discussion of potential applications in surgery, evidence to support their effectiveness in this context is often anecdotal. As this technology becomes increasingly prevalent, it is essential that decisions about integrating them into clinical care are based upon empirical evidence, rather than their novelty.

Smart glasses are one of several promising wearable technologies that could be used within the operating room (OR). These tend to consist of a wire frame integrated with a computerised central processing unit, camera for point-of-view pictures, video capture and a small head-mounted prism display that sits above the right eye. They have wireless capabilities and are equipped with sensors that can exert control with voice command, touch, blinking and head movement. Although this technology has the potential to improve operating procedures, most research to date on these devices has been explorative or 'proof-of-concept', limiting the ability to draw firm conclusions about their effectiveness. Such studies have also highlighted a number of limitations of this technology. This includes functional issues, such as inadequate battery life, insufficient resolution and rudimentary voice control. ▶

As wearable technology becomes more prevalent, it's vital that its implementation into clinical care is based on evidence, rather than novelty.

Usability problems have also been identified, including incompatibility with surgical loupes and a mismatch between the user's natural line of sight and the position of the display. There are also privacy concerns that have hindered the implementation of this technology into clinical practice.

"We hope our research into designing this wearable system will help to expand the range of surgical procedures that can use robotic assisted systems so that more patients and hospitals can gain the benefits from this type of surgery."

Sanja Dogramadzi, Bristol Robotics Laboratory

The case for camera systems

Camera systems have also been proposed as offering value within the OR. These are typically commercially available 'action' cameras often used in extreme sport photography. They usually consist of a high-definition camera, encased in a compact frame that can be strapped to either the head or body of the user. Most of the research on these devices has been clinical studies evaluating different features, which have demonstrated that the technical specifications of these systems could be adjusted to optimise both quality of picture and video capture in order to view the fine details required for use in surgery. However, similarly to smart glasses, a number of issues have been identified with this technology. Particularly significant is the lack of an integrated screen and the weight of these devices, which would prevent them being used within the OR.

A number of studies have explored the potential of head-mounted displays (HMD) for surgery. These are capable of superimposing computer-generated imagery over the user's field of view. There are two main classes of see-through HMDs – optical and video. The former allow the user to view the real world through a semi-transparent mirror, enabling the superimposition of electronic images or text over the user's natural view. The latter features non-transparent screens that instead display a video feed of real-world scene, captured with an external camera, in front of the user's eyes. Key barriers to implementation were device ergonomics – usually weight – and usability issues – including wire connectivity and intentional blindness. There have also been documentations of negative physical side effects, including eye fatigue, dizziness and headaches.

There have been four main clinical applications of wearables within the OR. The first is communication, particularly via teleconferencing, where a live feed is provided to observers remotely using the video-streaming capabilities of a device. Teleconsultation has also been tested, where clinicians in different geographical locations discuss issues via video.

Education is another promising area. Point-of-view recording and video-steaming abilities have been identified as valuable tools for training surgeons via telemonitoring. One study by researchers from Thomas Jefferson University tested the use of smart glasses within ophthalmological surgery education. This involved an ophthalmologist wearing the glasses while performing scleral buckling surgery, a procedure with a small operative field that is not conducive to conventional trainee instruction. The device allowed trainees to visualise a video stream of the primary surgeon's field of view on a monitor with real-time narration, thus proving a valuable learning resource.

Safety can also be aided by wearable technologies within the OR. Studies have investigated a number of devices for this purpose, including a see-through HMD for monitoring physiological data from patients that enables anaesthesiologists to limit time spent looking away from the patient. Wearables have been explored in terms of their ability to enhance efficiencies, such as the use of smart glasses to display and facilitate the completion of surgical checklists and HMSs to provide clinicians performing minimally invasive surgery with individual endoscopic displays.

Wearables also offer the potential to improve information exchange within the OR. This involves managing textual, pictorial and numerical information intraoperatively. Applications include photo documentation via both picture and video capture, voice-initiated intraoperative dictation and the collection of personal movement data to facilitate the assessment of specific surgical skills.

