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# Medics urged to organise refugee screening

Late-breaking refugee health research at ECCMID 2016 conference

Politicians and health professionals worldwide face a number of unique public health challenges due to migrations.

Thousands upon thousands of humans have taken and are continuing to take flight from wars, persecution and economic stress, seeking the chance of survival in European and other countries. They arrive not only physically exhausted, but also in mourning for those killed in their own countries, or during hellish journeys – therefore many also suffer unimaginable mental traumas. Clearly they need healthcare on several levels.

This April in Amsterdam, for the 2016 European Society of Clinical Microbiology and Infectious Disease (ECCMID), 340 late-breaker abstracts were submitted, 25 of which related to refugee health. Seven among those were chosen for airing. What they highlighted is the need for comprehensive screening programmes, improved therapy, and vaccination coverage in countries that have received and/or are receiving refugees.

Why? On top of the obvious physical and mental damage to these incomers, as Winfried Kern Programme Director of ECCMID said, researchers in various countries have observed an increased prevalence of resistant pathogens, or emerging or re-emerging infectious diseases, including HIV, TB, salmonella, shigella, scabies and other parasitic infections. 'Healthcare services across the world are facing a number of new challenges as a result of recent mass migration,' Kern confirmed. 'Refugees may carry both resistant pathogens and microbes, causing the emergence or



re-emergence of infectious diseases that have become less prevalent in host countries.

'These include methicillin-resistant Staphylococcus aureus, HIV and tuberculosis. Infectious diseases carried and transmitted by travellers and migrants increase the disease burden.

'We recommend that public health facilities maintain and step up screening programmes and put the appropriate precautions and procedures in place to most effectively protect migrants and domestic populations in host countries.'

Clearly, politicians and health professionals worldwide face a number of unique public health challenges due to migrations. The refugee health researchers presented

evidence from health services in Denmark, Germany, Switzerland, Taiwan, Norway, Brazil and the Netherlands regarding some of those challenges.

### Denmark

A study of HIV care among refugees and family-reunited migrants compared to Danish-born individuals compared 405 migrants and 279 Danish-born citizens. The incidence of HIV infection among the immigrants proved higher than that of Danish-born individuals.

The highest risk was observed in sub-Saharan Africans and heterosexual cohorts, and refugee and family-reunited migrants were also more likely to seek medical treatment late, further increasing the risk

of spreading the infection.

The researchers postulated that these results indicate migrants experience barriers in accessing HIV testing and call for a more systematic medical reception of newly arrived migrants in recipient countries.

### Switzerland

An abstract on the prevalence of drug-resistant pathogens – MRSA and ESBL – at four Swiss refugee centres showed that refugees (irrespective of origin) had colonisation rates that were ten times higher for methicillin-resistant Staphylococcus aureus (MRSA) and five times higher for extended spectrum beta-lactamase (ESBL) compared to the local population.

The researchers also observed

that more than a third of refugees from the Middle East were colonised by ESBL compared with less than a quarter in the general refugee population.

The authors concluded that the increased rate of colonisation at body surfaces with resistant bacteria among refugees from certain areas needs to be taken into account in case of illness and admission to a hospital.

### Norway

An analysis of the impact of immigrants and importation in Norway from 2006-2015, showed that the reporting rate of MRSA infections continues to increase there, boosted by imported cases, particularly in younger people and those with an immigrant background.

The presented data suggests that tourism and immigration may be important drivers for the current rise in MRSA infections.

### Germany

A screening of 20,312 stool samples taken at refugee centres in Thuringia, Germany, showed that, in 2015, one in every 300 refugees carried Salmonella or Shigella. As many as six ESBL-positive Shigella strains were isolated from Syrian children – two of them were resistant to ciprofloxacin. As a result of these findings, the surveillance programme with screenings for Salmonella and

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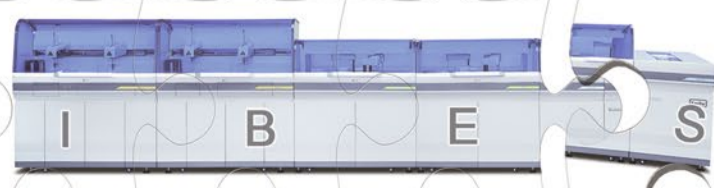
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The launch of a novel rehabilitation service bodes well

# NHS tackles bed blocking crisis

Report: Mark Nicholls

**Bed blocking** is a major problem within NHS hospitals across the UK, with thousands of patients sitting in hospital beds facing a 'delayed discharge' until the necessary next stage of their care becomes available.

A delay may be non-availability of a temporary or permanent space in a residential home, or rehabilitation unit, or a smaller community hospital, or lack of a supportive care package for their return home.

The latest figures from England's National Health Service (NHS) on Delayed Transfers of Care revealed 159,100 delayed days in January 2016 alone, of which 103,500 were in acute care. This is an increase from January 2015, when there were 150,400 total delayed days, of which 103,200 were in acute care.

This was also the second highest number of delayed days reported in a month since monthly data was first collected in August 2010.

Some 61% of all delays in January 2016 were attributable to the NHS, 32.3% attributable to Social Care and the remaining 6.7% attributable to both NHS and Social Care. The main reason for NHS delays was 'patients awaiting further non-acute NHS care' while the main reason for Social Care



delays was 'patients awaiting a care package in their own home'.

An independent review by Labour peer Lord Carter found nearly one in 10 beds was taken by someone medically fit to be released and that delays in discharging patients from hospital after treatment could be costing the NHS in England £900 million a year.

His report described the issue as a 'major problem' causing operations to be cancelled and resulting in the NHS paying private hospitals to see patients.

Critics say the lack of social care in the community is a key reason why people cannot be discharged from

hospital and the latest figures come at a time when spending on social care in the UK has fallen £4.6 billion over the last five years.

However, one health charity in the east of England – working with NHS partners – has taken steps to offset this blockage in the system.

The Papworth Trust, a charity for disabled and older people, has opened a £2 million residential scheme designed to ease the growing bed-blocking crisis in hospitals across the surrounding area. This consists of 28 purpose-built, self-contained flats that will bridge the gap between a hospital stay and discharge by replicat-

ing a resident's home, providing each patient with more than four hours of social care and one-and-a-half hours of occupational therapy daily.

The accommodation, to be known as MacFarlane Grieve House, will help residents regain practical skills, confidence and independence, while also providing short-term care 24-hours a day.

The new rehabilitation service is run on behalf of Cambridgeshire and Peterborough Clinical Commissioning Group (CCG), Cambridgeshire County Council and Uniting Care, with nursing services provided by the Cambridgeshire and Peterborough



Vicky McDermott is chief executive of Papworth Trust, a charity for disabled and older people, which has opened a £2 million residential scheme designed to ease the growing bed-blocking crisis in hospitals

NHS Foundation Trust.

Papworth Trust hopes that the NHS and charities working closer together will introduce the rehabilitation model across the country.

Papworth Trust chief executive Vicky McDermott said: 'MacFarlane Grieve House is a radical new approach to rehabilitation that will save the NHS money, reduce the likelihood of a patient re-presenting at hospital and provides a model that can be rolled out nationally.'

'One of the biggest challenges in our current healthcare system is people returning to A&E after they have been discharged from hospital without appropriate rehabilitation. This is expensive for the NHS and detrimental to the health of every individual who is left vulnerable after acute care.'

'We believe our rehabilitation model will allow hospitals to discharge patients into our care, happy in the knowledge that they will receive first-class social care and occupational therapy that will enable them to return home and go about day-to-day tasks with improved mobility. This will also mean that hospitals can discharge patients quicker, which will free up more beds.'

Finding out what high-tech can do for home care

# Pioneering NHS 'test beds'

A 'technology' project to modernise healthcare for patients with long-term medical conditions is being trialled in the United Kingdom in seven 'test bed' initiatives Mark Nicholls reports

**Test Beds**, a term used to describe a technology project resulting from collaborations between the UK's National Health Service (NHS) and international innovators, aims to harness technology to address issues facing patients and the service.

The first wave of seven Test Beds was announced last January by NHS CEO Simon Stevens at the World Economic Forum in Davos, Switzerland, who predicted that this will reform the NHS to meet 21st Century challenges – particularly from an ageing population and increase in patients with long-term health conditions – while remaining financially sustainable.

Frontline health and care workers in seven areas are to evaluate the use of novel combinations of interconnected devices, such as wearable monitors, data analysis and ways of working that will help patients stay well and monitor their conditions themselves at home.

## The five NHS Test Beds

- Care city innovation – to promote healthy ageing across a million-strong population in North East London.
- In the early intervention programme for long-term conditions the NHS in Heywood,

Middleton and Rochdale are working with Verily (formerly Google Life Sciences) and other organisations, e.g. the Greater Manchester Academic Health Science Network, to help healthcare professionals improve identification and support of at risk patients using advanced new predictive techniques.

- In the Lancashire and Cumbria Innovation Alliance (LCIA) the NHS will partner with Philips and several small business and social enterprises to support the frail elderly and people with long-term conditions to remain beyond the hospital and avoid unnecessary admissions.
- The Perfect Patient Pathway (PEPPA) test bed aims to create the 'perfect patient pathway' for those with long-term conditions, e.g. diabetes, mental health problems, respiratory disease, hypertension and other chronic conditions in the Sheffield City Region.
- RAIDPlus integrated mental health urgent care test bed will see Birmingham and Solihull Mental Health NHS Foundation Trust partner with organisations such as Accenture, West Midlands Academic Health Science Network, Birmingham



Sir Andrew Cash, of the Sheffield Teaching Hospitals NHS Foundation Trust, foresees a uniting of healthcare providers with tech and research groups



Des Breen MD, Medical Director for the Working Together Programme believes the test bed idea could potentially revolutionise healthcare delivery

Community Healthcare NHS Trust and West Midlands Ambulance Service and Police to provide more proactive support for those at risk of a mental health crisis.

## Two further projects – the Internet of Things (IoT) Test Beds

- The diabetes digital coach project, led by the West of England AHSN in partnership with Diabetes UK and technology companies including Hewlett Packard.
- In Surrey, Technology Integrated Health Management (TIHM) – a collaboration of a range of health technology providers to help dementia patients to live at home.

The test bed programme is part of the NHS Five Year Forward View,

published in October 2014, and sees the UK Government and the Academic Health Science Networks (AHSNs), and NHS England working with organisations from across the world deploying and testing various innovations.

The Sheffield's Perfect Patient Pathway test bed includes more than 30 partner organisations; there technology coupled with new ways of delivering care will be used to keep people with long-term conditions well at home, often avoiding hospital admission or further support.

A range of home-based monitoring devices and smart phone apps will mean patients can be supported to understand their condition and how they can manage at home with data received from the devices being collated and interpreted in an integrated intelligence centre.

Sir Andrew Cash, Chief Executive

of the Sheffield Teaching Hospitals NHS Foundation Trust has observed that 'The Perfect Patient Pathway test bed is a fantastic way of bringing together the region's health and social care providers with a number of technology as well as research organisations.'

Medics urged to organ

Continued f

Shigella in children is being continued throughout 2016.

## The Netherlands

Researchers observed high rates of scabies and its complications among asylum seekers from Ethiopia, Eritrea and Somalia. This represents a considerable burden for the healthcare system, especially where refugee centres already are under considerable strain due to high numbers of new arrivals, the researchers commented.

They suggest that scabies must be rigorously controlled in asylum seekers to reduce the risk of complicated cases, the strain on healthcare, and to prevent the spread to other patient groups in the proximity of individuals from high-risk countries.

## Taiwan

Surveillance study of tuberculosis among immigrant workers following pre-entry screening in Taiwan, 2011-2014 identified 2,080 cases of

# The free ride is over!

Medtech industry will stop paying physicians to attend medical conferences

At Europe's most prestigious medical conferences, as many as half of the doctors attending are only there because of the generous sponsorship by pharmaceutical and medical technology companies. John Brosky reports.

The practice has been going on for decades, to the point that continuing medical education (CME) in Europe is heavily dependent on the largess of these companies.

In 2018 it all comes to an end when a new Code of Conduct adopted by the European Medical Technology Industry Association comes into effect.

'We are aligning our association's code of conduct with the United States, China, and many countries of Latin America where the direct sponsoring of a physician is not allowed and you can only support CME through educational grants,' said Serge Bernasconi, who leads Europe MedTech, an alliance of European medical technology industry associations.

'This is making some of the medical societies very nervous,' he added.

Annual medical congresses with large industry exhibitions have become a rich source of revenue for many professional medical societies, and what is worrying them is that without industry support, many congress participants simply would not have the budget to be able to attend.

The USA enacted the Physician Payments Sunshine Act Sunshine act in 2010, to create greater transpar-

ency in doctor-industry relations. When the law was put into effect in 2013 with enforcement by the Centers for Medicare & Medicaid Services, physician participation at annual congresses dropped by as much as 50 percent.

The European Society of Radiology, which puts on the annual European Congress of Radiology in

Vienna, has discussed the impact of the new Code of Conduct internally, but has not made public any decision about actions it will take, according to a spokesperson.

Europe's interventional cardiologists did go public with their protest with an editorial in EuroIntervention, urgently calling for a delay in enactment of the Europe MedTech rules.

Patrick Serruys, M.D., Editor-in-Chief of EuroIntervention, wrote in an Expedited Editorial Publication published in November, 2015 that the new Code of Conduct 'will probably not affect key opinion leaders, but will affect the more vulnerable categories of healthcare professionals such as younger colleagues, nurses and technicians. The juniors

of today may not benefit from the grants allocated to hospitals, especially at the early stages of their careers, nor will nurses and allied professionals.'

Joining Serruys as co-authors of the editorial were William Wijns, MD, Chairman of the PCR (Paris Revascularisation Course) group that organises a series of highly successful conferences for interventional cardiologists implanting stents and heart valves, and Stephan Windecker MD, President of the European Association of Percutaneous Cardiovascular

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Dr Des Breen, Medical Director for the Working Together Programme said: 'This test bed has the potential to revolutionise the way healthcare is delivered. By reshaping the care pathways and with the aid of technology, patients will be empowered to take care of their own long-term conditions.'

Innovations that prove successful will later be made available for other parts of the country to adopt and adapt to the particular needs of their local populations.

ise refugee screening

rom page 1

tuberculosis in immigrant workers between 2011 and 2014. Immigrant workers from South East Asian countries, where tuberculosis is highly endemic, had a two-fold higher risk for TB than domestic residents. Active screenings increased the number of cases diagnosed at an earlier stage of the disease, when it is less infectious, thereby reducing the diseases burden.

#### Brazil

Another challenge in the management of diseases affecting immigrants was illustrated by an abstract presented by researchers on adherence for anti-parasitic treatment in primary care centres in the city of São Paulo.

The researchers reported a lack of adherence in Bolivian immigrants with Chagas disease, a parasitic disease that is in rural areas where poverty is widespread and where it is easily transmitted to people by insect vectors. B.M.

Lufthansa and the DGOU bring aviation training to hospitals

# Physicians will learn assertiveness

Interactive exchange between trainers and trainees. Professor Bertil Bouillon (top left), certified DGOU IC trainer.

Most accidents result from 'the human factor' – long acknowledged in aviation. Thus all crew members receive regular safety training to help prevent errors on board and on the ground. Now experts at the German Society for Orthopaedics and Trauma (DGOU) with those from Lufthansa Flight Training have developed a similar training programme for physicians. This Interpersonal Competence Training was presented in Berlin during October's German congress for orthopaedics and trauma surgery (DKOU)

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In the 1970s aviation researchers found out that roughly 70-80% of all aviation accidents were caused by human error. Thus specialised training formats were introduced to help prevent errors both by on-board crew members and air traffic controllers on the ground. An important component of this training is Crew Resource Management (CRM). This aims to build an extremely important though often neglected factor: social skills. That is not so much about being polite, but being assertive in critical situations.

Neither a comparable research discipline nor a comparable training approach exists in healthcare, despite how much more difficult it is for physicians to detect critical events or incorrect treatments – not to mention identifying their causes. Obviously errors do happen. According to international estimates each year approximately one per million hospital patients die due to avoidable treatment errors. With roughly 19.1 million patients admitted to German hospitals in 2014 that would translate to 19,100 patients who died from avoidable treatment errors.

The fact, as such, is not new. Then why have leading members of the German Society for Orthopaedics and Trauma (DGOU) decide now to approach experts at Lufthansa Flight Training GmbH to develop a CRM-like training for physicians? 'It was an idea whose time



had come,' said Professor Bertil Bouillon, Director of the Clinic for Orthopaedics, Trauma Surgery and Sports Traumatology in Cologne-Merheim, Germany, who is also a certified trainer for the new programme. He underlined that economic pressure in hospitals increases physicians' workload – which in turn increases stress and the error risk. In the end, however, it was the individuals' dedication that made the new training format happen.

What is unique about the interpersonal competence (IC) training is that it was developed jointly by physicians and safety trainers, explained Martin Egerth of Lufthansa Flight Training. A certified CRM trainer he is one of the main architects of the new course format. Egerth sees many parallels between the work environment in aviation and in hospital care: a strict hierarchy, much routine work, complex situations, high stress levels and the need for effective communication.

For Egerth, who seized the chance to gain an in-depth look behind the scenes of a hospital, there is one particularly important skill: assertiveness. What is known in avia-

tion is that airplane crashes usually happen after a chain of five to six errors. If this chain can be broken, an accident can be avoided. However, that requires errors to be recognised early and corrected immediately. Whoever is on the scene needs to speak up as soon as he or she notices an error. 'But when you are new in the team, when you have the feeling the others know more and when you are a bit scared to make a fool of yourself, speaking up can be really difficult,' Egerth says. Therefore assertiveness is the core social skill that is being looked at in IC training.

The new programme was designed for junior physicians, but an extension up the entire clinical hierarchy is planned. In the long run other disciplines might be included because, right now, IC training targets only orthopaedic and trauma surgeons. Anaesthetists as well as nurses, for example, would benefit from such training, in line with the core idea of safety training in aviation: a team where everyone works hand in glove – the best way to avoid errors and break the error chain.

The free ride is over!

Continued from page 3

Interventions (EAPCI).

The cardiologists call for a postponement of the phase-out of payments to physicians, as the societies' congresses are planned far in advance and they need an opportunity to determine how deeply the new rules will cut into attendance at meetings.

The editorial followed a crash meeting held by the three authors and other leading cardiologists with Bernasconi and Europe MedTech executives in October, 2015 at a hotel in the Charles de Gaulle Airport (Paris, France).

The physicians position in the discussion was that the proposed code of conduct is a one-sided document written by-and-for the interests of industry without consultation from the physicians and that this has provoked, 'a lot of confusion and misunderstanding within our professional community,' according to statements in an editorial.

'Whilst both parties agree that direct sponsorship can be perceived by the public as an issue in creating inappropriate interactions, we as physicians are concerned that [the] proposal may significantly impact the future of CME, create major restrictions for smaller meetings,

and severely impact larger conferences,' the editorial states.

In Europe, France led the charge toward greater transparency passing a Sunshine Act in 2011 that was enacted in May 2013. Portugal, Denmark and Slovakia have also enacted rules for greater physician-industry transparency.

The impact of these fragmented actions have not tipped the scale as the reformed Code of Conduct among Europe's leading companies in the medical technology industry.

While there is not currently a movement by the European Union to enact a pan-European Sunshine law, Bernasconi said, 'perhaps that would be better.'

'What we have today are different legislation and recommendations at various country levels, which becomes very complex. We have 28 different ways to manage the relationship. In France every time you buy a cup of coffee for a physician you need to report it.

'The Netherlands says you can subsidise half the expense of a physician going to a congress. The Italians say you cannot pay for a doctor going to a congress, unless he has the approval of his boss. The Nordic countries say you cannot pay

for a physician to go to a meeting,' Bernasconi added.

According to Bernasconi the pharmaceutical industry in Europe has taken an approach to transparency that leaves current practices in place, but requires sponsorships and financial support to be made public.

'We looked at that, but saying it publicly, posting it on a website does not address the conflict of interest that is evident to anyone, and no one today is going to believe there is not an influence,' he said.

'We have gone one step further into what we call transparency-plus. What we want is that if industry is going to continue supporting medical education, we want to be sure we are not going to be criticized for the way we do it,' he said.

'The objective of industry is not to suddenly take away its funding of medical education, but to change to a different model,' he said.

'They will have two years to figure this out, to create educational activities and programs that industry wants to support,' he said. Otherwise in a given specialty area, companies will figure out ways to create their own programs for CME.

Opening up a new view for laparoscopy

# The ultra high-definition monitor

High-def is suddenly so-yesterday for minimally invasive and endoscopic surgery

Report: John Brosky

The same 4K ultra-high-definition (UHD) technology that is surging as the next wave in consumer television has broken into the medical market with the presentation of two first-to-market laparoscopes.

For those trying to get the big picture, 4K ultra-high definition offers four times the resolution of the current generation of surgical high definition displays and, critically for keyhole surgeons, the camera on the laparoscope inserted into a patient's body captures four times greater clarity of the surgical site and target organs.

In 2013, consumer electronics giant Sony formed a joint venture with the dominant leader in endoscopes Olympus Medical systems to develop the 4K technology for surgical endoscope systems and further applications of the technology to medical imaging systems, such as video microscopes.

At that time Sony said it expected the market for surgical endoscopes would reach \$4 billion in 2020.

Three years later, Olympus is showcasing the Visera 4K UHD system that captures and displays 8.2 million pixels, which surpasses the company's own Visera Elite introduced in 2011 with two million pixels.

For an industry driven by incremental product changes, where products introduced in the past 18



The Visera 4K UHD system captures and displays 8.2 million pixels

months generate a third of annual revenues, the 4K overhaul of operating rooms could fuel growth in the surgical segment for years to come.

A sales representative with Olympus responsible for Germany said there are 1,200 hospitals in his territory and there is 100% penetration of HD systems some nine years after the first product was introduced.

Even costing twice as much as

HD, 4K systems will follow a similar adoption curve, he said, adding that Olympus had sold four Visera 4K UHD systems ahead of the market launch to two German hospitals.

Still, Sony-Olympus were not the first to reach the market.

### The Synergy UHD4 imaging platform

That honour belongs to orthopaedic surgical specialist Arthrex (Naples,

Florida), which introduced the Synergy UHD4 in March 2015, at the annual meeting of the American Academy of Orthopaedic Surgeons.

The Synergy UHD4 imaging platform features a programmable camera head, a xenon-bright LED light source, an image management system and fibre optic video over IP (internet protocol) integration all in one tablet-controlled device.

Medical display specialist Barco connects the Arthrex Synergy UHD4 to its Nexxis OR Management Suite

in order to demonstrate that its digital OR-over-IP system can easily handle the enormous data packets from the 4K camera and display them in medical-grade 4K monitors.

In early November, Barco demonstrated its ability to plug in the 4K technology to the operating theatre (OT) in AZ Groeninge hospital in Kortrijk for a laparoscopic liver resection.

Camera images encoded as IP packets can be sent to any display device by cable or wirelessly, which cleans up the clutter in an OT and makes live images available for sharing at any authorised locations, explained Johan Stockman, Barco's vice president for Strategic Marketing for Surgical Imaging.

