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New biospleen blood cleansing excites experts

Molecular diagnostics for infectious diseases takes a forward leap

A new extracorporeal nanotech device addresses the root cause of sepsis by removing pathogens and endotoxins simultaneously from blood even before their identification – this genetically engineered mannose-binding lectin protein can also latch on to the Ebola virus...

Report: Cynthia E Keen

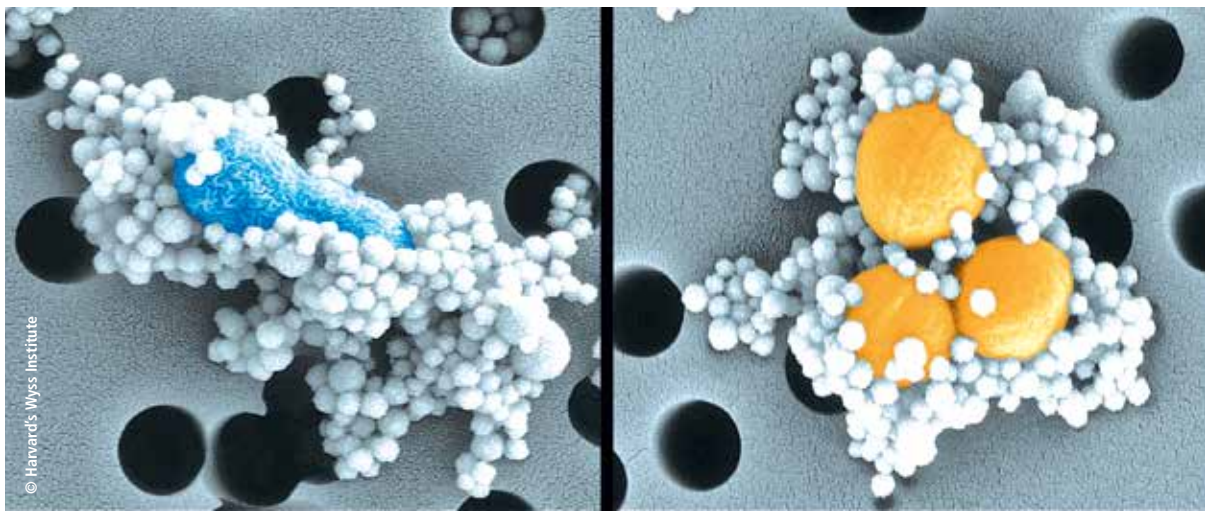

Image demonstrates the effectiveness of the genetically engineered protein-coated magnetic beads binding to pathogens. Here, the magnetic beads (128 nm) are bound to two pathogens (*E. coli* on the left and *S. aureus* on the right)

Sepsis is on the rise worldwide, in all likelihood exceeding the 2003-2013 estimates of 18 million cases. 30-50% of patients die, whether treated in a high-tech intensive care unit (ICU) or a resource-constrained hospital ward. In developing countries, sepsis causes 60-80% of all deaths (source: Global Sepsis Alliance). It also kills around six million infants and young children and 100,000 new mothers annually.

No specific anti-sepsis drugs are commercially available. Thus the presentation from Harvard University's Wyss Institute for Biologically Inspired Engineering in Boston of a dialysis-like blood cleansing biospleen device that can filter live and dead pathogens from human blood, generated tremendous excitement at the 6th Annual Molecular Diagnostics for Infectious Disease conference held in Washington, D.C. in late August*.

Inspired by the spleen, the extracorporeal blood-cleansing device is revolutionary in its ability to continuously remove pathogens and toxins from blood without first identifying the infectious agent. Time is vital – sepsis mortality rates increase as much as 9% for every hour before a correct antibiotic therapy is administered – the device offers the potential to rapidly treat systemic blood infections and prevent sepsis progression.

'The biospleen device addresses the root cause of sepsis by removing pathogens and endotoxins simultaneously,' principal investigator Michael Super PhD, Senior Staff Scientist, told *European Hospital*. 'Blood pathogen load is known to be a major contributor to both disease severity and mortality in patients with sepsis. Many patients respond to appropriately targeted antibiotic therapies that work exclusively by lowering the number of live pathogens, but antibiotic therapy does not treat endotoxins in a patient's blood. Therefore, we set out to develop an extracorporeal blood-cleansing therapy, similar to dialysis, that can rapidly remove microorganisms and endotoxins from the blood without the need to first identify the source of the infection and without altering blood contents – and it has exceeded our expectations, by being able to filter these out in a matter of hours.'

Magnetic micro-bead magic

The biospleen unit uses magnetic nanobeads coated with a genetically engineered human opsonin – mannose-binding lectin (MBL) that binds to a wide variety of pathogens. In its innate state, MBL has a branch-like 'head' and a stick-like 'tail'. In the body, the head binds to specific sugars on the surfaces of all types of bacteria, fungi, viruses, protozoa and toxins. The tail cues the immune system to destroy them. 'The protein is part of the innate immune system that has been binding sugars for 500 million years. It's a very robust pathogen capture mechanism,' he explained.

Because other immune system proteins can bind to the MBL tail and activate clotting and organ damage, Dr Super used genetic engineering tools to remove the tail and graft on a similar one from an antibody protein that does not cause these problems. This genetically engineered 'secret sauce' protein binds the pattern of sugar on the surface of the pathogens – more than 100 different species, but does not bind to mammalian host cells.

Dr Super described how the engineered MBL 'secret sauce' protein is attached to magnetic beads 128 nanometers in diameter. The beads are added to blood removed from the patient and bind to the pathogen. Magnets in the biospleen device pull the now pathogen-coated magnetic beads through the channels to cleanse the blood, which is then returned to the patient.

Dr Super and his colleagues tested the device on anaesthetised laboratory rats infected with bloodstream infections that human sepsis patients experience. Approximately 90% of live *S.aureus* and *E. coli pathogens* were removed within 60 minutes. Rats were challenged with lethal doses of endotoxin and 90% of the biospleen-treated rats survived, while only 14% of the control rats survived.

Tests of human blood *in vitro* removed more than ninety percent of key sepsis pathogens when the blood flowed through a single device at a rate of half to one litre per hour.

Dr Super advised that many devices could be linked together to obtain levels required for human

Continued on page 2

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Dressing up for Ebola's unlikely EU epidemic

Report: Lisa Chamoff

Unlike some news reports the Ebola virus is not as easily transmitted as influenza or other infections. Still, healthcare and laboratory workers must take precautions to quickly identify those infected and prevent an outbreak.

In an October webinar, hosted by the American Association for Clinical Chemistry, Dr Nancy Cornish, a medical officer at the Centers for Disease Control, emphasised that Ebola is transmitted by direct contact with blood and body fluids, and not spread by air or water. However, research laboratories making viral cultures so that pathogens achieve high concentrations, must increase safety precautions.

Anyone testing specimens from a possibly infected patient should wear gloves, water-resistant gowns, and full-face shields, or goggles and masks. Certified class II Biosafety cabinets or Plexiglass splashguards should be used to protect workers' skin and mucous membranes.

Anyway, medics should anyway ensure minimum infection prevention practices in patient care, including hand washing, using gloves, gowns and masks, safe injection practices and cough etiquette, Cornish said, also stressing that African facilities dealing with Ebola specimens have a different set of challenges, including no reliable running water and limited access to disinfectants.


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Dr Sheldon Campbell, Director of laboratories at VA Connecticut Healthcare and Professor of laboratory medicine at Yale School of Medicine, said facilities should come up with plans to include assessing the route and risk of transmission of certain organisms, and determine how common the pathogen is. When developing policies, Campbell said it's important to balance laboratory staff risk with the possibility of compromising care for 100 or more patients.

'When planning, plan for what's reasonable now, and that's really small numbers of at-risk patients to rule out for Ebola,' Campbell said. 'Don't try to plan yet for 100 patients with Ebola, or even for five. Plan for one and get that in place and watch what happens over the next few months. You might have to plan for more, but start with small numbers of cases and then reassess as time goes by.'

The CDC has also developed interim guidance for specimen collection, transport, testing, and submission for patients suspected of Ebola infection, which can be accessed at *www.cdc.gov/vhf/eb ola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html.*

Could the virus endanger Europe?

The welcome logic of a World Bank expert

Report: Michael Krassnitzer

'Ebola does not present a direct epidemiological danger for Europe,' according to Dr Armin Fidler, Lead Advisor on Policy and Strategy at the World Bank, but, he added, 'Inevitably some Europeans will become infected with Ebola, such as those in the healthcare professions or aid workers.'

Dr Fidler made that statement when interviewed by European Hospital during the European Health Forum Gastein, in very early October – well before the first known case of an Ebola infection in Spain emerged.

'Numerous current analyses and commentaries assume that Ebola could be quickly and effectively brought under control if the disease had not started in three West African states but for instance in a European country,' he explained. In countries with highly developed healthcare systems, people with suspected infections can be quickly and consistently isolated. Health service providers are adequately equipped to minimise the risk of contagion. Doctors and nurses can offer the best possible treatment, such as treatment for dehydration, impaired liver and kidney function, bleeding and impaired electrolyte metabolism.

'Contaminated materials can be appropriately disposed of and there is extensive information available to the public on the disease, its transmission and the correct behaviour during an Ebola epidemic.'

However, Ebola does indeed pose an indirect danger for Europe, as Fidler explained: The disease has a destabilising effect on those countries already known as *fragile states*: 'If these countries experience political unrest or waves of refugees this would obviously also have political or economic consequences for Europe.'

'The problem around Ebola is an indication of the fact that there has not been enough long-term and sustainable investment into the healthcare systems in these countries over the last few decades,' he stressed. 'The main investment has been into *quick wins*, i.e. areas where it's easy to quickly achieve positive results.'

Development aids in the healthcare sector, he said, are often earmarked for projects and measures that are comparatively easy to implement and effective in the short term, such as against HIV/AIDS. 'In vaccination programmes, for instance, results are easy to measure.

It's easy to estimate how many lives have been saved. These projects are important, but there is also a need for systematic, long-term and strategic investments into the healthcare system.'

Some damaging effects

'Many of these funds develop parallel structures, with doctors and nurses enticed away from the public sector because pay is better.' Long-term investment in healthcare systems is not as 'sexy' and harder to evaluate. In human resources investment, it takes a decade to train a doctor, which covers two legislative periods – 'so no politician would be interested,' he said.

Furthermore, health also depends on structures that appear to have nothing to do with a healthcare system. Fidler mentioned containers filled with medical supplies decaying in a harbour because the authorities are inefficient or corrupt: 'People in highly developed countries find it hard to perceive that investments into harbour and customs administration are also important their healthcare system.'

The agenda for Ebola is obvious to Fidler. There is an urgent need for additional healthcare providers who need to be adequately supported. The affected countries also need more mobile laboratories, hospitals and rapid tests, but also more communication about the disease, spread and treatment. 'Theoretically, it should not be difficult to stop the epidemic – if we succeed in isolating people with suspected infections or those who have been in contact with people who have had the disease diagnosed.'

However, the situation will become critical if the disease reaches the slums of a large African city with millions of inhabitants: 'The worst-case scenario assumes a potential 1.4 million cases by the end of the year. We all hope this will not happen.'


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Armin Fidler MD MPH MSc, who joined the World Bank in 1993, is Lead Adviser on its Health Policy and Strategy, based in Washington D.C. A medical graduate from Innsbruck University, he also holds Masters in Public Health (MPH) and Science (MSc) in Health Policy and Management, both from Harvard University's School of Public Health. Dr Fidler studied management at Harvard Business School and Public Finance and Welfare Economics at the London School of Economics and Political Science.

Biospleen blood cleansing excites experts

continued from page 1

blood cleansing at dialysis-like rates. Alternatively, a patient could undergo multiple rounds of the cleansing treatment.

The next step is to test the device on large laboratory animals, starting with pigs. He anticipates that initial human clinical trials would be carried out with patients in ICUs with severe sepsis. Patients with earlier-stage disease would likely require confirmation of septicaemia before starting the biospleen.

The device also might be able to reduce the spread of infectious agents to organs and additionally might lower levels of circulating endotoxin and inflammatory cytokines. It also may be the only option to fight sepsis caused by antibiotic-resistant bacteria.


© Harvard's Wyss Institute

Michael Super, PhD, Senior Staff Scientist at the renowned Wyss Institute for Biologically Inspired Engineering

'One of the huge advantages this device offers is that it is not necessary to perform a culture. Septic patients need treatment immediately. An accurate pathogen diagnosis takes one day to a week. Culture followed by antibiotic susceptibility testing (AST) takes two to seven days. Today, doctors are forced to make a decision on how to treat a patient without ever getting the lab data. We are working to change that paradigm,' Dr Super said.

Dr Super added: 'We see this technology being used as a 'front-end' technology for pathogen collection and concentration before doing molecular diagnostic tests such as Mass-Spectrometry, PCR and Next Generation Sequencing (NGS). The pathogen capture can be used to 'clean up' the sample, removing human proteins and DNA that interfere with molecular diagnostic tests. 'For example, when human DNA contaminates a bacterial DNA sample, a polymerase chain reaction (PCR) for bacterial DNA will not work reliably. We are focusing on how to clean up the sample so that we can do PCR.'

He anticipates that the biospleen device will be a platform technology with the ability to remove proteins like cytokines or autoantibodies as well as other types of cells, e.g. cancer cells from the whole blood volume of patients by coating the magnetic beads with appropriate cell- or protein-specific ligands.

Could such a device help curtail a future Ebola-like epidemic? The team confirms that the 'secret sauce' MBL protein does bind to Ebola. Dr Super did not know if a dialysis-like technology would work in view of the scale of the disease. 'But we could imagine having this technology available as a safety net for medical staff treating Ebola patients.

'What is so powerful about this technology is the ability to remove pathogens from a person's blood even before having the time to identify it.'

* See 14/9/2016 article in Nature Magazine online: (www.nature.com/nm/journal/vaop/ncurrent/full/nm.3640.htmlhttp:/www.nature.com/nm/journal/vaop/ncurrent/full/nm.3640.html

Dropping in from sea and sky

More than 750 British military personnel as well as RFA Argus – the country's medical ship – have arrived in Sierra Leone, for front line duties in the battle against Ebola

Report: Brenda Marsh

In a deep darkness before dawn uniformed medics, each bearing a red cross on one arm and some a beret embellished with the polished metal badge that includes the caduceus and crown of England, symbol of the Royal Army Medical Corps, gathered at RAF Brize Norton.

Awaiting their flight each already looked tired; but these people are the 'right stuff', a term coined to describe astronauts decades ago, but now certainly applicable to these highly trained, highly committed medics.

Sitting placidly in their bulky army uniforms, women had pulled back long hair to twist into a neat bun. Sleepy, they looked serious and quietly committed. These are full-time army personnel, doctors, nurses, consultants, who serve with the Catterick-based 35 Squadron, 5 Armoured Medical Regiment and Royal Army Medical Corps and they have already undergone extensive training ready for their vital roles in Sierra Leone. In Strensall Barracks, York, a hangar converted into a mock-up of a field hospital, they have worn full protective suits to treat simulated casualties.

Their purpose is to staff an Ebola Training Academy along with 90 personnel from 22 Field Hospital already in Sierra Leone.

The training academy is not the only establishment created there. A British-funded 92-bed treatment facility is also ready for use in Kerry Town, in the Western Area province.

Meanwhile, in Falmouth, Cornwall, the towering, grey, fully-equipped hospital ship, Royal Fleet Auxiliary (RFA) Argus, housing critical care and high-dependency units, had loaded up with vital supplies (aid, food, water, medical equipment and three Merlin helicopters).

Following the 10-day journey to the Ebola battle zone, no viral cases will be taken aboard, to ensure containment on land. What these highly trained people will do is provide transport and support to medical teams and aid workers.

As medics, marines, aircrew, engineers and sailors waved farewell from the decks of the Argus and slowly disappeared from the seascape, one couldn't help feeling a tug of pride as well as empathy for them for what they will experience in stricken Sierra Leone.

Medics from 22 Field Hospital take a key role in GRITROCK, the UK's military op. in Sierra Leone

France: Ready for Ebola

With strong links with the West Coast of Africa, France is among countries most likely to experience Ebola, with an estimated 20% chance of cases in the homeland before October ends - a few suspected cases have arisen.

On daily flights to France from Conakry, Guinea, questionnaires record passengers' destinations for later contact if necessary. Disembarked, they also undergo checks by Red Cross and Civil Protection Unit medics.

President François Hollande has announced that France would help the Guineans to build more anti-Ebola treatment centres (one is already constructed in Macenta), and French Civil Protection personnel will be deployed for training purposes.

The Bégin military hospital has 60 staff highly trained in infectious diseases and intensive care and has successfully used an experimental treatment for a Médecins Sans Frontières nurse who caught Ebola in Liberia.

Two other Paris hospitals and 12 French reference hospitals are also ready to handle cases.

In a patient's negative pressure room, all initial laboratory tests are performed at the bedside in a specialised mini-laboratory. Results from samples sent to Lyon for analysis at the central high security reference laboratory, come within six hours

Plasma treatment allows up to 80% of pressure ulcers to be healed within two weeks

Dr. Gustav Lohse, Ludwigshafen · Germany

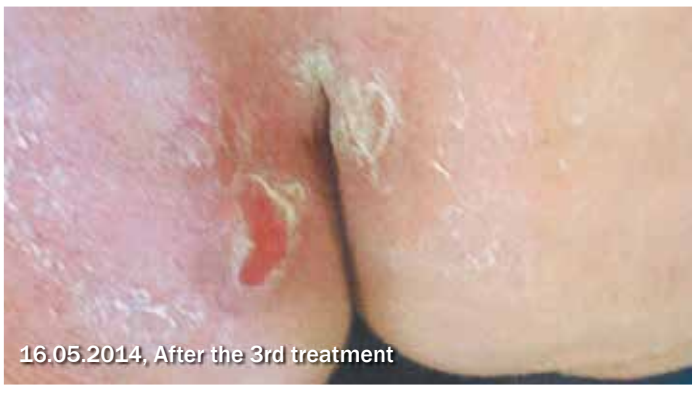
After just four rounds of treatment on a pressure sure (pressure ulcer) in a patient's coccyx area using cold plasma, improvement of up to 80% was achieved within two weeks.