Hands-on approach to robotics

More recently, the use of wearable robots is being explored in surgery. A collaborative team of researchers from the University of Bristol within the UK are currently developing a system for keyhole surgery, which will offer surgeons natural and dexterous movement as well as the ability to navigate

66%

The increase in surgical errors due to the effect of short-term stress.

British Journal of Surgery

through the surgical environment. Scientists will develop modern biomedical devices that are able to replicate complex human dexterity and senses. These wearable robots can be worn by the surgeon and will transmit their movements to the closed surgical interface without restrictions, reducing their overall cognitive, manipulation and training demands.

The systems involves three pieces of hardware – an exoskeleton, an instrument and smart glasses. Exoskeletons will fit over the surgeon's hands, controlling the instruments inside the body, This includes a newly developed surgical 'gripper', which mimics the thumb and two fingers of the hand. "In our project the exoskeleton will record the position of the fingers and communicate this to the robotic tools inside the body using tele-operated technology," said Professor Sanja Dogramadzi from the Bristol Robotics Laboratory, in a 2017 video for the University of the West of England, Bristol. "We want to give existing processes a more natural interface – operating surgeons will not have to do any unusual or unnatural movement. They will be able to use their hands as they would in open incision surgery."

The instrument, which goes inside the body, will have haptic abilities, allowing the surgeon to feel the tissues and organs inside the body, similarly to conventional surgery. The glasses will allow surgeons to position themselves anywhere in the OR. "This is an advance compared to current systems, which use a flat TV-like screen to relay images back to the surgeon," said Dogramadzi.

Researchers will collaborate with clinicians to ensure that these are fit for purpose. "The research will use the expertise and feedback of senior surgeons to develop the tools. We will use rapid prototyping to make prototype tools that the surgeons will test and we will incorporate their feedback into the next stage of design," said Dogramadzi. "This means we can adapt tools to the needs of different surgical procedures and this user-centred design process places surgeons at the heart of the development of this system."

Heartbeat monitor

Although still ongoing, this technology offers huge potential to improve procedures within the OR. "We hope our research into designing this wearable system will help to expand the range of surgical procedures that can use robotic assisted systems so that more patients and hospitals can gain the benefits from this type of surgery," said Dogramadzi. Wearables have also been used for research purposes. A 2018 study, published in the open access branch of the *British Journal of Surgery*, used technology that captured the electrical activity of a surgeon's heart. Scientists found that during periods of short-term stress, which can be triggered by a negative thought or a loud noise, surgeons are much more likely to make mistakes that can cause bleeding, torn tissue or burns. Medical errors currently result in 250,000–440,000 deaths annually in the US, with a proportion of those mistakes occurring in ORs, highlighting the significance of the issue.

The research used a smart shirt, which was worn underneath the surgeon's scrubs while he performed surgery. Originally designed for athletes to provide them with precise physiological data during workouts, the technology is able to measure the electrical impulses that trigger heartbeats. Using this data, lead author Peter Dupont Grantcharov was able to obtain heart rate variability information, which is a marker of momentary stress levels.

During the study, Grantcharov was allowed into the OR, where he collected laparoscopic video recordings of Dr Homero Rivas, associate professor of surgery at Stanford Medical Centre, as he worked. Another researcher reviewed the recordings and documented the mistakes that were made, and stress levels and errors were time-stamped to check for an association.

This data yielded the alarming finding that the effect of short-term stress on surgical error is as high as a 66% increase. "I was surprised by that, as well as by the amount of distractions in the OR," said Grantcharov. "Many machines have alarms that go off periodically, equipment malfunctions, side conversations take place, people walk in and out of the OR – I could go on. My hope is that other researchers will build upon our work to make further strides in learning about the causes of stress on surgical personnel. If our study helps make the OR a safer place for patients, I'd be thrilled."