Sony-Olympus utilises a similar approach to handle the 4K image files.

In marketing the new products the phrase end-to-end becomes a key differentiator.

Critically, the images from a live surgery must also be displayed on a 4K screen. Without closing the loop, the vivid value of the captured images is lost.

It is also a signal that hospitals face significant end-to-end investments in cameras, processors and monitors to upgrade to the 4K technology.

'4K has emerged, it is coming and it will arrive,' said Stockman. 'It is on everyone's agenda in the R&D labs right now, and will be on every surgeon's wish list,' he added. 'If it improves surgical outcomes, hospitals are going to invest in it.'

Medical heads turn to eye 4K and even 5K

## In sight: greater clarity for pathologists

The equivalent of HD or Ultra-HD for home television and video is now entering the world of medicine. Although 4K technology with its high-resolution display quality is already used in radiology, there are areas that do not yet benefit from this advanced technology. However, the Japanese company Totoku Electric Co., Ltd. now offers a simple and effective solution for pathology where 4K technology is yet to be used. In our interview with Marcel Herrmann, Marketing Manager for the Medical Displays division at Totoku Europe, he underlined: 'Pathology still works with analogue procedures in many areas, but high resolution images would be of huge benefit especially for these areas.'

Since talk about 4K technology, and even 5K, is widespread in medical circles, we asked Marcel Herrman of Toktoku Europe, why interest is so keen. 'This technology delivers the type of high-resolution images that we already have in our homes and which are now conquering the world of medicine. In certain areas of medicine, such as radiology, high-resolution images are nothing new. Displays with five million to 15 million pixels are standard here. However, other areas, such as pathology, don't yet benefit from these high-resolution images, although the advantages are obvious. Pathologists need more details in their images than radiologists. To date they have viewed these through microscopes.

'The current procedure in pathology involves scanning sections and then digitally viewing them at the workstation. Once the sections are digitised it's easy to obtain a second

opinion by digitally sending the sections on. This also makes diagnosis easier. The practical implementation of 4K technology is relatively easy: All you need is a computer, a dis-

play and a graphics card that can convert 4K, and almost all graphics cards these days are capable of this.'

With that simplicity, surely this

Pathologists more than welcome higher resolution images



### technology should be far more established?

'The difficulty is that apart from the computer and technical prerequisites for the technology display you also need sources that can deliver 4K. The technological solutions for this are comparatively expensive.'

### Is this where Totoku's solution comes into play?

'We know that many people shy away from large investments but still want to jump from working with analogue procedures straight to 4K because they see the huge benefits, particularly for pathology. This is why we have developed a competitive solution, which still offers all the advantages of 4K technology.'

'Many microscopes can connect to a single-lens reflex camera. This interface has been used for documentation. However, if the interface is used to connect a 4K camera, which is then connected to the respective digital display, this delivers an effective and affordable 4K solution, which we presented at the ECR in Vienna.'

'We are basically connecting two different areas here, using the experiences gained in professional broadcasting, TV and video production has long worked with very



Qualified as a radio and television engineer, Marcel Herrmann went on to complete a course in Marketing and Communication at the Academy for Marketing and Communication, Dusseldorf. He then spent seven years as a product manager before becoming Marketing Manager in the Medical Displays division at Totoku Europe in 2007.

powerful cameras, which makes post-editing easier. Our technology solution is essentially based on experience with professional video equipment. Our answer to the problem is basically a plug and play solution.

'It would probably take years, or even decades, until the entire pathology workflow is digitised in the conventional way – and it will be expensive. Our solution shortens this process.'

### Could the company venture into endoscopy with this solution?

'Theoretically, yes, although endoscopy requirements are higher because even smaller sensors and camera technology are needed. This will most likely be possible in future

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'Unmatched quality that has never been seen'

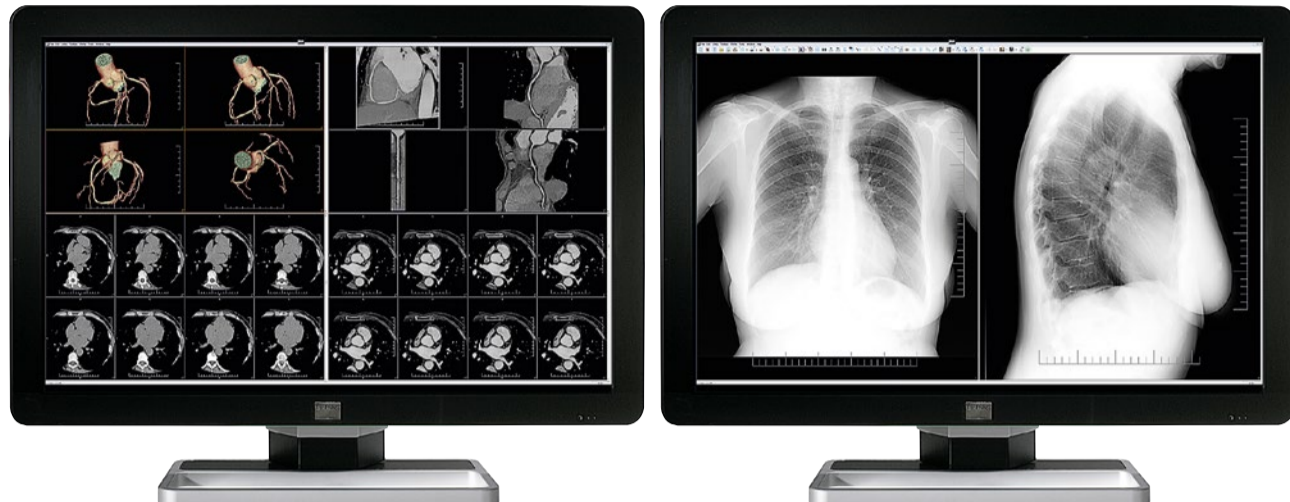
# At the speed of light

Pumping up brilliance on the Coronis Fusion accelerates productivity for a next generation of diagnostic displays, John Brosky reports

Here is a quick formula for accelerating the time spent reading diagnostic images. If you can see it faster and with greater confidence, you will save time. Asking how much time can really be saved is a fair

question, and considering the significant investment Barco has put into improving diagnostic displays, the company wanted to know the answer as well.

'One day a week,' said Bjorn



Belpaeme, the manager for Barco's Coronis Fusion portfolio. The evidence comes from a study at the Montefiore Medical Centre, a teaching hospital for the Albert Einstein College of Medicine in New York City that compared a dual three-megapixel (MP) display system with the next-generation Coronis Fusion 6MP display. The result was a time-savings of 19%, and importantly, a significant reduction in eye strain during reading sessions.'

Yet adding more pixels is only one link in the complex chain of elements that need to pull together for sustained improvements in productivity, day-in and day-out, he explained.

#### 'Nothing else compares with the new line'

Enhancing display ergonomics needs to take into account things like the screen size, viewing angle, image detail, or light calibration and then there are tools and software a radiologist might use to improve workflow.

Belpaeme said that, by revisiting and re-engineering these elements from the ground up, Barco today is bringing forth a next-generation of the Coronis Fusion line with what he called, 'an unmatched quality that has never been seen, and frankly, there is nothing else in the industry to compare to the new Coronis Fusion.'

While Barco has not yet completed a clinical study to back up his claim, Belpaeme said he could

The stand-out feature of the renewed Coronis Fusion family is a 50% increase in luminance

offer one proof that is irrefutable. 'We never get our demos back,' he said, explaining that the Coronis Fusion models Barco sends to medical centres for a trial period don't come back. 'We send out a truck and they send us back a cheque in the mail. They always want to keep the system,' he added.

The stand-out feature of the renewed Coronis Fusion family is a 50% increase in luminance, powered up to 600 candelas compared with the 400 candela brightness that is the industry standard. 'This means more than just more light. It means radiologists can see details more quickly, such as a small fracture in bone or tiny lung nodules, structures that they simply cannot see on a standard display, and this saves a lot of time,' Belpaeme explained.

Barco notes there are 10% more of what radiologists call JNDs, or Just Noticeable Differences, that reveal more subtle details on the Coronis Fusion.

The system also offers the highest real estate of any diagnostic display with a generous 30-inch screen, and the new generation now additionally provides the best contrast ratio at 1,500:1 compared to 1,000:1 previously.

Screen size is another vital link in the productivity chain, providing a wide surface to accommodate multi-modality imaging and flexible posi-

tioning of images on a single screen.

According to a recent study by The MarkeTech Group, about 85% of radiologists use three displays or more, which explains why 87% of radiologists complain of physical discomfort, such as back pain, neck strain and eye fatigue when reading images.

#### Boosting site luminance while dimming the rest

The super screen size and the wide viewing angle of the Coronis Fusion displays helps to reduce head and eye movements as well as minimising image manipulations for a more ergonomic reading experience.

Bundled with the next-generation line of Coronis Fusion displays is a tested and proven suite of intelligent tools to help improve viewing control and enhance reading productivity.

Barco's proprietary SpotView technology can boost the luminance in a region of interest while dimming the surrounding image area to provide a sharp focus on selected details more efficiently. Filling out the toolkit are DimView, SmartCursor, Find Cursor, Application Appearance Manager, and VirtualView.

Like all of Barco's medical display systems, Coronis Fusion 6MP comes with MediCal QAWeb, a cloud-based technology for automated calibration and Quality Assurance to ensure maximum up-time of the display with no need for human intervention.

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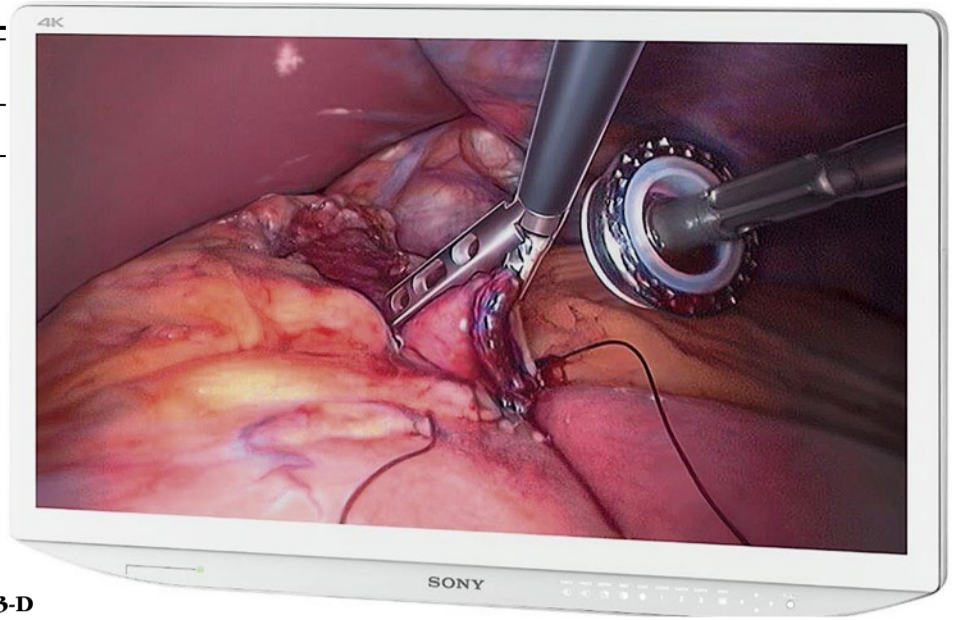
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Refining the depth of field for greater surgical precision

# Out goes pixellation

John Herman, European Marketing Manager of Sony Healthcare Solutions, explains the potential of 3-D and 4K technologies in medicine



“ Display technology for medicine has advanced rapidly from analogue, to digital, to high definition, to 3-D and now 4K.

High-quality displays will continue to be invaluable tools, whether it's the enhanced depth of a 3-D image, or the increased contrast, resolution and level of detail enabled by 4K. State-of-the-art visual technology should now be a part of every medical team's arsenal.

3-D imaging provides enhanced depth of view during procedures and enables effective training and education. Physicians are provided with a level of visualisation that they were unable to realise in 2-D, with the ability to record and display in 3-D providing a more realistic depth of field, helping them better navigate procedures. For example, 3-D medical head mount displays provide an in-depth surgical training experience – a recent study by La Sapienza University of Rome indicated that the use of 3-D viewing 'represents a huge improvement in terms of depth of surgical field, manoeuvrability, image detail, and suture times'.

When advancing medical technologies, Sony builds upon the expertise developed in 4K broadcasting and cinematography from feature films, TV shows, documentaries, commercials, videos, sports and more, to create the best possible tools for the high pressure medical environment.

4K capture and display is rapidly expanding the limits of what medical teams can visualise. 4K offers four times the resolution of standard HD, resulting in virtually no pixelation and giving surgeons greater detail, as well as more faithful colour reproduction. With its improved clarity and detail, 4K displays allow surgeons and their teams to monitor a procedure more precisely, proving invaluable in microscopic operations and keyhole surgery in

Continued on page 8

In sight: Greater clarity ...

Continued from page 5

generations of equipment, but it's not yet feasible.'

**There is already a lot of talk about 5K. Where will all this end?**

'All of this is a question of what makes sense. The human eye has a limited capacity and the display size has to increase along with the increasing resolution.

'It basically comes down to a calculation as to the maximum possible size for a monitor on a desk. At some stage the capacity will be reached and I believe that anything beyond 4K, or a maximum of 5K, no longer makes sense.'

Leading the way in 4K

4K

Introducing Sony 4K surgical monitors LMD-X550MD and LMD-X310MD.

4K means detail and lots of it. These 4K surgical monitors from Sony allow medical professionals to see vessels, tissue and organs in detail never before possible with current Full HD technology.

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4K - detail when it matters most

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Ultra-High Definition (UHD)

# Conferences demand large size and high-res

NEC Display Solutions Europe reports that it manufactures a large range of display products, such as medical displays, large format displays or projectors as well as desktop versions, to provide cross-departmental integration to a common standard.

This means catering for multi-disciplinary team meetings, tumour board and trainings.

Efficient communication and discussion between patients and cooperating physicians is crucial for success. 'Modern medicine is

team work,' explains Dr. Thomas Egelhof, head of Radiology in the Merian Iselin Klinik für Orthopädie und Chirurgie Basel, Switzerland. 'It works best, if you can assess and discuss examination results with the doctors and patients involved. For this purpose, the image display must be so precise that, from the different viewing angles and distances in the meeting room, good conditions are found to carry out and obtain an in depth analysis.'

The state of the art UHD medical conference room solutions offer a 1:1 resolution clone from an 8MP diagnostic display onto an UHD

(3840 x 2160) large format DICOM display, the company adds. 'The NEC XUHD series is available in display sizes ranging from 65" to 98" to meet any size of conference room and viewing distance. The X841UHD-2 diagonal dimensions of more than two metres allow several images to be shown alongside each other for direct comparison.

'The sheer size permits groups of up to 10 people to gather in front of the screen with unrestricted views. Thanks to the high display brightness, images remain stable regardless of the ambient room lighting. While in operation, the monitor does

not emit any audible sound; therefore concentration is not impaired, even in larger groups, or sensitive meeting situations. The NEC XUHD series delivers unequalled medical image quality combining reliable 10-bit colour reproduction with a high luminance and contrast ratio. A semi-matt surface restricts the effect of reflections on the screen.

'The internally programmed DICOM GSDF curve optimises the display to human visual performance in compliance with the DICOM Part 14 standard, drastically improving the accuracy at which images can be reviewed,' the firm continues. 'The NEC Professional large format displays can be DICOM calibrated with NEC GammaCompMD QA client software and an external MDSVsensor3. The LED backlit S-IPS (LCD) panel technology eliminates colour shift regardless of the viewing angle, which could be an issue for horizontally positioned conference rooms around a commercial PVA (LCD) panel technology large format display.

'The replacement of projector lamps is eliminated reducing the total cost of ownership (TCO) of the solution. Thanks to the wide variety of connection options, several signal and cable types allow a flexible choice of playback sources alongside PACS display.'

Size and resolution are key factors in medical imaging displays, thus NEC points out 'radiologists will benefit greatly from the 31.5" sized NEC MD322C8 diagnostic monitor with 8MP (UHD) resolution for daily reporting outside conference sessions'.

Details:  
[www.medical.nec-display-solutions.com](http://www.medical.nec-display-solutions.com)

TOTOKU

## Realistic Color

Everyday and Everywhere

TOTOKU pathology solutions convince with perfect color reproduction, covering 99% Adobe RGB.

Advanced software tools for calibration and color management are the perfect addition here.

The Merian Iselin Hospital for Orthopedics and Surgery has a reputation for highest quality standards and the use of advanced technology



Out goes pixellation

Continued from page 7

particular.

4K provides the highest resolution available today as a window into the body, which is important for minimally invasive, microsurgical procedures such as neurology and ophthalmology, as well as open general surgery, and for education and training. Endoscopic 4K camera systems are already being introduced into the market as improved visualisation also can help to improve surgical workflow.

In addition, medical teams using 4K displays have the capability to see a 'quad-split' view of four full

HD signals (1920x1080) on one display, helping them view different angles and sources. HD monitors on the market today would only be able to display one quarter of HD in each quadrant. This means that surgeons are can now see four simultaneous fully high definition sources, such as an endoscopic camera, room camera, radiology signal and patient vitals.

Another great example for the use of 4K and high-resolution displays is in patient distraction and entertainment. Hospitals, as well as General Practices, have had increasing suc-

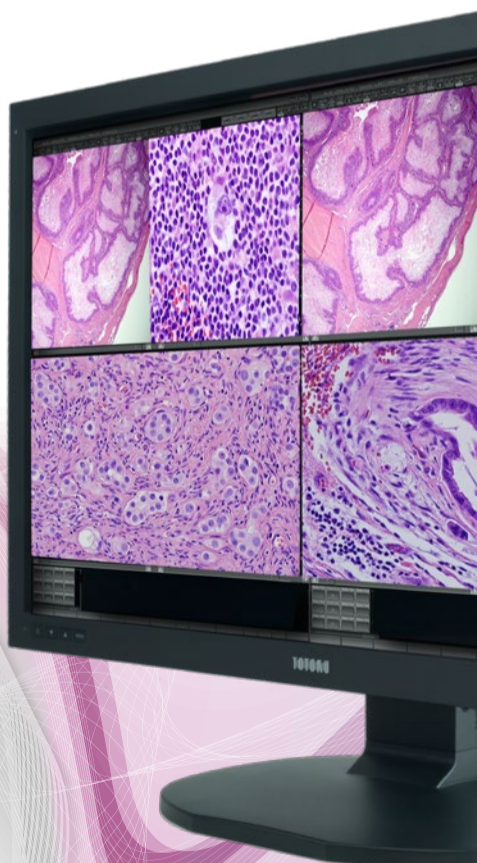
cess in reducing patients' anxiety by installing displays in waiting rooms and common areas to provide entertainment and a welcome distraction in an otherwise potentially stressful situation.

Patient distraction is perhaps most important for physicians dealing with children. With the goal of reducing anxiety in pre-surgery patients and parents, the Alder Hey Children's NHS Foundation Trust, for example, has installed a digital aquarium in the day surgery waiting room, featuring the first digital aquarium in any hospital in the world and the first installation anywhere outside of Japan.

The digital aquarium draws on a combination of exceptional display technology and touch screen capability, resulting in an interactive experience that provides an entertaining distraction and helps to alleviate some of the stress that children and parents experience prior to procedures.

Whether for operational use in OTs or entertainment, both 4K and 3-D technologies still have huge untapped potential for medicine, and companies like Sony will continue to innovate and evolve its solutions to fit the ever-expanding and increasing needs and requirements of medical professionals, and ultimately support patient care in all forms.

Another advantage – while staff study images, children can be in the Day Surgery waiting room interacting with a digital aquarium with touch screen – the first to be installed in any hospital in the world



4K



[www.totoku.eu](http://www.totoku.eu)





Presenting precise colours and outstanding sharpness

# Even displaying a beetle's hair



With simultaneous dual-channel-output the micro camera can combine with various systems, so an existing 2K infrastructure is useable

Although having one of the smallest camera heads available, the new 4K micro camera's resolution is 3840x2160/60p and it has a capacity of up to 1600 TV lines



'4K technology is the future - a fact which hasn't gone unnoticed by Panasonic. The company presented its new 4K Ultra HD Micro camera GP-UH532 in Dusseldorf in November 2015. We are very pleased to introduce this innovative system,' says Margarita Zoussevitch, European Marketing Manager at Panasonic.

Panasonic reports that the 4K micro camera also offers various options for colour enhancement and can zoom in to previously selected image sections and also is particularly user-friendly. The new camera's resolution is 3840x2160/60p and its capacity is up to 1600 TV lines. 'Our 4K micro camera outclasses everything. It delivers very precise colour reproduction and outstanding sharpness and detail,' Zoussevitch points out. 'Previously undetectable areas or objects become visible and sharp. Structures and details which were previously imperceptible - such as the fine hairs on a beetle - become clearly visible.'

Additionally, six different personal profiles for the camera can be stored on, and accessed from, a USB stick.

The system has the medical standard IEC60601-1 certification and can be connected to a number of medical devices or procedures via several HDMI- or SDI ports, Panasonic adds. 'This makes the camera suitable for different medical or microscopic applications in hospitals, research facilities and laboratories.'

The device consists of a micro camera head, control unit, cable and adaptor. 'It has one of the smallest 1/3 camera heads on the market,' the manufacturer points out. 'With different cable lengths of three, six and 15 metres available, the camera head can be used for various applications.'

Patrick Linder, European Product Manager at Panasonic Industrial Medical Vision, adds: 'The 4K Micro camera GP-UH532 offers simultaneous dual-channel-output in 4K/2K. Users can therefore use the GP-UH532 with their existing 2K infrastructure without the need for a buck converter.'

The micro camera can be combined with various systems and facilitates many different individual solutions, offering a cost-effective interoperable solution, the manufacturer notes.

Zoussevitch: 'We cannot expect customers to immediately convert their entire infrastructure to 4K - and this is not necessary with our new system. Thanks to the simultaneous dual-channel-output users can also use the camera in an existing 2K infrastructure.'



## NEC 8 MEGAPIXEL MDT ROOM SOLUTION SETS NEW STANDARD FOR RADIOLOGICAL PRACTICE

The NEC MDT Room Solution is a complete solution including everything needed to provide the latest medical meeting room infrastructure. The Medical Desktop and Large Format Display - both 8MP - can be cloned on a pixel to pixel level to provide outstanding image quality without any loss of data or visual detail. This solution helps to establish efficient reviewing processes and diagnostic investigations as well as providing hospitals a future-proof investment in a state of the art technology and quality.

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Orchestrating a brighter world **NEC**

Needed: an umbrella organisation to link path, lab and IT experts

# Morphological medicine and pathology will boom

Professor Klaus Kayser, former Head of the Institute of Pathology at Heidelberg University Hospital's Thorax Clinic, may be retired but he continues to be a leading figure in his discipline, a visionary, famous for this critical and 'out of the box' thinking. During the run-up to the European Congress on Digital Pathology (ECDP), Ralf Mateblowski asked the expert about telemedicine and standards and, even more importantly, a discipline in transition

As a mere communication tool, telepathology crosses time and space barriers by enabling data analysis from anywhere and at any time, no matter when and where the data were generated. The crucial advantages of digital pathology (DP) lie in its time independence and the ability to 'turn back the hands of time': the evaluation of histological specimens involves much more than looking at the slide and wobbling it back and forth; rather, it requires returning to the original, switching between the original specimen and its stained or marked version.