Pressure ulcers are sometimes due to immobility and may even be lifethreatening in certain forms. In the general report of the UlcPrävent collaborative research project, which was supervised by the Institute of Textile Technology and Process Engineering Denkendorf (ITV), part of the German Institute for Textile and Fibre Research Denkendorf (DIFT), information was published in 2012 showing an estimated 800,000 or so new cases of pressure ulcers in Germany, of whom around 10,000 people die due to decubitus ulcers each year.

At the dermatological practice in Ludwigshafen, a patient treated by Dr. Lohse had suffered for several months from a pressure ulcer in the coccyx area. Despite months of applying ointments and cushioning, no improvement was seen in the pressure sore. Accordingly, the patient was prescribed *plasma ONE* as treatment by the dermatologist.

As early as the first treatment with cold plasma, the treating dermatologists noted a documented improvement in the pressure ulcer, while the patient also experienced relief from pain. From the second treatment, the patient was fully free of pain.


9.05.2014, Starting point and 1st Plasma treatment


16.05.2014, After the 3rd treatment

After three rounds of follow-up treatment within two weeks with *plasma ONE*, the pressure ulcers showed continual improvement.

This example from dermatological practice shows that treating with plasma can be an effective and successful approach to healing pressure ulcers within a much shorter period than if using ointments and cushioning treatments alone.

Structural and interdisciplinary improvement

Invigorating Medica's Education Conference

Collaboration with Europe's largest specialist medical society brings rewards

Interview: Brigitte Dinkloh

With around 140,000 visitors annually, Medica is doubtless *the* showcase for medical manufacturers. However, although the world's largest medical fair, the venue is not yet very well known for continuing medical education. This is set to change. With the re-orientation of the Medica Education Conference (MEC) during a collaboration with the German Society for Internal Medicine (DGIM), the organisers hope for a bigger response and an increased number of visitors. We asked Congress President Professor Hendrik Lehnert MD, Director of Medical Clinic One, at the University Hospital Schleswig-Holstein, Campus Lübeck, about his expectations and the education programme design.

Explaining how the collaboration with Medica evolved and the importance of the congress for the DGIM, Professor Lehnert said that Messe Düsseldorf sought a new partner for the Medica Education Conference and the DGIM submitted its tender. 'It must have impressed the organisers because we were selected,' he explained. 'We are very pleased to be organising this conference because it gives us an opportunity to prove that we can organise another, large congress with a different aspiration and bigger target audience, alongside our own annual Internal Medicine Congress in Wiesbaden.

'This is a very exciting opportunity and challenge to go beyond the bounds of internal medicine, to work in an even more interdisciplinary manner than before and to design a programme encompassing many neighbouring disciplines, from surgery to radiology and pathology.'

Asked about the interest shown to date and the potential number of participants, the professor explained that the application procedure is continuing, so there is no popularity indication as yet. 'We are hoping for more than 2,000 participants – a good start for us and significantly more participants than in previous years. In the long run we are aiming for between 8,000 and 10,000 participants,' he added.

How can that ambitious target be achieved? Prof. Lehnert pointed out that the high quality conference programme is structured in a completely new way and the organisers have gathered outstanding national and international speakers. It is also backed by advertisements in the specialist press and in daily newspapers.

'Overall, the conference is definitely set to become more international. As yet the English language part of the programme is only about 10% of the total; however, in the future, the plan is to develop a successive transition from German to English as the congress language.

'To date, education has tended to be side-lined by the large fair; with 140,000 visitors the smaller training and education part has definitely been dwarfed by the exhibition.' He expects change and that the MEC will become very successful.

'There are four superordinate key topics, which have been laid out as broad and transdisciplinary as possible,' Prof. Lehnert pointed out. For 2014 these are infection and inflammation, telemedicine and robotics, gastrointestinal oncology and interventional medicine, involving representatives from many other disciplines, such as surgeons and radiologists.

'We have a very diverse programme committee who will also cover areas beyond the expertise of internal medicine. Gastrointestinal oncology is obviously a classic topic within internal medicine, but it is also complemented by surgery and radiology. The key topic interventional medicine strongly involves gynaecology as well as urology. We have obviously ensured that the expertise of the programme committee members is taken into consideration. A clearly structured daily timeline with standardised parallel events provides all participants with a diversified, all-day scientific education in combination with a visit to the exhibition. In the first instance the programme is naturally aimed at doctors and interested company representatives, but there are also some programme points that will interest other medical professions.'

10-15% of the programme will be practical seminars and hands-on courses to include, for example, ultrasound seminars, nutrition, endoscopy and diabetes. Although an hour a day has been set aside for industry symposia, so far there has not been much participation. 'However, this is not decisive for the success of the congress,' the professor noted, adding that there will be industry symposia on laboratory medicine. 'Many are probably waiting to see what the first MEC under our management will be like and then decide to participate next year.

Our annual congress includes around forty industry symposia and I am 'sure this kind of participation will develop for the Medica Ediucation Programm as well.

Swedish-born **Hendrik Lehnert**, an internal medicine specialist with a focus on endocrinology, has directed Medical Clinic I at Campus Lübeck, Schleswig-Holstein University Hospital since 2007. After gaining psychology and medicine degrees, Lehnert worked at the Laboratory of Neuro-endocrine Regulation at the Massachusetts Institute of Technology and the Cardiovascular Laboratory at the Harvard School of Public Health in Boston. Before his Lübeck role he had been a Medical Director in Magdeburg and Chair of Medicine at Warwick University Medical School, Coventry University Hospital, United Kingdom. This year he became President of Lübeck University – and he will head Medica Education until 2016.

Healthcare stands to gain the most from RFID

Identifying the best hospital safety technology

On the occasion of the upcoming Euro ID and ID World International Congress 2014 in November in Frankfurt am Main, Germany, Cornelia Wels-Maug asked about the role of Radio Frequency Identification (RFID) in healthcare, during her interview with H Sprague Ackley, Technical Fellow at Honeywell Scanning & Mobility, and a member of the ID World International Congress Committee

Euro ID 2014, the only global conference covering all the technologies of automatic identification (AIDC), will provide an overview of technologies used for identification purposes across a diverse set of industries, H Sprague Ackley explained, qualifying these as 'technologies like barcodes, biometrics – such as iris and facial recognition, RFID, RFID in connection with voice, smart cards, magnetic stripes, Optical Character Recognition (OCR) and voice recognition will be on show.'

Are certain ID technologies better than others for healthcare?

'Today, basically all common AIDC technologies are used in healthcare. The technologies work together. For identity purposes in a hospital, you can, for example, use a wristband with either a barcode or an RFID chip integrated. The decision as to which technology to employ is typically not taken out of a technological rationale, but on business considerations. A cost-benefit calculation determines which technology to use; in most cases the answer is barcode. That's why the healthcare world is full with barcodes. However, there is a trade-off between price and level of security. Although barcodes work well, especially for tracking specimens, they do not offer authenticity benefits and can be easily copied.'

What role does RFID play in healthcare?

From the time a patient is on the way to hospital, through the admission process, on to diagnosis and treatment, and all the way to final discharge, everything about his or her health and needs must be ensured – particularly in terms of personal identification, medications, nursing care and much more. Safety is a vital part of successful care

'RFID is used in various applications, from patient, document and file tracking, medication authentication, management of facilities, assets, inventory, laundry and access control – and not all uses have been invented yet.

'An RFID system is based on the usage of radio waves, RFID tags and RFID readers. The tag, which has a unique identification number and an antenna to send and receive radio waves, can be attached to

Facing a commercialised healthcare system

Generation Y in hospitals today

Will today's junior doctors ultimately change tomorrow's structures?

Could the widely predicted shortage of qualified staff in German hospitals soon lead to tough competition for members of Generation Y, ultimately resulting in a change in hospital structures and a revolution in the country's total healthcare system? Perhaps. EH correspondent *Bettina Döbereiner* spoke with Professor Christian Schmidt – among the first to scientifically examine the needs and desires expressed by today's German medical graduates to future employers – and also with consultant surgeon Professor Henne-Bruns, who has lengthy experience of cooperation between different generations of co-workers.

'In the future the hospital market will be strongly affected by competition for qualified staff,' predicts Dr Christian Schmidt, referring to Germany's demographic change, which he believes will soon lead to a massive shortage of qualified staff. This belief – and his personal experiences of dealing with the young doctors of generation Y (born after 1981) prompted Dr Schmidt and colleagues to scientifically examine what they have noticed about that generation. 'We wanted to obtain, as much as possible, empirically sound evidence about this new generation of doctors, so that we can gear our management culture and Personnel Development Programmes specifically towards this generation.'

Work commenced in 2011 (Der Anaesthetist, 60:517-524) by way of a comprehensive literature research on the internet. The bottom line of the evaluation: Members of Gen Y 'live while they work' – unlike the post-war generation (baby boomers), for instance, who 'live to work', but also unlike the members of Gen X, who 'work to live'.

According to this meta-evaluation, members of Gen Y place much importance on sticking to agreed working hours (ideally nine to five), refuse to work unpaid overtime and would consider working part-time for certain periods to achieve a better balance between job and family life. This could obviously lead to potential conflict for work in the hospital, a place where unpaid overtime is not a rarity and long shifts of work are the order of the day. Apart from their literature research and evaluation, Dr Schmidt and colleagues also conducted numerous surveys of their own. The largest and most important to date was published in the specialist magazine HNO (HNO 2012, 60:993-1002). Asked about their choice of future employer, young medical students said that a good working atmosphere was the most important aspect for them. In second and third place came a good training structure and breadth of training and in fourth place was a family-friendly employment policy.

Looking at these results, Dr Schmidt said, 'Attracting members of Generation Y to our hospital means creating lifestyle-adapted career paths for them.' He has very recently – having only been in Rostock for the last six months – helped to introduce a target agreement for consultants, which, among other points, calls for feedback and development dialogue with employees. When it comes to being family friendly, Schmidt pointed out, Rostock University Hospital is already set up very well. 'Ultimately,' he added, 'I'd like to strategically embed a management style that fits in with the new generation in our organisational culture – but this will take time.' Unlike Schmidt, Dr Doris Henne-Bruns, at Ulm University Hospital, believes the issue of the generation gap to be irrelevant in her daily clinical routine. She also queries the classification of certain birth years into generations and the common up or devaluation of the different generations against one another. 'This whole evaluation stating that the "economic miracle" generation worked hard and enjoyed it, and that Generation Y, although committed, only want to work for eight hours a day and otherwise prefer to focus on leisure and pleasure – there is a message here saying that the older generation did things correctly and the young ones are a little lazy,' she criticised, encouraging us also to ask what the older generation may actually have done wrongly and what the new generation is doing well.

Furthermore, in more than ten years of management experience she has not experienced any generation-based conflicts in her hospital: 'We employ some very young assistants and I can see that they want to work just as hard and although they may have an eye on the clock, just like everyone else, they are fully committed and immediately prepared to step in when there are staff shortages.'

The only generation gap issue the professor has observed is that parental leave is more to be expected nowadays among males. 'That's very positive; I've always supported it,' she confirms.

Unlike the generation issue, Dr Henne-Bruns believes that there is greater relevance in the commercialisation of medicine resulting not only in problems for daily routine but most significantly a change in values. Among excesses are liberal diagnoses and over-diagnosing due to financial pressure on hospitals, and also millions of euros drained from the healthcare system through indirect payments to shareholders via medical insurance premiums by yield-driven private hospital operators.

In this, Dr Henne-Bruns holds high hopes for the younger generation: 'I hope that future generations will no longer be prepared to tolerate this system in its commercialised shape and that they will drive a shift in thinking.'

Christian Schmidt, Medical Director and Head of the Board at Rostock University Hospital since 2014, belongs to 'Generation X' (those born between mid 1960s and '70s). He studied medicine at the universities of Muenster, Germany, and Durban, South Africa, and specialised as a surgeon at Kiel University Hospital. He also studied Public Health with a focus on Healthcare Management in Bielefeld, Germany and Boston, USA. Working in hospital management since 2005, before his Rostock role he was Managing Director of the City of Cologne Municipal Hospital Group. With colleagues, Schmidt is currently writing a comprehensive practice handbook on Generation Y, with publication planned for late 2015.

Consultant, visceral and thoracic surgeon **Doris Henne-Bruns** is part of the German 'economic miracle' generation (i.e. born just after WWII war (1945-'55). Having studied medicine at the University of Hamburg she trained as a surgeon at Reinbek Hospital and Hamburg University Hospital, where she was awarded her professorship in 1988, writing her habilitation on Auxiliary Liver Cell Transplantation. Following her Hamburg professorship, in 1992 she moved to Kiel University Hospital where she became professor for oncology and transplantation at the General Surgery and Thoracic Surgery Clinic. From October 2001, Prof. Henne-Bruns has been Medical Director of the general, visceral and transplant surgery clinic at Ulm University Hospital. Her specialty: cancer surgery.

Courtesy of Honeywell Scanning and Mobility

H Sprague Ackley, Technical Fellow at Honeywell Scanning & Mobility, and a member of the ID World International Congress Committee

Courtesy of Honeywell Scanning and Mobility

CN70 RFID

an object; this allows the object to be tracked. In many supply chain applications a single tag can be used over and over again but for authenticity applications, once a tag has been used, it must be destroyed. RFID operates in an unlicensed spectrum space and the specific frequencies used in a country depend on national regulation.

'Although RFID is more secure, it is more expensive than barcodes and therefore is an uphill sell to push RFID in apps that have, so far, worked well with barcodes. Nonetheless, RFID can also do more than barcodes. Take the example of a medication that needs to be kept at a certain temperature – a barcode cannot keep track of environmental data. However, by attaching sensors to the packaging of the medication, an RFID tag can log information about the medication's environment at certain intervals and it is possible to obtain this data at any time simply by reading the tag.

'In the above example, a thermal sensor would be required, but there are other sensors to determine whether a specific object was dropped, exposed to light, or where it is actually kept. RFID offers a cost effective way of monitoring medication freshness and authenticity – but will RFID ever replace barcode? I think this is unlikely because barcode symbols are much less expensive than RFID tags and barcode scanners are competitively priced.

'However, there is also a case for using barcode and RFID in tandem, as an additional layer of security, for example in tracking patients, because barcodes can be damaged and RFID readings can be jeopardised. The latter can occur if there are multiple RFID tags in close proximity to each other. In this incident, an RFID reader might be scanning more tags than intended or not reading the right one. To remedy this, a supplementary barcode can be used to ensure the correct readings are taken.'

Where and why is RFID particularly useful in healthcare?

'RFID really excels when stakes are high, for instance when patient identities are confounded, or something valuable goes to waste because it's handled incorrectly. This is particularly true for medications. Patients die due to the administration of wrong drugs, so medication authorisation screams for RFID because its usage for this purpose is still miniscule.

'The second high profile use for RFID is in to ensure the freshness of an item, to demonstrate that the supply chain has not been breached; for example, has the medication or sample been kept at the stipulated temperature? 'In my view, these two are big and exciting opportunities for RFID. 'Healthcare, of all industries, stands to gain the most from RFID, ultimately because lives are at stake.'

Gastrointestinal medicine and surgery

A genuine interdisciplinary way for specialists to work

At the close of the Gastrointestinal Medicine and Surgery meeting in Leipzig, Professor Peter R Galle, Congress President of the German Society for Gastroenterology, Digestive and Metabolic Diseases, spoke with of European Hospital about today's emphasis on interdisciplinary exchange and the need to augment cooperation even further

'Gastrointestinal medicine and surgery without interdisciplinary working would be inconceivable,' Prof. Galle emphasised. 'We specialists in internal medicine are closely networked with surgeons and other specialists. In the case of stomach cancer, for example, if a patient is diagnosed via endoscopy the endoscopist carries out the biopsy, the pathologist makes the histological diagnosis, the surgeon operates on the patient and, before this, the radiologist would have been consulted to assess the potential extent of the disease in any other areas away from the stomach. Gastrointestinal medicine and surgery are prime examples for a real interdisciplinary way of working – in daily clinical practice.'

Surgeons, he pointed out, expect real-time, good quality imaging to help procedures. 'We also expect high quality support from pathologists. They have to make frozen sections during surgical procedures, have to attend clinical-pathological meetings and also need to provide information regarding the aggressiveness of tumours.'

Personalised medicine

'The development of personalised, molecular-genetically based diagnosis will lead to treatment in the next step. In this context, RAS oncological diagnosis for colorectal cancer plays the most important part. If a mutation in the RAS gene is present, the use of biologically active substances, so-called antibody therapies, will be different to cases where the mutation is not present.

Furthermore, we can learn from other diseases, in haematology for instance. With liquid tumours there is no limit to the availability of sample material. In gastrointestinal medicine this is much more difficult – sometimes we have no tissue available at all.

Therefore we work in all possible manners and, in the case of liver cancer for instance, utilise personalised diagnosis and treatment.'

Health insurers' negativity

'During the initial phase it is an additional service provided that is not billed separately.

'The flat rates per case system works with full settlements, meaning that when a new method of treatment becomes available there will initially be no allowance for it in the reimbursement system.

'We do indeed have initial problems with most of the new or experimental procedures.'

Quality assurance – compliance entails lots of work

'Initially, more quality also means more work. However, quality also can help to relieve strain. A quality-based approach can, for instance, ensure that junior doctors work in the safest possible way.

'Quality assurance is basically an investment. We have to improve our documentation and develop more standard operating procedures (SOPs). These provide guidelines and are therefore indispensable.

'Personally, I would even say there are only two things that should be important in medicine regarding billing: Indication and quality. The first question is whether a treatment is necessary and whether it can be specifically developed – and, if so, whether it is of good quality. Once these two simple questions have been answered, everything else is of lesser importance.

This is why we included quality assurance measures in the whole series of events at our congresses, ranging from topics such as gall stones to stomach cancer, to do this subject justice.'

Guidelines and recommendations

'The aims of guidelines developed through the DGVS (German Society of Gastrointestinal Diseases and Nutrition) and (American Board of Medical Specialties) are to achieve consistent diagnosis and treatment strategies for certain diseases. Guidelines provide a helpful framework for orientation – the reason why the DGVS has been developing guidelines for many years on topics such as stomach cancer, hepatitis B, pancreatitis, obstipation, diverticula etcetera.

'On the DGVS board, our colleague's responsibility is to ensure that certain guidelines are followed and updated. In some areas this is particularly difficult because things are very fast-moving. Hepatitis C, for instance, is characterised by incredible dynamics. Every few months we have to deal with new substances, and regular guidelines would not keep up with things here. In these situations we try to give updated recommendations several times a year, which are published in the Journal of Gastroenterology.