Over the next few years, we are likely to see these technologies increasingly used not only within surgery but in healthcare as a whole. Although still an emerging field, wearables clearly offer huge potential for optimising OR procedures, saving time, costs and improving the lives of both clinicians and patients. ●

The SMARTsurg project to develop wearable robotics for surgery

The SMARTsurg project aims to develop an advanced system for performing R-A MIS, in order to reduce the surgeon's cognitive load related to the system's operation that will ultimately allow for a shorter training time, while delivering increased accuracy, safety, reduced MIS procedure time and expanded applicability.

The main vision of the SMARTsurg project is to enable complex, minimally invasive surgical operations by developing a novel robotic platform for assisting the surgeon in such tasks. This system will use highly dexterous anthropomorphic surgical instruments, wearable hand exoskeleton with haptic feedback for controlling the surgical instruments and wearable smart glasses for augmented reality guidance based on real-time 3D reconstruction of the surgical field.

SMARTsurg developments will employ a user-centred approach for efficient technology adoption and commercialisation, which will be achieved using short prototyping and testing cycles supported by focused end-user and commercials requirements. Ultimately SMARTsurg technology could provide a more dexterous, natural-to-use system with much improved interfaces that would render fast learning and acceptance by surgeons.

Source: *British Journal of Surgery*

Non-invasive treatment for vaginal health

We speak with Professor Marco Gambacciani, director of the Menopause Centre at Pisa University Hospital, about the benefits provided by **Fotona**'s non-invasive laser gynaecology treatments in treating a variety of gynaecological disorders.

You have been working with laser systems for treating gynaecological disorders since 2013, after being introduced to non-invasive FotonaSmooth Er:YAG technology. What convinced you that traditional treatment methods weren't enough?

Professor Marco Gambacciani: I can say that the management of postmenopausal patients requires extreme personalisation. One choice doesn't fit all. Consequently, I was excited by this new opportunity to treat vaginal atrophy with the laser. With one machine, we have the ability also to treat stress urinary incontinence and initial stages of vaginal prolapse. It's a great achievement for improving women's well-being and quality of life.

There are many laser manufacturers on the market. You chose the FotonaSmooth gynecological laser. What makes them different from other laser manufacturers?

I reviewed all the available literature when I approached this new technology. No other machine was able to provide the option to treat – with the same non-invasive technology – vaginal atrophy, stress urinary incontinence or vaginal prolapse. Since adopting the product, we have established strong new evidence that the FotonaSmooth technology offers the best choice for the practicing gynaecologist in terms of safety, results and patient satisfaction.

Clinicians are often seen to be averse to new technology, but you appear to have embraced it. Which are your favourite features of the FotonaSmooth laser system?

The FotonaSmooth Er:YAG laser technology is not just minimally invasive, it is a completely non-invasive procedure. It is not ablative, and causes no bleeding, pain or scars. The gentle, but intense, heating of the vaginal tissues can guarantee positive results in more than 80% of patients.

"No other machine was able to provide the option to treat, with the same non-invasive technology, vaginal atrophy, stress urinary incontinence or vaginal prolapse."

Vaginal atrophy is a very common indicator of a number of disorders, and affects over half of women in their 50s. What is your experience with RenovaLase compared with standard therapies?

I have treated hundreds of women, and we have published many papers about the significant and quick effects of RenovaLase. In normal postmenopausal women, the effects of FotonaSmooth are rapid compared with the standard hormonal therapies, but also longer lasting – up to 12–18 months. FotonaSmooth is also the best treatment for breast cancer survivors. With these women, hormonal therapies are not allowed. With RenovaLase, the effects are astonishing and their sexual life is not jeopardised by atrophy anymore.

You also have a lot of experience with IncontiLase treatment for stress urinary incontinence. Could you tell us more about that?

The effects of IncontiLase on urinary incontinence are surprising. The significant improvement is evident after the second or third laser application. The effects are there in more than 80% of our patients, with significant improvement of continence for up to 12–18 months. More than 70% of our patients later repeated the treatment, thereby avoiding surgery. I think that with IncontiLase we can avoid unnecessary surgical procedures, save money as well as patient distress and pain.

With the introduction of the ProlapLase non-invasive laser treatment for prolapse, the future of treatment is bright. What do you see are the main benefits?