A modern routine lab that processes 50,000 to 60,000 cases per year covers two major areas: lab and pathology.

At first, digitisation creates more work in the lab, since the scanner has to be loaded with slides, a cumbersome procedure that requires some getting used to. The process is speeded up when the pathologist receives his specimens pre-sorted, e.g.

Controversial thoughts of a whistleblower (Kontroverse Gedanken eines Nestbeschmutzers) from a presentation by Dr Gerhard Stauch at the European Conference on Telepathology 2000, in Aarich, Germany

the liver and lung specimens. If – and only if – DP is optimally organised, the lab technician no longer needs to move around, but can perform all necessary steps at the workstation, such as transferring the digitised slides, including suggestions for analysis, to the pathologist. Ideally, results are made available to the departments via the HIS.

Efficiency, however, is not only a matter of the degree of digitisation and organisation; to a large extent it is a matter of having access to pathologists who are specialised in certain organs. They can be found in large institutions such as Charité in Berlin, or the University Hospital in Heidelberg. Currently, 'human' routine pathology, unlike experimental pathology in the pharmaceuticals industry, is struggling with standardisation even though defined strategies are available for all parameters in order to reduce imprecise measurements, such as thickness, intensity of the dye, or correct lighting in order to be able to assess suspect areas in a tumour specimen.

In Heidelberg, algorithms were developed that provide high sensitivity and specificity (95%) for difficult-to-diagnose tumours such as mesothelioma, or metastatic adenocarcinoma, and can be applied for breast and lung carcinoma. Even if the software programme itself is not yet perfect, the algorithms work and routine usage is

around the corner with confirming parallel studies the only component missing.

Nevertheless, morphological medicine and pathology will experience an enormous boom as scanners with a €100,000 price tag are becoming obsolete since US-American drones feature entirely new optics. Cheap iPhone lenses can be combined with scanners – such projects are underway in China, Finland and the US. If these ideas really pan out, scanner prices will drop by factor 10 and high investment costs will be a thing of the past. While developments in terms of data transmission are stagnating – whether the hoped-for revamping of the internet with fibre optics, or the use of satellite telephones. For example in Africa, will spell progress remains to be seen – the imaging market is immense with hardware and software solutions becoming more and more affordable.

What's really missing is an umbrella organisation bringing together pathologists and lab and IT experts. The wait-and-see attitude of the industry is a definite obstacle: many companies have excellent IT staff who potter about without understanding the work of the pathologist.

On the other hand there are many specialist physicians who are highly interested in IT but lack the necessary knowledge. Communication does not really happen!

In the now defunct GDR frequently mathematicians and physicists worked in institutes of pathology alongside their colleagues in medicine and to a large extent it was this direct access that enabled them to develop inno-



Klaus Kayser MD PhD, Professor of Pathology and Epidemiology, Dr. rer.nat. (Physics), Dr. med, Dr. honoris causae mult. headed the Institute of Pathology, Thoraxklinik, University of Heidelberg until 2005. The former faculty member of Heidelberg and Berlin University (now Charite Berlin) is a pioneer in electronic medical communication, research on image analysis, lectins, structural entropy, and lung cancer.

ventions. This very effective cooperation was abolished and today in Germany there is a slew of institutes – Fraunhofer, Max-Planck and the German Cancer Research Centre – all of which work in different and distinct areas. However, when it comes to application-specific issues, close spatial proximity is the ne plus ultra.

The almost philosophical contemplation of the relationship between structure and function is a topic only very few pathologists are interested in. In biology it is a matter of the inside and the outside. When observed long enough, a structure will turn into a function. This approach opens a different view on pathology: Today, no theory, be it energy balance, metabolism, or any one of the common physical-chemical concepts, can explain why a cancer lesion of 2 cm diameter can destroy the entire system and kill the patient. 'Cardiovascular failure' is nothing but a catch-all phrase because, in the end, structure-associated functions defined on the gene level determine what does not function and why. Which parameter is it that triggers a domino effect that causes the human system to collapse? Digital pathology may well help to understand the construction of 'life as such'.

Challenges in digital pathology

## We expect to see some changes

Strictly speaking, digital pathology has not yet resulted in any groundbreaking changes for clinical diagnostics. The conventional light microscope introduced to pathology around 100 years ago continues to be the most important tool for pathologists. Nevertheless, in the future, according to private lecturer Dr Frederick Klauschen, Head of the Molecular and Systems Pathology Group and Consultant at the Institute for Pathology at the Charité Clinic Berlin, we can expect to see some changes from the introduction of digital technology.

Report: Marcel Rasch

'Digital pathology is supporting us already in making information from tissue sections more easily quantifiable with the help of computer assisted systems,' says pathologist Dr Frederick Klauschen. 'However, when it comes to pattern recognition, and therefore tumour typing and classification into malignant or non-malignant tumours, the pathologist will remain superior to the computer for the foreseeable future.'

### Let the computer do the counting

To date, the biggest innovation is a more objective and standardised view and quantification of certain tissue characteristics facilitated by image analysis procedures. 'One example of this is the measurement of the proliferation index,' Klauschen says. This can be determined via the immunohistochemical detection of the protein Ki67, which is found in the cell nucleus of proliferating cells.

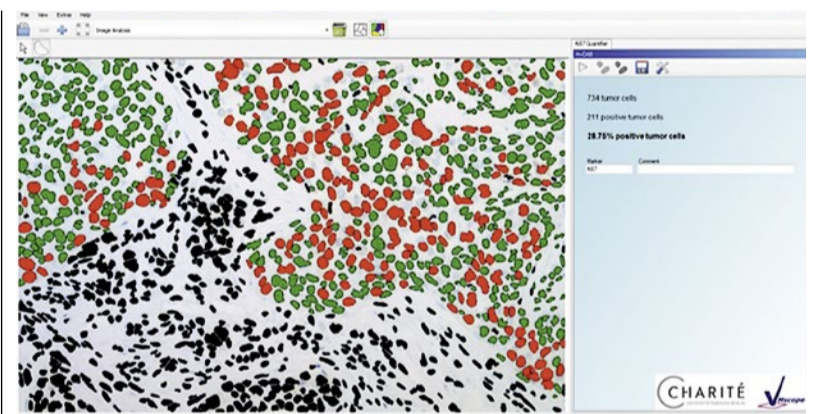


1. Ki67 Quantifier: Determination of the Ki67 proliferation index in breast cancer. The image shows the original immunohistological image (brown: Ki67-positive (proliferating) cells, blue: Ki67-negative (non-proliferating cells))

The result normally shows some individual cell nuclei in the normal histological colour (blue) and other cell nuclei where Ki67 is detected in brown or red shades.

Counting the frequency of the brownish colours was once something the pathologist had to do 'manually'. Now, however, the count-

ing can be done with the help of a computer, using representative image regions. 'We have developed a specific programme for this purpose, the so-called Ki67 Quantifier. This software supports us with the counting and determination of the proliferation index. It facilitates standardised, automated and precise quantifi-



2. Ki67 Quantifier: Computer-assisted diagnosis for the determination of the Ki67-proliferation index in breast cancer. This shows the analysis result of the original image 1. Black: Stroma, red: Ki67-positive tumour cells, green: Ki67-negative tumour cells

cation,' Klauschen explains.

'We work very closely with the German Breast Group with regards to breast cancer, for the validation of such procedures.' Tumour samples that arrive, from all over Germany and other countries, are examined in the Institute for Pathology at the Charité Clinic, which acts as a pathology reference centre. The above-mentioned software is then utilised in the context of these studies and validated based on clinical data.

Digital procedures are currently being developed and tested to examine different types of tissue char-

acteristics and markers. 'However, many of these procedures are not yet ready for use,' the pathologist points out, adding: 'although some Institutes are already using these software solutions it will take some time before all areas of diagnostics will benefit from them.'

### Common problem – lack of standards

One big problem with the practical application of image analysis procedures is the lack of standards. Although there is a dialogue and exchange between the various areas

A Utrecht medical centre now operates a fully digital workflow for primary diagnostics

# The digital age in diagnostics dawns

Pathologists in Utrecht step away from the microscope as the first fully digital workflow goes live for primary diagnostics, John Brosky reports

'The whole world wants to stop by and see the show,' said Paul van Diest MD, who leads the Department of Pathology at the Utrecht University Medical Centre. Why? In March 2016 the centre began to run a fully digital workflow for primary diagnostics. The centre is now overwhelmed with requests for visits.

It was a bold move into the digital age where van Diest convinced the University Medical Center to roll forward the next five years of capital spending for the pathology department to pay for the new system in the first year. 'We replaced the old scanners, we set up a completely new server architecture and a work-

flow system, so that we can now do the diagnostics in a different way,' he said. 'For primary diagnosis we no longer use the microscope, we are looking at a digital image on a screen.'

'I can not give you a precise percentage because, during this transition period, we haven't logged any numbers, but my gut sense is that at least 90%, possibly as much as 95% of the diagnostic work, is now done in a completely digital way, which I think is pretty good for the first month.'

In May 2016, a highlight of the European Congress of Digital Pathology in Berlin will be a Roundtable Session on 'Digital Pathology Workflow Integration,' where van Diest will share with fellow pathologists his pioneering experience and some lessons learned.

'Change management will be my first bullet point,' he said during our interview. 'Stepping away from the microscope is a revolution for the average pathologist, so you have to make sure you have everyone on board to do something this radical. This means influence and involvement, the key terms.'

**It's about the people you need on-board to help with project management**

'My second point will be to make sure you get the right stuff, because it's difficult to make an optimal system with the wrong stuff,' he said with a laugh, adding that 'It's not just about the hardware, it's also about the people from the company, who you will need to have on-board to help with project management, because it is very complicated to bang this down.'

'Then it becomes important to design upfront exactly what you want,' van Diest advises. 'This sounds obvious, but you need to get the design really right – the architecture for the system. To know what you want to have in the end becomes critical at the beginning.'

Following a pan-European tender, the Utrecht pathologists selected a line of scanners from Hamamatsu Photonics of Japan and a workflow informatics system from Sweden's Sectra.

The conversion, over five months, to digital for diagnostics was less a revolution than an evolution for the pathology group in Utrecht, which has been regularly handling digital images with an archiving system



Paul J van Diest MD, took charge of the Department of Pathology at the Utrecht University Medical Centre in 2003. He is a full professor at the university's medical school where, to date, he has personally supervised 57 PhD theses. He is also an Adjunct Professor of Oncology at the Sidney Kimmel Oncology Centre at Johns Hopkins in Baltimore, Maryland, USA, and serves on the editorial board of 23 international journals. Professor van Diest has also served as president of several international societies and published more than 600 papers in peer-reviewed journals.

set up in 2007 for the retrieval of old cases, whether for comparative study, for research or education.

Thanks to this early experience with archiving, the Utrecht group was also prepared for the massive storage challenge the new

Continued on page 13



Strategies and demands for digital pathology workflow integration

## Three-step process for digital pathology

As laboratories in Europe shift to systems for digital pathology, they must ensure the technology not only works, but works for them, says Dr Liron Pantanowitz, director of pathology informatics at University of Pittsburgh Medical Center (UPMC). Lisa Chamoff reports

On 27 May, at the 13th European Congress on Digital Pathology in Berlin, pathologist Dr Liron Pantanowitz, from the Pittsburgh Medical Center will give the keynote address 'Strategies and demands for digital pathology workflow integration', discussing how to bring digital technologies into a laboratory without disrupting the processes already set up.

'Just because you're bringing in new technology doesn't mean you're going to do a better job,' Pantanowitz confirms. 'The people have to be willing to work with the technology and be efficient.'

Later in that 3rd day of the congress, Pantanowitz will also participate in a roundtable discussion on Digital Pathology Workflow Integration.

In his keynote address, the pathologist will go over the three-step process for digital pathology: pre-imaging, imaging and post imaging, providing strategies for incorporating scanning of slides into a lab's workflow, and discussing the importance of training people to do high-quality imaging to create the best slides and how laboratories

can make decisions about saving immense amounts of data.

Going digital could have a negative affect on a laboratory's workflow if, for example, employees batch all the work of scanning slides, or if there's downtime, Pantanowitz points out.

If laboratories follow the right integration strategies, he adds, they can take advantage of the many benefits of a digital system -- using computer-aided diagnostic tools and conducting image-based searches,

Pantanowitz will also touch on his work with Onyx, a company that provides digital pathology technology and is a joint venture between GE Healthcare and UPMC

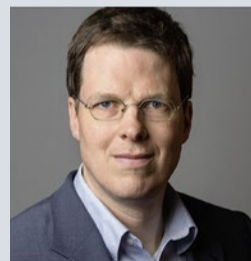
Digital pathology is gaining ground in Europe faster than in the USA, Pantanowitz points out, with less stringent regulations governing its use.

The country's Food and Drug Administration (FDA), which regulates medical devices, states that digital pathology cannot be used for primary diagnosis. While the USA's laboratories can use digital pathology technology 'off label', they risk being held liable if there

of pathology, the analysis of tissue slides from different labs is difficult, the specialist regrets. There are no unified standards regarding histological colourings. 'Each laboratory produces slightly different depths of colours, so the sections differ from one another. Pathologists are not normally worried by a stronger pink or blue – a computer, however, then may have problems with the classification. The objective is the development of procedures which are independent of colour,' he emphasises. Although previously not an important topic in pathology, these types of standardisation are works in progress, having gained importance only with the introduction of digitisation.

Klauschen sees a further difficulty in the practical implementation of digitisation in day-to-day pathology. 'Although we have the technology available, scans of sections are only compiled for special studies, conferences, or for research projects. The actual pathology workflow is not digitised.' One reason for this is the vast number of tissue sections produced at the Institute every day and the related expenditure of time for the digitisation of each section.

The data volume of the images still represents a big problem as pathological images have much larger file sizes than those in radiology, for instance. 'We have amounts of data which simply represent big challenges for the IT infrastructure. There is



Frederick Klauschen MD is a pathologist, physicist, lecturer and consultant as well as Head of the Molecular and Systems Pathology Group in the Institute for Pathology at the Charité University Clinic in Berlin. Up to 2009 he worked at the National Institutes of Health in Bethesda, USA and he is currently a Junior Fellow at the Einstein Foundation in Berlin.

room for development here, particularly regarding the archiving of all this data.' Klauschen is aware of only two institutes where the workflow is completely digitised – one in the Netherlands, the other in Sweden.

Despite the numerous challenges the pathologist believes that digital pathology means progress, which, in future, will also play an important part in the integration of conventional-morphological and molecular pathology. 'Fluorescence-in-situ hybridisation visualises genetic changes in the tissue. Digitisation and computer-assisted evaluation can be of enormous benefit here.'

'I also believe that digital pathology will become important for the interpretation of molecular profiles in the tissue context.'



Dr Liron Pantanowitz is Director of Cytopathology at UPMC Shadyside. He is also Director of the Pathology Informatics Fellowship Programme and Associate Director of the Pathology Informatics Division.

should be a malpractice case. As a result, three laboratories in Europe have gone fully digital, according to Pantanowitz, while he is not aware of any fully digital laboratories in the USA.

UPMC runs a digital pathology consultation service, providing second opinions to pathologists, clinicians and patients around the world, which provides the facility with an additional revenue stream.

The Pittsburgh Medical centre is in the process of collecting data regarding the use of digital methods for primary diagnosis to help make the case for using digital technologies for primary diagnosis, Pantanowitz adds.

SPECIAL: DIGITAL PATHOLOGY

# Goodbye to the microscope? Not yet!

Carol I Geppert MD, from the Institute for Pathology at Erlangen University Hospital, Friedrich Alexander University Erlangen-Nuremberg, debates the impact of digitisation on pathology

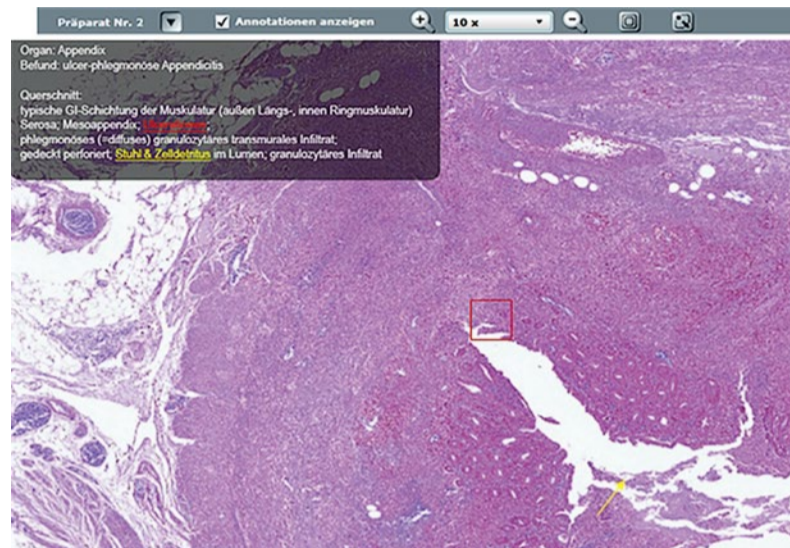
Digital Pathology (DP) is the fastest growing area of pathology, along with molecular pathology. However, the use of digital tools such as scanners and analysis software, as mentioned in a previous article, is mainly limited to academia (volume 24, issue 6/15). Academic medicine benefits most in teaching and research where larger investments can be applied for without the pressure of daily clinical routine, or the economic pressures of the health system.

In Erlangen, DP has been an established part of teaching in human, molecular, and dental medicine.

Using an online-microscope, students from Würzburg,

Regensburg and Erlangen (Cooperation partners: the universities and university hospitals as well as the Fraunhofer Institute Erlangen) can access digital slides from their respective courses browser-based via the internet, from anywhere and can study with superimposed texts and annotations (image 2). In addition, in recent research some projects have also been driven with the help of DP within the Comprehensive Cancer Centre Erlangen-Nuremberg, addressing problems from different clinical fields. DP already plays an important part in national and international cooperation projects.

Naturally, new and fast-paced technology also has its limitations, which need to be clearly stated. The error rate of the scanners with slides or low contrast, or errors in digital image analysis (DIA) caused by artefacts can negatively impact on trust



Digital pathology is already an important part of teaching at the Institute for Pathology, Erlangen University Hospital. Via the internet, students can access all course contents, browser-based with annotations and texts, as well as for monitoring achievements (online microscope based on development in cooperation with Fraunhofer IIS Erlangen, [www.pathoskopieren.de](http://www.pathoskopieren.de)).

in this new technology. Therefore, there is also some criticism and scepticism amongst pathologists.

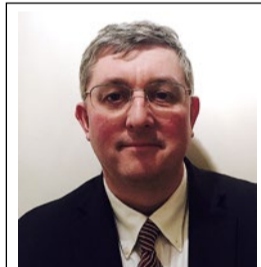
Furthermore, next to the many advantages of DP there are also clear disadvantages, such as high

initial investment costs for scanners and data storage, as well as the ongoing costs for maintenance and support. Pathology will be confronted with similar problems to those seen in radiology years ago, during the initial conversion to digital image processing. Although terabyte (TB) mass storage is now comparatively affordable, the amount of data involved in DP is extremely high. One case with five sections can take up between 2.5 to 20 gigabytes (GB), i.e. the equivalent of a vast storage requirement of several 1,000 TB, which converts to several PB per year, assuming all cases from one large centre were to be digitally stored every year. This new dimension of data exceeds the requirements in radiology by tenfold and would therefore be unprecedented in clinical medicine.

By contrast, there is the new dimension of the interpretability of an immeasurable number of cells with their colourings for immunohistochemistry, CISH or FISH. New analysis software – digital image analysis (DIA) – from companies such as Definiens or Indicalab, can quantitatively evaluate all cells from one section. This can be a routine section for one patient or samples from many patients via tissue micro arrays (TMAs), where more than 400 samples can be put on one slide (such as GrandMaster, 3-D-histech, Hungary). This will deliver completely new and detailed views of

Digitisation will take patient care to new levels

## Pathology departs from a dark back room



South Africa born **Daniel du Plessis** gained his MB, ChB degree from the University of Stellenbosch, where he also studied anatomical pathology. Appointed consultant histopathologist at Tygerberg Hospital, in Cape Town, he then moved to the Walton Centre for Neurology and Neurosurgery in Liverpool, England, holding training and research posts from 1998 to 2003. Additionally, in 2002 he became a Fellow of the Royal College of Pathologists, with subspecialty accreditation in neuropathology. Appointed consultant neuropathologist at Salford Royal Hospital NHS Foundation Trust and the Greater Manchester Neurosciences Centre in 2003, he is now the Clinical Lead at the Department of Cellular Pathology, at the hospital, and an honorary lecturer at the University of Manchester Medical School.

ing for far greater cross talk than in an individual isolated practice and that will be of much benefit for patients.'

Pathology digitisation is inevitable du Plessis believes, concluding: 'If a number of high profile departments implement digital pathology, word will spread about how beneficial this system is, then there will be peer pressure on other departments to conform.'

Report: Mark Nicholls

A UK-based neuropathologist has highlighted how the digitisation of pathology will play a pivotal role in taking patient care on to a new and more efficient level. Speaking in a recent Webinar under the heading The Adoption and Benefits of Digital Pathology for Primary Diagnosis, Dr Daniel du Plessis also noted how the digital era would raise the profile of pathology and 'bring it out of the dark backroom'.

Using a Sectra digital pathology system within his department at Salford Royal NHS Foundation Trust in north-west England, a pilot study highlighted how digital pathology speeded up diagnosis and workflow, and particularly had advantages within the context of the multi-disciplinary team (MDT) meeting.

With his neuropathology unit at the 728-bed Salford Hospital used to pilot the system by Sectra – which has an established track record in PACS systems for radiology – the benefits quickly became apparent; the digital system was used to navigate through a slide on screen. 'We soon felt far more confident and at ease navigating through a digital image than the slide on the platform,' du Plessis said. 'I've been doing microscopy for 20-30 years, but it only took me 2-3 days to almost abandon one in favour of the other.'

'The digital screen was definitely

my preferred first port of call and, for most of the cases, I was happy to do all reporting on the screen without having to look at slides under a microscope. What was so enjoyable about the Sectra system was the confidence it instilled; you felt more in control of a slide on a screen than using a standard microscope.'

Currently, his network is not fully digitised; for real-time diagnostic smears, surgeons send a sample to the lab and await a rapid stain and assessment, but digitisation will speed that up considerably and also facilitate wider information sharing over secure internet links, such as with neighbouring centres in Liverpool and Preston.

With storage space at a premium within the NHS, having everything digitised rather than on glass slides

will avoid the expense of maintaining a large slide archive, either on-site, or with a commercial storage organisation off-site, and from a clinical governance perspective obviates the risk of slides breaking, being lost or misfiled.

The ultimate driver in having a hospital move to digital pathology, he said, is cost and time; more rapid turnaround and more efficient use of pathologists' and lab staff time. This was particularly visible in MDT meetings, where previously slides had to be retrieved by support staff, carried to the meeting, shown on microscopes and then re-filed.