'Medicine is characterised by fast progress and large amounts of new information that affect diagnosis and treatment. This means we also generate high costs. There will never be guidelines for all diseases, especially not current ones.

'Currently this can be seen in the case of Ebola. There are experimental drugs that have not been licensed yet and therefore they should not really be used.

'Ultimately, this is about an ethical consensus rather than a scientific issue. According to the WHO, the current, threatening constellation justifies over-riding the established, normally required multi-stage testing procedure. This is understandable. If the need is this extensive, we should be able to compromise. We medics are well aware of this – take the example of the classic triage, which is the answer to ethical conflicts of this kind.'

A specialist in Internal Medicine and Gastroenterology, **Professor Peter R Galle** has directed the Medical Clinic and Polyclinic at the Johannes Gutenberg University of Mainz since 1998. He has also served on the supervisory board and board of directors at the same University Hospital.
A graduate from Marburg University and the Free University of Berlin, he wrote his doctorate in 1985, followed by his habilitation on the 'Replication of Hepatitis B viruses in vitro' in 1993.

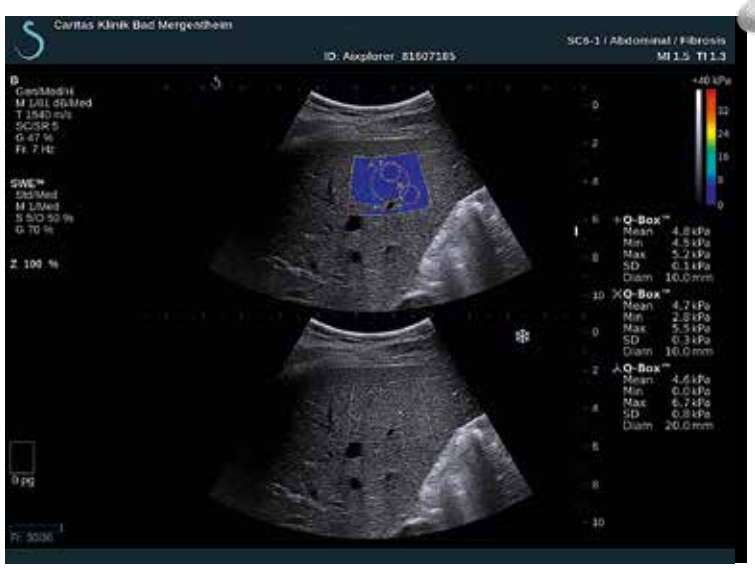
Shear wave elastography detects more than liver disease

A little revolution in sonography

Results are potentially better in 2-D and 3-D ultrasound

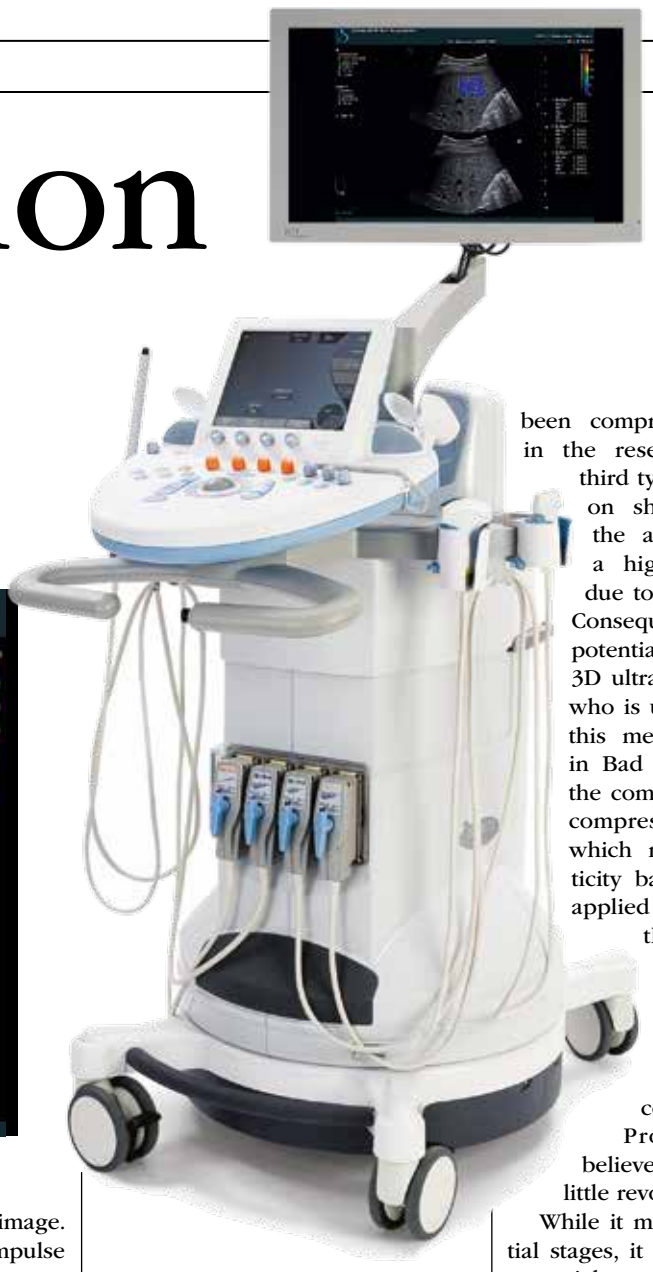
Until recently liver biopsies were performed to stage hepatic fibrosis in order to identify the suitable therapy. 'Since any intervention in the human body is associated with risks – haemorrhage and infection for example – we have long been looking for an alternative method to determine liver tissue elasticity. Today shear wave elastography is exactly such a method,' says Professor Christoph F Dietrich MD, Medical Director of Clinic II at Caritas Hospital in Bad Mergentheim, Germany.

Shear wave technology uses not only the b-mode image, which is based on information provided by the longitudinal ultrasound waves as they travel through the tissue with a speed of around 1.560 metres per second, but also at the transverse shear waves. The propagation of the shear waves in the tissue correlates to tissue elasticity: wave velocity is proportional to tissue elasticity. Consequently, the propagation velocity in fibrotic tissue is higher than in healthy liver parenchyma. Currently, there are four different elastography procedures.



Normal liver parenchyma in shear wave ultrasound (Aixplorer/SuperSonic)

Fibroscan, also called elastometry, is the most widely used procedure, although it does not generate a typical ultrasound image. Acoustic Radiation Force Impulse Imaging (ARFI) provides a conventional ultrasound image. Shear wave elastography, introduced in 2009 by SuperSonic's Aixplorer system, is the most recent and most innovative type of elastography.



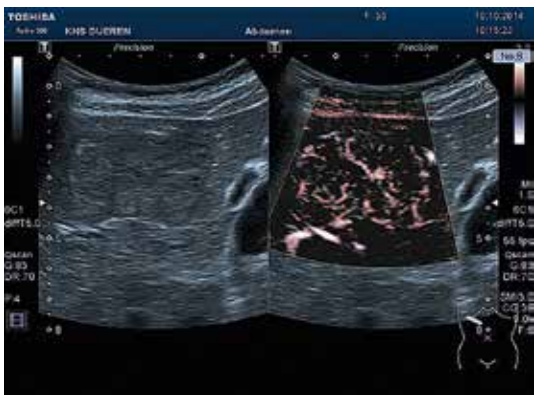
'The first two procedures have been comprehensively evaluated in the research literature. The third type, however, is based on shear waves and has the advantage of offering a high processing speed due to superfast processors. Consequently, the results are potentially better in 2D and 3D ultrasound,' says Dietrich, who is using and researching this method in his hospital in Bad Mergentheim. 'Unlike the competing procedure, the compressional elastography, which measures tissue elasticity based on the pressure applied via the transducer, the results generated by the Aixplorer show a comparability of about 90 percent as soon as identical parameters are being compared,' he adds.

Professor Dietrich believes the Aixplorer is a little revolution in sonography. While it might still be in its initial stages, it does show enormous potential as a non-invasive imaging method that can provide information on several other tissue characteristics. Moreover initial results

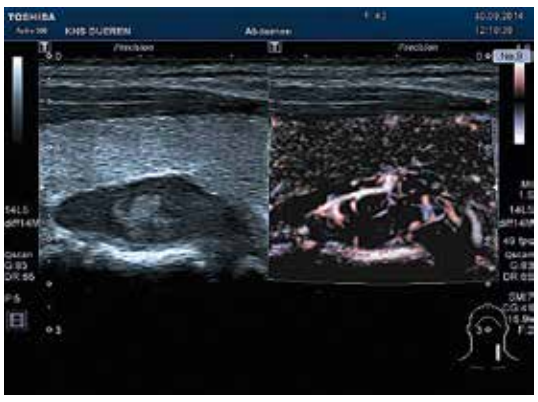
Continuity, consistency and clinical benefits

Refinements and advancements galore

In essence an upgraded flagship ultrasound scanner is a new system



Microcirculation in a parathyroid adenoma with monochrome SMI (mSMI)



Vascular architecture in a focal, nodular hyperplasia with mSMI

Terminal ileitis in Crohn's Disease with mSMI

The Aplio, Toshiba's flagship ultrasound scanner, has been extensively advanced and essentially turned into a new system. The highly innovative Japanese company in imaging diagnostics has refined the successful Aplio series of scanners and introduced it internally in Frankfurt at the beginning of October. International clinicians who were given the opportunity to test the equipment before the launch were enthusiastic about the precise imaging, compact and smart design and the traditionally high processing quality. Gastroenterologist and liver specialist Dr Horst Kinkel, Assistant Director of the Medical Clinic II at Düren Hospital, confirmed: 'Compared to the previous version of the Aplio, the technology has become more sophisticated and powerful.'

With its innovative technologies, unique applications and a newly developed hardware and software architecture, Aplio raises the bar in ultrasound diagnostics. Precision imaging, differential imaging and other technologies based on high-density beamforming have advanced ultrasound imaging. The intuitive and flexible operational concept iStyle simplifies complex examination processes.

QuickScan facilitates fast patient-specific optimisation in the B-image and Doppler.

The 3-D FlyThru Tool has been further perfected and is now probably a competitor for hysteroscopy in gynaecological examinations.

The real-time fusion of CT and MRI images with ultrasound scans has become faster and easier.

The new advanced real-time applications in turn expand the diagnostic spectrum and provide additional information to the user through parametric visualisation of tissue changes. The new shear-wave elastography function supports the localisation and assessment of stiffness of tissue inside the body with high precision, sensitivity and reproducibility. The different grades of elasticity can be visualised with colour coding in parametric images and, importantly, can also be quantified – an exciting technology to assess liver diseases such as fibrosis.

SMI with and without contrast media

With the help of special new algorithms the platinum version of the Aplio can show even the smallest amounts of contrast media selectively in the contrast-imaging mode, making it possible to visualise the finest vascular structures and subtle blood perfusion in lesions and organs. The new Superb Micro Vascular Imaging (SMI) on the other hand shows the blood flow in the vessels right down to sub-millimetre levels – without the addition of contrast media. With the addition of contrast media even in the smallest dose the resolution and sensitivity for blood flow is increased to levels previously unattainable. This facilitates new opportunities for diagnosis in different clinical applications.

SMI visualises organ perfusion right down to the surface layers or the complete vascular architecture in lymph nodes and indeterminate space-occupying lesions. 'This means that, in the future, it will probably be possible to use contrast media more efficiently,' Kinkel hopes. This obviously has financial but above all timesaving advantages: 'All I have to do to utilise SMI is press a button. However, the administration of contrast media, necessitates the availability of syringes and emergency equipment.' he adds. 'The scanner shows me at the touch of a button whether there is something there or not – this is a big advantage in this technology. Therefore I rate this innovation so highly – it makes my daily clinical routine easier.'

Detail resolution provides diagnostic safety

'SMI is a new Doppler-technology with the advantage that tissue artefacts, which normally interfere with the colour Doppler image and make it unusable, can be extremely efficiently suppressed,' he explains.

'SMI facilitates high detail resolution and a high frame rate. This provides the doctor with improved morphological understanding and therefore more assurance and safety in making a diagnosis.

'The complex SMI algorithms make it possible to analyse echo signals and to achieve a distinct differentiation between blood flow and tissue artefact.

'At the same time they make it possible to recognise the correlations of tissue structures more clearly, which helps, for example, in the diagnosis of patients with abscesses resulting from inflammatory bowel diseases, for example diverticulitis.

'Now I can determine far more precisely whether there is oedematous tissue, or still healthy, perisigmoid tissue without the presence of abscesses; or I can recognise tissue that's only of low echogenicity in the normal image despite being well perfused. This,' Kinkel concludes, has a large impact on my treatment of patients.'

After gaining his medical degree and doctorate at the University of Cologne in 1994, **Horst Kinkel** began his career at Düren Hospital. He qualified as a specialist for internal medicine in 2001 and was awarded the Instructor Level II of the German Society of Ultrasound in Medicine in 2004. At the end of 2008 he became Assistant Director of Medical Clinic II at Düren Hospital, where his focus is on contrast ultrasound, interventional ultrasound, haepatology and chronic inflammatory bowel disease. Dr Kinkel is a member of numerous scientific societies, co-author of textbooks and of an interactive instructional CD for ultrasound.

A senior consultant at Caritas Hospital in Bad Mergentheim, Germany, since 2002, **Christoph Frank Dietrich** is also the current President of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB). With a scholarship from the German National Academic Foundation, he studied at the Medical University Hannover and, in 1988, passed the US-American FMGEMS exam. A specialist physician for internal medicine since 1997, he received his habilitation in 1999. Professor Dietrich is also a certified specialist in several other disciplines such as gastroenterology and haematology/oncology.

on shear wave elastography exams of kidney, spleen and pancreas are promising, albeit requiring further research. Professor Dietrich: 'With regard to the pancreas, real-time elastography has up to now a higher value, since we only have to find out whether a certain tissue region is harder or softer compared to surrounding tissue to be able to tell whether a tumour is present or not. Thus colour coding with blue indicating hard tissue and red indicating soft tissue is sufficient.'

Anaesthetist guides flight docs on the routine use of portable machines

POC ultrasound takes to the skies

Given their quality, small size, portability and robustness, SonoSite point-of-care ultrasound systems play vital roles in hectic A&E and surgical departments, and also in monitoring patients in transit. Working in Berufsgenossenschaftliche Unfallklinik (BGU), Tübingen, anaesthetist Dr Rüdiger Eichholz believes in the importance of POC ultrasound and has set up a training programme for clinicians who accompany patients with International SOS.

Europe has many air ambulances and commercial aircraft available for patient transfers, but facilities in some geographical regions are more basic and unpredictable. Thus the Middle East Asia branch of International SOS, in Dubai, keeps its own Lear jet ambulances around the region, fully staffed and equipped as intensive care units.

Point-of-care (POC) testing aims to gain faster diagnostic results and treatment by assessing a patient at the bedside or during transit. Surgeons, emergency doctors, and sometimes paramedics use Focused Assessment Sonography for Trauma (FAST) to screen for pericardial effusion or fluid around the abdominal organs following trauma.

For years, Dr Rüdiger Eichholz has found point-of-care (POC) ultrasound invaluable in anaesthesia, ICU and trauma medicine for FAST scanning (Focused Assessment Sonography for Trauma), ultrasound-guided nerve blocks and vascular access, plus general cardiac, chest and abdominal scanning.

At BGU, a trauma, orthopaedic, plastic and craniofacial surgery centre, a large part of his work involves performing regional anaesthesia under ultrasound guidance. As a certified DEGUM trainer, he also spends considerable time travelling, demonstrating ultrasound's advantages and encouraging and training clinicians to routinely use the technique.

As a co-ordinating doctor for the German branch of International SOS, Dr Eichholz talked to patients, assessed their needs and helped to solve all kinds of medical problems. This included undertaking face-to-face consultations and often evacuations or repatriations. Although termed 'emergencies', the SOS flights do not go directly to or from an accident or major incident, but focus on patient transfers. All journeys are elective, with some degree of planning and preparation involved, consent from the patient or relatives, payment and insurance details, and agreement and discussion with the releasing and accepting hospitals. While some patients are quite ill, others are not; sometimes the team moves a fairly healthy patient. Some repatriations are simply about transferring a patient to a more sophisticated medical centre to ensure nothing serious is overlooked, especially if surgery is needed.

When Dr Eichholz was approached to join the International SOS Abu Dhabi team as a flight physician he found the aircraft was equipped with a new NanoMaxx system, which proved invaluable during patient transfers. 'While I'm very familiar with using POC ultrasound in this setting, I discovered that many of the team only occasionally used ultrasound and were not entirely at ease with the technique, or aware of its full potential in performing diagnostic procedures and needle guidance,' he said. 'So, we established a training programme at International SOS, using my knowledge and teaching experience to explain the advantages of POC ultrasound to help flight doctors to make the most of its diagnostic capabilities.'

Based on the AEN (Armbruster Eichholz Notheisen) training concept developed by Dr Eichholz and fellow anaesthetists Dr Wolf Armbruster (Evangelisches Krankenhaus Unna) and Dr Thomas Notheisen (BGU), the teaching programme (English language) is adapted to aero-medical issues; it uses similar methods, 3D imaging and hands-on sessions with small classes.

The M-Turbo and the NanoMaxx are ideal devices, both for the application and for teaching, as Dr Eichholz pointed out. 'The system's robustness, portability and quick boot-up time are all very important on air ambulances and, although we have power packs on board, it's also very convenient to have a good battery life.'

Dr Rüdiger Eichholz, anaestetist, Berufsgenossenschaftliche Unfallklinik (BGU)

'For training purposes, it's important to have a system that's small, simple to operate and easy to understand from the technical perspective, and both these systems, especially the NanoMaxx, fit this profile perfectly. The ease of use has been especially important in establishing the programme because, while most of the doctors could see a role for POC ultrasound, many were cautious and not happy with their knowledge and skill levels.'

To help build confidence, the team introduced pre-flight scans for even healthy, walking, talking patients. 'In this way, flight doctors practise their ultrasound skills, develop a routine pattern of examination, learn to differentiate between normal and abnormal images, and ultimately gain confidence in their scanning abilities. The pre-flight scans also give a comprehensive baseline picture of each patient before a flight, and are entered into that individual's electronic file for future reference.'