First and foremost, that it is non-surgical. The effects of ProlapLase on the initial stages of POP are really encouraging, mainly when we are dealing with a defect of the anterior vaginal wall and vaginal laxity.

What emerging trends do you see in non-invasive laser gynecology in the future?

I do believe that in the near future the laser functional vaginal restoration and urinary incontinence treatment will be a common practice in gynaecology, not only for therapy but also for prevention. We will see a real turning point in the coming years in laser treatment for prevention in order to maintain normal vaginal functions. ●

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Lessons to be learned

Medical imaging has revolutionised healthcare delivery and the next generation of imaging technology promises to be even more powerful, further enhancing the ability of physicians to diagnose and treat an increasingly wide range of diseases at lower radiation doses. Developments in AI are helping improve both efficiency and effectiveness of diagnosis and care. **Ajay Kohli**, physician at Drexel College of Medicine in Philadelphia, speaks about the recent technological advances within AI.

Only a few years ago, AI was barely discussed within medical imaging. This has all changed and there are now numerous conversations taking place, both online and offline, about its significance in influencing multiple industries, including healthcare. Its growth has been rapid and it shows no signs of slowing. Based on data from the marketing intelligence company Tractica, AI in radiology will reach $19 billion by 2025.

Within the buzz about the technology, there is both excitement and concern among healthcare professionals about the opportunities it provides. Although there is consensus that AI could improve the speed and accuracy of diagnoses, there are also anxieties that it could replace humans, leaving jobs at risk. As a radiology resident physician with a deep entrepreneurial background, Ajay Kohli offers a valuable insight into both sides of the coin.

Failure to launch

Applications in radiology have not always been effective, contributing to ongoing worries about the technology among healthcare professionals. "In the late 1990s, computer-aided diagnosis (CAD) was used in mammography but this was in a rudimentary way," explains Kohli.

Despite the excitement and high hopes for AI at the time, the technology was simply not advanced enough to be relied upon for clinical decision-making. In a 2018 paper published in the *Journal of the American College of Radiology*, Kohli discussed the lessons that could be learned from the failed application of CAD.

Due to its limitations, healthcare professionals had to re-examine all the areas flagged by the technology, which was not a productive use of their time. "Not only did CAD increase the recalls without improving cancer detection, but, in some cases, even decreased sensitivity by missing some cancers, particularly non-calcified lesions," Kohli said. "CAD could lull the novice reader into a false sense of security. Thus, CAD had both lower sensitivity and lower specificity, a non-redeeming quality for an imaging test."

The failure to offer anything beyond the role of a 'second reader' or 'spell-checker' was due to the technology's limited processing power and, more fundamentally, because of its reliance on supervised learning. This type of AI, unlike deep learning, demands the identification and labelling of the inputs of the system, which means that it is heavily reliant on the skill of the radiologist.

"In supervised learning, the computer is trained on samples with known pathology (truth) and then tested for its ability to predict the likelihood of malignancies in a test sample (truth and lies)," Kohli said. "Despite the allure of supervision, the pedagogy is not neutral. Because the computer sees more cancers during its training than its test, there is verification bias, and the specificity drifts."

Deep thoughts

Since the late 1990s, AI efforts have mainly focused on deep learning, a type of machine learning that is based on the way the human brain processes information. "There are three common applications of these technologies within radiology," explains Kohli. "These are deep learning to recreate CT and to automate workflow, as well as apps for physicians."

Based on recent figures, Frost & Sullivan notes that among the 114 start-ups active in the AI for medical imaging space, a significant majority are targeted at the image analysis aspect of radiology. As decisions about a diagnosis are based on this work, it is clearly a hugely important clinical task. AI can be used to recreate CT image scans to assist in this process.

"Neural networks called autoencoders can boost the quality by generating similar images with 'repaired' pixel values, which has been learned from training on similar data," explains Kohli. "This could prevent the need for the patient to have as many follow-up scans, which can lower exposure to radiation and allow for quicker diagnoses to reduce healthcare costs."