With images digitally available, they can be retrieved and easily displayed with a focus on specific areas of interest. 'It rekindles people's interest in histology because it's

done in such an efficient and quick way,' he said. 'You can show how a tumour has changed over time, with just a few clicks; you can't do that with the microscope set-up.'

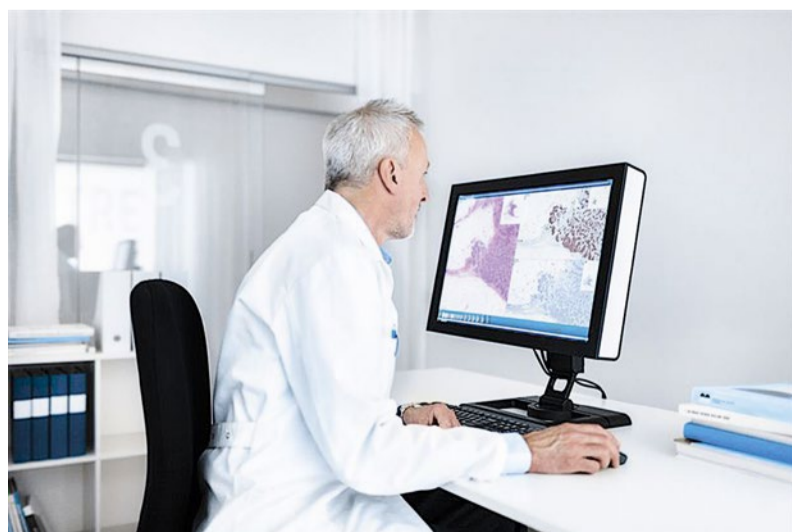
It enables the MDT to be linked to different centres, with second or third opinions, and the pathologist can marry images with radiology on the same platform.

'It has boosted pathology, which has become a far more efficient partner in the MDT meeting,' said du Plessis, adding that there are also work-life balance opportunities, with pathologists able to do some of the reporting at home, and there are also patient benefits in that a growing proportion of cases need to be double reported.

'Neuropathologists tend to be in smaller units within a larger general pathology unit, so there might be only one or two people to look at a case,' he pointed out. 'Digital pathology allows units to link up and benefit from forums that can contribute to consensus diagnosis. Difficult cases can be quickly shared in a network that enhances diagnostic accuracy and reliability.'

This has huge advantages for the patients in terms of quality assurance, robust objective reporting, and less subjective vagaries of individual reporting.

Significant benefits at his practice: 'Our basic skills will remain the same, but I think we will become far more efficient. As said, it will bring us out of our dark backrooms, allow-



tumours and their specific biomarkers. Although previously we could gain good and realistic estimates with the bare eye, we can now generate far more exact evaluations of hundreds of thousands of tumour cells in one section, for instance for each individual tumour cell. Until recently this was completely impossible.

The integration of individual parts of DP into clinical routine is already happening in interdisciplinary tumour boards and conferences, in telepathology and through the transmission of digital slides in the context of studies or consultations. It has facilitated a much faster, worldwide exchange between experts and colleagues without the need to physically send sections. As there has been an abundance of new technologies and innovations over the last few years and a continuously expanding market for imaging equipment (scanners and the camera technology used in them) for image processing (reconstruction and visualisation software) as well as for digital image analysis (DIA) the need for standards for diagnosis and research has become equally imperative.

If, one day, DP was to become established in daily routine it will have to withstand comparison with the microscope in daily practice, in terms of practicability, sturdiness and, most importantly, speed. The microscope is unlikely to disappear. Some areas, such as quick section diagnosis where a diagnosis has to be achieved within 15 minutes during on-going surgery, there can

be no digitisation. However, we (including Professor Peter Hufnagel at the Charité Berlin and Professor Gian Kayser at Freiburg University Medical Centre) believe that, more and more pathologists will mainly work digitally, and also beyond university settings, in the distant future, because the requirements from this field will continue to grow and the investment costs for scanners and data storage are likely to fall due to increased competition. In our view the full potential of DP, which is as versatile as it is promising, has not yet been exhausted, by far. However, high quality standards in image generation, processing and analysis must be established independent of manufacturers. They should be the basis for the continuously growing and ambitious community of pathologists in diagnostics, research and teaching. DP can help achieve a new measure of quality, particularly in the growing field of cancer diagnostics (companion diagnostics) with immunohistochemical biomarkers such as Her2 or PD1/PD-L1, which are decisive for treatment.

The tool will become a robust, reproducible, secure, comprehensively quantitative and observer-independent aid for diagnosis. With the help of DIA, important biomarkers, such as prognosis parameters, can be completely, quantitatively, digitally evaluated (e.g. Her2-FISH in Z-stack) even three-dimensionally. DIA is therefore superior to the previous methods, as it makes millions of tumour cells analysable, if necessary even in several layers (for FISH signals).



Carol I Geppert MD from the Institute for Pathology at Erlangen University Hospital

Furthermore, observer-independent, digital evaluations will lead to a location-independent, comprehensive increase in diagnostic quality for certain problems, be it in a large centre or a peripheral practice.

Along with many well-known pathologists we believe that DP will have become an established part of a hybrid workflow consisting of DP and conventional microscopy in clinical routine within the next 10 years. The advantages speak for themselves and there is no end in sight for the rapid developments and resulting opportunities for application.

I believe many pathologists are following the rapid developments in digital pathology with excitement and interest, as well as with scepticism. Most of them are not yet happy to swap their microscopes for computers. However, within the next ten years I believe that a hybrid diagnostics workflow, consisting of conventional microscopy and digital image analysis, will be established. A comprehensive change to purely digital diagnostics is still a long time coming.

## The digital age in ...

Continued from page 11

digital diagnostics system presents. Reaching 800 terabytes the archival system was pushing the internal capacity. 'We had a chance to be part of a bulk central storage initiative at this big academic we are part of, so we joined as a customer,' the professor explained. 'The archives were transferred to the new system, which he said is safer, more secure and more affordable than maintaining a dedicated storage facility. Also, it is faster: flashing requested images on the screen in seconds, rather than in minutes.'

### Challenges and compromises

If the transition to working digitally has been fairly smooth, there remain both challenges and compromises. 'There are things that are simply not possible for digital processes yet,' van Diest pointed out. 'Here we simply go back to the slides. It is always possible to return to the slides. This does not mean the images are not good. It may be a difficult case. We certainly don't force someone to do a diagnosis in a digital way only to make a wrong diagnosis.'

There also remains the controversy of depth-of-view on digital slides versus the microscope view, which he said is 'a compromise we have to live with today'.

'We'd prefer to have three to five focus layers within every image. Yet that increases scan time by a factor of three to five, and increases storage requirements by a factor of

three to five. This is something we simply cannot afford, both in terms of time and financially in terms of storage.'

Now that the diagnostic system is operational, the next stage is optimisation, working through what he called a long wish list that will keep the vendor companies busy for the next three to five years. The group, he said, is also keen to begin implementation of image analysis algorithms.

'The one we will start with, one we have developed ourselves, are algorithms for the recognition of mitosis, something very important in cancer diagnostics that is now done in a subjective way. By using algorithms it can be done more quickly and more reliably,' van Diest pointed out.

Pleased by the high level of interest in visits, van Diest added: 'We are pioneers here. We had to invent the wheel, which means that other people who plan to do this will probably be able to do it slightly faster, perhaps better, and likely in a cheaper way than us.'

# Digital pathology is evolving...

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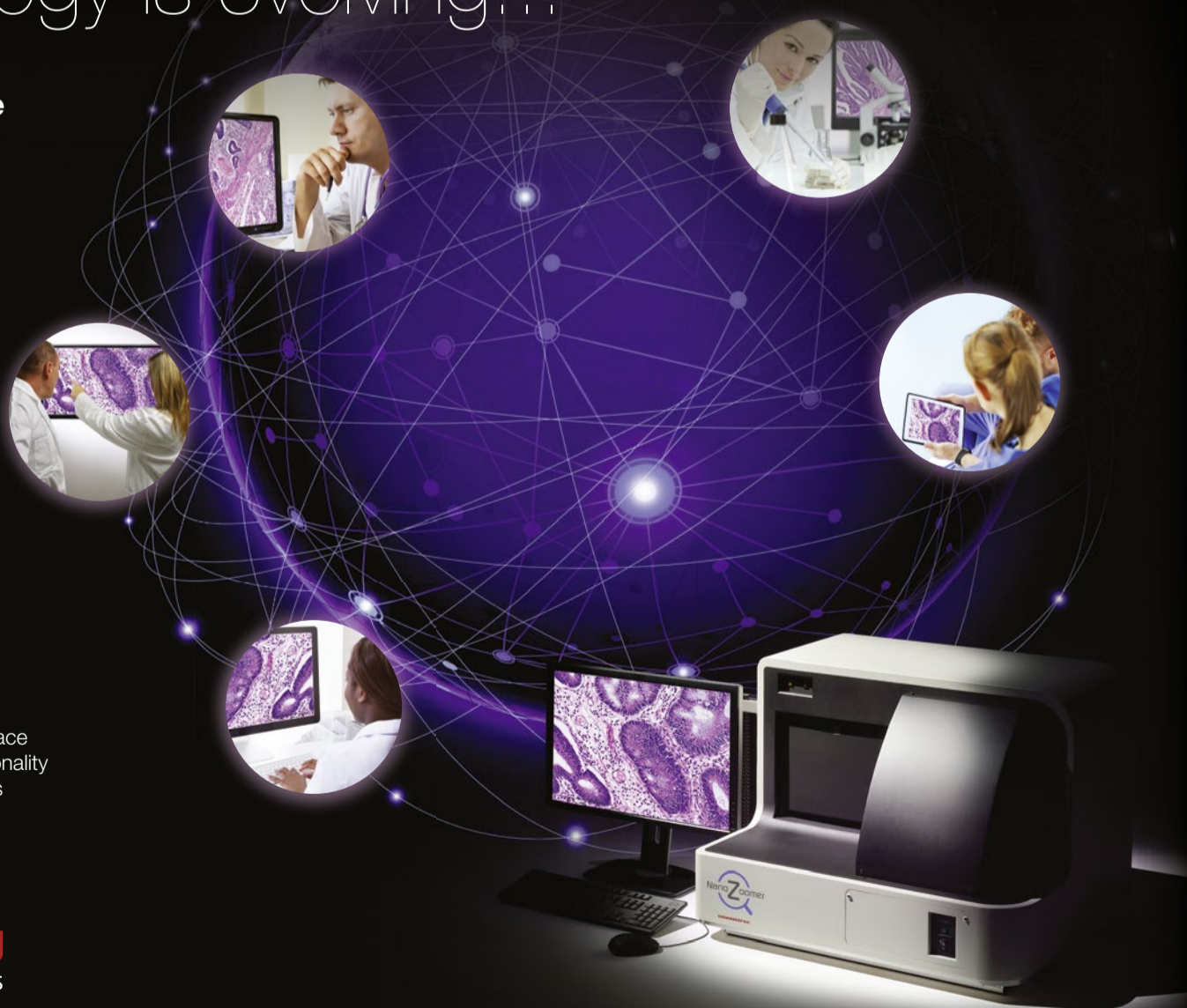
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ECCMID highlights why MMR infections are emerging viral illnesses

# Measles, mumps, rubella threaten youngsters

In a European Hospital interview before his presentation at ECCMID 2016, Infectious Disease Specialist Dr Guillaume Béraud spoke of the results from his modelling of the three 'childhood' diseases, measles, mumps and rubella.

Report: Jane MacDougall, Paris

Explaining the reason why measles, mumps and rubella were presented in the same session as viruses such as Ebola and Zika, during the 2016 ECCMID meeting, infectious disease specialist Dr Guillaume Béraud, from the Centre Hospitalier Universitaire de Poitiers, said this was an 'organisational short cut on the part of the ECCMID organisers, or we could reconsider our opinion of these 'common and benign childhood' viral infections. Because, since the introduction of vaccination in the 1960s, these can certainly no longer be considered as "common and benign".

'Also, and this is of particular importance,' he stressed, 'one effect of widespread vaccination – which has been extremely effective but has not, of course, achieved 100% coverage – is that these viruses have not, unlike smallpox, been eradicated. To do so, we'd need to reach 95% vaccine coverage. This has had an interesting impact on the spread of these viruses, none of which has an animal reservoir, they can only survive by infecting humans, and this is why their spread has slowed down. 'From a modelling point of view, we can see that the circulation of the viruses is slower than in the pre-vaccine era, therefore the population being infected has changed. The population now at risk to get infected is no more children, but teens and young adults. Why? Because, in addition to the shift in age of onset due to a slower viral circulation, these are the generation that socialise the most and therefore are the most likely to come into contact with the virus and, if they have not been vaccinated, develop the disease.'

'One important downside of catching measles, mumps or rubella, when older, is that the disease is much more severe than in a younger person (<5 year old). These cases are often much more serious, with far more risk of sequelae and, in the worst case scenario, mortality and therefore, from this perspective these can certainly be considered as new emerging viral diseases.'

#### Why, if adequate vaccination exists, is there resurgence?

In France vaccination has been recommended for all children since 1985 and is 100% reimbursed by Social Security. The MMR vaccine requires two doses to be given before the age of 24 months. However, vaccination is not obligatory and therefore a number of children each year either receive only one, or no dose of vaccine, which enables the virus

to propagate. 'The actual vaccine coverage (which is highly variable by region) never exceed 90% for the first dose and 85% for the second dose, with much lower coverage for some departments, which is far too low for herd immunity to be protective (>90-95% is required). Therefore outbreaks can and do occur, particularly in areas where coverage is lowest, such as in south-east France. With continued suboptimal coverage the risk of epidemics can be easily be modelled – and are a real threat for 2016.'

#### Why are vaccination rates low?

'The reasons for low vaccine uptake are multiple and complicated. One very real problem is because vaccination has been so successful for so long, the potential seriousness of these illnesses has been forgotten and people do not consider protection against them as a priority.'

'Also, of course, there is the anti-vaccine lobby, which is extremely articulate and convincing in its arguments and can sway a parent who

has fears about vaccine safety. Of course the importance of vaccine safety is now primordial as the fear of the disease is so low.'

'As a profession, healthcare providers need to learn to communicate our message to the public in an equally meaningful way, we need to learn what triggers a mother to have her baby vaccinated. It most certainly is not the highly scientific data that excites us, and our colleagues!'

#### In this 21st century, why are these viral diseases potentially dangerous?

'These diseases are entirely preventable by vaccine. The vaccines we have are very effective and provide immunity for life and, therefore, no research has been directed towards specific antiviral therapy for measles, mumps or rubella. Today, our standard of care for patients with these infections is much as it was in the 1950s and '60s, when epidemics were frequent in the under 5s, meaning standard symptom control; fluids, rest, control of fever etc.'



Dr Guillaume Béraud, at the Centre Hospitalier Universitaire de Poitiers, Poitiers, France, recently completed his PhD, which focuses on mathematical modelling of the spread of infectious diseases. For this he worked in two centres – EA 2694 'Epidemiology and healthcare quality assessment' in Lille, France and the Centre for Statistics in the Institute for Biostatistics and Statistical Bioinformatics at Hasselt University in Hasselt, Belgium.

This also means that, with the more severe cases we are seeing, we have no real therapeutic options, hence the real probability of serious complications.'

#### How might the cases in France affect European neighbours?

'This problem is not unique to France; many other EU countries have low vaccine coverage, for example, the United Kingdom and Germany. The adolescent population also travels to other countries in groups.'

'We had a good example of how this helps virus spread last year. A group of school children from Alsace visited Berlin and contracted measles from the children with whom they had exchanged.'

'Fortunately, for France, Alsace is a region with higher than average vaccine coverage and the number of cases soon petered out. This was fortunate because our modelling shows quite clearly how, in another region, an epidemic could easily have broken out. Measles is a highly contagious virus.'

#### How can this resurgence be stopped?

Dr Béraud: 'Only by vaccination; we need to work together to eradicate these viruses. It should be possible, but will require a concerted effort from parent groups, healthcare professionals and governments working together, which is not as easy as it sounds.'

*Clostridium difficile* remains a difficult foe

# Fresh insight into an old pathogen

Report: Anja Behringer

Hospital-acquired *Clostridium difficile* infection (CDI) is on the rise. Symptoms range from non-typical mild diarrhoea that can develop into pseudomembranous colitis up to a toxic megacolon, which often leads to death. Not only are there are hardly any efficient antibiotics nowadays, the use of antibiotics has turned out to be a significant risk factor in the spread of CDI. Since CDI occurs in many countries, rich and poor, an international team of researchers, supported by the German state of Lower Saxony, compared the incidence of CDI in countries with different levels of antibiotic use.

When patients carry the bacterium upon admission to the hospital and the infection develops during the patient's hospital stay, the body not only has to fight the original

disease, which was the cause for the hospital admission, but also CDI. Particularly older and immune-compromised patients are at risk: the extended hospital stay also translates into a considerable increase in treatment costs. CDI furthermore has a high recurrence rate and

can develop into a chronic disease because most antibiotics destroy healthy as well as harmful bacteria, which can cause allergies, autoimmune, metabolic or psychological disorders, with the latter ones rarely diagnosed as being tied to the status of the colon.



According to the Robert Koch Institute, every year around 65 million adults worldwide suffer some form of gastrointestinal disease. While only one third of the people affected consult a doctor, those who do seek treatment should be aware of the risks associated with antibiotics. The German Gastroenterological Society (DGVS) points out that antibiotics themselves can cause diarrhoea and recommends limiting their use to certain cases, such as shigella or salmonella infections. While antibiotics do cure diseases they can cause long-term damage to the enteric flora – not to mention environmental damage.

For hospital therapy the DGVS Guideline recommends judicious use of antibiotics and strict compliance with hygiene rules. In particularly severe cases, the patient must be isolated – with unavoidable additional staff and treatment costs.

Despite many warnings from physicians there are only a few pharmaceuticals left whose efficacy has not been wasted by over-prescription. These drugs of last resort are limited to particularly severe cases. Understandably pharmaceutical companies are urged to develop new antibiotics. However, the call goes largely unheeded despite steadily progressing research. Obviously in the future an antibiotic has to attack the specific pathogen rather than damaging the entire microbiota. Indeed, an active ingredient for targeted use against *Staphylococcus aureus* already exists.

In Europe, the influx of young migrants may well increase pressure on the pharmaceutical companies to intensify efforts – particularly since the Zika virus, for example, is spreading without a vaccine or a therapy in sight.

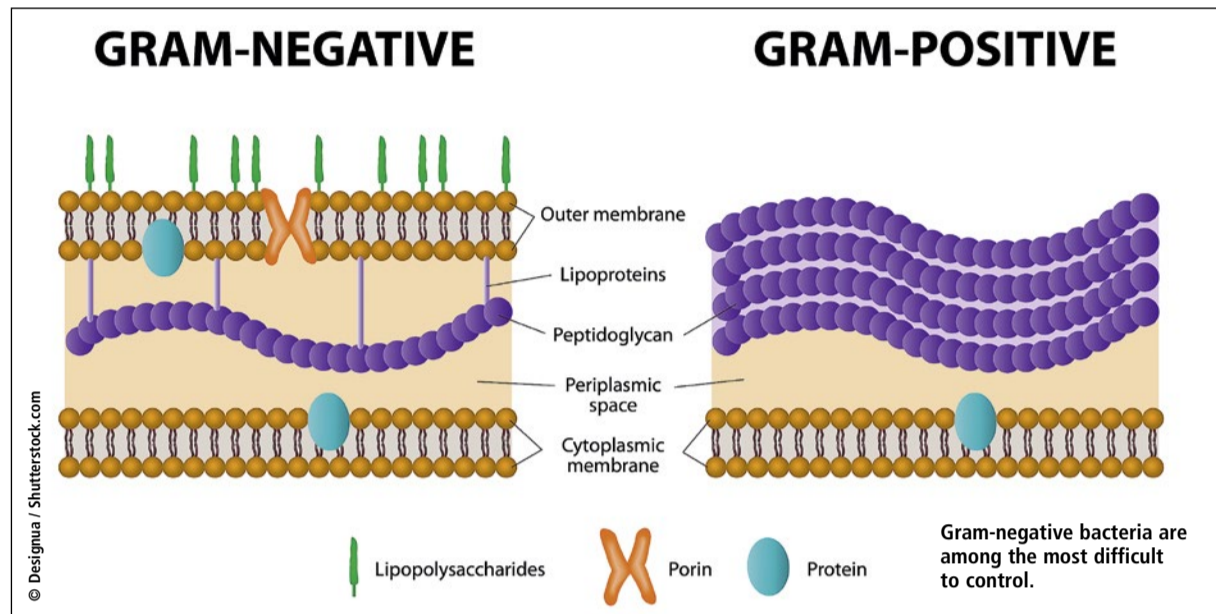
*Destroying the bacterial defence membrane*

# Scientists gain ground against resistance

British-based scientists report a breakthrough in combating antibiotic resistance



**Changjiang Dong** is Professor of Molecular Medicine at the University of East Anglia's Norwich Medical School. His research into antibiotic resistance was named 'Research Project of the Year' at the Times Higher Education (THE) Awards 2015. Last year he received a Wellcome Trust Investigator Award for £1.7 million to continue his research.



linked to disorders such as diabetes, Parkinson's and other neurodegenerative diseases.

**Report: Mark Nicholls**

The mechanism by which drug-resistant bacteria maintain a defensive barrier has been identified by researchers at England's University of East Anglia (UEA) and their findings could result in a new wave of drugs that can bring down those defensive walls rather than attack the bacteria – thus they may not develop drug-resistance at all.

Diamond Light Source technology, which generates extremely intense pin-point beams of synchrotron light enables scientists to explore almost any material in atomic detail, and thus to investigate Gram-negative bacteria. The latter are particularly resistant to antibiotics because of the cells' impermeable lipid-based outer membrane, the barrier that defends against attacks from the human immune system and antibiotic drugs.

It allows the pathogenic bacteria to survive, but the loss of the barrier causes them to become more vulnerable and die.

Previously the researchers had found an Achilles heel in the defence barrier but how this cell wall is built and maintained – the 'assembly machinery' – remained

unknown.

Lead researcher Professor Changjiang Dong, from UEA's Norwich Medical School explained: 'Gram-negative bacteria are among the most difficult to control because they are so resistant to antibiotics. All Gram-negative bacteria have a defensive cell wall. Beta-barrel proteins form the gates of the cell wall for importing nutrition and secreting important biological molecules.'

The beta-barrel assembly machinery (BAM) is responsible for building the gates (beta-barrel proteins) in the cell wall. Dong confirmed that stopping the beta-barrel assembly machine from building the gates in the cell wall would cause the bacteria to die.

The research - funded by the Wellcome Trust with collaborators including Dr Neil Paterson of Diamond Light Source (UK), Dr Phillip Stansfield from the University of Oxford, and Professor Wenjan Wang of Sun Yat-sen University – saw scientists study the gram-negative bacteria *E. coli*, in which the beta-barrel assembly machinery contains five sub-units, known as BamA, BamB, BamC, BamD and BamE.