Several training courses have taken place and a systematic in-flight manual has been prepared, with a checklist and 'how to' guidance on the device, plus specific example guides for the most frequently used techniques, e.g. how to examine the chest, heart or vessels before vascular access. 'My main aim has been to continue to pass on my enthusiasm for using ultrasound – and so far so good! The programme has been very warmly received, with the potential to make it available to International SOS doctors worldwide,' Dr Eichholz concluded.

September in Vienna: The Trauma Imaging symposium

From head to toe – not forgetting the face

Report: Michael Krassnitzer

The number of radiological accident and emergency examinations had doubled within five years because many accident and emergency (A&E) patients are given CT scans even before having a comprehensive clinical examination. This means that patients are scanned who do not really need urgent treatment, according to Associate Professor and private docent Gerd Schueller MD MBA, President of the Austrian platform Trauma Imaging. 'So, it has become ever more important to look at the radiation doses involved, which has not really been an issue in accident and emergency radiology to date,' he points out

The solution has been to develop iterative reconstruction – i.e. a new algorithm, which may be very time-consuming but which also facilitates a reduced radiation dose during examination by around 50% – with consistent image quality. 'All major CT manufacturers now offer such scanners,' he says. 'In recent years, this is the most important technological development in our field.'

Head injuries are always an important issue in emergency radiology. However, at the *Emergency – Head to Toe conference*, held by the firm Trauma Imaging in Vienna this September, those body parts that are usually given less attention in this context, were also part of the programme.

One of those parts is the face. 'In the case of facial injuries, surgery is not always urgent – unless there is bleeding in the eye,' he explains. If this occurs, retinal detachment can be a risk. However, trauma affecting the face or neck tends to go hand in hand with a high mortality rate (12%) because it often occurs in conjunction with craniocerebral injuries. A substantial, radiological description of the fracture(s) of those parts of the cranial bone responsible for facial stability is very important here. The face is divided into four vertical and four horizontal sections for this purpose. It is also important to check whether the muscles and tendons that hold the eyelids in place are intact.

In the case of abdominal trauma, 3-10% of cases involve urogenital injuries, with renal trauma the most common occurrence.

Urogenital traumas are particularly dangerous in a polytrauma case. Isolated injuries, on the other hand, tend to heal spontaneously in 95-98% of cases. 'We can't really determine whether a patient needs surgery or not,' the professor admits.

Here the examination procedure of choice is a CT scan, with or without contrast media administration.

Radiology is obviously also used for urological emergencies such as haematuria, flank pain, colic and infection. Differentiation between colic and acute appendicitis is a particular challenge. Here, the radiologist also falls back on clinical diagnosis – patients with appendicitis experience relief from pain when lying down with their legs pulled up, whilst colic patients feel a strong need for movement.

Incidentally, MRI scans are used increasingly to diagnose appendicitis. 'If the appendix is located behind the large intestine, there is no chance of diagnosing this with ultrasound,' Schueller emphasises. Diffusion-weighted MRI scanning is very helpful by enabling radiologists to diagnose appendicitis within 15 minutes without contrast media administration.

'Unfortunately,' he adds ruefully, 'there tend to be bottlenecks when it comes to the availability of MRI scanners.'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Gerd Schueller is founder and president of Emergency Radiology Schueller, a teleradiology firm based in Zurich.
He qualified in medicine and radiology at Vienna University's Medical Faculty, and became an Accident and Emergency Radiology consultant in the Department of General and Paediatric Radiology, at the University Hospital for Radiodiagnostics in the same city. He served as consultant radiologist and board member at the Spital Bülach in Switzerland from 2012-2014.
He is a founder and board member of a numerous international radiology societies and, in June this year, was president of the Annual Congress of the European Society of Emergency Radiology (ESER).

Swiss consider an end to mammo screening

Benefits: Are they a question of beliefs?

Experts who oppose an end to screening argue that its value far outweighs the harms

Report: Mark Nicholls

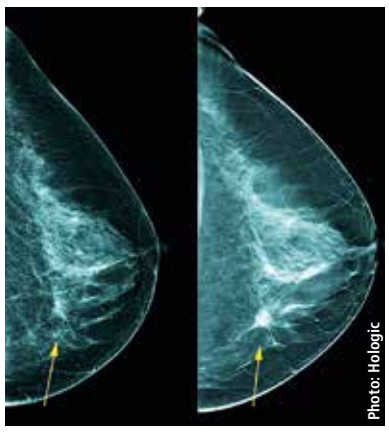
A panel of experts has recommended that existing programmes be phased out and that systematic screening programmes be replaced with systematic screening information that would give women the opportunity to make individual choices.

The move has been suggested by the seven-member Swiss Medical Board, an independent health technology assessment initiative, which, although sanctioned by some of the country's leading medical bodies, makes non-legally binding recommendations.

The board initially published its recommendations in February, triggering a degree of opposition from cancer experts. However, the move was later discussed again by members of the board, which confirmed its position over winding down the breast cancer screening programmes in Switzerland on the basis that screening does not clearly produce more benefits than harm.

Two members of the Swiss Medical Board - Dr Nikola Biller-Andorno and Dr Peter Jüni – underlined the position with an editorial in the *New England Journal of Medicine*, stating: 'We were struck by how non-obvious it was that the benefits of mammography screening outweighed the harms.'

With 5,400 women contracting breast cancer every year in Switzerland, and with 1,400 deaths from the disease, the board assessed



Mortality rates from breast cancer can be reduced by screening

the positive aspects of systematic mammography screening, such as earlier detection of tumours, alongside the potentially negative aspects such as excess therapy and psychological stress in the event of false positive results, as well as cost effectiveness.

It concluded that mortality rates from breast cancer can be reduced slightly by screening but added: 'This desirable effect is offset by the undesirable effects: specifically with about 100 of 1,000 women with screening, erroneous results are produced, which lead to further investigations and, in part, to unnecessary treatments. Furthermore, the cost-effectiveness ratio is very unfavourable.'

This led the board to recommend that no new systematic mammography screening programmes be introduced; a time limit set on existing programmes and a call for all forms of mammography screening to be evaluated with regard to quality and for desirable and undesirable effects. They acknowledged criticism of the recommendations as contradicting 'the global consensus of leading experts in the field' but maintain they are looking at the issue from an unprejudiced standpoint rather than as part of past consensus-building efforts by specialists in breast cancer screening.

Medical ethicist Dr Biller-Andorno is Director of the Institute of Biomedical Ethics at Zurich University and Dr Jüni is an epidemiologist in the Department of Clinical Research at the University of Bern.

Other board members are a clinical pharmacologist, oncologic surgeon, nurse scientist, lawyer, and health economist.

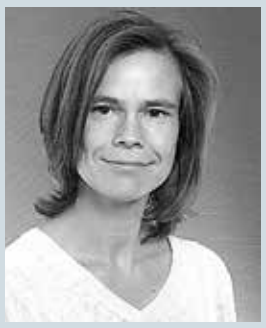
The Swiss Medical Board – appointed and sanctioned by the Conference of Health Ministers of the Swiss Cantons, the Swiss Medical Association, and the Swiss Academy of Medical Sciences – has been reviewing mammography since the early part of 2013 and had concerns because they feared the debate was re-analysing out-dated trials, with none focused on more modern breast cancer treatments.

Drs Biller-Andorno and Jüni wrote: 'The relative risk reduction of approximately 20% in breast cancer mortality associated with mammography, which is currently described by most expert panels, came at the price of a considerable diagnostic cascade, with repeat mammography, subsequent biopsies, and over-diagnosis of breast cancers – cancers that would never have become clinically apparent.'

They suspect there is 'pronounced discrepancy between women's perceptions of the benefits of mammography screening and the benefits to be expected in reality.'

Their editorial stated: 'It is easy to promote mammography screening if the majority of women believe that it prevents or reduces the risk of getting breast cancer and saves many lives through early detection of aggressive tumours.

'We would be in favour of mammography screening if these beliefs were valid. Unfortunately they are not, and we believe that women need to be told so.'



Nikola Biller-Andorno, Professor and Director of the Institute of Biomedical Ethics at Zurich University, studied medicine at the University of Erlangen-Nuernberg as well as philosophy and social sciences at the University of Hagen in Germany, and between 2002-04 worked as an ethicist at the World Health Organisation. In 2004 she was appointed Professor of Medical Ethics at the Charité, Joint Medical Faculty of the Free and Humboldt University, Berlin, and a year later joined Zurich University as Full Professor of Biomedical Ethics. In 2007 she became the founding director of the Institute of Biomedical Ethics. The professor is a member of the Central Ethics Commission of the Swiss Academy of Sciences, a temporary advisor to WHO and deputy editor of the Journal of Medical Ethics. Her bioethics works have been published widely.

New No

Much will now depend o

Report: Mark Nicholls

A new study has suggested that mammography screening of healthy women can help to significantly reduce deaths from breast cancer.

The study used information about women in Norway from 1986-2009 to reach its conclusions and followed all women aged 50-79 years during that period.

Principal investigator Lars Vatten, Professor in Medicine/Epidemiology at the Norwegian University of Science and Technology, Trondheim, said: 'The main finding was that invitation to mammography screening every two years among women 50-69 years of age was associated with 28% reduced risk of dying from breast cancer. The second finding was that 368 women need to be invited to mammography screening to prevent one breast cancer death.'

He explained that a national mammography screening programme was gradually implemented in Norway's 19 counties between 1996-2005 and that gradual implementation by county, and the near random distribution of invitations within the counties, provided a setting similar to a natural experiment, enabling researchers to compare breast cancer mortality among women who were invited to screening and women who were not (yet) invited.

'In the analyses we carefully separated breast cancer deaths that occurred among women diagnosed before invitation – without potential for a screening effect – and deaths that occurred among women who had been invited before diagnosis (with a potential for effect),' Prof. Vatten said.

With the research likely to trigger further debate over mammography and the timing of breast cancer screening for women at average risk of the disease, the professor hopes the findings will further inform that debate and underline the need for exact information about screening patterns (date of invitation, date of

Researchers have found out that mammography screening of healthy women can help to reduce death from breast cancer

Mammography screening can reduce deaths

orwegian breast cancer research

n new treatments and more systematic management of patients

Since 1996, **Professor Lars Vatten** has chaired the Epidemiology Department at the Norwegian University of Science and Technology, Medical School, Trondheim, where his research interests focus on cancer, perinatal and cardiovascular epidemiology. Initially a family doctor, he became a research fellow at the Norwegian Cancer Society in 1987 before moving to the Norwegian Medical Research Council in 1990 as an epidemiology researcher before taking up his current role. Prof. Vatten has published more than 300 papers, is a member of The Norwegian Royal Academy of Sciences and, in 2010, he received the King Olav V Prize for Cancer Research.

diagnosis and date of breast cancer death). 'That's because it is imperative to distinguish between women who could benefit from screening and women who could not benefit,' he added. 'Actually, this corresponds to the elementary distinction between exposed and unexposed individuals in observational studies.'

Benefits and harm

'Benefits are typically indicated in terms of mortality reduction, and our study adds to the evidence that mammography screening reduces the risk of dying from breast cancer,' he said. 'However, screening picks up a certain proportion of breast cancer cases with limited malignant potential, and unnecessary treatment of these cases will be regarded as harmful. The challenge is that the proportion of these latter cases is very difficult to estimate, and that the cases cannot be identified on the individual level.'

While the professor said that the results suggest a clear mortality benefit, he believes health professionals need to realise that there are costs and that an important challenge is to identify women with breast cancer who have a disease that is not likely to be lethal. 'In fact,' he suggested, 'it is extremely important to identify cases with low malignant potential, because these patients should probably receive a different treatment from that which is currently the conventional choice.'

As for the future of mammography, he believes that, with increasing improvement in treatment, gradually more women need to be screened to provide the benefits reported in the study. However, he points out that much depends on new breakthroughs in treatment, and more systematic management of breast cancer patients. The potential impact on clinical practice, of course, depends on the results of future research.

'With increasing breast cancer awareness among potential patients, better organisation of diagnostic work up and improved treatment, the need for screening may be reduced but… just when these requirements are fulfilled is difficult to predict,' concluded Professor Vatten.

Creating the Holy Grail of medical imaging

Phase-contrast X-ray

Report: Sascha Keutel

Among new medical imaging innovations exhibited at Medica 2014 is a phase-contrast X-ray technique to bring greater precision to breast cancer assessment and improve biopsy diagnostics.

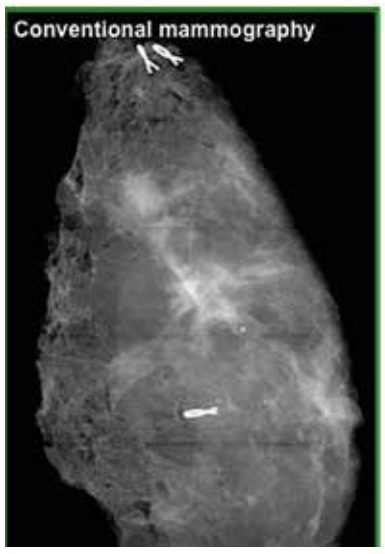
We asked research pioneer Professor Marco Stampanoni, a key figure in the development of this technique, to explain how it works.

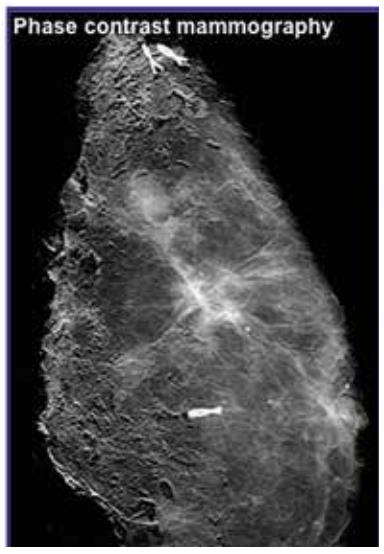
'Phase-contrast X-ray imaging can be considered one of the holy grails of medical imaging,' he pointed out. 'Since the first discovery of X-rays in 1896 by Röngten, scientists have worked very hard to address a fundamental issue: how to increase contrast in soft-tissue while keeping the dose deposition under control? Namely, in conventional X-ray imaging (radiography or CT) as it is performed daily in hospitals, the contrast is essentially determined by the absorption of X-rays in the body – which, as the name suggests, is directly related to the dose deposition.

'On the other hand, to generate contrast, phase-contrast imaging, exploits refraction and scattering signals from the body. It can be shown that while the absorption signal might be small for a soft-tissue specimen such as the breast, the phase contrast signal can be much larger. Being able to detect such a signal and convert it into an interpretable image might provide a formidable new radiological tool: high soft-tissue sensitivity (so far a prerogative of MRI) at excellent spatial resolutions within a short time, which are typical features of CT scanners.'

Back to the beginning

'The development of phase sensitive X-ray techniques goes back to the mid-sixties, first with interferometric experiment using crystals. Further, with the advent of synchrotron facilities, X-ray imaging experienced a first revolution, as coherent X-rays were finally in reach. Coherence is the intrinsic property one needs in order to observe interference phenomena which, in the end, allows access to the phase information.





In the last decade we saw the development of many approaches: propagation-based imaging, diffraction enhanced imaging, coherent diffraction imaging, gratings interferometry and ptychography, to cite a few.

'These methods perform phase-contrast imaging at different length scales, from a single cell up to whole organ imaging.'

Further objectives for phase-contrast X-ray

'Out of the many techniques developed so far, gratings interferometry seems to be the most promising, with respect to potential clinical applications. This approach, pioneered at the Paul Scherrer Institute in Switzerland, has been proven to work very efficiently on conventional X-ray sources, i.e. without the need of a large-scale facility like a synchrotron. This raised the interest of the medical community, which, as mentioned, is eager to improve soft-tissue differentiation at high-resolution keeping dose under control.

'Our research aims to develop the technology (hardware/software) to finally bring phase-contrast imaging into hospitals, to improve diagnostic capabilities to benefit the entire population. An ideal entry point for this technology is mammography, a popular radiologic technique to investigate breast tissue. It is well known, also in relation with many active screening programs, that dose delivery is critical issue. It would be of paramount relevance if a technology were to be available that could significantly improve sensitivity to soft-tissue, sharpness as well as lesions delineation and microcalcifications visibility.

'The identification of microcalcifications is one goal of breast cancer screening and early detection of pre-malignant and malignant lesions. Breast calcifications are common on mammograms, being especially prevalent after menopause. Although they are usually benign, certain morphologic (e.g. fine pleomorphic or fine linear) and distribution (e.g. clustered or segmental distribution) descriptors may indicate breast cancer.'

Other possible applications

'Currently, it looks like mammography is very well suited for a first clinical application of phase contrast imaging. Whether this technology will make it into more complex systems, for instance a human-body CT, still needs to be verified and many teams worldwide are working toward this aim. Further, it has to be pointed out that phase contrast imaging promises to be very useful for applications outside the medical field, for example in non-destructive testing or homeland security.'

Radiation exposure comparisons

'This is obviously a critical issue, which cannot be answered yet with a comprehensive quantitative statement, because there are no clinically compatible phase-contrast systems available that have been pushed to perform at their physical limits, as is the case, for instance, for conventional, absorption-based instruments. The theory is very promising and the hope is that one day a phase contrast mammography system, with dose constraints within the actual regulation limits and significantly improved image quality, can be deployed to a hospital.'

Advantages and disadvantages over others

The most fascinating aspect of phase contrast imaging is that it should be possible to achieve a significantly improved soft-tissue differentiation compared to conventional X-ray based systems. Being an X-ray technique, it is also supposed to be significantly cheaper and eventually provide a better spatial resolution than conventional MRI.

'However, phase contrast is based on ionising radiation, and therefore the minimisation of the dose delivered to a patient as well as the delicate balance between such dose and the desired and/or required diagnostic information have always to be taken into account.'

Research results

'With clinical partners we have contributed to the early period of phase contrast imaging in a clinical environment. For the first time, we presented images of the human breast investigated by this novel technology (outside a synchrotron) and we statistically evaluated the potential impact of such a technology in a diagnostic context. From our studies it appeared clear that sharpness, contrast, lesion delineation and microcalcifications detection are improved.

'We recently indicated that it might even be possible to discriminate between two types of microcalcifications. If statistically confirmed, this could eventually provide an additional descriptor for a scoring system to improve risk stratification.'