Of the 114 start-ups active in the pursuit of AI in the medical industry, the majority are focused on radiology.

Beyond image analysis, automating workflow is another hugely valuable application of AI. The technology could help to reduce the burden on radiologists and improve efficiencies within their daily activities. Unsurprisingly, this is an area of concern among clinical professionals as deep learning is capable of performing tasks that they would otherwise be completing. However, there currently remains a need for 'human-in-the-loop' systems where healthcare staff are making the final call in order to ensure patient safety.

"Neural networks called auto encoders can boost the quality by generating similar images with 'repaired' pixel values, which has been learned from training on similar data. This could prevent the need for the patient to have as many follow-up scans, which can lower exposure to radiation and allow for quicker diagnoses to reduce healthcare costs."

Apps have also be developed for physicians using AI technology to help support them to enhance the level of care they can provide to patients. "You can help to ensure that care is similar in different countries and healthcare systems by replicating the workflow of the radiologist," says Kohli. This can be particularly helpful in overcoming language barriers.

Despite the exciting AI applications within radiology, there are a number of weaknesses with current technologies. One of these relates to the errors that the technology can make, such as the potential for the neural network to 'hallucinate' by adding together two images. Similarly, worrying results have occurred with 'backdoor poisoning attacks' where mislabelled images enter into the

$19 billion

The estimated value of AI in radiology by 2025.

Tractica

data set, causing malicious actors to insert 'backdoors' into learning systems by tricking them into reliably predicting particular incorrect labels.

Mistakes aside, an inherent problem with AI is termed the 'black box' issue, which means that results are difficult to explain and validate. Although inputs and outputs can be monitored, it is unclear exactly how these technologies arrive at a decision. "You can make a few tweaks to the system, which can create big changes in the results being generated," says Kohli.

In some instances, these systems use shortcuts, which can lead to false conclusions being made. Such evidence should serve to further reassure radiologists that their jobs are not in immediate danger of being replaced.

Lending a hand

To help address some of these issues, Kohli suggests that healthcare can gain a lot from looking to the application of AI within finance. Although not intuitively compatible, they do have certain similarities that are beneficial for sharing knowledge. "Both industries have lots of data and use automation," Kohli says. "Also, neither one can discount the role of humans in making decisions."

"Not only did CAD increase the recalls without improving cancer detection, but, in some cases, even decreased sensitivity by missing some cancers, particularly non-calcified lesions. CAD could lull the novice reader into a false sense of security."

The technologies implemented so far have fundamentally changed the financial industry. Examples include the use of natural language processing in detecting anti-money laundering and fraudulent activity, cognitive computing to analyse variables to build more effective training algorithms and leveraging deep learning to explore consumer decision patterns and provide personalised 'chatbots'. Hedge funds are an area of finance that has been particularly transformed by the integration of AI. Systems using these technologies are already outpacing those run by humans alone.

In the same way that global financial markets had a metamorphosis into the electronic and digital versions that we see today, we are also currently witnessing a similar shift in the medical industry. In the past several years, there has been an influx of technologies such as electronic medical records, data from implantable and wearables. All of these have created large amounts of data but the industry remains behind the financial sector in optimising the use of this data.

Kohli has suggested that healthcare can learn a number of lessons from the application of AI in finance. The first of these is truly personalised medicine. Instead of merely using the imaging data, this could be integrated with more general information about the patient as well as their preferences to inform treatment options.

Comprehensive communication, characterised by video visits, telemedicine, outpatient imaging, patient-centred documentation and other aspects of convenient care are set to become the new norm for healthcare delivery. In the same way that natural language processing is being applied in finance in the form of 'chatbots' to educate people on how to make better investment decisions and track their spending, these could be used to inform patients on their condition and treatment options. They could also be used to track symptoms in between appointments so that time in clinic can be more productive. Ultimately, AI can be conceptualised as an ally to enhance the standard of care provided to patients, making it more personalised and accessible.