The researchers wanted to know

exactly how these sub-units work together to insert the outer membrane proteins into the outer membrane or cell wall.

Dong: 'Our research shows the whole beta-barrel assembly machinery structures in two states - the starting and finishing states. We found that the five sub-units form a ring structure and work together to perform outer membrane protein insertion using a novel rotation and insertion mechanism... Our work is the first to show the entire BAM complex. It paves the way for developing new-generation drugs.'

'The beta-barrel assembly machinery is absolutely essential for Gram-negative bacteria to survive. The sub-unit BamA is located in the outer membrane and exposed to the outer side of the bacteria, which provides a great target for new drugs.'

In human mitochondria, he pointed out, a similar complex – called sorting and assembly machinery complex (SAM) – is responsible for building the proteins in the outer membrane of mitochondria.

The research team also believe that unravelling this mechanism could lead to better understanding of human cell dysfunctions

*Probably available this autumn*

# New test for the early detection of Lyme disease

As part of the EU 'ID Lyme' project, the infection immunology working group at the Institute for Hygiene and Applied Immunology at the Centre for Pathophysiology, Infectiology and Immunology at Vienna's Medical University is working to develop a test to detect Lyme disease (borreliosis) early, thus improving the ability to detect an active infection easier than before, so that healthy people with Lyme disease antibodies in their blood do not receive unnecessary antibiotic treatment and so that appropriate

treatments can begin early. "Unfortunately, the current standard laboratory test is often unable to detect Lyme disease at an early stage of the infection," explains Hannes Stockinger, Head of the Institute for Hygiene and Applied Immunology of the Center for Pathophysiology, Infectiology and Immunology of MedUni Vienna. "On top of that, the current test often interprets a mere antibody reaction as an infection and people are treated with antibiotics unnecessarily, because the infection is way in the past

or is already completely resolved." The current test can only analyse part of the human immune system, namely B-cells but not T-cells, which are needed to fight infection and whose activity indicates infection. The experts are therefore helping to develop the world's first point-of-care test to detect an active infection so that patients could start appropriate treatment. The test, known as the 'Ixodes Kit' should be available in the autumn of 2016, said the scientists, speaking on the occasion of World Immunology Day 2016.

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*Post-ebola syndrome is the next healthcare challenge*

# Ebola leaves a health legacy

First the good news: the most severe ebola outbreak ever has been contained. Last December, Guinea, where the first infection was reported in late 2013, was declared free of ebola cases. Liberia was considered free of ebola in mid-January after no new case had been reported for 42 days (the WHO criterion for 'free of ebola').

Report: Anja Behringer

For a 'post mortem' to know what could be improved for next time – and experts do not doubt that a 'next time' ebola outbreak will come. The first lesson learned: the WHO needs to be strengthened – more money, more power, more support. Second: in poor countries sustainable healthcare structures should be established and targeted efforts are needed to raise awareness among the people about health risk. Third: the outbreak prompted the pharmaceutical industry to develop and distribute medication and vaccines at a previously unknown speed. However, apart from success for one particular vaccine, research efforts did not yield successful results.

## The survivors

According to the WHO, 11,000 people died during this recent ebola epidemic in Western Africa. 17,000

patients, more than during any previous outbreak, survived ebola virus disease (EVD) but are struggling with a range of sequelae, such as eye pain and decreased visual acuity, head and joint pain, hair loss, abdominal pain, loss of appetite, nausea, sleeping disorders or chronic fatigue. Neurological symptoms include short-term memory impairment and disorientation and women report menstrual abnormalities. The virus may persist in the eye, liquor (meningitis) and, nine months after the infection, even in semen.

It is only due to the large number of survivors that the sequelae become visible. Now, that the disease itself has been contained, the post-ebola syndrome is the next healthcare challenge that needs to be mastered.

What exactly causes the symptoms is unclear – the virus itself, the massive immune response to it, or the use of aggressive disinfectants.



The Ebola-virus may persist in the eye, liquor (meningitis) and even in semen.

Currently, data on the type, frequency and duration of symptoms are being collected and analysed. Maybe we are dealing with a chronic phase that follows the acute phase.

## Studies of survivors

A study involving 49 patients who survived the 2007 Ugandan outbreak pointed at a number of long-term sequelae that persisted as long as two years post infection. Whilst in Uganda a different sub-type of the

ebola virus caused the infection, the symptoms are very similar to those reported by survivors in West Africa.

In Liberia, researchers are collecting data on the long-term sequelae of the ebola infection. The team of the Partnership for Research on Ebola Virus in Liberia (Prevail) is trying to find out whether survivors develop immunity and whether, after the acute phase of the disease, they transmit the virus to sexual partners and other close contacts.

Over a five-year period the Prevail team will regularly examine 1,500 survivors and 6,000 people in those survivors' immediate vicinity and analyse blood, tears, sweat and semen. Another focus will be vision disorders that appear to be a typical sequela of an ebola infection. Lassa fever patients report similar sequelae, as severe infections in general can weaken a patient over a long period of time. On the other hand, different symptoms can have very different causes.

While all these physical issues need clinical care, the mental effects must not be neglected. The disease itself, the loss of loved ones or social marginalisation upon discharge from the treatment centres – these are traumatic experiences, which leave scars. Moreover, tight family units were torn apart and many children are orphaned. For many survivors, 'back to normal' – to a day filled with hard physical labour – is impossible, in view of the many sequelae.

Addressing the medical and psycho/social needs of EVD survivors is thus a major focus of the WHO action plan.

*Rapid medical tests in disaster areas*

# Winners on the firing line

Jens Hahn MD is an Internal Medicine and Intensive Care Specialist who works with the international, independent, medical humanitarian organisation Médecins Sans Frontières (MSF in English: Doctors Without Borders). Here he describes his work in Afghanistan and South Sudan, and the use of rapid diagnostic tests in the field.

Interview: MEDICA.de

Infectious diseases are widespread in conflict areas, and without basic medical care on location, people cannot be appropriately treated. Laboratory tests are limited in the field. However, rapid diagnostic tests enable medical personnel to test patients for several infectious diseases, e.g. for the presence of malaria or HIV infection.

Speaking of the Sudan and Afghanistan, Jens Hahn said it is hard to generalise about the work involved: 'Every conflict area has its own structure that depends on the respective security situation. How freely can you move as a medical team? Can you actually perform the classic work of MSF? Can you drive to the site with your jeep and provide primary healthcare to people, or does the security situation not allow it? In Afghanistan for example, treatment needs to focus on the centres. Here you can move freely only in the hospital or your living quarters.

## What diseases and injuries do you prepare for there?

'That also strongly depends on the situation. In classic settings, like in South Sudan, these can be tropical diseases such as malaria, hepatitis or tuberculosis. A large number of war wounds is added in the increasing conflict areas with violent battles. Here you need to increasingly treat gunshot wounds. Infections that result from bullet or stab wounds, and other acts of violence, are also a part of our daily routine.

'The battle involves classic infec-

tious diseases such as transmissions of bacteria, viruses and parasites. But there are also many cases where people with bullet wounds cannot be medically treated until after a few weeks have gone by.

'The severely infected wounds need to first receive first aid and then generally require subsequent surgery.'

## Resources available on location

'You also need to differentiate in this instance: when we need to drive a long way from our base camp to a village, we can only take a limited amount of material with us, meaning only those items that fit into two Jeeps, for example.

'In terms of primary healthcare, malaria or respiratory diseases in children, for instance, can be treat-

ed on a larger scale. Therapeutic foods for malnourished children and hygiene products, like soap, also have room in the Jeep. Many infectious diseases can occur because the simplest resources are not available on site.

## On site lab testing

'Laboratory tests can only be done on a limited scale, especially in remote areas. A small test kit, for example, could make it possible to detect anaemia on location. Yet this test is rarely conducted because, typically, you can't perform a blood transfusion in this kind of setting. By now, we commonly use rapid tests that can detect malaria within a

MSF doctors use Jeeps to reach people who otherwise would have no medical care



Jens Spahn MD works with Médecins Sans Frontières.

few short minutes, for instance. You can envision this like a pregnancy test, only the test isn't done with urine but with one drop of blood and an indicator.

'The HIV rapid diagnostic test also plays a relatively big role in the field. These types of tests are not available for all diseases, however. From a medical point of view, it is rewarding to fall back on your manual skills and get away from just treating people with medical

devices.

## Which rapid diagnostic test is used most frequently?

'The malaria test; in the best-case scenario, we regularly visit different places after we've informed the community members in advance. Oftentimes, about 250 children are waiting for us in a malaria-infested area.

'If a child exhibits an increased body temperature or other symptoms, we perform a rapid diagnostic test. Since this is often the case for at least one-third of the people or more, you quickly need dozens of tests. Yet not all of them turn out positive. The children frequently also have other diseases.'

## In conflict areas, are you personally more susceptible to infections and take special precautions?

'That strongly depends on the area. During the Ebola epidemic, for example, where MSF could set up tents very quickly, you definitely had to protect yourself. We are dealing with a disease where drugs don't provide any protection. This is why we are just as vulnerable as the people that live in this area.

'I didn't perceive the risk as much greater in Afghanistan than I did at home. Sure, TB is a major problem there but this is a disease that primarily affects people with weak immune systems. Yes, there is an increased risk in some countries for certain diseases, such as malaria, for example. However, the risk to get sick yourself is not exorbitantly higher.

'We need to pay more attention to hygiene. The local standards often don't meet our own standards.

Source/author: MEDICA-tradefair.com/Kilian Spelleken





More effective drug delivery meets targets

# Biotherapeutics strike cancer cell growth

Report: Mark Nicholls

Many drug treatments do not work due to their poor ability to reach their intended targets inside patients' cells. To address this, researchers at Cardiff University's Schools of Pharmacy and Pharmaceutical Sciences, and Biosciences have designed a highly efficient method to improve the delivery of therapeutic molecules into diseased cells such as those in stomach cancer, breast cancer and tuberculosis.

In this new approach, called 'receptor crosslinking', the team specifically worked to improve the delivery of a relatively new class of drugs called biotherapeutics.

The researchers explain that cancer cells often contain a unique protein on their surface that acts as a barcode, identifying these cells as cancerous against their healthy counterparts.

In their findings, they characterised new ways of targeting breast cancer cells with Herceptin, which interacts specifically with a barcode protein called Her2 – a protein barcode widely recognised to be a major driver of cancer cell growth and division.

Lead author Professor Arwyn Jones, from the School of Pharmacy and Pharmaceutical Sciences, said: 'The striking thing is that we have tested our approach on both Her2, as well as other barcode proteins, and each one gave the same result.'

'It looks like this could be a universal strategy to increase the uptake of drugs into different kinds of cells involved in many types of diseases.'

The research team has manipulated how Herceptin interacts with Her2, which results in both being rapidly engulfed by the cancer cells that then proceed to destroy the protein barcode.

Professor Jones: 'The fact the same approach has worked for three very different receptors suggests that we should be looking at many different targets here, to do the same with them, spreading it away from cancer to other diseases.'

As well as different cancer types, the approach could be used to target inherited genetic diseases and infectious diseases such as tuberculosis. TB is a potential target, he explained, because it hides within macrophages (immune cells) and

this delivery method might have potential to drag the drug to the inside of the macrophage 'to hit the tuberculosis where it is hiding'.

Having highlighted the 'universality of the approach', the Jones' team would now like to see other

researchers try it with specific antibodies and models on which they are working. 'Our approach is about more effective delivery of therapeutics to the inside of cells,' he said. 'If we think of cancer, many anti-cancer antibodies have now been developed to target receptors on the plasma membrane – some loaded with anti-cancer drugs.'

'The problem lies in then getting the antibody to the inside of cells, as its fate and that of its drug payload is governed by the targeted receptor.'

However, he added: 'If you can force this interaction and have the receptor and antibody driven to the inside of a cell, you have a much better chance of getting that drug to its target site.'

Still, the expert acknowledges the approach is a long way from clinical use, despite its wide-reaching potential, but this a critical step forward. 'The next stage,' Professor Jones pointed out, 'is to understand what happens inside a cell and then design drugs that specifically target that process.'

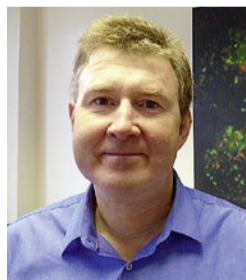


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**Arwyn T Jones** is Professor of Membrane Traffic and Drug Delivery at Cardiff University's Schools of Pharmacy and Pharmaceutical Sciences. He is closely involved in the school's main research themes of experimental therapeutics & pharmaceutical sciences; and drug discovery, design and synthesis. With a major interest in cancer and cell biology, his current projects fall under the overall themes of breast cancer cell biology, drug delivery and regulation of endocytosis. These include targeting and endocytosis of plasma membrane receptors, design and characterisation of drug delivery vectors and cellular delivery of therapeutic macromolecules.

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Automatic tasks: inoculation of patient specimens, sorting, imaging, processing

# Fast, efficient, cheaper microb



A fully automated clinical microbiology laboratory system went into service at Heidelberg University Hospital this April. Produced by the Dutch medical technology firm BD Life Science, this first installation at a German university hospital will play a major role in a study exploring the potential benefits of lab automation in containing the spread of pathogens in a hospital

Report: Sylvia Schulz

Set up in the Department of Medical Microbiology and Hygiene, at Heidelberg University Hospital, the BD Kiestra TLA (Total Lab Automation) offers fully automated inoculation of patient specimens as well as sorting, imaging, processing and slides transportation to predefined work stations and diagnostic instruments, such as a mass spectrometer. Sixty-eight systems have been installed worldwide; Germany has four in use in private microbiology labs.

The ambitious aim is to offer results within 26 hours from receiving the specimen – a major improvement over the 48 to 72 hours required today to identify a pathogen and test for possible resistances. 'Currently available and feasible methods and hospital routines do not allow for further acceleration of microbiological diagnostics – this can only be achieved by automation,' explains Professor Klaus Heeg, who is head of the Department.

The new system is not only expected to speed up processes but also to increase safety and the quality of the results. The incoming specimens are prepared right away and processed after a defined incubation period. Whilst previously incubation times differed due to a wide variety of workflows, TLA offers a standardised procedure that provides homogeneous results and documents them – thus serving as a helpful quality assurance tool.

Patients will benefit from lab automation through faster treatment onset, e.g. antibiotics therapy, while the hospital expects to reduce length of stay. 'With this new lab solution we want to show that even a university hospital can offer efficient, quick and inexpensive microbiology diagnostic services,' says Irmtraut Gürkan, Commercial Director of the University Hospital Heidelberg. 'Whenever a diagnosis is unclear, the patient is separated which hampers clinical workflows and binds capacities. Thus a quick diagnosis is always desirable in terms of economics.'



At this point, the hospital is leasing the lab solution, which comes with a price tag of €3 million, since public funding was denied. However, by the time the leasing contract runs out, the initial results of the study will be available – and hopefully support a second application for public money.

New tube with powder additive aids diabetes diagnoses

## Inhibiting rapid glucose breakdown

Along with the increasing need to diagnose diabetes mellitus cases, gestational diabetes (GDM), the most common disease during pregnancy, needs to be detected/ruled out at an early stage. If not identified, GDM can lead to complications such as infections, premature births and long-term effects for the mother and child.

However, the rapid breakdown of glucose (glycolysis) in venous blood samples complicates accurate diagnosis of diabetes and can lead to a false negative result. Thus it is necessary to inhibit glucose breakdown immediately after blood collection.

Various institutions, such as the Deutsche Diabetes Gesellschaft (German Diabetes Society), Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (German Society for Gynaecology and Obstetrics), and the American Diabetes Association have drafted guidelines, which recommend the addition of a citrate-fluoride additive to maintain the 'in vivo glucose level'.

For this reason, Greiner Bio-One has launched a new tube, explaining: 'The special feature of the new Vacuette FC Mix tube is the powder additive. It stabilises the glucose level immediately after collection for 48 hours. This allows a reliable diagnosis of diabetes conditions and avoids false negative analysis results. The stabilisation is carried out in the whole blood and therefore does not require immediate centrifugation. Unlike in tubes where liquid is added, the finely granulated addi-



In the new Vacuette FC Mix tube the glucose level is immediately stabilised after collection

tive does not cause a dilution effect. There is no need to convert the measurement result.'

### How the additive works

'The citrate/citric acid buffer reduces the pH value in the sample,' the manufacturer reports. 'As a result, enzymes needed for the glycolysis process are inhibited and the actual "in vivo level" is stabilised from the start. The additive is completely dissolved, and therefore optimally mixed with the sample, after swivel-

ling ten times. In the case of storage between 4°C and room temperature, a further sodium fluoride additive ensures long-term stabilisation for 48 hours.'

The transparent PET plastic, shatterproof tube comes with either a grey or pink security cap, allowing differentiation from standard glucose tubes. The cap is particularly easy to open and allows for hygienic working in the laboratory.

Further details: [www.gbo.com](http://www.gbo.com)

Company banishes white from medical

## Colour up yo

This January, Kugel Medizintechnik, from Regensburg, Germany, announced an interesting new venture. Although a leading manufacturer of equipment for pathology, histology and the laboratory for over 15 years, the firm launched its new Colour up your Lab design service.

A month later, at the German Pavilion at ARAB LAB 2016 in Dubai, the firm was presenting lab personnel with this concept and reports: 'We received a lot of questions: What's high pressure laminate? What makes it eco-friendly? What kind of laboratory furniture can be colour matched? Why is it antibacterial?'

Along with a 'Colour up your lab' leaflet, the company showed its histo-pathology equipment, e.g. grossing tables, staining tables, preparation cabinets, stainless steel furniture and more, and also presented a new brochure about exhaust systems for histo-pathologies.

### Leave behind those sterile white worlds

However, Kugel was keen to point out that it not only manufactures this equipment but also provides planning. 'No matter if you're looking for a partner for a sophisticated furnishing of an entire building complex or perhaps a partial fit out, we are your point of contact concerning the designing, developing and planning.'

Kugel is encouraging medical personnel to leave those traditional sterile white worlds behind, stating that the 'design possibilities are almost endless. The combination of different materials like wood with granite or the mixture of cold and warm tones gives your laboratory design that little extra something.'

'We do not limit ourselves to laboratory furniture and laboratory table plates, but rather we also colour

match our preparation cabinets with the corporate identity of your laboratory. All woods and raw materials that we use for our eco-friendly high pressure laminate solution come from sustainable managed forests with PEFC and FSC certificates.

'Additionally, daily adjustments of production processes guarantee that 10 times less water and 40% less energy are used and 75 % of the waste is recycled or recovered.

'During production of high-pressure laminate, fine paper layers as

Color concepts in laboratories instead of sterile white



ng, slides delivery

# iology diagnostics



hospitals or patients who had previously stayed in countries where widespread resistances are reported – a total of 40,000 patients per year. Additionally, Heidelberg is presently conducting a large countrywide resistance-screening programme, which translates into around 8,000 specimens being processed and read every single day.

Joint opening (from left): Silvia Hardenbol, Business Director Central Europe, BD Life Science, Diagnostic Systems, Patrick R. Murray, PhD, Sr. Director, Worldwide Scientific Affairs, BD Life Science, Diagnostic Systems, Irmtraut Gürkan, Commercial Director of the University Hospital Heidelberg, Prof. Klaus Heeg, Head of the Department of Medical Microbiology and Hygiene, Prof. Guido Adler, Medical Director.



The study, a joint project by the hospital research team and BD, is designed to evaluate how the new system combined with a newly developed imaging procedure can help to significantly speed up diagnosis. The study will also show whether a fully automated lab solution can handle the gigantic sample throughput in a microbiology lab of a top-tier hospital. At Heidelberg University Hospital every newly admitted patient who is considered likely to carry resistant pathogens is routinely tested. This group encompasses patients transferred from care facilities, senior citizen homes, other

interiors

# our lab!

well as a thin eco-friendly melamine resin film are applied on top and bottom of a wooden base plate.

**Colour-fast, high-temp and moisture resistant**

'Then, the different layers are pressed together under high pressure of 75 kg/cm<sup>2</sup> and temperature of approximately 150°C, making the furnishings colour fast and light insensitive; moisture resistant and hence suitable for damp environments; resistant against high temperature and most chemicals; easy to clean and scratch and impact resistant.'

The firm also reports that its high-pressure laminate laboratory furniture 'is coated with the antibacterial Sanitized coating, with silver ions, which kills 99.9% of bacteria within 24 hours'.



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Early warning of future brain disease – up to 20 years before onset

# Blood test detects early Alzheimer's

The cause of Alzheimer's disease remains unknown. Early diagnosis is currently not possible as clinical symptoms only occur once a large number of neurones in the brain have already been destroyed. There is no treatment available either. Imaging procedures such as PET-MRI are expensive and not covered by routine care. This situation hinders the early confirmation of a diagnosis. A new blood test now makes it possible to diagnose Alzheimer's up to 20 years before the onset of the first clinical symptoms. Amyloid-beta peptides, i.e. proteins, and an infrared sensor, play key parts in this process. In our interview, Professor Klaus Gerwert, Head of the Chair for Biophysics at the Ruhr University Bochum, Germany, discusses the procedure



Professor Klaus Gerwert is Head of the Chair for Biophysics at the Ruhr University Bochum. As Chair of Biophysics, the professor, and his colleagues, investigate structure, function and interaction of proteins at the atomic level, using a wide variety of interdisciplinary methods from biology, biophysics, biochemistry and computing. In the post-genome-era the focus of research has moved more towards proteins, which are, besides DNA, key players on a molecular level.

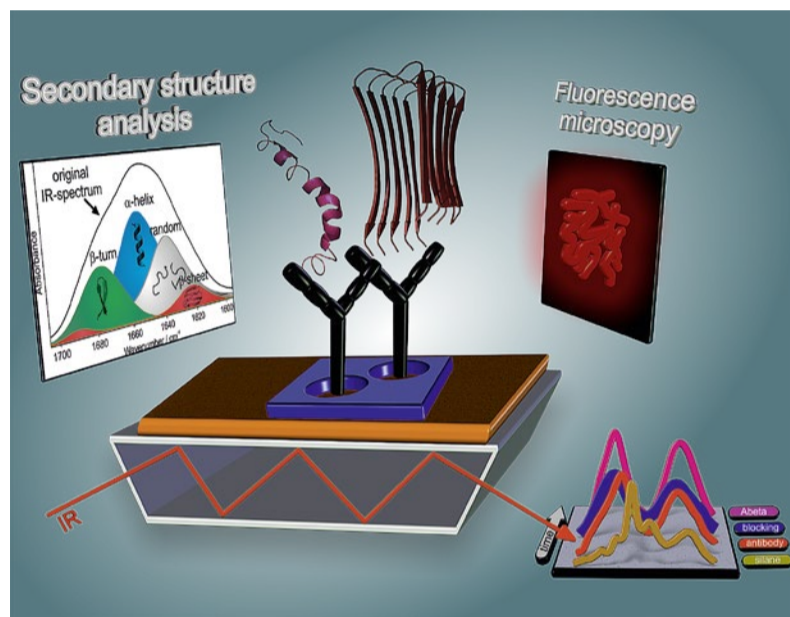
Report: Melanie Günther

'There are different hypotheses that describe how Alzheimer's develops, but none of these has been conclusively proven,' explained biophysics expert Professor Klaus Gerwert, when asked about the role of amyloid-beta peptides in Alzheimer's disease. 'We assume that, at the beginning of the disease, there's a change in the amyloid-beta peptide. This means that the peptide changes from a healthy alpha-helical form into a diseased, beta-pleated sheet form; the secondary structure of the protein changes. The pleated sheet structures can attach to one another and form oligomers. We believe that the formation of soluble oligomers is the critical point at the beginning of Alzheimer's disease. The oligomers develop into fibrils and finally into visible plaques.'