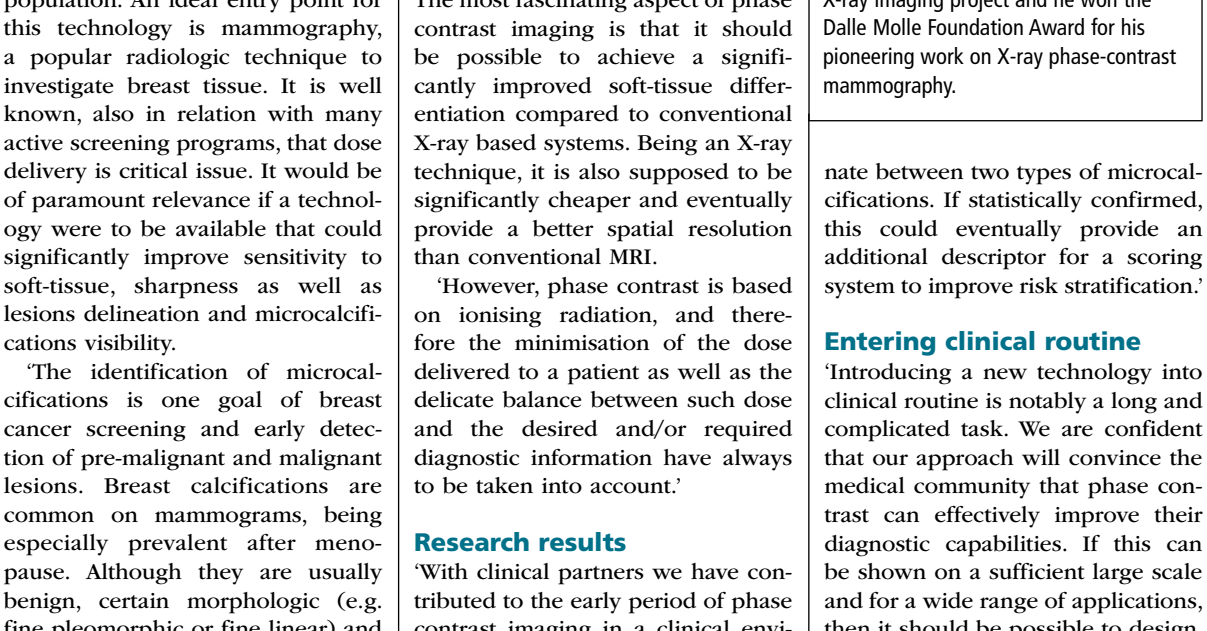
Entering clinical routine

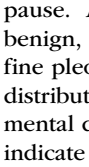
'Introducing a new technology into clinical routine is notably a long and complicated task. We are confident that our approach will convince the medical community that phase contrast can effectively improve their diagnostic capabilities. If this can be shown on a sufficient large scale and for a wide range of applications, then it should be possible to design, build and certify an instrument, which will make it.

'As technology developers we must show that this technique can be brought so far that it can be efficiently transferred to a hospital.

'Then, the radiologists need to assess the capability of this technique and confirm that it indeed provides a significant benefit to their diagnostic process. These are the two fundamental pre-requisites for a successful story.'

A physics graduate (1998) from ETH Zurich, in 2002 **Marco Stampanoni** also graduated in synchrotron-based tomographic microscopy. In 2013 he became an associate professor there, focusing on X-ray imaging in the IT and electrical engineering department. Today he is a professor for the Institute of Biomedical Engineering at the University and at ETH Zurich, where he leads the X-ray Imaging and Microscopy Division. At the Paul Scherrer Institute he also heads the Swiss Light Source (SLS) X-ray Tomography group consisting of 19 people – two staff scientists, seven post-docs, eight PhD students, a computer engineer and technician. Dr Stampanoni's research encompasses phase contrast X-ray imaging and microscopy, real-time tomographic micro-imaging, nanotomography and novel radiological methods for clinical applications and more general non-destructive testing. In 2012 he received an ERC Grant for his phase-contrast X-ray imaging project and he won the Dalle Molle Foundation Award for his pioneering work on X-ray phase-contrast mammography.





Absorption image - conventional radiography (1895)

Differential phase image

Scatter image

Adopting intelligent foreign practices

Radiology around the world

In a 'travelogue' of clinical practices, Carestream turns up some unique solutions to shared challenges

Report: John Brosky

Responsible on a global scale for sales and marketing development with Carestream, Todd Minnigh does a good bit of travelling around the world.

'It all happens out there, in clinics and hospitals. This is where you find the people who are responding to patients' needs, and who tell us what they need so we can develop products to help,' he said. 'We like to get out there, to talk to these people, to see what they are doing, how they have solved problems and the challenges they continue to face in their work.'

Minnigh explained that there are common issues for every radiology operation, but there are also specific solutions to these shared problems, approaches that are unique, and often sometimes specific to a region or a culture.

In August 2014, at the annual meeting of Association for Medical Imaging Management, he shared what he calls a radiology travelogue in a presentation entitled 'Patient Care Over There: What We Can Learn from Radiology Practices Around the Globe'.

Examples of clinical practices were drawn from visits in the United Kingdom, Chile, Brazil, Germany, France and Russia, all illustrated in true travelogue form with snapshots.

'I'm not a clinical expert, so I am not going to tell people this is what they should or shouldn't do,' said Minnigh. 'Yet there are distinct differences in radiology practice that provoke ideas, that may speak to health care providers about how they might do things differently.'

At the highest level, people everywhere want to help the patient, he pointed out. 'They all have a shared concern and try to use the least amount of radiation exposure. Some are more meticulous about how they manage dose.'

As an example he cites visits to German radiology clinics where he found a greater concern for what is called scatter radiation, or second-hand dose. Where it is common in North America to use mobile X-ray units in the emergency department, in Germany emergency patients who are able to move are taken to the protected area of the radiology department for the X-ray exam. Trauma patients not able to be moved are directed to a dedicated CT scanner rather than undergoing an X-ray.

The travelogue then moved to South America for a fresh look at another shared problem of patient scheduling to maximise the use of imaging equipment.

Noting that it can take three times as long for a patient to undress and dress again during an exam than it does to actually shoot an X-ray, Minnigh said, 'This clinic asked the question: What if we create three dressing rooms? If we add three times the capacity for patients to change, can we then make the X-ray unit three times more productive?'

'This is exactly what they did in Argentina to make the fullest use of their digital radiology room,' he said. 'The dressing rooms cost very little to build compared to the cost of an X-ray machine and the space required,' Some people might call this a mass-production approach, he acknowledges, but he counters that clinics are confronting a growing demand for radiology services. In many Western countries, this demand is coming from the increasing medical needs among an aging population, many of whom are over 65 and typically require 15 times greater service on average than people just 45-55 years of age.

Beyond imaging equipment, clinics need to consider that, as this senior population swells, the number of younger people available as employees will shrink, requiring fewer people to do even more by being more productive.

'Rather than be overwhelmed, the challenge to radiology operations is to prepare for a potential increase in business in a way that assures the same safety and quality of service,' Minnigh advised, adding that the benchmark he shared from Argentina is a way of teasing this question.

Todd Minnigh, VP Sales & Marketing Development at Carestream Health

Neurosurgery aided by flight simulation technology

Virtual assistance during procedures

SNAP is used as a rehearsal and training platform for neurosurgeons and residents

Report: Cynthia E Keen

The adage 'practice makes perfect' is applicable to every profession – but even more so for pilots and surgeons. Flight simulation technology has been used for decades to hone aviators' skills, and this technology is now being used by neurosurgeons to plan as well as practise surgical procedures and for real-time virtual assistance in operating theatre. Interestingly, products from Surgical Theater of Cleveland, Ohio, are the brainchild of a career Israeli Air Force flight simulation designer, Moty Avisar.

Working with Dr Warren Selman, neurosurgeon-in-chief at the UH Case Medical Centre in Cleveland, Surgical Theater first developed a Surgical Rehearsal Platform (SRP) that received the USA's Food and Drug Administration 510(k) clearance in 2013.

The SRP uses CR or MRI images to create 3-D models. The model enables surgeons to plan and practise a surgery, such as clipping an aneurysm. It enables users to make recommendations on what size, shape, and placement of a clip would be best for a given patient, thus eliminating wastage of expensive clips that may be tried and rejected during surgery because they do not provide the best fit. Alternatively, a surgeon could virtually position a patient and plan the point of entry that provides the best access to the surgical target.

Courtesy of Mount Sinai Hospital, Department of Neurosurgery

Dr Bederson using the SNAP in the operating theatre

The Surgical Navigation Advanced Platform (SNAP) is an extension of SRP. It connects to a navigation system (such as the Brainlab Curve or the Medtronic Stealth), which allows a surgeon to view a 3-D representation of the patient's cranial anatomy in the operating theatre and navigate off it. SNAP provides the ability to rotate an image or make it semi-transparent to see behind arteries and other critical structures, something not previously possible to do. Dr Selman, who is also chief medical officer of Surgical Theater, has used SNAP's automated reality and simulation capabilities to pause the navigation scene during surgeries to rotate a 3-D image to verify that he had completely removed a tumour.

The neurosurgery department of Mount Sinai Hospital in New York City started using SNAP in July 2014, immediately following FDA clearance on 30 June 2014. Department chair Dr Joshua B Bederson advised *European Hospital* that he has been using SNAP in the operating room for a rapidly growing number of surgeries. He compared the technology with that of watching football on television, where multiple cameras positioned in a stadium can show different angles of an image, or freeze it, zoom in, and enable the viewer to think about other 'what if' scenarios.

'I currently use the SNAP to pause navigation during surgery, allowing me to rotate, expand, or cut away parts of the image. This allows me to confirm that vital structures are safely protected, that I removed a specific portion of the tumour, and that I am not threatening critical brain arteries,' explained Dr Bederson. 'I've also found that connecting Snap to an intraoperative navigation platform enhances coordination among team members.'

Steven Philemond, a clinical research coordinator in the hospital's neurosurgery department, said that Mount Sinai has not compiled any quantifiable data to determine whether SNAP use has minimised the length of a surgical procedure. 'However,' he said, 'it does reinforce a neurosurgeon's confidence in the approaches to cases. Failing to pick the proper trajectory may also add on time to the case. The 3-D rendering that the SNAP provides allows both neurosurgeons and residents to have the ability to re-orient themselves during the case.'

Other valued uses: Mt. Sinai uses the SNAP as a rehearsal and training platform for neurosurgeons and residents. Philemond said that residents use the system to review cases where surgery has already taken place, plan their approach and rehearse the procedure. They then view the intraoperative video to see how the actual procedure compares to the approach they outlined. The SNAP system also can interface with videoconferencing and video streaming systems, offering residents and neurosurgeons throughout the world the chance to view the surgical procedures in which it is used.

Dr Bederson presented the technology in a scientific session at the annual meeting of the European Association of Neurosurgical Societies this October in Prague. Surgical Theater also will be an exhibitor at EANS 2014.

The company anticipates receiving a CE Mark approval for both SRP and SNAP within six months.

Radiology and imaging

Delivering on dose reduction promises

System shows 41% lower dosage than others

With more than 60 years in radiology, Zwanger-Pesiri is one of the largest non-hospital-based radiology practices in the USA. Among its 60 radiologists the number of specialties include interventional, neuro, abdominal and cardiovascular radiology as well as musculoskeletal, breast and vascular imaging.

With such a diverse, large patient base, and many radiologists to manage, workflow is a key consideration, which is why the DX-D 300 DR system, with its Cesium Iodide detector technology and immediate image availability, was chosen.

Workflow was the initial driver

'We installed our first Agfa HealthCare DR solution, the DX-D 300, in our Elmont site in August 2013. We chose it primarily because the workflow was so efficient, it was easy for the technolgists to set up and images were quickly available. At the time, Agfa HealthCare was telling me about its dose reduction capabilities but, to be frank, I didn't really believe them. They kept on about it, so we set up a study to compare results.

'We had two competitive units from other suppliers on the same site, so that provided the ideal opportunity to test what they said.'

Study parameters

The aim was to determine if the DX-D 300 needed less exposure and patient dose than two other systems used at Zwanger-Pesiri Radiology. It also compared doses used to those used for similar exams in other facilities, based on available published studies*. It comprised PA Chest, Lateral Skull and AP Hand exposures taken on phantoms used to simulate patient exposures.In each case the phantom was positioned just as a patient would be and the standard exposure made.

41 percent average dose reductions

Results showed that, while the amount varied depending on the type of exam, the average dose on most was 41% lower with the Agfa HealthCare system versus the other systems – an admittedly unexpected result for Zwanger-Pesiri.

'Much to my surprise, the DX-D 300 was able to provide high image quality at a lower dose,' Dr Mendelsohn said. 'For me, that's great in one way and possibly bad in another. It's good because we can promote our commitment to dose reduction to our patients and now have the figures to prove it, but,' he adds laughingly, 'it could possibly be bad, because the company will want to raise the price we pay! Although, to be honest, I would be prepared to pay a little more for the level of dose reduction we achieved. Agfa HealthCare has done a really wonderful job with it.'

A compelling story

'Dose reduction has become a very compelling story; all radiologists need to be cognitive of is patient dose and aware that patients are becoming better informed and will increasingly ask questions,' Dr Mendelsohn said. 'Change will ultimately be driven from the grass roots rather than by radiologists because our financial model does not currently place a premium on it.'

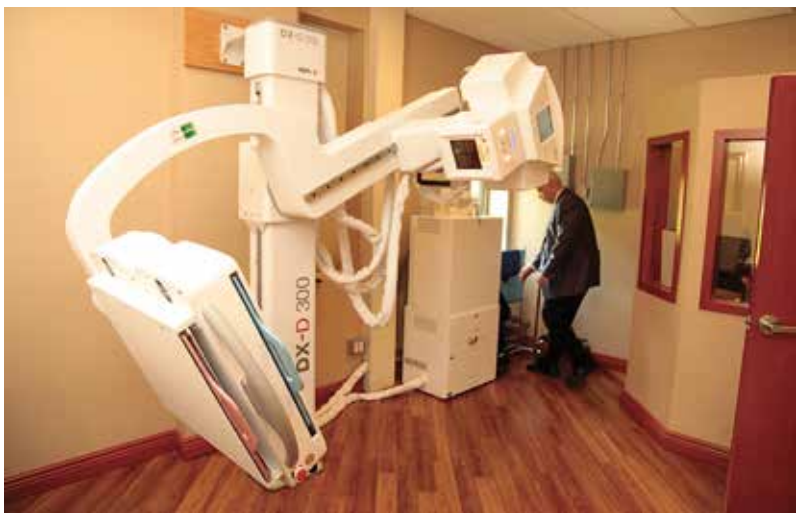
Dr Mendelsohn acknowledges that, with the advent of Cesium Iodide phosphor detectors and Musica imaging processing software used with the DX-D 300 solution, the firm can now achieve the best of both worlds – significant dose reduction while radiologists still gain high quality images with which to work.

Committed to dose reduction, Steven L Mendelsohn MD, CEO and Medical Director of Zwanger-Pesiri Radiology, New York, believes a change in attitudes will be driven by patients rather than radiology professionals

'With so many sites, and such a large population to serve, our biggest challenge is one of workflow,' says Jeanine Sartorelli, Zwanger-Pesiri's Chief Technical Officer. 'To meet demand, we have a lot of teams that rotate across our sites, so ease of use when switching between solutions is paramount.'

A happy patient is the ultimate aim. 'With the advent of Google and other information sites, patients are more knowledgeable and more prepared to question their dose exposure,' Janine explains. 'It's great to be able to say that we are using the lowest possible dose for their images. With the automation and accuracy offered by the DX-D 300 with Cesium Iodide detectors and Musica, we can speed them through the process and make it easier for referrers to access their information.'

* Ernest K. Osei and Johnson Darko 'A Survey of Organ Equivalent and Effective Doses from Diagnostic Radiology Procedures' ISRN Radiology Volume 2013, Article ID 204346, 9 pages http://dx.doi.org/10.5402/2013/204346



The DX-D 300 DR system in use at Zwanger-Pesiri Radiology

Magnetic resonance imaging

Applications in paediatric cardiology

MRI can replace cardiac catheterisation

'In paediatric cardiology, echocardiography is the method of choice for preoperative diagnostic purposes,' explains Professor Dr Emanuela Valsangiacomo-Büchel, senior cardiologist and director of cardiovascular imaging at the University Children's Hospital Zurich, Switzerland. 'Although we are quite aware that echocardiography does not show everything,' she adds. 'Therefore we used to perform cardiac catheterisation. Today we prefer magnetic resonance imaging.'

Magnetic resonance imaging (MRI) has the major advantage of being a non-invasive procedure that does not involve radiation exposure, which makes the modality particularly well suited for the diagnosis of complex congenital heart defects in, such as complex anomalies of the aortic arch or pulmonary arteries. 'A prime example where MRI replaces cardiac catheterisation is pulmonary atresia with multicentric lung perfusion, Dr Valsangiacomo-Büchel explains. Non-invasive procedures avoid thrombosis in peripheral vessels.

'Today, the treatment of children with congenital heart defects often involves cardiac catheters and open rather than occluded vessels make things much easier for both surgeon and patient,' the cardiovascular imaging specialist points out. At Zurich's University Children's Hospital quite a number of neonates with complex heart defects undergo an MRI scan rather than catheterisation.

Dr Valsangiacomo-Büchel's institution is, however, the exception rather than the rule, because cardiac MRI requires a mature and sophisticated interdisciplinary infrastructure. Anaesthesia and ICU teams, for example, must be accustomed to working in an MRI environment. This is the case at the University Children's Hospital, where the paediatric cardiology department is involved as well as radiology, anaesthesia and the ICU. Other facilities also offer MRI but tend to focus on older children.

MRI in children with congenital heart diseases is most frequently indicated postoperatively when 'certain residual findings' are present after surgery. MRI provides functional and morphological information – a crucial feature, since both types of information need to be considered in the evaluation of peripheral pulmonary atresia.

Images and data of differential lung perfusion allow a precise evaluation of the patient situation. 'We no longer perform lung scintigraphy,' the expert says. Typical indications for postoperative MRI are tetralogy of Fallot after total repair with pulmonary valve insufficiency in follow-up: measurement of size and function of the right ventricle, quantification of pulmonary insufficiency and finally the decision whether a pulmonary valve replacement is required.