Collaboration between individuals is also needed in order to overcome the challenges of AI within imaging. Currently, software engineers, data scientists and venture capitalists are dominating the conversation about these technologies and radiologists remain silent. In order to maximise the use of AI in any healthcare setting, it is essential that developers understand the clinical relevance and significance of the data.

Critical thinking and reflection can also be prompted though collaboration. Kohli recalls an instance where he spoke about heart failure and was asked about his reasons for using that term and the potential negative impact of the word 'failure' for patients. As an established healthcare professional, it was not something Kohli had considered before but his experience highlights the value of conversations with individuals and organisations both inside and outside the healthcare industry.

Back to the future

Although AI is the current trend, Kohli notes that only a few years ago, it was wearables that was the topic du jour and that in a few years it will be different developments that are creating a buzz within healthcare. This includes the emerging quantum computing, tokenisation and interoperability, all of which help to make best use of the wealth of data generated by these technologies. Regardless of the format, it is clear that imaging and healthcare as a whole can learn a lot by collaborating with other individuals and industries to ensure that innovation translates into better care provided for patients.

Radiological workflows – efficient, fast and stable

International IT system provider **medavis** focuses on the users and work processes of radiological facilities.

Headquartered in Karlsruhe, Germany, medavis has been a leading manufacturer of radiological workflow solutions since 1997. The medavis Radiology Information System (RIS) is one of the most innovative radiology software solutions worldwide. Approximately 37,000 users – at 700 locations in over 20 countries – already rely on medavis, taking full advantage of the potential of radiological facilities' efficiently and sustainably.

The company's RIS is available in many languages and is well established globally, seamlessly integrating workflow solutions into existing IT structures. With modular and scalable applications, medavis already networks radiologists with each other and

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with referring physicians across locations, providing relevant information reliably and securely. The company's strong international network of regional managers and local partners provides perfect service and support for customers worldwide.

Each radiological examination results in studies and reports that are transmitted to the referring doctor. The medavis Referrer Portal provides easy online access to reports and studies without a separate installation. Viewing previous studies and downloading the original DICOM data is also possible.

The platform is based on state-of-the-art web technology and thus guarantees independence from infrastructure and systems, while maintaining the highest security standards, increasing referrer loyalty and the reputation of radiological institutions. With this service, treatment cycles become shorter and faster, and work is more comfortable. ●

For further information

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RADIOLOGY WORKFLOW SOLUTIONS

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The future of hybrid operating rooms

Practical Patient Care talks to Dr Sven Seifert, chief physician at the clinic for thoracic, vascular and endovascular surgery at Chemnitz Hospital, Germany, about how mobile C-arms are helping to make the concept of hybrid operating rooms an increasingly achievable reality. Since 1996, he has worked successfully with the mobile C-arms of **Ziehm Imaging** in a hybrid OR set-up.

What does a hybrid operating room look like, and what kind of clinical applications are performed there?

Dr Sven Seifert: A hybrid operating room, or 'OR', represents a prime example of how to unite the technology of a sterile operating room setting with imaging modalities like C-arm-based X-ray and MRI approaches, or even robotic solutions. This, in turn, creates new possibilities for performing operations such as vascular, neurosurgical, or even abdominal procedures. The greatest changes and developments in this respect have occurred in the field of vascular procedures. It is now possible to perform a wider range of angioplasty procedures and stent implantations for vessel recanalisation or aneurysm repair in just one step, or in combination with conventional open repair techniques.

Which financial and workflow advantages do you see in the inclusion of a hybrid operating room?

At first glance, hybrid solutions may appear to be a fairly costly investment. This, however, depends on which solution you ultimately decide upon, given that there are other, less costly options – such as mobile hybrid OR solutions – available. In addition, there are savings and benefits resulting from the shorter operating times arising from the integration of these technologies, namely improved image quality and the provision of various new operating procedures thanks to the combination of open and interventional techniques. In the case of Chemnitz Hospital, new software solutions like 3D or 2D-image fusion, needle guiding and carbon dioxide angiography imaging were incorporated into the hardware. It should also be noted that developments made in the field of robotic surgery point to the potentially pioneering role of a multiple hybrid OR in the near future.