Along with other scientists, Gerwert has developed a test to detect change in amyloid-beta peptides and thus diagnose Alzheimer's earlier.

**How does the test, or procedure, work?**

'We have developed an infrared sensor. This detects the secondary structures and differentiates between alpha-helix and beta pleated sheet forms. However, various different types of proteins are found



in the blood or spinal fluid. The difficulty is being able to look only at the amyloid-beta. Other substances impair this and interfere with the actual signal. We utilise antibodies as 'interceptors' to specifically bind amyloid-beta peptides. These are covalently bonded to the surface of the infrared sensor, meaning that we have a type of ELISA-test (Enzyme-Linked-Immunosorbent Assay).

'We then measure the bonded amyloid-beta peptide with the infrared sensor and analyse whether it is present in its healthy or diseased form. We utilise structure-sensitive

infrared bands, i.e. so-called amide I bands. When these bands are below a certain threshold we know that Alzheimer's disease is present.

'We determined the threshold level based on experimental investigations.'

**What does the importance of amyloid-beta peptides distribution mean?**

'This is the key part of the test: There are antibodies that can only selectively bind one form of amyloid-beta peptides – either the healthy or diseased form. The blood

of a healthy human contains a large number of healthy amyloid-beta peptides, but naturally also some diseased ones. An antibody that only selectively looks for the beta pleated sheet form would therefore also find diseased forms in a healthy person. Therefore the test is initially confusing.

'The advantage of our technology is that we can determine the secondary structure distribution of all amyloid-beta peptides extracted from body fluids label-free. When the peptides are healthy we can see alpha-helical dominated bands above the threshold level. When the majority of peptides are of the beta pleated sheet form, the band goes below the threshold level. Unlike the ELISA procedures we measure the distribution of all amyloid-beta peptides and not only specific conformations.

**Early detection timescale**

'Our primary objective was to detect an early stage of Alzheimer's, i.e. before the onset of clinical symptoms. Therefore, we selected the amyloid-beta peptide, because the change occurs around 15 – 20 years before the beginning of clinical symptoms.

'We've already carried out a mini-study which, although not yet statistically significant, has delivered some promising results. We analysed samples from a cohort from the year 2000, at the Heidelberg-based German Cancer Research Centre (DKFZ). We could analyse, conclusively, which of the initially healthy study subjects developed Alzheimer's disease within the following 8-15 years. To substantiate our analysis with statistical accuracy,

we are currently examining 1,000 samples from study participants. Once we can make this prediction for all 1,000 samples we'll have achieved the necessary statistical significance. So far we have tested 300 out of the 1,000 samples.'

**Other neurodegenerative disease**

'The sensor is also potentially suitable for the detection of Parkinson's disease. In the case of Parkinson's the so-called alpha-synuclein plays an important role. We assume that this protein also converts from an alpha shape to a beta shape. We are currently looking for a specific antibody for alpha-synuclein, allowing us to use the sensor for the detection of Parkinson's disease.'

**When might the test enter clinical routine?**

'The procedure is very robust in the laboratory. It is suitable for the detection of Alzheimer's. It is a good, additional clinical-chemical test to confirm an Alzheimer's diagnosis.

'We need to await the results of the current study to assess its use for early detection. We are currently optimising the sensor and are trying to increase the sample throughput so that large collectives can be measured in short periods of time.'

A new photo-switchable molecule for oxygen-independent PDT therapy

# Advanced photo-dynamic therapy

Researchers develop an oxygen-independent, photoswitchable molecule and successfully test this in the lab to observe effects on tumours. Photoswitchable agents may reduce chemotherapy effects

So far, photodynamic therapies have been dependent on oxygen in the tissue. But hardly any oxygen exists in malignant, rapidly growing tumours. A group of researchers at the KIT Institute for Biological Interfaces and the University of Kiev has now developed a photo-switchable molecule as a basis of an oxygen-independent method.

The researchers' successful laboratory tests on tumours have been reported in the journal 'Angewandte Chemie' (Applied Chemistry – DOI: 10.1002/ange.201600506).

Photodynamic therapy (PDT) in medicine usually uses a substance that reacts to light and converts the oxygen in the tissue into aggressive radicals. These reactive substances

are toxic and damage neighbouring cells, in such a way that tumours, for example, are decomposed. As a result of their quicker growth, however, many tumours have a high oxygen consumption. This reduces the concentration of oxygen available in tissue, which may aggravate conventional PDT.

What the researchers at the KIT Institute and the University of Kiev have developed is a new photo-switchable molecule for oxygen-independent PDT. The effect of the GS-DProSw molecule can be 'switched off' by ultraviolet light prior to therapy. Only upon application is it 'switched on' in the tumour tissue by visible light to damage the tumour tissue there. 'The sur-

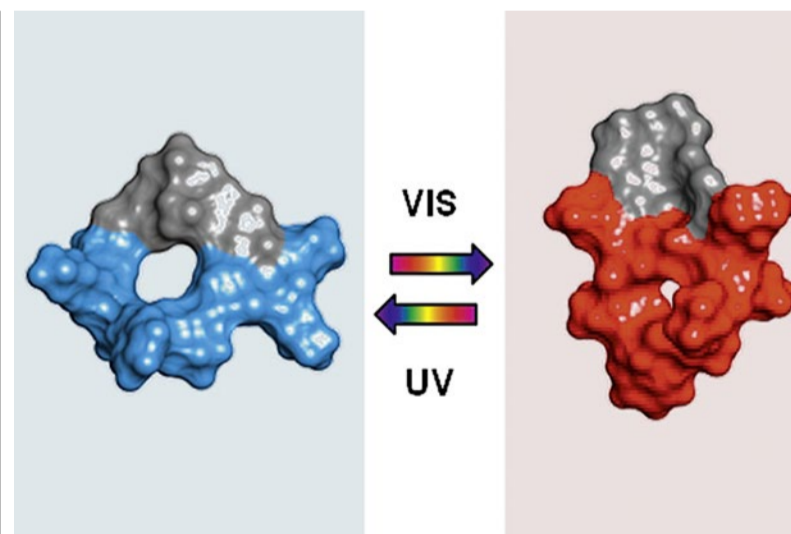
rounding organs remain in the dark and are not affected by the active substance,' Anne S Ulrich, Professor of Biochemistry and Director of the KIT Institute for Biological Interfaces, explains. 'As a result, side effects are reduced significantly.'

**Animal testing**

Now, for the first time, this new concept has been tested on animal models.

Once per day, the photo switchable GS-DProSw molecule was administered. Then, the tumours were irradiated locally with visible light for a period of 20 minutes. After ten days of PDT treatment, the tumors were found to be far smaller than comparative groups not treated with light.

To initiate an oxygen-independent reaction in PDT, the molecule applied has to be of a cytotoxic



The GS-DProSw molecule in its inactive form (blue) can be activated by visible light (red) and 'switched off' again by UV light. (Figure: KIT)

nature. This means it has to directly attack the tumour tissue irrespective of other reaction partners. A suitable molecule with cytotoxic properties against tumours is the biomolecule gramicidin S (GS), which is a natural antibiotic.

To prevent it from damaging healthy tissue, the research team inserted a photo-switchable diaryl ethene segment into the ring struc-

ture. As a result, the GS-DProSw molecule can be switched between two states with the help of light: The agent can be administered in the inactive state and is activated at the desired location by specific irradiation with light. There, it attacks the surrounding tumour tissue and, contrary to conventional PDT, it does not require any oxygen for this purpose.

New technique shows OxLDL in atherosclerotic plaques

# Identifying a likely heart attack

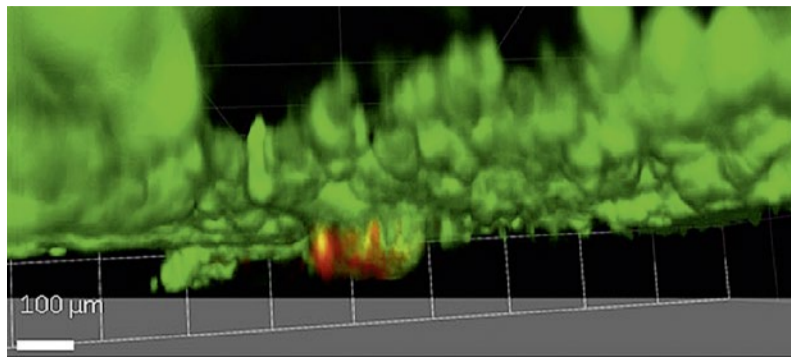
UK researchers have identified a new approach, which could make it easier to identify fatty plaques that could cause heart attacks or a stroke, Mark Nicholls reports

A team from Imperial College London is using fluorescence molecular tomography (FMT) optical imaging technique to determine oxidised LDL (OxLDL) – known to play a major role in atherosclerosis and present in high quantities in plaques most likely to lead to a heart attack or stroke.

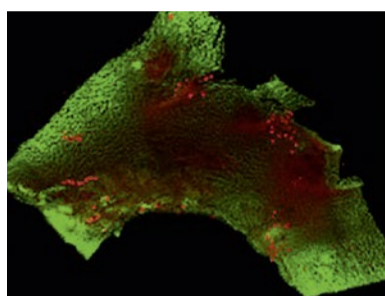
The method proved promising when identifying atherosclerotic plaques in mice models and potentially could show how likely an atherosclerotic plaque is to rupture in human patients. Once identified doctors could then treat those plaques, either with targeted drugs or a stent implanted in the affected areas.

Atherosclerosis is the build-up of fatty plaques in arterial walls that lead to the brain or heart. If an atherosclerotic plaque ruptures, it can form a clot, causing either a heart attack or stroke. Over 100,000 people die annually in the United Kingdom after suffering such events.

The team's method to detect and visualise amounts of oxidised LDL (OxLDL) in atherosclerotic plaques involves near infrared optical imaging. For this, the researchers experimentally used a specially designed antibody that targets OxLDL, adding

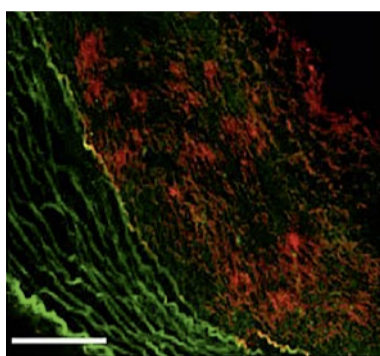


Injected L01-750 (red) homing in to aortic oxLDL deposits underneath stained endothelium (green)



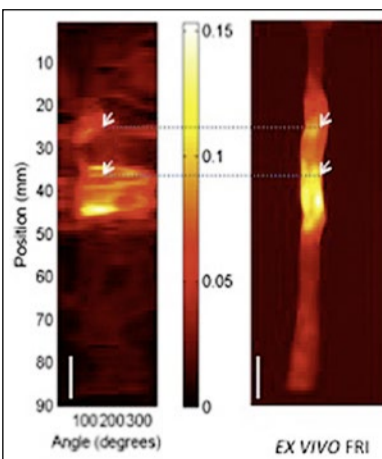
L01-750 (red) identifying oxLDL in a mouse aorta

a fluorescent marker to visualise plaque areas that contained large amounts of OxLDL. The first part of the research utilised Fluorescence Molecular tomography (FMT), which is new technology that allows full-body optical molecular imaging of murine models. During a second part of the research, performed with



Injected L01-750 (red) as seen on fluorescence microscopy of rabbit atherosclerosis

Harvard Medical School, an infrared catheter was used to look inside the artery of atherosclerotic rabbits and detect any fluorescently-labelled antibody. The researchers hope that this approach will make details vis-



Injected L01-750 Identifying oxidised LDL in rabbit aorta with ex vivo intravascular NIRF imaging and fluorescence reflectance imaging.

ible that are usually invisible to doctors using current technology to visualise atherosclerotic plaques. They are now working towards using the technique in people and can already detect the human form of OxLDL.

Consultant cardiologists and lead researcher Dr Ramzi Khamis: 'We are excited about this step in the challenging field of optically imaging molecular activity of atherosclerosis. Most of the imaging techniques out



Dr Ramzi Khamis is a consultant cardiologist and clinical research fellow at the National Heart and Lung Institute at Imperial College, London. He splits his time between treating patients and translational research, primarily in the area of the immune system and atherosclerosis.

there in the clinic look at morphology, the structural kind of components of atherosclerotic plaque, and although that tells you quite a lot, it does not tell you about the inflammatory status or molecular activity of plaque.

'With this research we're trying to pick out the plaques that are most likely to rupture before they cause a heart attack. Our next step will be to modify the technique that we've used here so that it can be used in patients to detect dangerous plaques.

'We are also looking at the possibility of using the same antibody that we've developed to image the plaque to deliver drugs directly to the plaque itself. So, we have not only found a possible new diagnostic tool, we may also have discovered a new way to treat this deadly disease.'

Exporting more Asian medical imaging devices

# Chinese firm reaches into Europe's market

Neusoft Medical Systems, a limited company, is the leading supplier of medical imaging equipment in China, a country with more than 46,000 hospitals. The firm also provides equipment to hospitals in 109 other countries, amounting to 9,000 customers. Now Neusoft reports preparations to tap into European market

'China remains our home market and is definitely our largest base of customers, yet we have expanded with great success establishing operations not only across Asia but in South America, South Africa, and the Middle East,' Neusoft Medical Systems CEO Patrick Wu pointed out. The company is now turning strongly to building on a customer base in North America, he said, and this year he will oversee the opening in Frankfurt of a direct subsidiary operation for Europe, with a special focus on Germany.

'Europe is a highly competitive market with very well established companies, and arguably, Germany is the toughest place to compete. Perhaps for this reason, we want to go there first, to put our systems up against the best,' Wu explained. 'Yet, our strategic approach is not to compete against big companies at big medical centres,' he added. 'Instead, our focus in Europe is on private imaging centres, and there are about 2,000 of these in Germany alone. We can offer an excellent product portfolio for smaller community hospitals, as well. In this segment of the German market, we can help them meet their

need for high performing imaging systems while at the same time helping them to meet demanding budget requirements.'

Last year, at a German clinic, Neusoft installed its flagship product NeuViz 128 CT a 128-slice scanner that was launched in May 2015. At this reference site the company is also able to showcase a second product in its scanner line, the NeuViz 64, a 64-Slice CT System.

For smaller hospitals, Neusoft also extended the NeuViz CT product line to include a premium performance 16-slice system, as well as the NeuViz 16 Classic.

Building on proprietary technologies and an in-house research and development expertise for CT, the expanded NeuViz product line includes variations on a unique dual-

slice CT system and the NeuViz Twin.

Software technology is a core competitive strength for the company, as it is an integral part of the Neusoft Corporation, the largest IT solutions and services provider in China. As a result, Neusoft Medical Systems has continuously enhanced its imaging technologies with a powerful command of algorithms to improved image quality and accelerate workflow. The complete Neusoft Medical Systems imaging portfolio includes a range of CT scanners, MRI scanners, diagnostic X-ray and a best-in-class premium ultrasound platform.

In oncology, the company has developed a line of linear accelerators for radiotherapy, and launched the NeuSight PET/CT worldwide that is both CE certified and approved by the USA Food & Drug Administration in January 2016.

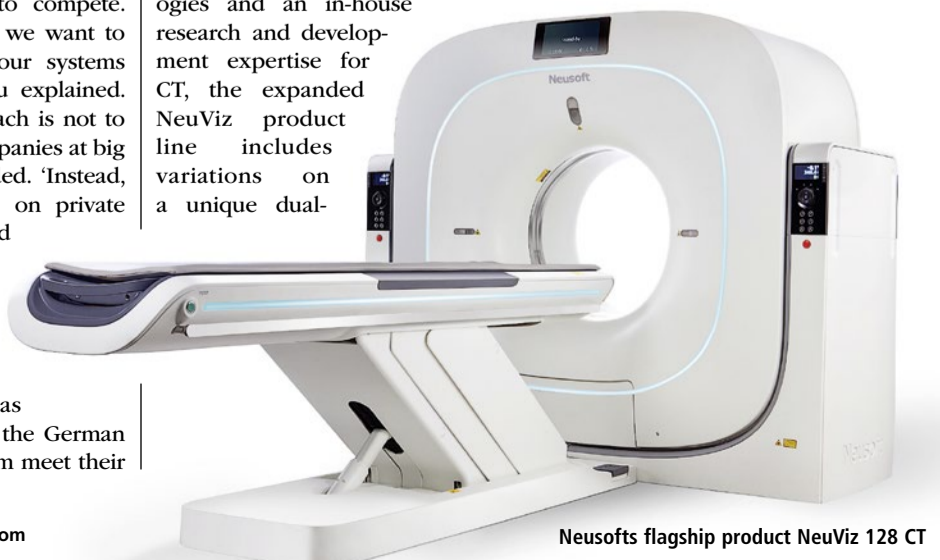
'When we bring together our

complete portfolio, Neusoft Medical Systems can present a very competitive package,' said CEO Wu, adding: 'Customers find that we are exceptionally strong with healthcare informatics to support our systems in image processing capabilities and image management, including a



Patrick Wu, the CEO of Neusoft Medical Systems

cloud-based technology for storage as well as technical support.'



Neusofts flagship product NeuViz 128 CT

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2-D/3-D scaled for 360-degree breast biopsies

# NEW: The dedicated prone breast biopsy table

Breast tomosynthesis imaging, Hologic calls it 3-D mammography, is proving to be the best modality to image breast cancer. 'The Hologic tomosynthesis system has demonstrated superior clinical performance to conventional 2-D mammography in a number of metrics, in particular showing improved detection of invasive cancers and reductions in recall rate,' the manufacturer reports, adding: 'Now Hologic is offering its tomosynthesis technology on a dedicated, prone breast, biopsy table.'

'The CE-marked 'Affirm' prone biopsy table provides enhanced 2-D/3-D biopsy imaging and fast, easy access to the breast,' Hologic points out. 'The new product is an important step forward in biopsy technology — allowing radiologists to better target lesions found with 3-D mammography exams, as well as other screening modalities — with exceptional imaging, improved workflow and seamless, 360-degree access to the breast.'

Clinicians trust prone patient positioning for breast biopsy because it supports the patient stably throughout the procedure while isolating them from the biopsy needle — certainly improving patients' experience.

The Centro de Patología de la



Among the first to provide tomosynthesis guided breast biopsies on the new Hologic Affirm prone 2-D/3-D biopsy table are Alejandro Tejerina (second from left) and colleagues at the Centro de Patología de la Mama, Tejerina Foundation, Madrid

Mama, Tejerina Foundation, in Madrid, Spain became one of the first sites in the world to offer the new system. Alejandro Tejerina MD, a radiologist with the Centre, reports that the feedback from the first wave of patients is very positive. 'We are performing these [prone biopsy] procedures now with an average of 20 minutes,' he said. 'That's a big change, not only for our time but

also for the patient experience. I have a colleague in the Netherlands who also had one of the first systems installed, and she said she did one procedure in just 12 minutes. That is perhaps exceptional, but it shows what is now possible.'

According to Tejerina, conventional breast biopsy systems are restricted to 2-D imaging with a narrow window for targeting the

lesions. Often it requires multiple X-ray exposures to find and position the suspect tumour for the biopsy needle. With tomosynthesis imaging on the new Affirm table, he said there is a much wider field of view and, critically, the biopsy device can now be positioned anywhere in a 360-degree circle.

Hologic built many other innovative features into the new Affirm prone system that make it easier to work with and faster for the procedure, Tejerina noted.

The Hologic MultiCare Platinum system had to be positioned manually, 'now the system does this for us automatically, which saves time. The software really streamlines our workflow, so that goes faster. The paddles for compressing the breast are clear instead of metal, and this makes things easier.'

Even the positioning of the patient improves the experience, he said. With upright systems, the woman undergoing the biopsy is looking directly at the biopsy needle. If the woman is lying down, she does not need to witness the procedure directly.

The new Affirm prone system offers a more efficient, more accurate procedure and the woman's breast is under compression for less time, which adds to her comfort,

he said. The Foundation has led the way in women's breast health for over 40 years. Offering tomosynthesis guided breast biopsies on the Affirm prone 2-D/3-D biopsy table is another first for the Centre, Hologic pointed out. 'In 2000, the Centre pioneered the use of digital mammography in Spain. It was the first centre to install a stereotactic guided prone biopsy table in 1997.'

'In 2010, it led the way again, installing a Hologic Selenia Dimensions breast tomosynthesis system, the first site in Spain to use the innovative technology to improve the early detection of breast cancer. Later in 2010, the Centre was the first site in Spain to combine the Hologic Affirm upright biopsy system with the Hologic tomosynthesis system.'

'In 2015 the Centre began offering Hologic's I-View contrast enhanced 2-D imaging along with a 3-D scan, further increasing the value of a contrast mammography procedure.'

'The Affirm prone biopsy system expands the Centre's breast biopsy portfolio, complementing their Selenia Dimensions 2-D/3-D mammography system and Affirm upright biopsy system,' Hologic concludes.

Towards personalisation of ovarian cancer care

## Imaging the invisible killer

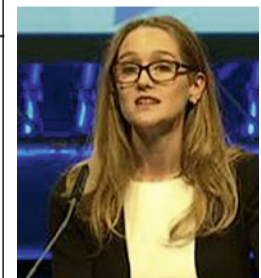
Andrea G Rockall, Consultant Radiologist at the Royal Marsden Hospital and Visiting Professor of Radiology at Imperial College in London, delivered the prestigious Wilhelm Conrad Röntgen Honorary Lecture at ECR 2016 on 'Imaging the invisible killer: towards personalisation of ovarian cancer care'.

then develops resistance to the treatment: 'A better understanding of this disease is urgently needed and imaging developments have an important role to play.'

The radiologist offered several suggestions to improve early detection, such as MRI-supported ultrasound, which may lead to successful screening and a radiological lexicon. Rockall introduced an algorithmic approach for the characterisation of masses, which is currently being validated in large multi-centre studies.

Furthermore, the professor introduced current radiomic studies that are exploring imaging characteristics of underlying tumour biology. They aim to stratify ovarian cancer into distinct gene expression subtypes that may enhance therapeutic targeting.