Ultrasound continues to be the preferred method to document the success of a paediatric cardiac intervention. If the ultrasound exam does not yield any suspicious findings, no MRI is necessary. If however residual findings are present which might require another intervention, MRI can be useful both for diagnostic and planning purposes.

An MRI scan for example facilitates the decision whether catheterisation or surgery is indicated.

'MRI is currently the diagnostic standard to plan a transcutaneous pulmonary valve replacement,' Dr Valsangiacomo-Büchel explains. The modality measures all necessary parameters in the right ventricular outflow tract and generates a 3-D image. Based on these data the cardiologists decide whether a transcutaneous valve replacement is possible or whether surgery is required.

MRI can visualise the coronary arteries and their anomalies – an important issue Dr Valsangiacomo-Büchel believes: 'If a coronary artery runs across the right ventricular outflow tract, a Melody valve implant is contra-indicated.'

Professor Emanuela Valsangiacomo-Büchel directs cardiovascular imaging in the paediatric cardiology department at Zurich's University Children's Hospital, Switzerland, where she also heads the foetal cardiology programme. Her paediatric cardiology training was taken mainly at her current institution. However, during her stay at the Hospital for Sick Children in Toronto/Canada and the Children's Hospital in Boston, USA, between 2000-2002, she focused on cardiovascular imaging.

The potential of cardiovascular magnetic resonance imaging

Cardiomyopathy – the chameleon disease

MRI benefits and potential should be communicated better and to a wider clinical audience to be used more frequently

Cardiomyopathy is a disease with many faces, a 'chameleon', according to Professor Jeanette Schulz-Menger. As Head of the working group Cardiac MRI at Charité, Campus Buch and head of Non-invasive Cardiac Imaging at Helios-Klinikum Buch, Berlin, she uses cardiac MRI to understand the disease better. 'Cardiac MRI plays different roles in the diagnosis of the different forms of cardiomyopathy,' the professor explained during our EH interview.

The 'crucial feature' of this imaging modality is its ability 'to differentiate possible myocardial damages' in all forms of this cardiac disease, she pointed out, even when the pump function of the heart is intact. Even if echocardiography, for example, recorded normal cardiac performance in a patient, cardiac MRI can detect scar tissues and inflammations.

Cardiac MRI is the modality of choice to record right ventricular pump function, because echocardiography cannot handle the complex anatomy of the right heart. 'The right ventricle is shaped like a backpack –it simply does not fit in any geometrical assumption,' Prof. Schulz-Menger explained. While echocardiography tries to cut the right ventricle into many sections to be able to calculate pump function, she added, 'MRI can generate a 3-D image of the heart, which allows us to evaluate the actual pumping performance.'

In dilated cardiomyopathy – the pathological enlargement of the heart muscle – MRI is used to identify the cause of the condition, such as perfusion problems, inflammations or scar tissue. 'Scar tissue is easily visualised with contrast-enhanced techniques,' she said. This is of utmost importance because patients with scar tissue on the myocardium are at a higher risk of sudden cardiac death or on-going weakening of the heart muscle.

Moreover, cardiac MRI is increasingly used to examine the hearts of professional athletes, although this particular area has not yet been acknowledged in the relevant guidelines. Here, the task of cardiac MRI is to show whether a heart is enlarged due to intensive activity or due to a hypertrophic cardiomyopathy.

While echocardiography can visualise a thickened heart muscle, unlike MRI it cannot unambiguously identify cardiomyopathy. Furthermore MRI can identify heart muscle inflammation. Athletes who suffer this condition, and continue training, might experience life-threatening arrhythmias, which may lead to sudden cardiac death.

Professor Schulz-Menger is particularly pleased that other disciplines have begun to recognise the value of this: 'Cardiac MRI is used for risk stratification purposes in non-cardiac diseases.' In certain lung diseases such as sarcoidosis MRI can contribute to a more complete picture of the patient status. 'Many young sarcoidosis patients die of sudden cardiac death due to conduction disorders,' she explained. Conventional diagnostic methods, however, detect only eight percent of cardiac involvement, while pathological studies have shown cardiac involvement in 40 percent of patients. Cardiac MRI could identify these patients – 'and,' Professor Schulz-Menger said, 'that's great'.

She would like to see MRI used more frequently and in a more targeted fashion, but that would need its benefits and the potential to be communicated better to a wider clinical audience. Close relatives of patients with hypertrophic cardiomyopathy also need to undergo an MRI scan because there could be a familial predisposition for the disease. 'If I am serious about diagnostics, each relative has to have a cardiac MRI,' the professor pointed out, particularly since echocardiography is known for its poor detection of early signs of a hypertrophic cardiomyopathy. Additionally, a cardiac MRI scan is indicated when contradicting findings are reported, for example when an ECG yields different data than the echocardiography.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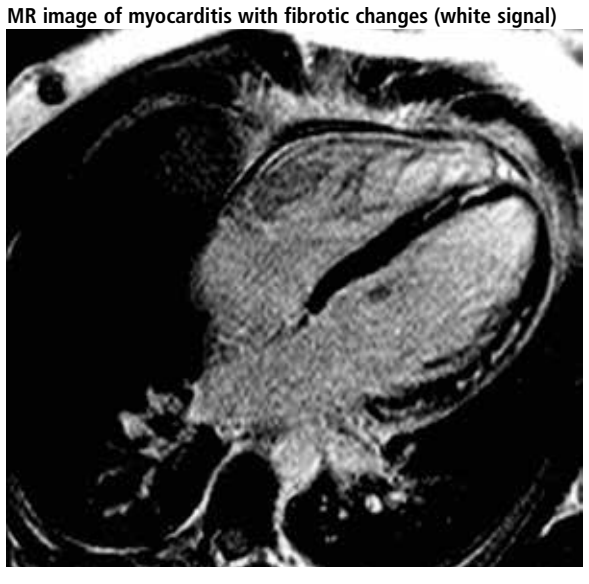
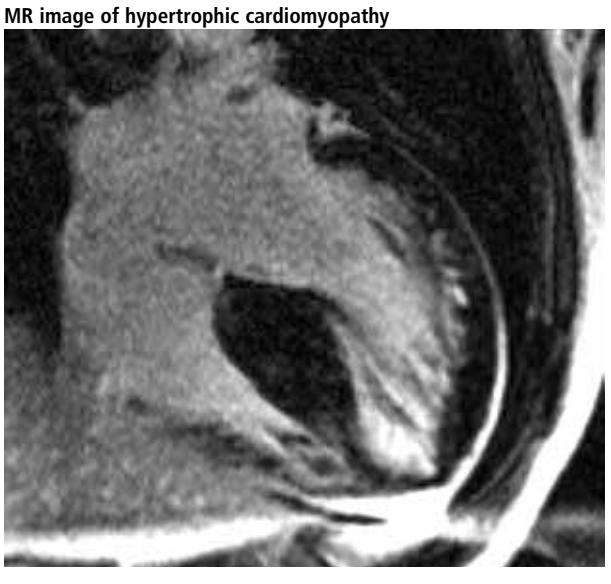
Jeanette Esther Schulz-Menger has chaired cardiovascular magnetic resonance imaging at the Experimental and Clinical Research Centre (ECRC) in Berlin since 2008. The Max Delbrück Centre (MDC) and Charité jointly operate the centre. The professor's research focus is on the evaluation of myocardial damage with cardiac MRI. A driving force behind the implementation of a 7T MRI scanner at MDC, she also sets great store by translating MRI research results into clinical practice.

MR image of myocarditis with fibrotic changes (white signal)



MR image of hypertrophic cardiomyopathy



Spain's Institute for Cardiovascular Research

Stepping towards CD disease prevention

Report: Dr Eduardo de la Sota

Cardiovascular disease develops in a slow and subclinical manner over decades, only to manifest suddenly and unexpectedly. Prevention is crucial, both before and after clinical appearance, and evidence is ample of the effectiveness of early detection of at-risk individuals and lifestyle modifications or pharmacological approaches.

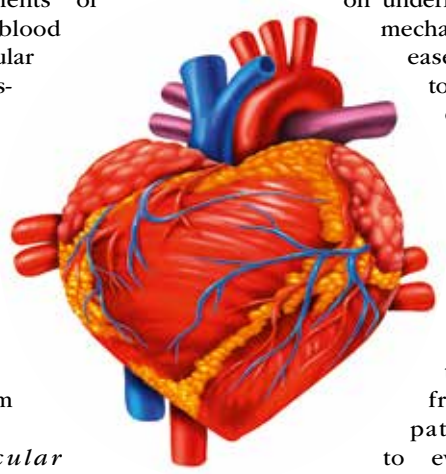
However, those approaches require time, perseverance, and continuous development. Special focus must be made in e.g. diet, weight control (obesity is a disease) and physical activity, among others.

Led by Dr Valentín Fuster, The Spanish Institute for Cardiovascular Research (CNIC) was founded because – despite enormous advances in diagnosis and treatment over the last 20 years – cardiovascular diseases remain the major cause of death in the developed world. The costs generated in economic, social and human terms are also immense.

In response, the Spanish Government, through the Carlos III Institute of Health, created the CNIC to amalgamate the best Spanish cardiovascular research and provide a modern infrastructure and ample funding for biomedical research.

CNIC research is grouped into three departments:

- *Vascular biology and inflammation* (VBI). Here the complex interactions between the components of circulating blood and the vascular wall are investigated, with emphasis on vessel wall remodelling, inflammation and cell-cell biology and signalling in metabolism and disease.
- *Cardiovascular development and repair* (CDR). Researchers are investigating cell-cell interactions and signalling pathways operating during heart morphogenesis and vascular development, the origin and maintenance of the pluripotent state, and the metabolic regulation and repair of the adult cardiovascular system.
- *Atherothrombosis, imaging and epidemiology.* This department develops non-invasive technologies for molecular-resolution imaging that can identify and characterise vulnerable plaques. Combined with epidemiologic analyses, this approach provides invaluable information on underlying molecular mechanisms of disease, leading to tools for accurate diagnosis and targeted drug delivery.



At the 19th World Congress on Heart Disease in Boston, MA, topics ranged from clinical pathophysiology to evaluation and stratification techniques and molecular and cellular biology, including neurohumoral, immunological and genetic studies. The most relevant studies presented approached cardiovascular disease prevention and prognostic algorithms. These included two interesting Spanish studies.

In the first, according to Dr R C Hermida from the University of Vigo, sleep blood pressure (SBP) is an independent predictor of cardiovascular events. That study involved 11,255 subjects, 6,028 men/5,227 women. Dr Hermida concludes that mean SBP, but not daytime clinically measured BP, is a significant and independent prognostic marker of cardiovascular disease morbidity and mortality. These findings indicate ABPM (Asleep Blood Pressure Measurement) is a clinical necessity to accurately detect abnormal sleep-time BP and assess cardiovascular disease risk.

In the second study, Dr M J Sanz from the University of Valencia), presented a study to address effective strategies to treat and prevent atherosclerosis, using combined concentrations of Rosuvastatin (Rosu) and bexarotene (Bex) on angiotensin II (Ang-II)-induced arterial mononuclear cell (MC) recruitment. Research data suggest that combined administration of Rosu+Bex at suboptimal doses may constitute an alternative therapy to control vascular inflammation, minimising the appearance of drug-associated adverse effects.

Thus, CD prevention is advancing slowly, but showing clear evidence that physical and mental hygiene, medical controls, education and healthcare information will minimise mortality and morbidity of cardiovascular diseases, which cause much suffering, mortality and healthcare expenditure.

2nd artificial heart implanted in France

Firm imposes press embargo over new transplants

Another patient in the final stages of heart failure has received an artificial heart at Nantes University Hospital Centre, according to Carmat, the manufacturer of the device. John Brosky reports

Carmat announced, in a press release, its active recruitment of two more patients to complete its first-in-human clinical trial of the artificial heart against a primary endpoint of 30-day survival with secondary criteria for assessing the impact of the reinvigorated blood supply from the mechanical heart on internal organs. 'We warmly thank, particularly today, the experienced team at CHU-Nantes,' stated Carmat CEO Marcello Conviti. 'Passing this step was made possible thanks to their confidence as well as that of our participants, partners and investors.'

The company was forced to issue the press release after the newspaper Liberation reported a second implantation.

Although the news leak was reported by all French media, none could report any further detail about the patient's condition. The company imposed a news blackout regarding implantations after the media circus that followed the news of the first implantation and the subsequent death of the patient 74 days later. The company's stock price jumped on the first news and then fell dramatically with the death of the patient and statements by the inventor of the mechanical heart, renowned cardiac surgeon Alain Carpentier MD, that the device had stopped abruptly.

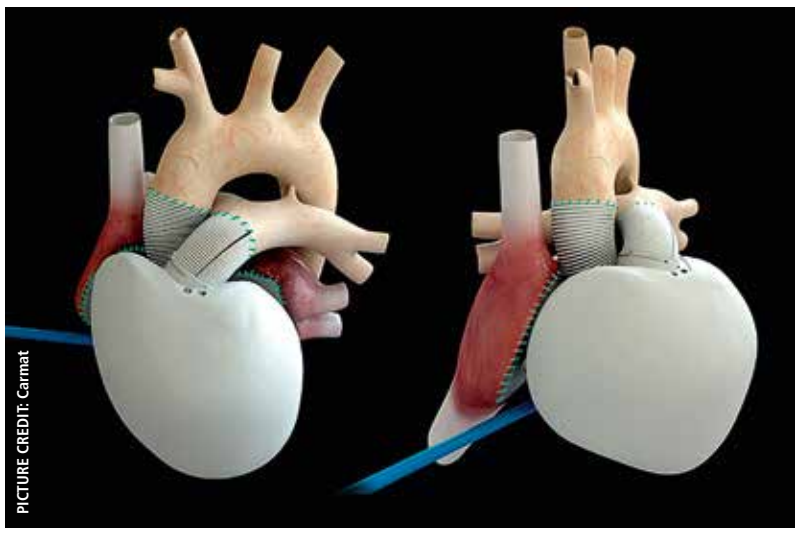
One of the surgeons who participated in the implantation procedure, Daniel Duveau MD, said that the heart did not stop brutally. 'During two hours, each time the device stopped, the system did everything it could to restart the pump. Despite a possible dysfunction, the system intelligently demonstrated its capabilities,' he said, comparing the action to that of a doctor performing a cardiac massage.

Dr Duveau was the lead surgeon for the implantation procedure at CHU-Nantes.

The first patient, Claude Dany, 76, lived 74 days, which, noted lead surgeon Christian Latremouille MD, from the Hôpital Georges-Pompidou in Paris, widely exceeded the end point for the safety study.

After a four-month review of the device and the causes of death of the first patient, French authorities approved the continuation of the clinical trial for safety and feasibility. In its press release, Carmat reported that two independent control committees monitoring the trial had met on 4 September 2014 and issued a report approving a continuation of the trial for the final two patients.

The Carmat artificial heart is the first device to completely replace a human heart and is fully contained within the thorax requiring no external pumps. Only two wires exit the body at the abdomen, one to supply power and the second to monitor device performance.


PICTURE CREDIT: Carmat

Carmat's artificial heart

It is also the first artificial heart capable of adapting the blood supply according to a patient's activity, varying from three to nine litres per minute, rather than having a constant blood supply.

Carmat repeated in its press release that, in conformance with good clinical practices, there would be no reporting of results of any of the implantations until the end of this safety and feasibility trial, unless required by 'particular circumstances'.

Low energy, cold light, long life

A surgical led lamp illuminates countless conditions

The Starled3 NX suits many applications in the operating theatre and diagnoses in, for example, gynaecology, dermatology and general medicine.

'The lamp grants a homogeneous and shadow-less light thanks to its special LED optics created by ACEM Medical Company, which directs light beams at best according to the needs,' the Italian manufacturer reports. 'The visual area is perfectly illuminated assuring both excellent visual comfort and working conditions. Its next generation LEDs produce an unparalleled quality of light with a colour temperature (CCT) of 4.500 °K and a colour rendering index (CRI) of 95.'

Light intensity is 130.000 lux with low energy consumption of 69W, and the life cycle of their LEDs is around an impressive 50,000 hours.

The model has three reflectors producing a blended and intense cone of light, focused through automatic adjustment of the light spot diameter, the firm points out. 'The slim, practical, compact design makes it perfect for several uses. The lamp is ergonomic, easy to move and to position and suitable for the laminar flows of the operating theatre.'

The Endo function (light for endoscopy) also enables the lamp's valuable use during Minimally invasive surgery. Other functions include touch-screen adjusted via the I-Sense control panel – covering light intensity, DoF (depth of field), Size (light spot diameter adjustment), Sync (optional - to synchronise controls of the Acem Medical Company's combined lamps when also used for exams or proceduresC).

Details: www.acem.it

The 2014 European Society of P

Mismatched reports from clinicians and pathologists

Surveying discrepancies

Undiagnosed co-morbidities were found in a quarter of deaths following recent discharge

A limited survey of patients who died soon after being discharged from hospital found that almost a quarter had an undiagnosed co-morbidity with a potentially avoidable cause of death.

Lukasz Adamczyk, a pathologist in training at Southmead Hospital, Bristol, UK, presented the findings at the European Congress of Pathology in London.

Adamczyk and his colleagues looked at 8,971 adult deaths recorded in the Bristol area between 2012 and 2013, focusing on 123 patients who passed away within 30 days of being discharged from hospital. From the available information they found that, in almost 25% of cases, there was a major discrepancy between the clinical diagnosis recorded on the discharge summary and the findings of an autopsy [http://www1.esp-congress.org/guest/ID730f32b5450d8a/AbstractView?ABSID=8142].

The data was drawn from several locations, as autopsies in the region are conducted in a central mortuary. In addition to the two main hospitals in Bristol, deaths in the community that fell onto other hospitals in the wider Avon area were included. In the majority of cases, death was directly related to previously recorded risk factors, or the cause of most recent hospital admission – nearly half of the patients studied were over 80. In 38% of cases, some discrepancy was discovered between the clinical notes and the results of an autopsy.

'The main finding is that, in our cohort, where patients die within the 30 days of discharge the majority of cases are in full agreement between what the clinicians have diagnosed and what was found in the autopsy,' commented Adamczyk, noting that malignant diseases were rarely missed.

'Our findings broadly reflect what is already recorded in the literature,' he added. 'About thirty percent of the time, there's a mismatch between what the pathologists says and what the clinician says, which has been studied and meta-analysed for quite a few years now.'