Dr Sven Seifert has worked successfully with mobile C-arms in hybrid operating rooms since 1996.

What opportunities do you see in the provision of a mobile imaging system in a hybrid OR?

A mobile hybrid X-ray solution provides the surgeon with nearly all the options and features that a stationary X-ray system offers. There are various costs associated not only with procurement of the system itself, but also with regard to installation and placement. However, if the next operation doesn't require hybrid assistance, you can simply offer the system to other departments, or move it out of the OR to create added space. All of this allows the effective use of this equipment, especially for low-volume hospitals.

How important is dose management for the surgeon and their staff, as well as for patient care?

Dose management is an incredibly important topic. The official data reveals that hybrid and angiographic procedures are those that expose the population to the highest levels of radiation. After all, hybrid procedures are becoming increasingly complex and lasting longer. And compared to a normal angiography conducted in a radiology unit, the surgeon and staff members are in closer proximity to the source of radiation. As a result, we place a great deal of importance on implementing measures that protect both the staff and the patient.

What trends have you perceived when it comes to imaging in the hybrid operating room?

I expect some developments in terms of software features and improved operating functionalities. In the future, I foresee the surgeon being able to operate the system without requiring any other workstation aside from the system itself. Furthermore, the surgeon should be able to use fusion and measuring techniques. CT or MRI imaging serves as the basis for the fusion techniques and improved 3D navigation. Additional opportunities will arise in the near future and will include contrast enhanced sonography, endoscopy and different imaging techniques, as well as new needle guiding procedures in the hybrid OR setting, coupled with new robotic systems. ●

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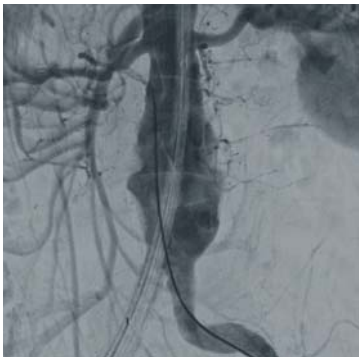

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[1] Ziehm Vision RFD Hybrid Edition represents a group of optional hardware and software that creates an option package on the device named Ziehm Vision RFD. [2] The SmartDose Concept includes a variety of hardware and software features. Due to regulatory reasons, the availability of each feature may vary. Please contact your local Ziehm Imaging sales representative for detailed information.

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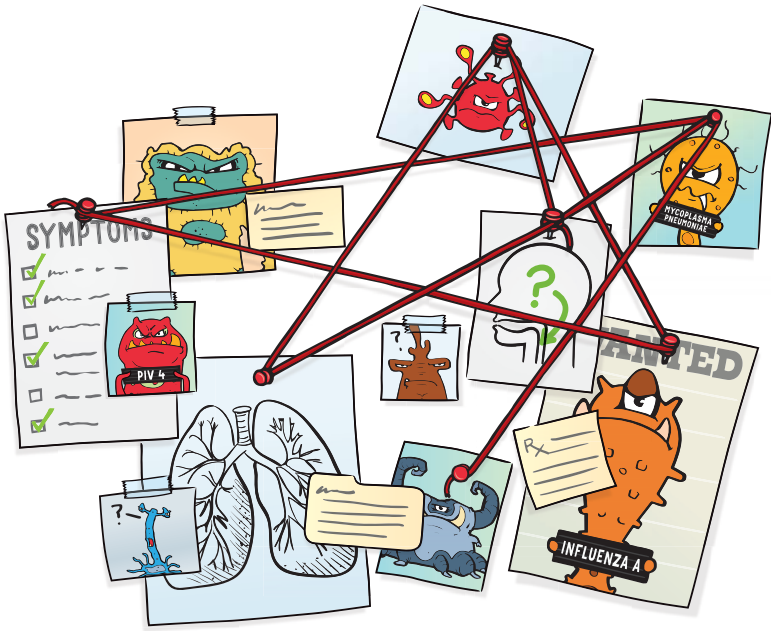

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