'I hope I could convince you



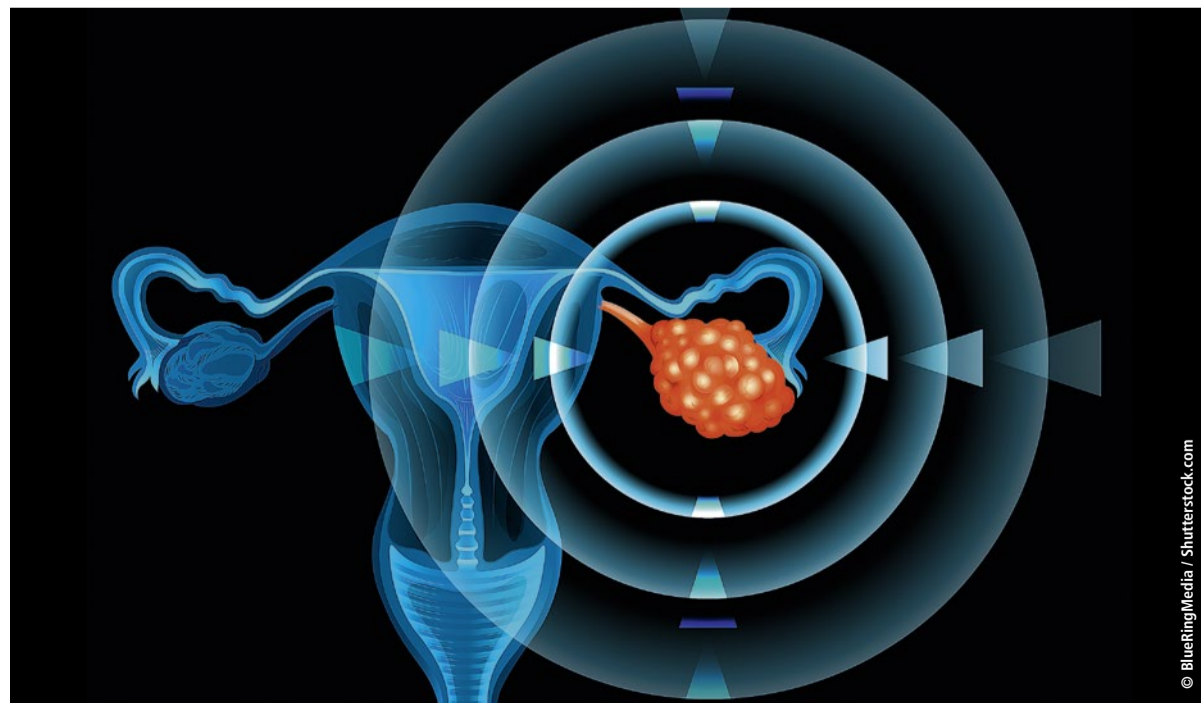
Andrea G Rockall is a Consultant Radiologist at the Royal Marsden Hospital\* and Visiting Professor of Radiology at Imperial College in London, UK. She graduated from King's College Hospital, London, in 1990 and received her radiology training at St Mary's Hospital and University College Hospital, London. The professor was president of the International Cancer Imaging Society for 2015 and is a member of numerous organisations, including the British Gynaecological Cancer Society, the RCR and the National Cancer Intelligence Network.

### Sascha Keutel reports

For many cancers there has been a steady improvement in patient outcomes, due mainly to early detection and novel therapies. However, with ovarian cancer, the most lethal gynaecological cancer in Europe, no such success can be reported.

The major problem with ovarian cancer is detection because, in the early-stage, the disease is rarely symptomatic and screening is not supported by trial evidence. Most patients present with disseminated peritoneal disease that can be surgically complex, Professor Rockall explained and added that CT is still inconsistent to predict surgical findings, which limits its contribution only to surgical planning.

Another problem, according to Professor Rockall, is that the initial response to chemotherapy is often followed by disease relapse, which



that imaging can personalise chemotherapy. Early detection of non-responders using advanced imaging techniques and potentially radiomics may play a significant role in the future. Imaging can indeed personalise the planning of surgery. The challenges of CT, which are very real, may be overcome through multiparametric MRI allowing optimisation of the surgical approach', Professor Andrea Rockall concluded her presentation.

\* The Royal Marsden Hospital was founded by Dr William Marsden in 1851 as the Free Cancer Hospital, was the first hospital in the world dedicated to the study and treatment of cancer.

The whole is greater than the sum of its parts

# Top topic: Hybrid imaging

'The combination of nuclear medicine and modern imaging procedures such as CT and MRI is becoming increasingly important in the diagnosis, treatment planning and after-care of cancerous diseases,' explains Professor Katrine Åhlström Riklund, Deputy Head of the Department for Radiology, Senior Consultant at the Department of Nuclear Medicine, and Director of Sweden's Umeå University Medical School, who also presides over the newly established European Society for Hybrid Medical Imaging, ESHI.

Hybrid Imaging was among the main topics at this year's European Congress of Radiology (ECR 2016) in Vienna this March. Riklund, this year's congress president, said, 'The molecular, biochemical and structural information obtained through hybrid imaging is greater than the information gathered from the respective individual procedures.' Or, as Aristotle put it: 'The whole is greater than the sum of its parts'.

PET/CT, the combination of positron-emission-tomography and CT, and SPECT/CT, the combination of single photon emission CT and CT, are already fixed components of radiological and nuclear medical diagnosis. However, there are also new developments in this area of medicine.

Researchers from the Statistical Imaging Group at University College Cork, Ireland, as well as researchers from the Department for Radiology and the PET/CT Unit at the University Hospital Cork, reported on statistical methods they have developed to analyse 18F-FDG-PET/CT examinations.

With the help of the tracer 18F-fluorodeoxyglucose a lot more information can be gained about heterogeneous tumours than with conventional PET/CT. Lung cancer for instance is characterised by a particularly high tumour heterogeneity, i.e. the tumours contain a number of genetically different cancer cells with different biological characteristics – a fact that must be considered during treatment.

Even more is happening in PET/MRI, i.e. the combination of positron emission tomography and magnetic resonance tomography. 'PET and MRI are still in their "honeymoon period",' Professor Goh, Chair of Clinical Cancer Imaging at King's College London, points out, although she can also see a shift in paradigm. 'The times where we simply used to measure whether a tumour has grown or shrunk are over. Now we actually have access to the biology of the tumour.'

Professor Gary Cook, Chair of Clinical PET Imaging at King's College London is somewhat less euphoric: 'It's not yet clear how important PET/MRI will become as a diagnostic tool.' However, even he ultimately sees a rosy future for PET/MRI. 'There is mounting evidence that PET/MRI delivers a more precise diagnosis for some types of tumours, such as those in the brain or prostate, than PET/CT or MRI alone.' The use of new tracers, such as Gallium 68 (68Ga) could also give PET/MRI a boost.

As multiparametric MRI is acquiring a key role in the diagnosis of prostate cancer, now PET/MRI is also becoming of interest in this field. 'Particularly in the case of recurrences, PET has proved to be a useful tool



Combined imaging makes it possible: Images taken with the PET/MRI scanner show high resolution structures and detailed biological information

to differentiate between potentially curable local recurrences and metastases,' explains Dr Egesta Lopci, from the Department for Nuclear Medicine at the Istituto Clinico Humanitas in Milan, Italy. Choline tracers (11 C-Choline and 18F-Choline) are used for this purpose. Prostate cancer cells have a high requirement for choline, which means that this respective radionuclide is found there in particularly high concentrations.

In the case of dementia, PET/MRI could also play a more important role in the future. Although MRI makes it possible to differentiate between the typical patterns in the brains of Alzheimer patients, and those suffering vascular dementia, this is only possible for the typical forms. 'Individual patterns often don't look like those found in textbooks and there are patients who suffer Alzheimer dementia as well as vascular dementia,' explains Dr Sven Haller, neuroradiologist at the University Hospital Geneva, Switzerland. There is also the problem of the 'blind spot', which MRI is affected by during the detection of Lewy Body Dementia:

'MRI is nonspecific when it comes to the detection of this type of dementia,' he adds.

Thus PET comes into play: 'This procedure makes it possible to determine the reduced dopamine transporter reception in the striate nucleus that occurs with Lewy Body Dementia. PET also facilitates a clear differentiation between Alzheimer dementia and vascular dementia. 'The crucial point is the detection of beta-amyloid in vivo,' emphasises Dr Valentina Garibotto, specialist in nuclear medicine at the University Hospital Geneva. There are no fewer than four tracers that can be utilised to detect typical plaques of beta-amyloid, which accumulate in the nerve cells and blood vessels of the brain in Alzheimer sufferers.

'The availability of PET/MRI opens up new possibilities in oncological radiotherapy,' confirms Professor Ursula Nestle, of the Department for Diagnostic and Therapeutic Radiology at the University Hospital Freiburg (Germany): 'The hybrid procedure facilitates very precise therapy planning.' This applies in

particular to tumours which can only be visualised with difficulty with CT but very well visualised with MRI and which can also be examined very well with PET, such as those found in the upper abdomen, prostate and brain.' Nestle is expecting a lot from the combination of molecular PET and molecular MRI.

Recently launched is a new EU breast cancer research project, 'Digital Hybrid Breast PET/MRI for Enhanced Diagnosis of Breast Cancer' (HYPMED). The European Institute for Biomedical Imaging Research (EIBR) runs this, as project coordinator, and the University Hospital Aachen, Germany is scientific coordinator. The project envisages the integration of a PET detector into an MRI surface coil so that high resolution PET imaging and high resolution MRI imaging can be carried out synchronously in breast cancer patients – including the opportunity to carry out minimally invasive MRI- and PET-guided biopsies. 'This approach is basically aimed at upgrading any conventional MRI scanner into a high resolution PET/MRI system,' confirms Professor Volkmar Schulz Dr-Ing, from the Institute for Experimental Molecular Imaging at University Hospital Aachen.

The growing importance of hybrid imaging also has an impact on the relationship between radiologists and nuclear medics. 'This combination of nuclear medical and radiological procedures requires specialist knowledge of both disciplines and also respective training,' emphasises Professor Osman Ratib, Head of the Department for Nuclear Medicine and Molecular Imaging at University Hospital Geneva.

However, this is not quite so easy: 'Whilst hybrid imaging is developing at a rapid pace there is still room for improvement when it comes to the

cooperation between both disciplines involved,' believes Professor Gerald Antoch, Director of the Institute for Diagnostic and Interventional Radiology at the University Hospital Dusseldorf. Nuclear medics should not simply regard CT or MRI as tools for the precise anatomic positioning of their PET images, and radiologists should not only see PET and CT as types of additional contrast media, Antoch believes: 'We need training programmes that cover both sides of hybrid imaging.'

ESHI president Riklund taps it in a nutshell: 'In the future hybrid images should be interpreted by one single specialist.'

Whole body PET/MRI image



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The mainstay of patient identification

# Go biometric or risk a botch up

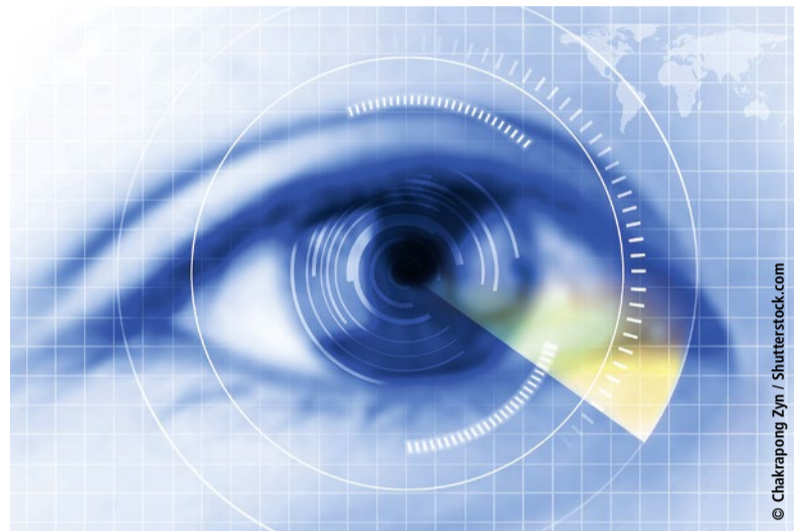
Today, most healthcare systems rely on text-based matching: A patient's identity (ID) card or driver's license is considered sufficient proof of identity. However, this 'identification system' puts patients at risk of death, improper treatment, insurance abuse and lawsuits the provider and hospital cannot defend. Informatics expert Dr Raymond D Aller, a renowned authority on the use of information technology (IT) to enhance and ensure patient safety and operational efficiency, urges healthcare providers: 'Move toward biometrics as the mainstay for patient identification!'

Interview: Sascha Keutel

Questioned about the risk of current identification systems for hospitals and insurance cover, informatics expert Dr Raymond D Aller explained, 'If patient "A" comes to our hospital and we mistakenly identify him as patient "B", we risk treating him for diseases he may not have, giving him medications to which he is allergic and could have a serious or fatal reaction and we might fail to give him vital medication or treatment because we do not realise the conditions he does have.'

'In that scenario, the misidentified patient might sue the hospital. It's very difficult for a hospital to convince a jury that it was excusable to treat the wrong patient. Typically, such cases are settled out of court.'

'If patient "F" lacks medical insurance, but his brother "G" has good coverage, our present practices make it possible for patient "F" to give the hospital a driver's licence borrowed from "G". "F" then receives treat-



ment, let's say knee replacement, and the bill is sent to "G's" insurance company – which constitutes insurance abuse. Furthermore, the hospital may not recognise critical conditions in "F" such as a pre-existing atypical blood bank antibody and give a blood transfusion that could be harmful or fatal.'

## Shortcomings in text-based patient identification and matching

'Text-based patient identification has several critical shortcomings. Firstly, there's a high possibility that more than one person in the population served has the same name, sometimes even the same date of birth.'

Secondly, clerks tend to treat close text matches as exact. Third, different ethnic groups handle names differently, Hispanic women, for example, have two surnames one of which might change when they get married, or some Hindus of southern India who consider it heretic practice to provide the family name.

Moreover, as the number of patients in the database is expanding, the likelihood of matching non-corresponding people increases.

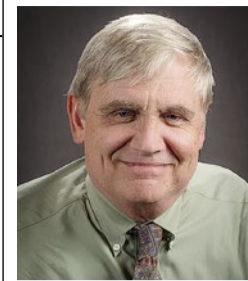
'Even the US Joint Commission on the Accreditation of Healthcare Organisation (JCAHO), and others, promulgate the fallacy that matching two text identifiers is somehow "positive" identification. Unfortunately, a driver's licence is not much better than other forms of text. Humans are not very good at unique matching of a picture on a driver's licence. Interestingly, biometric face recognition algorithms do a much better job. Last but not least, don't forget that if a patient is admitted comatose, or confused, obtaining text information may be difficult.'

## Biometric identifiers used in healthcare

'Biometric identifiers are used to identify and authenticate patients. Biometric identifiers currently used in healthcare include iris pattern, palm vein pattern, face recognition and fingerprint. Others show promise, such as handwriting tempo and cardiac rhythm, and further experience will show their roles.'

## Are biometric identifiers superior to other identification methods?

'I've listed some shortcomings of



Raymond D Aller MD is Director of Informatics at the University of Southern California Laboratories and Pathology. A Harvard Medical School graduate, for his medical thesis he designed the first online surgical pathology information system in the USA. This became the prototype of the anatomic pathology automation tools now used in most hospitals there. He was elected Fellow of HIMSS, Fellow of the American College of Medical Informatics and awarded the Lifetime Achievement Award/Honorary Fellow of the Association of Pathology Informatics. Aller is currently focusing on a major unsolved problem in healthcare: the definitive identification of the patient and the need to move from text matching to biometric identifiers.

text-based patient identification and matching and the difficulties encountered when asking patients to identify themselves, based on what they know or what they have, such as an ID card. Biometric identifiers on the other hand have a precise relation to who the patient IS – biologically. With a precision often reaching one in several hundred thousand! I urge those responsible to move toward biometrics as their mainstay for patient identification!'

A futuristic communication strategy cuts nurse ward walks by 2 km daily

# Humber River Hospital is oh so smart

'Humber River Hospital, Toronto, Canada, could come straight out of a science fiction series that provides Star Trek-like healthcare services with hall-cruising robots delivering food, medications and supplies to staff, electrochromic windows, video conference capabilities at patients' bedsides and real-time location systems, to name but a few futuristic features. Yet, this is now and for real!' Cornelia Wels-Maug reports

## Workflow automation at the centre:

Opened in October 2015, the new Humber River Hospital in Toronto is a 656-bed acute care facility aims to offer a new level of staff and patient experience with everything involved being 'lean, green and digital'. The hospital's underlying mantra is workflow automation to maximise efficiency and patient outcome. More than three-quarters of its supply chain are automated. Physicians order tests, deliver samples and receive results completely electronically.

Given its high level of computerisation to support the day-to-day care delivery, this could well be called a 'smart' hospital. To achieve that, a high degree of integration efforts had to be mustered to connect the various pieces of technology into a coherently working system. 'We are using technology to advance high quality, safe and efficient patient-centred care,' says Kevin Fernandes, CTO for Humber River Hospital. When it comes to communication, he makes it clear: 'Our technology

strategy includes equipping our care team with some of the latest communication tools at the point of care (POC).'

To this effect, the hospital chose to work with Ascom Wireless Solutions, which provides wireless on-site communication system and has built up an international presence in hospitals, senior care and independent living. The hospital installed this vendor's nurse call system, Myco, and its Unite software platform, both designed to improve quality and efficiency of care. 'Myco's seamless integration with other hospital systems enables us to deliver everything from time-sensitive, bedside nurse calls and notifications to real-time electrocardiograms and waveforms directly to the mobile caregiv-

er device,' Fernandes adds. 'Ascom Myco increases the time our staff and physicians have to meaningfully interact with patients at the bedside.'

## Communication experience

Why did Humber Hospital choose Ascom? Claes Ödman, General Manager of Wireless Solutions at Ascom, explains: 'The Myco is already used by other technically advanced institutions, such as the Cancer Centre in Melbourne,

Australia. In particular, we have a strong presence in North America, due to Ascom purchasing GE's nurse call system back in 2011.'

His colleague, Fritz Mumentahler, CEO of Ascom Switzerland, adds to this: 'We have



Humber River Hospital, billed as the first fully digital hospital in North America, selected customised communication solutions from Ascom including more than 600 Ascom Myco smartphones, purpose-built for healthcare, combined with the Ascom Unite software platform.

an extensive mobile portfolio. What sets us apart is that we bring mobile devices, middleware, connectivity and infrastructure together. When it comes to the execution we also have a strong local deployment operation and local technical presence.'

## Myco and middleware optimise workflow

The Ascom Myco is a purpose-built smartphone geared for deployment in hospitals. 'It's a workflow optimising tool,' Tim Whelehan, President & CEO of Ascom North America, points out about the product's core feature. Combined with the vendor's middleware 'Unite', it supports access to information from medical equipment and clinical systems – e.g. patient monitoring devices and patient health records – when on the move. Thus patient-related information is available whenever needed to take decisions at the POC, extending the solution's capabilities well beyond those of a pure nurse call system. 'Using the Myco helped one of our clients to bring down the time spend running around the



wards from 11.5 km per day to 9.5 km just by optimising the workflow,' Whelehan points out.

The phone is based on Android open-source OS and supports the integration of existing hospital apps. 'We chose an Android platform to make it open for developers. Currently, there are about 80 apps working on the platform,' Whelehan explains. 'The system can support up to 250 different workflow systems on the Unite platform.'

Furthermore, by filtering alerts so that nurses are only notified of alarms triggered by their assigned patients, or those devices that monitor their patients, the solution significantly contributes to reducing alarm fatigue. Nurses can use the phone functions to either call the patient or forward or escalate the alarm.

The top display allows reading notifications at a glance, which adds to ease of use. Although the solution can host a range of healthcare applications, mission-critical alerts are prioritised.

The built-in barcode scanner is



*Criminals could target personal medical data*

# Managing the risk of cyber crime

Cybercrime cases grow annually, which demonstrates the possibility, not only for banks or companies, but also for insurers, because criminals also steal data and whole databanks containing private information. At this year's HIMSS conference in Las Vegas, Stephen Cobb, Senior Security Researcher at ESET North America, spoke of the growing risk and the need to manage health IT security risks

Report: Marcel Rasch

'Companies and consumers need to know that there is a thriving global black market in personal information', Cobb points out and specifies: 'This includes everything from basic data like name and email address to data such as a Social Security number, date of birth, account passwords, and of course, medical records.' Criminals steal this data wherever they can. That includes trying to take these data from healthcare organisations often having large databases of personal information. Criminals who steal personal information can sell it on the black market to other criminals who have figured out ways to monetise it. 'They do this through a wide range of fraudulent schemes, many of which involve some sort of identity theft. The result can be anything from your income tax refund being delayed to someone getting medical services in your name', Cobb states.

The risks are many and varied, but Stephen Cobb sees four main categories:

- Some risks have monetary impact, such as losing money by fraudulent bank transfers made using stolen credentials.
- Health risks can arise if medical data is abused to obtain medications or procedures.
- The organisation from which data was stolen risks a damaged reputation.
- Trust in technology will be eroded by criminal activity, undermining the great potential

of digital technology to improve healthcare delivery.

## How can we prevent those risks?

There are well-documented security practices that can greatly improve an organisation's resistance to attacks by cybercriminals. These start with data mapping and risk analysis, in which all the personal information handled by the organisation is identified and the potential threats to that data are evaluated. 'After



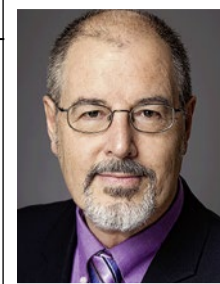
documenting the risks an organisation can plan how it will mitigate them through security measures', the expert explains. 'Low probability risks might be accepted, while high impact risks might be transferred through cyber risk insurance.' A weak spot in this process is the underestimation of the level of certain risks, particularly new and emerging risks. Thus a regular update of the risk analysis is indispensable.

Cobb: 'It should be noted that, whilst there is a high level of interest in, and concern about, complex new security vulnerabilities, many security breaches come about because basic security measures were not correctly, or not uniformly, applied. More than one major breach has been announced as "a sophisticated nation state attack", but later found to be much more mundane in origin and execution.'

## Who is responsible in a case of abused data?

There are often multiple parties and different levels of responsibility involved in data handling. A hospital may collect and store information about a patient, but send some of that data to a billing company, which then shares it with an insurance company. 'If criminals break into a hospital's network and steal data then the hospital is responsible, even if it has outsourced its data processing,' Cobb points out.

This is important when consid-



Stephen Cobb has spent 25 years on computer security and data privacy research as well as advising firms, consumers and government agencies on sensitive data and systems protection. He qualified as a Certified Information Systems Security Professional (CISSP) in 1996 and currently leads a San Diego-based research team for security software maker ESET. He is also studying for his MSc degree in criminology at the University of Leicester in England.

ering the risks in cloud computing. 'However, the data processor may also be held responsible,' Cobb adds. If personal information, or a medical record, is stolen from an insurance company that is processing a claim, then that insurance company is responsible. This shows that data security is an important topic that involves every organisation dealing with personal data. 'In other words, you cannot outsource responsibility,' Cobb concludes, and is apprehensive. 'I worry that the level of criminal activity targeting personal data will erode trust in digital technologies, although these have great potential to improve quality of life and living standards around the world.'

Now more than ever we need to manage the risks in an appropriate way as we move forward with new technologies.