Why these discrepancies occur is very difficult to assess, Adamczyk explained. 'This is the first such survey, and our goal was to determine the proportion of discrepancies and to subtype them. Finding out the cause of discrepancies would need a more extensive study.' He pointed out that at the time of autopsy, a full background medical history of the deceased might not be available. Often it is also not included in the discharge summaries. Cases such as these are more challenging to correlate.

'The interesting finding is the 25% figure. If those people had received different treatment, knowing what the pathologist knew, it would have changed their outcome.'

'It's seems like a big number,' admitted Adamczyk. 'But overall it's a very small proportion of patients.' Nonetheless, Adamczyk emphasised the importance of carrying out autopsies whenever there is doubt over the cause of death.

Adamczyk said the study would have to be carried out within a much larger cohort of patients before stating specific conclusions, but highlighted the importance of providing the pathologist with the full medical history. 'A relatively small proportion of patients die after being discharged, and autopsy confirms clinical diagnosis, these are the main features here. Further studies are required to determine why some diagnoses are missed.'

Lukasz Adamczyk MD is a specialist trainee in histopathology. He works in the Department of Cellular Pathology at the Southmead Hospital in Bristol, UK. Adamczyk graduated the Medical University of Gdańsk, Poland, in June 2007. His current research is on 'Large cell neuroendocrine carcinoma of the urinary bladder – a morphometric, clinicopathological and immunohistochemical study focusing on a large-cell subtype'. He is a member of Royal College of Pathologists, the British Division of the International Academy of Pathology and Pathological Society of Great Britain and Ireland.

The righ

Patients are no longer content to be passive re
ing a more active role in their treatment, says

Kathy Oliver, Chair co-director of the International Brain Tumour Alliance (IBTA [www.theibta.org]), was speaking at a 'Pathology, Patients and the Public' workshop at the European Congress of Pathology in London. Han van Krieken, president of the European Society of Pathologists, and Suzy Lishman, president-elect of the Royal College of Pathologists, chaired the session.

Oliver, whose son Colin was diagnosed with a brain tumour in 2004, drew attention to rare cancers – affecting fewer than six in 100,000 people, they nonetheless make up 22% of cancers diagnosed in Europe [http://www.cancerresearchuk.org/about-cancer/type/rare-cancers/about/what-is-a-rare-cancer/], affecting over four million people. She called for these patients to receive greater access to their medical records, especially pathology test results, and promoting the right of patients to seek a second opinion.

The IBTA was formed in 2005 to raise awareness of the needs of brain tumour patients and their families, and to build greater links

Low-grade ductal cancer in situ

The issue is not over-diagnosis but over-treatment

We desperately need a 'no treatment' trial for DCIS

Clive Wells is Chairman of the European Working Group on Breast Cancer Pathology, and London Regional Co-ordinator for the United Kingdom's National Health Service (NHS) National Breast Cancer Screening Programme.

During the European Congress of Pathology he used his lecture to speak out about the risks facing healthy women who were found to have low-grade tumours during screening programmes.

Frank Swain: Your lecture at the recent congress on pathology focused on the issue of over-diagnosis. Tell us more.

'Over-diagnosis in breast screening is the big issue that's becoming a problem in the literature. The phrase suggests to the general public that the doctors have diagnosed benign issues as cancer, but in general that is not true.

'What over-diagnosis describes is the detection of cancers by screening that would have never been otherwise recognised during the patient's lifetime, or would never have killed the patient. Screening is great and can and does save lives, but some women will be found to have cancer that wouldn't have been an issue in their lifetime.'

Why does it matter if we find cancer in otherwise healthy women?

'Estimates of the rate of over-diagnosis are around one and 10 percent. Ten percent is a lot, and significantly tips the balance between benefit and harm. For those women, screening has been a disaster, because they've been diagnosed with cancer and had treatment, and yet they would never have known they had a tumour if they hadn't been screened.'

What's the root of the problem?

'Lead-time is the time between the cancer diagnosis by screening, and when it would have become symptomatic. Current estimates suggest lead-time is two years on average. Length bias is the detection by screening of a tumour that is so slow growing that it never would have become symptomatic within a patient's lifetime. Therefore, length bias also contributes to this over-diagnosis, as does the detection of tumours that, even if you hadn't screened for them and detected them, could have been effectively treated anyway when they surfaced two years later.

'You have to ask if we are doing harm to women by detecting these kinds of tumour. We are detecting things we call cancer, which are cancer by all current criteria, and yet they're not going to kill the patient. So we're doing the patient a disservice by saying, "You've got cancer, you need treatment".'

How can those running screening programmes overcome this issue?

'You say we need a test for aggressiveness of tumours. Studies have shown that screening-detected cancers have a less aggressive molecular signature than interval cancers. These low-grade tumours could be responsible for the over-diagnosis we see. We are in an awkward situation where we don't know which cancers will recur and which will not, so we must treat them all. The issue is not really over-diagnosis but over-treatment.'

What is the next step?

'Adequate funding of research and universities is needed to uncover new molecular markers of aggressiveness. It's much more expensive to treat a patient with chemotherapy than it is to apply a test for aggressiveness of the cancer.

'There are tests for long-term recurrence, such as EndoPredict. However, these tests are not seen to be cheap in the first instance, so aren't always carried out.

'We also desperately need a trial of "no treatment" for low-grade DCIS (ductal cancer in situ) cancers. The planned LORIS study by researchers at the University of Birmingham is one example.

'Of course, it will be difficult to recruit enough people – not a lot of women would say they don't want treatment for precancerous tumours.'

Clive Wells MD qualified from Cambridge University in 1978 having attended clinical school at St. George's Hospital in London, and trained in histopathology at Oxford. He was appointed Consultant in Histopathology and Cytopathology at St Bartholomew's Hospital in London in 1989 and worked there for 20 years until moving to University College Hospital in October 2009. He is now a Consultant and Honorary Senior Lecturer in Histopathology and Cytopathology. Dr Wells publishes widely on breast pathology and is Chairman of European Commission Working Group for Breast Screening Pathology (EBCN).

Pathology Congress

Patients are becoming experts in their own diseases

t to a second opinion

As August turned to September almost 3,350 people from 87 countries gathered in London for the 26th European Congress of Pathology (ECP 2014), organised by the European Society of Pathology in partnership with Pathology London 2014 Ltd, a trading subsidiary of The Pathological Society of Great Britain and Ireland. Representatives included experts from the United Kingdom, Greece, Spain, Germany, Turkey and many more countries. UK science journalist Frank Swain attended on behalf of *European Hospital* to report on key issues

ecipients of medical care, and are instead tak- the co-director of a patient advocacy group

between patients, healthcare providers, research institutes and pharmaceutical companies working in the field. 'Pathologists are the link between lab-based research and clinical practice,' said Oliver. 'Yet, we as patients and caregivers, rarely see them, know their names or indeed have a chance to thank them.'

The IBTA manages events such as the Walk Around the World for Brain Tumours, which has been supported by 200 brain cancer charities and other relevant organisations over the past eight years, and the International Brain Tumour Awareness Week, held in October.

Oliver added that accurate diagnosis is essential for improving patient care, but better knowledge about rare cancers like brain tumours was held back by a lack of tumour material. Telling the audience that 'tissue is the issue', Oliver identified the lack of tissue donations as a crucial bottleneck preventing improved research into rare cancers. She encouraged pathologists to meet with patients before surgery to explain the value of these donations and to seek informed consent so that the tissue could be used in urgently needed research. Examples of tissue banking initiatives that actively involve patients include the PATH Biobank in Germany, which collects tissue from breast cancer patients, and the US-based Life Raft Group, which gathers samples of rare gastrointestinal stromal tumours (GIST).

Because of the limited tissue available for rare cancers research, the IBTA encourages greater data sharing between hospitals, and increased collaboration amongst researchers through the management of tissue banks and European Reference Networks. 'Arriving at an accurate diagnosis is essential for optimal treatment of rare cancer patients,' she said. 'It's crucial that rare cancer patients are dealt with by specialised, expert pathologists, who are very familiar with their specific type of disease.' To meet this goal, the IBTA is promoting the development of Centres of Expertise at national level, with pathologists who are knowledgeable about rare cancers and experienced in treating them.

Oliver is also on the advisory board of the European Patients' Academy on Therapeutic Innovation (EUPATI), which empowers patients' roles in guiding medical research, e.g. clinical trials.

Finally, she called for tools to help patients actively participate in their care, e.g. a 'patients dictionary of pathological terms'.

Kathy Oliver is Chair and Founding Co-Director of the International Brain Tumour Alliance (IBTA). Involved in a range of high-level projects and committees addressing brain tumour and rare cancer issues in Europe, she is also a frequent plenary and session speaker at international neuro-oncology and cancer conferences. Oliver was recently appointed to the European Commission's new Expert Group on Cancer Control where she will be the alternate representative from the European Organisation for Rare Diseases (EURORDIS) Policy Action Group on Rare Cancers. She was presented with The EANO (European Association for NeuroOncology) Award 2011, as well as the Advocacy Award conferred by the 5th International Conference on Future Trends in the Treatment of Brain Tumours.

Sending that vital hand hygiene message

A picture is worth a thousand words

Report: Brenda Marsh

Want to put a message across quickly? Answer: Show an image. A starving child with huge tearful eyes prompts an instant flow of charitable donations. The same message in words might go unread, or a response would take longer – or worse, be forgotten. So, how do you tackle that BIG hygiene message – *Wash your hands!?*

Promoters of the European Tissue Paper Industry Association (ETPIA) hit on the idea of offering top prizes to any young graphic designer who could devise an eye-catching cartoon. Aptly, the European Tissue Symposium Cartoon Contest winners were announced on Global Hand Washing Day*, and their work is now exhibited in Bologna, shown on Facebook, and will become part of a wider social media roll-out to stress hand hygiene importance in infection containment.

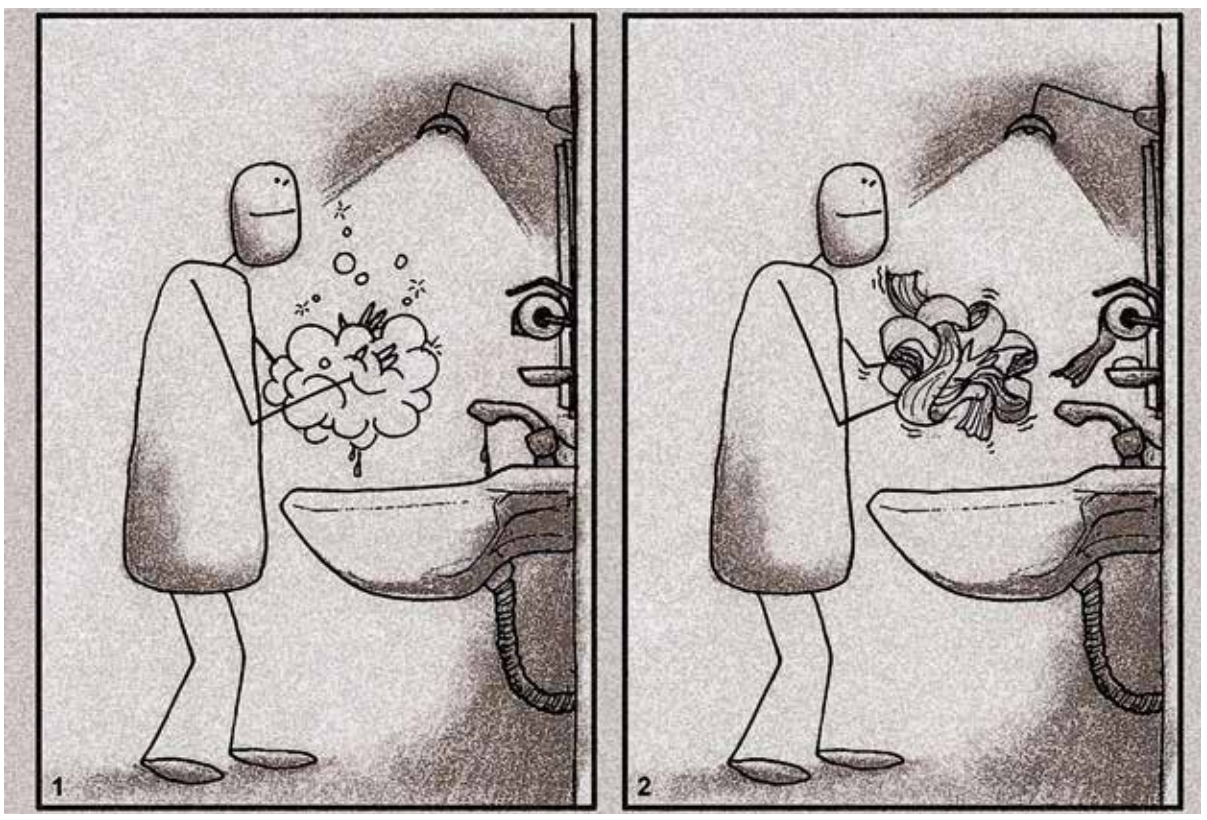
Elisa Canaglia's *Our Future*

The International Cartoon Contest Winner is Rahim Biyarash, from Iran, for his design 'Soap – paper'. Christian Ghisellini, chairman of the judges, said: 'Rahim charmed us with his extreme synthetic design and ironic approach. He has captured the concept and the theme perfectly.'

Elisa Canaglia, from Italy, won 1st prize in the ETS Academy Cartoon Contest for her design 'Our Future'. 'Hand hygiene is such a key part of our daily life; that's why I depicted its importance in a childhood memory almost everyone can relate to,' she explained.

Three specialist ETS prizes were also awarded to Erica Dalle Luche for 'Just relax with tissue'; Martina Tonello for 'Soapy Pirates' and Chiara Martinelli for 'Racoon'.

Handwashing with soap, ETPIA emphasises, '…could save more lives than any other medical intervention and is critical to meeting the Millennium Development Goal of reducing deaths among children under five years old by two-thirds by 2015. The importance of hand washing and drying is further underlined in the recent consensus statement* from six eminent European microbiologists and hospital hygienists. It concludes that hand drying completes the hand washing process by reducing the transmission of microbes and that a system should be chosen that takes into account the risk of contaminating hands, other individuals or the environment. This has significant implications for the spread of infection in public washrooms and healthcare environments.'



Rahim Biyarash's Soap – paper

* Global Hand Washing Day is on the annual calendar of governments, schools, NGOs, private companies and scientific organisations around the world to promote good hygiene and health.

* Consensus statement: http://www.europeantissue.com/hygiene/expert-consensus-statement/

Lessons fro

Diagnosing gastrointestinal inf

Continuous medical training for medical biologists and primary healthcare workers

Report: Jane MacDougal

The human gut literally teems with microorganisms from at least 1,000 different species that are increasingly considered to be a valuable resource for the prediction, aetiology and prognosis of disease. Their presence is necessary for healthy functioning of the gastrointestinal tract and, by default, the entire body. However, due to continual contact with the environment, primarily via food, the gut is susceptible to infection when a virus, parasite or bacterium enters the area and disrupts normal gut microbiota (or flora).

Common symptoms of gastroenteritis, while varying in intensity, include diarrhoea, vomiting and abdominal pain. While often mild, consequences such as dehydration can be dangerous especially in vulnerable populations – e.g. the very young or elderly. Rapid diagnosis so that appropriate treatment and infection control measures can be instigated is an important healthcare goal.

During JIB 2014, held in Paris this October, Medical Biologists attended a training course on the latest developments in diagnosis of infections caused by the bacteria *Helicobacter pylori*, *Campylobacter sp.* and *Clostridium difficile* and the enteric virus Norovirus.

Quick, accurate diagnosis of a gastrointestinal infection remains a challenge for the routine laboratory. A French study found that 55.6% of *C. difficile* infections were not diagnosed, either because of false negatives or clinicians not ordering the test. Classical serum antibodies are not useful in the diagnosis of gastrointestinal infection. Therefore, more traditional microbiological methods of culturing the invasive pathogen, carrying out enzymatic tests and performing an antibiogramme are used.

These are still completely valid, particularly for the wealth of information gathered, e.g. in terms of antimicrobial resistance and, in the case of *C. difficile*, are required for diagnosis confirmation. They do however, require expert knowledge and sometimes specialised media and culturing conditions. A major drawback is that the results are slow in coming e.g. campylobacter culture needs 72-96 hours in micro-anaerobic conditions.

Therefore, newer, molecular and enzymatic diagnostic tools and techniques have been introduced in an attempt to provide the rapid and accurate diagnoses required.

Unlike other invasive pathogens, *Helicobacter pylori* colonises the duodenum and stomach where it may remain asymptomatic or cause ulcers and/or gastric reflux from the excessive production of acid, or alternatively diminish acid production and lead to gastrointestinal cancers and lymphoma. While improved standards of living and hygiene have reduced the incidence of infection in Europe, approximately 15.5% of the adult population is infected.

Diagnosis of *H. pylori* is often made from biopsy taken during endoscopy, a highly useful analysis because histological data can be added to the microbiological work-up, but it is highly invasive. As an alternative to bacterial culture, real-time PCR (polymerase chain reaction) with FRET can rapidly detect not only the presence of the bacteria but also genotypic mutations, predictive for antibiotic resistance to clarithromycin and fluoroquinolones. A problem in France, however, is the difficulty in obtaining the kit to perform this PCR (GenoType HelicoDR from Hain Lifescience GmbH).

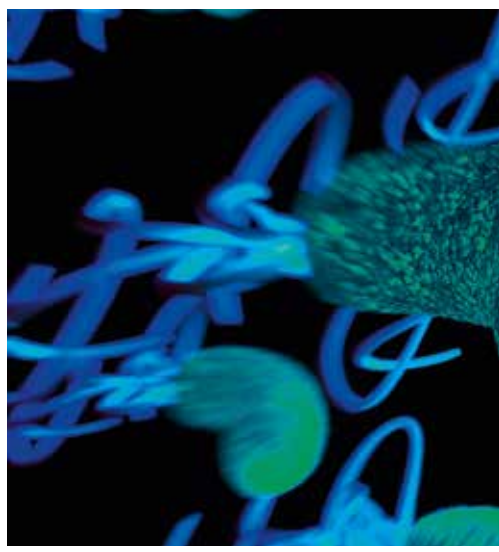
PCR diagnosis of *H. pylori* remains an invasive technique, unlike for the other three infections that are considered where the diarrhoeal stool, or even a rectal swab, provides the starting material for PCR.