*The advancing march of electronic technology*

# Intelligent machines have a place in healthcare

Report: Sascha Keutel

The Advisory Board Company is a global technology, research and consulting firm serving healthcare and higher education. They serve more than 230,000 leaders at 5,200 member organisations, enabling them to elevate performance and solve their most pressing problems. The Company provides strategic guidance, actionable insights, cloud-based software solutions, and comprehensive implementation and management services.

Knowledge modules, speech interfaces, robotics, analytics, and the Internet of Things demonstrate advances in intelligent computing in industries such as transport, retail and financial services. What role do they play in the healthcare industry? In his keynote address at the innovation pre-conference workshop at HIMSS 2016, Kenneth Kleinberg, Managing Director for The Advisory Board Company, identified that intelligent machines in healthcare 'include intelligent service assistants, remote patient monitoring systems, intelligent symptom checkers, (semi) autonomous medical devices, robot hospital or home assistants, and predictive modelling systems'.

There are different types of technological approaches used in intelligent computing. For example, constraint-based reasoning is often used for

scheduling problems; inference-based systems are used where experts can describe their knowledge in terms of rules but not the specific order that they rules need to 'fire' and machine learning and neural networks are often used where past data is available to train a model to produce useful results in new yet similar situations.

Kleinberg has categorised six key areas in which intelligent computing are affect the healthcare system and kinds of issues they can address:

- Intelligent Information Gathering and Sensing (Internet of Things) - What do we know about the patient and his/her changing environment to aid in his/her health? Example: Humber River Hospital in Toronto, working with CGI and ThoughtWire to help the hospital respond more efficiently to "code blues".
- Intelligent Interaction and Service - How can we communicate with our systems in a more natural manner? Example: MD Anderson's Patient Concierge using technology from Cognitive Scale to assist patients in choosing restaurants and housing.
- Intelligent Diagnosis and Care Plans - What's wrong with the patient and what kind of evolving treatment plan would be most effective? Example: Modernising Medicine using technology from IBM Watson to assist in diagnosis.
- Intelligent Medical Devices - How

can we automate and adjust medical devices to be more real-time, accurate, and responsive? Example: Johnson & Johnson's Sedasys for automated anaesthesiology.

- Robotics - What roles can robots take to assist with the mundane, dangerous, or complex jobs of humans? Example: University of California San Francisco Mission Bay, the use of TUG Robots by Aethon to deliver supplies throughout the hospital.

- Advanced Business Intelligence/Analytics - What can we learn from our data, and how can we predict future states and act on that knowledge? Example: Ayasdi use of Topological Data Maps at Mt Sinai to identify different types of Diabetes.

'These types of intelligent systems will examine large and varied sources of information, search literature, direct questions and information retrieval, provide ranked options and alternatives for providers to consider, predict outcomes, adjust with new data, and reduce and eliminate unnecessary workflow steps,' Kleinberg explains. Thus there is no doubt that those intelligent machines will transform diagnosis, treatment and workflow for patient care. However, do they have the potential to affect the healthcare industry? Kleinberg is positive: 'Absolutely - there are many tasks from the simplest to the most complex that can potentially be done more



As Managing Director for the Advisory Board Company, Kenneth Kleinberg, specialises in helping healthcare stakeholders in the US and abroad with IT strategy, including EHRs, HIE, and mobile computing. Kleinberg holds a BSc in biology from The State University of NY at Albany and an MA in neuropsychology from Queens College in New York. He is a HIMSS Fellow and is currently serving on the Connected Patient Committee.

accurately, efficiently and rapidly than by poorly trained, overworked, or overwhelmed healthcare workers and providers.

So, whilst intelligent systems could have an impact on healthcare, could they present a risk for patients? Kleinberg is cautious: 'They can be dangerous if not properly configured, "trained", monitored, and kept up to date. Training involves adapting the model to produce correct answers by showing the model combinations of correct situation/response pairings. Closed loop systems are especially risky and require considerable testing and often regulatory approvals.'



The new Humber River Hospital officially opened in October 2015

an important feature to ensure that the prescribed medication is administered to the right patient. The Myco works well in a shared Wi-Fi environment and has an interface permitting fast roaming, which enables non-interrupted calls for users moving across different wards while on the phone.

## Outlook - A prophet has no honour in his own country

This prestigious win further strengthens Ascom's market standing. The vendor aims to 'be present in every tier-one hospital in the world by 2020'. Although Ascom is a force to be reckoned with in North America and parts of Europe - mainly the Netherlands, Sweden, Finland and Norway - it will take more orders in leading hospitals to achieve its goal. Ascom particularly wishes to expand its presence in its home market Switzerland, as well as in Germany, the Middle East, Africa and Asia.

Delivering respiratory support and cardiopulmonary bypass

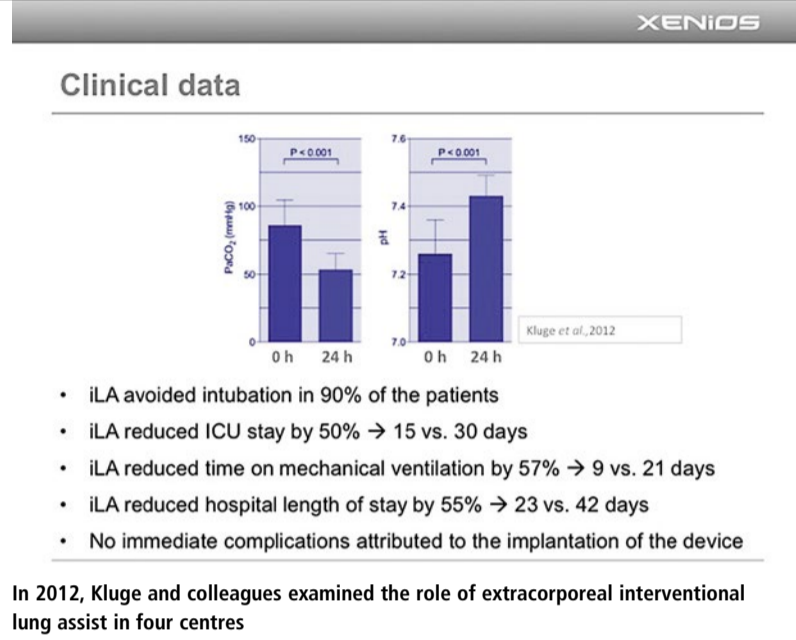
# Extracorporeal technology eases stress

Conventional therapy for ARDS patients and for patients with exacerbation of chronic obstructive pulmonary disease (COPD) has relied on invasive mechanical ventilation. Mechanical ventilation, however, has several major drawbacks: sedation has to be induced and the air being pressed into the lungs with positive pressure can damage the pulmonary alveoli or the diaphragm. Moreover, even maximum ventilation frequently does not provide adequate gas exchange.

Innovative artificial lungs, which breathe for the patient, offer less traumatic treatment for severe diseases such as acute respiratory distress syndrome (ARDS) or chronic obstructive pulmonary disease (COPD)

2013, German firm Xenios AG was founded by the two medical device companies Novalung GmbH and Medos Medizintechnik AG. Its focus lays on developing and manufacturing innovative devices for minimally invasive lung and heart support and offering groundbreaking solutions for lung failure as well as surgical and interventional solutions for the treatment of heart disease.

The Novalung product family is the first complete product range of state-of-the-art solutions for minimally invasive treatment of acute and chronic lung failure without mechanical ventilation and without the need for



patient sedation and mobilization.

XENIOS novalung products enable therapies for lung failure that are adapted to specific indications and patients. The duration and intensity of extrapulmonary lung support can be selected and adapted based on individual needs.

Thomas Bein, MD, University of Regensburg Medical Center: "Novalung's lung support therapies can be dosed as required in order to individualize to a patient's

specific needs, which is a very significant clinical benefit."

This new and easy-to-use alternative to invasive and trauma associated mechanical ventilation is usually comprised of a pump-driven pulmonary support system that removes carbon dioxide and adds oxygen.

A key component of such a device is the so-called membrane ventilator, which 'breathes' outside the patient's body to perform some of the gas exchange work of the native lung, at

**XENIOS**

**Interventional Lung Assist (iLA) - Revolutionizing today's standard of care**

**Interventional lung assist is efficacious and allows a broad range of application.**

the same time relieving the respiratory muscles.

A plasma-tight diffusion membrane is connected femorally, for example, to the body via a vascular access. The blood pump can be adjusted precisely and instruments control blood flow. The membrane ventilator can be used on a patient for up to 29 days. Because the lung assist system does not require sedation, in that period the patient is actively involved in the therapy and can eat and communicate.

The hardware fits on a trolley, providing patient mobility during the therapy, the manufacturer adds.

The membrane ventilator height can be adjusted quickly, for example, when the patient wants to lie down,

sit up or be moved around. In addition, subsequent therapies can follow sooner, bringing length of stay reductions and thus reduced costs.

The next generation of lung assist systems might well be portable, the report continues. The platform-based technology enables further developments, such as smaller and other types of vascular access plus increased efficiency as state-of-the-art gas exchangers provide better performance with a smaller footprint.

What might the far-off future bring? Perhaps bio-hybrid systems that mimic nature and are even colonised with cells.

Information: Xenios AG

New MRI system results in bigger throughput

## Children distracted by DVDs in scanner

Measures to improve the MRI scanning experience for young patients have had a dramatic impact on waiting times for a British hospital, Mark Nicholls reports

The Royal Sussex County Hospital, in Brighton, has installed a Siemens Healthcare Magnetom Aera 1.5-Tesla system incorporating special features to help relax younger patients. Within months of the installation of the wide bore machine, which has comfort enhancing features, there has been a significant fall in the number of patients aged 4-17 requiring general anaesthetic ahead of undergoing an MRI scan.

Other devices to help children relax include a TV - donated by Rocking Horse Children's Charity - to watch DVDs, and lighting control for young people to select the ambient hue.

John Wilkinson, the hospital's Imaging Services Manager, explained that in the nine months since the Siemens machine was installed, clinicians have found the number of children needing general

anaesthetic for their MR procedure has fallen by between one third and a half due to the increased compliance and comfort.

This has led to increased capacity, falling anaesthetic costs, and benefits to younger patients.

### In the bore, TV is key to patient relaxation

Under general anaesthetic (GA), the hospital can conduct MRI scans on three children per session, but up to ten children per session - depending on the nature of the scan - when they do not require GA because they feel more relaxed with the Aera's enhanced child-friendly features.

'This negates any anaesthetic risk for the children completely,' he said. 'The in bore TV is key, enabling children to lie down and watch their favourite DVD during a scan, while the wider bore makes the scanner much more tolerable from a claustrophobic point of view.'

'It is also quiet, which is much more acceptable to a child and this Siemens model has a variable LED lighting system, where children can say if they want blue, yellow or purple lighting. This way they feel as though they have more control of the scanning environment and as



a result they are happier and more relaxed.'

One of the main benefits is a reduction in waiting times. If a child needs anaesthetic, anaesthetic and radiology teams must be coordinated, with the child admitted to hospital as a day patient, and the wait for an MRI slot can be up to five weeks.

'Without GA, the wait is around two weeks and sometimes only three to four days, so we have been able to increase our capacity for paediatric scanning,' Wilkinson added. 'It is less resource intensive and from a patient - and parent -

experience, so much better with the new Scanner. It creates a more acceptable environment for a child to go into an MRI scenario.'

The trust has located the scanner between the adult hospital and The Royal Alexandra Children's Hospital, to use the equipment also for adults, and finds it has improved patient flow.

This particular move is part of the hospital's threefold operation to provide enhanced MR access to paediatric patients, and relocate the neurology department as well as ensure a better experience for the in-patients.

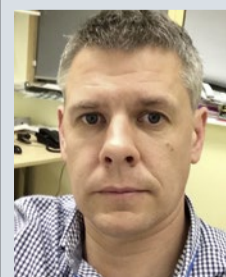
Two further Aera 1.5-Tesla systems have been installed as part of the planning to upgrade technology and further enhance the facilities within the hospital's radiology department.

### Systems will be in use for seven days a week

The systems are intended to be used for a range of services which include cardiac, breast, orthopaedic and prostate, and will also be used to ensure better throughput for neurosurgery patients following the move of neurosurgical procedures to the Royal Sussex County Hospital campus.

'We will be using the systems seven days a week, which will greatly impact the out-of-hours MR service with patients being seen more rapidly,' Wilkinson pointed out.

The three new Magnetom Aera will support a twenty percent rise in demand at The Royal Sussex County Hospital for imaging services compared to nine percent nationally in the UK.



Radiographer **John Wilkinson** is Imaging Services Manager at Royal Sussex County Hospital, Brighton, which is part of Brighton and Sussex University Hospitals, in the south of England. He is the professional lead for radiography within the hospital Trust.

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Portable US proves invaluable after Nepal earthquake

# POC ultrasound flies to work

The massive earthquake in Nepal in April 2015 killed more than 9,000 people and injured more than 23,000. Within days, medical teams from other countries had offered services to the disaster relief effort, among them a team from the UK's James Paget University Hospital (JPUH) in Gorleston-on-Sea, East Anglia. Here consultant anaesthetist Andreas Brodbeck explains how point-of-care ultrasound technology helped the team to provide long-term pain relief for earthquake victims, and support Nepalese doctors performing surgical procedures.

“ Spring 2015 saw vast areas of Nepal destroyed by an earthquake with a magnitude of 7.8, leaving local doctors trying to cope with huge numbers of seriously injured patients requiring urgent treatment. With a global relief effort underway, a team from the James Paget University Hospital volunteered to visit the earthquake zone, where they could use their medical expertise to assist Nepalese doctors dealing with an overwhelming workload.

Along with three other consultants from JPUH – orthopaedic surgeon Mike Flores, trauma consultant Emeka Nnene, and general surgeon Kamal Aryal, who originates from Nepal – I offered my services to

Kirtipur Hospital in Kathmandu. I had no idea what drugs and anaesthetics would be available at the hospital, but I knew that regional anaesthesia would be beneficial and so I took a SonoSite point-of-care ultrasound system with me, along with some local anaesthetics, needles and an Ambu-bag.

At Kirtipur, facilities were limited and the environment far from ideal. The majority of the patients we encountered were waiting for surgery to upper and lower limb injuries. Many were injured trying to escape from buildings, often jumping from some height, and so ankle, wrist and clavicular fractures were common. POC ultrasound was invaluable for treating these people; the instrument's small size and light weight made it easy to transport,

and I used it from the first day to the last.

With just one probe – a linear transducer – I could visualise the upper and lower limbs, allowing me to administer regional anaesthesia to one patient in the recovery room while another was in theatre undergoing surgery.

It's such a wonderful way to give an anaesthetic; you don't need general anaesthesia, which means people are not sick afterwards and recover faster. Patients are pain free after the procedure and experience fewer side effects, and it's safer, too, with a lower risk of developing complications. Using ultrasound, you can perform reliable blocks one after the other and, as the onset of anaesthesia is much faster, you don't have to wait a long time to find out whether or not it has worked. This quality is something that you can only get using ultrasound guidance.

The local anaesthetists, who were already very skilled at performing blocks with nerve stimulation, were fascinated by the use of ultrasound-guided anaesthesia and, after watching a few procedures, they were ready to use the technique themselves. It became a really good teaching experience.

The SonoSite system is very robust, intuitive and simple to use, and they picked it up so quickly. They saw how much the quality of the blocks improved, and I'm sure they will ask the hospital managers to invest in an ultrasound system at the earliest opportunity.

Within a couple of weeks, the



In spring 2015 an earthquake destroyed vast areas of Nepal

Medical staff from many countries worked together in the Nepal aid programme



workload was manageable and we could return home.

Nepal has since suffered a second earthquake and the monsoon has started. While the medical situation is reasonably well under control – there were fewer deaths and injuries during the second quake, largely because so many people were homeless and living under tarpaulins in the open air – there is still a great deal to do and it will be many years before the country is restored to its previous state.

The Nepal aid programme was a real team effort, with medical staff from many countries working together to treat as many patients as possible, providing support to our Nepalese colleagues, allowing them to take a much needed break.

As anaesthetists at Kirtipur and another hospital have expressed an interest in learning more about

ultrasound, I plan to return to Nepal in a few months' time, accompanied by Mr Aryal, to run a workshop on regional anaesthesia. This time I will take a newer point-of-care ultrasound system and more probes, allowing a range of additional ultrasound topics – echocardiography, abdominal or lung ultrasound, laparoscopic procedures and the use of ultrasound in ICU – to be covered, depending on what people want to learn.

I really appreciate the support we receive from SonoSite for our work in Nepal; it's a company that genuinely cares. Being able to contribute to the initial relief effort, with the backing of JPUH and the charity Nepal in Need, was very satisfying, and I look forward to returning to the country later this year. ”

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Advances and Controversies in Reconstructive Microsurgery (ACRM) 2016

# Robots hold a steady role in microsurgery

Embracing robotic technology in the realms of microsurgery will have significant benefits for patients, clinicians and hospitals, Mark Nicholls reports

Leading hand and peripheral nerve specialist Professor Philippe Liverneux believes using robots will not only enhance patient outcomes and improve cosmetic appearance but also bring significant cost benefits to health systems.

As Professor of Orthopaedics & Hand Surgery in the Hand Surgery Department at Strasbourg University Hospitals, he outlines his vision for bringing robotics and microsurgery closer together at the Advances and Controversies in Reconstructive Microsurgery (ACRM) 2016 conference (5-6 May, Norwich, UK).

During his presentation 'New horizons in robotic nerve microsurgery,' he discusses how the future of peripheral nerve microsurgery should be robotic and bring additional benefits within minimally invasive surgery (MIS).

Speaking in our pre-conference interview Professor Liverneux said: 'The goal is for microsurgery to become endoscopic super-microsurgery; we want to highlight the attraction of robotics for microsurgery within the philosophy of MIS.'

He also points to RAMSES (Robotic Assisted Microsurgical & Endoscopic Society) – a group of plastic, hand and orthopaedic specialists - which advocates the future benefits of microsurgery being robotic.

A particular aspect of this is the work of plastic surgeon Jesse Selber, who directs clinical research and is an Associate Professor in the Department of Plastic Surgery at the University of Texas MD Anderson

Cancer Center in Houston, Texas. A pioneer of robotics use in harvesting flaps, primarily from the latissimus dorsi and the rectus abdominis, to provide substance to cover other injured body regions, at the conference he tackles the subject of simultaneous skull, scalp, kidney, pancreas transplants.

Professor Liverneux: 'Usually you have to make very large incisions to harvest these muscles but, with the robot, we can make small incisions. This is important from a cosmetic point of view and patients will be happy with a small incision. A second advantage with small incisions is that patients will have less complications and recover faster, which will be cost effective because they will stay fewer days in hospital.'

## A robot improves the surgeons' skill

As a hand micro-surgeon, Liverneux finds the advances of robotic control offer particular benefits when patients sustain deep nerve injuries, such as a tear of the brachial plexus nerve network from the neck and shoulder down the arm, or injuries sustained by babies during some difficult births.

He explains that the operation to restore movement by making a nerve graft in the brachial plexus traditionally requires a large incision often of 20-30cm. 'These incisions are very bad from a cosmetic point of view and for nerve recovery,' he said. 'The goal of robotic microsurgery in peripheral nerve surgery is



to avoid this large incision.'

While data comparing robotic surgery to conventional techniques remains limited, Liverneux says common sense suggests it's preferable to make smaller, rather than larger, incisions.

Another area in which robotic surgery has benefits is in the long thoracic nerve responsible for the motion of muscle that gives stability of the scapula.

'With the robot, incisions are small and precise, fractionally away from the nerve to ensure when we suture we don't affect the nerve,' he adds.

Micro-surgeons still often use large incisions to carry out the finely detailed surgery within the body but Liverneux suggests the robot can conduct this with small incisions and precise instruments within the body. With the robot, instruments can move in three dimensions and have 3-D vision within the body, offering excellent optical magnification – currently one-to-five but potentially one-to-100 in the future – underlining the importance of imaging in robotic microsurgery.

A critical advantage of a robot in microsurgery is the facility of



Professor Philippe Liverneux has been Professor of Orthopaedics & Hand Surgery in the Hand Surgery Department of Strasbourg University Hospitals since 2006. He is also General Secretary of the French Society for Surgery of the Hand, and Past President of the French Society for Microsurgery and the Robotic Assisted Microsurgery & Endoscopic Surgery Society. His research projects include minimally invasive surgery and nerve transfer and elbow flexion restoration, using robotic techniques.

motion scaling and tremor filtration. 'In microsurgery, because all the tissues that you are dealing with are so small, less than 1mm, if you can increase the scaling of our movement this will increase the surgeon's precision. Motion scaling is very important for micro-surgeon because it makes the operation easier,' Liverneux points out.

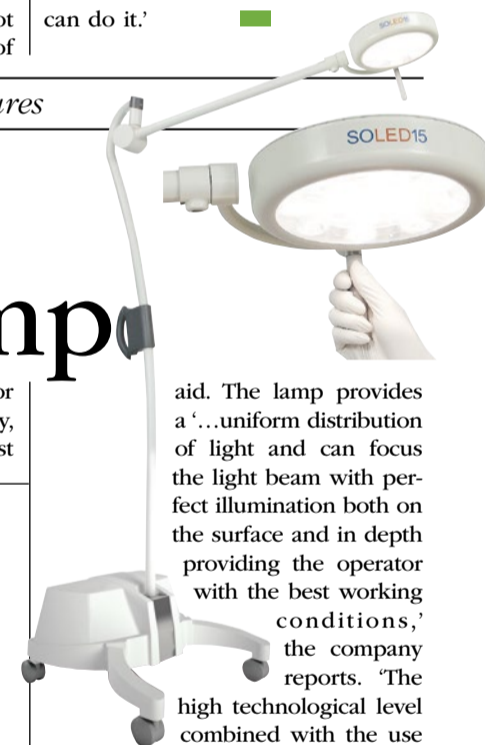
'Motion scaling and tremor filtration are two key features provided by robots compared to conventional human skills. The future of microsurgery is to make the technique easier and what else than a robot can do it.'

Lighting up medical procedures

## The smart Italian LED lamp

Soled15-F, which supplements the Starled range of lamps manufactured by ACEM Medical Company, is a

focusable LED examination light for diagnostics, minor precision surgery, intensive care, recovery room and first




aid. The lamp provides a '...uniform distribution of light and can focus the light beam with perfect illumination both on the surface and in depth providing the operator with the best working conditions,' the company reports. 'The high technological level combined with the use

of high-powered LEDs allow the lamp to have a very linear yield and a negligible performance decay for its entire life duration.' The light beam is IR-free.

Light intensity is 50,000 Lux (large spot light beam) increasable up to 77.000 lux (small spot light beam) and with low power consumption (24 W). Colour temperature (CCT) is 4.500°K. The colour-rendering index (CRI) is 95.

'The LEDs layout gives visual comfort and produces a uniform, homogeneous and shadow-less light,' ACEM reports, adding, 'The high technological level combined with the use of high-powered LEDs allow the lamp to have a very linear yield and a negligible performance decay for its entire life duration.'

The lamp's round shape also makes it handy and functional when in use and being moved, and so the structure fits well with work in diagnostics, test labs and dental surgery. With an iSense touch panel to control all functions, the lamp also has an easy-to-grip removable and sterilisable handle, making it suitable even for critical sanitary applications.



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