Additionally, PCR can be used to identify the campylobacter species *C. jejuni* and *C. coli*, but this technique has been developed in-house by reference laboratories, using FRET of the gyrA gene.

A commercially available multiplex PCR kit, Seeplex Diarrhea-B1 ACE Detection (Seegene, Bionobis) identifying *Campylobacter spp.*, *Salmonella sp.*, *Shigella sp.*, *Vibrio spp.*, and *Clostridium difficile* toxin B, is both sensitive and specific. Nevertheless PCR remains fairly expensive and requires specialist knowledge to perform correctly.

Despite this, real-time PCR is the gold standard for the diagnosis of norovirus gastroenteritis, a significant cause of gastrointestinal morbidity and mortality in young children, even in industrialised countries.

Immunochromatographic point-of-care tests (ICT) have been developed and several are commercially available in Europe. Simple and rapid diagnosis enables suitable treatment to be initiated early, but the existing tests are not yet considered standalone diagnostic tools.



Helicobacter pylori

In the case of *H. pylori* infection the commercially available test CLOtest Rapid Urease test (Kimberly Clark) again requires a biopsy for the starting material, but can provide an answer within one hour with 80% sensitivity. However, because it is known as a 'doctor test' it is not reimbursed by social security in France.

The two commercially available tests for *Campylobacter sp.* performed directly on the stool sample are ImmunoCardStat! Campy (Meridian Biosciences) and RidaQuick Campylobacter (R-Biopharm AG) while rapid – response within 15-20 minutes – their accuracy is low, with

New diagnostic tool for A&E teams

Toolkit for quicker sepsis identification

12,500 lives could be saved from sepsis every year

Report: Mark Nicholls

Accident and Emergency (A&E) teams play a key role in identifying patients with sepsis, followed by risk stratification for severe sepsis and septic shock, initiating resuscitation and treatment, and ensuring the correct onward management of patients identified with sepsis. Now a new clinical toolkit, developed jointly by the College of Emergency Medicine (CEM) and the UK Sepsis Trust, aims to help A&E teams to become more aware of the significant morbidity and mortality due to sepsis and provide the knowledge and skills for early recognition of its presence.

Designed to provide operational solutions for reliable sepsis identification and management the toolkit also complements clinical toolkits designed for other clinical areas and also offers guidance on screening and response to sepsis.

Dr Jeff Keep, a consultant in Emergency Medicine and Major Trauma at King's College Hospital in London and a member of the Quality in Emergency Care Committee at the CEM, hopes the kit will bring clarity for emergency doctors over the different definitions of the severity of sepsis. 'Time can be wasted diagnosing the severity of sepsis and by making the diagnosis simpler and having the confidence to treat sepsis before a definitive diagnosis has been made, we should improve door-to-antibiotic times,' he explains. 'Recognising sepsis is often easy when the patient is very unwell, but we want to recognise sepsis early on and this can be very difficult; the toolkit contains useful ways to achieve this.'

With emergency departments (EDs) using Early Warning Scores (EWS), performed very soon in the patient's journey in the ED, an EWS of three or four, or higher, should trigger a sepsis screen, he said.

The toolkit also summarises some key recommendations for better organisation of the hospital and its sepsis management. Dr Keep: 'Sepsis is a time-critical illness. Researchhas shown that early treatment with antibiotics has a significant impact on mortality, which increases by 8% for every hour's delay.

'Many patients with sepsis present to the ED and therefore the ED should manage sepsis patients as it does other time-critical illnesses, such as major trauma, myocardial infarction and acute stroke. In the UK, if managed properly, we estimate that we could save 12,500 lives from sepsis every year.'

Jeff Keep MD is a consultant in Emergency Medicine and Major Trauma at King's College Hospital, London, and a member of the CEM's Quality in Emergency Care Committee. With a particular interest in sepsis, he developed the national standards in 2009, and keeps the committee up to date with sepsis developments.

At present some 37,000 people die from sepsis annually in the UK, but steps are being taken to cut tackle this in bringing together professional organisations such as the College of Emergency Medicine, the College of Paramedics and the Royal College of Physicians to jointly tackle sepsis and advise a group of members of parliament (APPG) on how to fix sepsis.

The Parliamentary Health Service Ombudsman published a report on sepsis last year, the NCEPOD (National Confidential Enquiry into Patient Outcome and Death) is conducting a review of sepsis patients, and UK health guidance and advisory body NICE (National Institute for Health and Care Excellence) has fast-tracked sepsis through its system and will be issuing guidelines in the near future.

'NHS England [The National Health Service] has also joined the fight against sepsis and the momentum is currently strong and very positive. Of course, it is ultimately down to the individual healthcare providers to recognise sepsis early and start treatment, but the broad support from within the UK healthcare system is invaluable,' Dr Keep stated.

In 2009, CEM developed national criteria and standards for the management of severe sepsis and septic shock, and conducted the first national audit of these standards in 2011/12 and a second in 2013/14.

'The results have improved, and more patients with severe sepsis or septic shock are receiving IV fluids and antibiotics within an hour of attendance,' Dr Keep said.

He stressed the importance of data coding as being critical in combating sepsis and added: 'If every hospital collected accurate data on sepsis then it would be easier to monitor improvements and manage sepsis more effectively.

'Diagnosing the source of infection is also important and strategies for early investigations are crucial to patient survival. By identifying and treating sepsis earlier, costly treatments such as ITU admission can be avoided and these resources should be invested in hospital 'Sepsis Teams' that can respond rapidly with the necessary skills to diagnose and treat sepsis and not allow the patient's condition to deteriorate further.'

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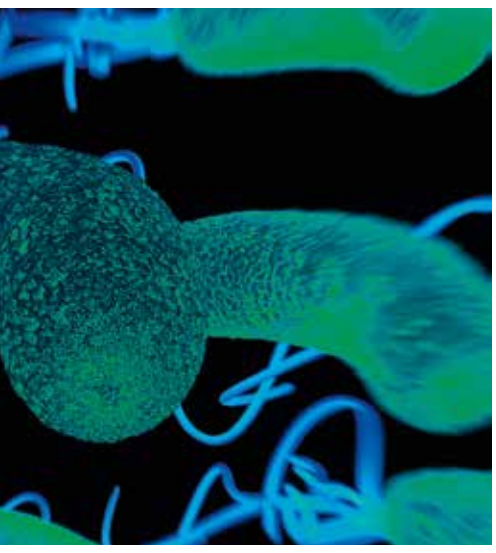

many false positives; therefore their use should always be complemented by culture.

Likewise for Norovirus the rapid enzymatic tests available require further confirmation because sensitivity is relatively low.

However, in the case of *C. difficile* commercial tests that detect glutamate dehydrogenase in the patient's stool and have a turnaround time of 15-45 minutes, compatible with routine laboratory needs, are highly correlated with culture and can be used as a first screening step in a diagnostic algorithm.

ELISA tests are also commercially available for some of these gastrointestinal pathogens. *H. pylori* can be detected in a stool ELISA test (HpSA, Meridian, Italy) based on monoclonal antibodies, with high specificity, but poor sample storage can affect sensitivity.

ELISA kits are much more reliable than ICT to diagnose *Campylobacter*. Available commercially are the Premier Campy (Meridian Biosciences) and RidaScreen Campylobacter test (R-Biopharm AG) and take about two hours to perform have high specificity and good PPV and PNV of 100%. They are recommended to screen before culture or when a patient is culture positive and also before faecal transplant is performed.

Another technique introduced in some laboratories and reference centres is to use mass-spectroscopy by MALDI-tof to identify causal agents. This is particularly effective for *Campylobacter sp.* enabling positive identification of more different species than is easily done by normal microbiological techniques.

The most accurate and widely used non-invasive test for *H. pylori* the 13C breath test, 97.9% specificity, 96.7% sensitivity requires the measurement of 13C02 by mass spectrometry, placing it beyond use among routine laboratories.

The lesson from this training session is that diagnosis of gastrointestinal infections is perhaps not as easy as it could be for routine biology laboratories and more could be done to provide the tools needed for rapid and efficient diagnosis for those at the forefront of infection.

25th International Symposium on Critical and POC Testing

POCTs will accelerate sexually transmitted disease diagnoses

About 350 million people worldwide suffer uncured but curable sexually transmitted diseases (STD). Accurate point-of-care testing (POCT) is one of the best ways to identify and treat them, Cynthia Keen reports

Trichomonias, with an estimated 187 million cases, and Chlamydia with around 100 million, are the most prevalent sexually transmitted diseases (STDs), according to the World Health Organisation (WHO). There are approximately 36 million cases each of gonorrhoea and syphilis. HIV1/2 cases are around 34 million.

In September, Professor Anne Rompalo MD (Johns Hopkins School of Medicine, Baltimore, MD) an expert in epidemiology and STDs, discussed current and impending POCTs for sexually transmissible infections at the 25th International Symposium on Critical and Point-of-Care Testing of the American Association for Clinical Chemistry (AACC) in San Francisco.

The importance of POCTs is simple: quicker diagnosis leads to faster treatment and the knowledge of having a STD might motivate a patient not to transmit it to others.

Any such test must have high levels of sensitivity and specificity, be very easy to use, robust and portable and very fast. Dr Rompalo: 'Only 10-20% of my patients who are tested and asked to return in a week for their test results do so. As for the rest, I hope any sexually active person seeking a partner doesn't meet them.'

The ideal situation is hard to achieve

In 2006, the WHO identified benchmarks for an ideal STD POCT, recognising the lack of access to laboratory diagnostic services in less industrialised countries, or those with limited funding. Dr Rompalo has conducted doctor and patient surveys at STD and adolescent outpatient clinics.

In one survey of clinicians primarily treating STD at out-patient clinics in the USA, she found the majority (62%) wanted POC tests for Chlamydia, followed by HIV early seroconversion (14%) and syphilis (8%). Ideally, tests needed to be cheap (US $20-50), have specificity and sensitivity in the 90th percentile, and fast – results in 30 minutes or less. Physicians wanted a urine-stick home test. Adolescents polled in focus groups are strongly in favour of home testing options, for convenience and privacy.

'Testing outside a lab will become a reality,' Dr Rompalo predicts. 'However, for the home tests of the future, and clinic-administered POC tests, quality control is very important. If a hospital offers POC tests, who is going to oversee quality control? How will this be administered? Who will enforce reporting to public health departments?'

Laboratories have very high adherence of reporting STDs, but although legislation requires physicians to report, Dr Rompalo believes the majority forget. She envisions future POC tests as having a chip embedded in the collection medium, which will be triggered when positive outcomes are identified. The module performing the test would then securely communicate this information via the Internet to the appropriate public health department.

Chembio Diagnostic Systems has developed the first dual HIV 1/2 and Syphilis Treponemal antibodies Point-of-Care (POC) test utilizing Chembio's patented Dual Path Platform (DPP) technology.
The Chembio DPP HIV-Syphilis Assay is single-use immunochromatographic rapid screening test for the detection of antibodies to Human Immunodeficiency Virus Types 1 and 2 (HIV 1/2) and Syphilis Treponema pallidum in fingerstick whole blood, venous whole blood, serum, and plasma.
Photo: Chembio Diagnostic Systems

The majority of her talk was on existing POC tests for various STDs as well as those currently in development and clinical testing.

Chlamydia trachomatis/ Neisseria gonorrhoea

Dr Rompalo believes that culture testing for Chlamydia is horrific: a hard, long, and painful process. Nucleic acid amplification tests are the new gold standard but, while their specificity is excellent, sensitivities are not nearly as good as they need to be.

Trying to interpret them as positive or negative can be difficult because it may not be easy to tell if a colour strip has changed colours.

She considers the Biostar QIA Chlamydia test of male urine (sensitivity of 59.4-78.8% and specificity of 98.4-100%), the Clearview Chlamydia cervical (49.7% sensitivity and 97.9% specificity) and vaginal (32.8% sensitivity and 99.2% specificity), and the C rapid test for vaginal (74.2% and 95.7%) and male urine (41.4% and 89.0%) are in this category.

Her preference is the cartridge-based assay Cepheid GeneXpert CT/NG – a rapid, real-time nucleic amplified test to detect DNA of Chlamydia trachomatis and Neisseria gonorrhoea –which is FDA cleared for use in female endocervical swabs, patient-collected vaginal swabs, and for male and female urine specimens from symptomatic and asymptomatic patients.

The Xpert is a modular platform for testing samples directly from patients, and requires no hands-on manipulation from specimen-loading until results are available 90 minutes later. It is 97% sensitive and has a specificity of 99.9%.

Because the test takes 1.5 hours, the patient must be told of an appointment in advance and the clinic's workflow adjusted so that a patient's sample is collected immediately after arrival, and the patient should be advised that he/she will receive the test results and begin treatment if either disease is confirmed. However, if more patients are routinely scheduled than a module can test simultaneously, multiple testing machines may be needed.

The Path OC-check using cervical swabs has a 60% sensitivity and 89.9% specificity; for vaginal it is 54.1% sensitivity and 96.25 % specificity. The Biostar QIA GC cervical test has 50% sensitivity and 96.25% specificity.

Tests for chlamydia and gonorrhoea

One interesting technology uses microwave accelerated metal enhanced fluorescence (MAMEF). It is a microwave-based lysing system that has ultra rapid and sensitive detection of biomolecules. Dr Rompalo described this as similar to taking a kernel of corn, zapping it, and having it break up like popcorn.

The system utilises a glass or plastic surface, gold metal, and an anchor probe (a fluorescent probe specific to the target). Pieces of Chlamydia DNA placed on the plate are hit with low energy similar to energy in a cell phone. When Chlamydia is recognised, the fluorescence close to the metal gets excited, and this enhanced fluorescence is what is read. Recent testing achieved 82% sensitivity and 91% specificity. The machine will cost about US $2,500, and each actual 10-minute test about US $1.50.

A similar test using MAMEF-based detection is being developed for gonorrhoea. Not only is a rapid test needed, but also one to detect the type of the strain and gonorrhoea-resistance markers. Due to the increase in antibiotic-resistant gonorrhoea strains, it is important at the outset not to prescribe antibiotics that will be ineffective.

Dr Rompalo considers the Atlas Velox TM System is very promising. Disposable cards are used, all reagents are stabilised on the card, and test results take 20 minutes. The portable, small-footprint test processor, with no fragile optical sensors, will be good for field use.

Once a user adds a sample to a testing card, DNA extraction, PCR amplification, and detection of the target are all performed automatically by the system. An electrochemical label released from the probe is hybridised to the target by the nuclease enzyme. The nuclease is double-strand specific, so no label is released in the absence of a target. Voltage is applied to a carbon electrode. At a known potential, the electrochemical label oxidises, generating a measurable current. Reports are produced.

For Herpes Simplex 1-2 (HSV), the 'hot' development is ISO AMP HSV POC. Testing using genital swabs has shown 97.1% sensitivity and 93.4% specificity. The test takes 20 minutes and an additional amplification test one hour.

Syphilis POC tests have proliferated due to the WHO. Determining if non-treponemal or treponemal antibodies are present and if the infection is active or inactive are important – difficult to determine in clinical examination.

The importance of POC screening tests cannot be underestimated, due to a high level of the disease in Africa, and maternal child transmission. Dr Rompalo recommended two: Trinity Sp Health Check using whole blood serum, with a sensitivity of 98.2% and specificity of 97.3%, and the Chembio Diagnostic Systems' DDP Syphilis Screen.

The U.S. Centers for Disease Control is currently working with the San Francisco Department of Health and Kaiser Permanente of North Carolina, with both testing five in-development POC syphilis tests.

These use whole blood serum or plasma specimens for analysis and the systems are easy-to-use, small and robust. Tests are also easy to analyse. Some have no timer. Several do not need refrigeration or water, so can be used in remote locations as well as in an STD mobile van.

'POC technologies may be global game-changers,' Dr Rompalo said, because of places where money or resources are too scarce for expensive tests, or clinic visits are limited, and labs overworked, or not on the premises at all. Globally, numerous STD-infected individuals simply do not know that they have a disease, she stressed.

Teaching POC diagnostics and testing in medical schools worldwide is vital. 'If physicians and healthcare workers are not willing to use POCs routinely in their practice, the point of this is lost. Sustainable business models are needed worldwide, to take STD POC testing to a larger audience.'

Built on MedMira's patented rapid flow-through platform, a diagnostic technology that showed good clinical performance in evaluations and inspections. Key Product Features of Multiplo Rapid Syphilis/HIV Antibody Test are: three minute test procedure, instant results, whole blood, serum or plasma specimens, no specialised training required, built-in procedural and reagent control line, 18 month shelf-life at 2-30°C, no refrigeration or cold chain required, no timers needed, results are easy to interpret, no specialised equipment is needed.
Photo: MedMira Inc.

Aspiration and infection

Zero percent and other illusions

The majority of nosocomial infections cannot be avoided

Interview Ralf Mateblowski

Professor Tobias Welte MD, President of the 24th International Congress of the European Respiratory Society, gave EH some personal views on the symposium 'New perspectives in the management of nosocomial pneumonia'

'A load of nonsense!' Such was the professor's spontaneous response to calls for complete avoidance of nosocomial infections. 'You always have to differentiate between nosocomial infections that are acquired and those which come from patients themselves,' he explained. 'When patients suffering chronic colonisation with nosocomial pathogens in the bowel have to undergo abdominal surgery then infections sometimes simply cannot be avoided - and the majority of all infections are based on this endogenous, intrinsic mechanism. It is therefore an illusion to believe nosocomial infections can be entirely avoided. On the contrary: The majority cannot be avoided!'

Nevertheless, there are noteworthy successes in prevention. 'For a long time the focus was on MRSA; ten years ago we had an increasing prevalence in Germany of 22-25%. Since then, we have seen a slight drop to currently around 17-20% because of more standardised infection prevention and control procedures. A further decrease is possible, but it would be an illusion to believe that the figure can be cut to below 10%.'

The main reason for this is that staphylococcus bacteria are different from other pathogens in their biology and disease mechanisms. 'Resistant coli, for instance, are almost never transmitted via the hands but, in the case of staphylococcus, hand hygiene is the key issue! The clean hands campaign, supported by the Federal Ministry of Health, was very successful. Standards were developed for many procedures where staphylococcal infections play a part, such as for inserting catheters.

It's all the more incomprehensible then that the coordinating manager of the national reference centre, Professor Gastmeier, is currently having to look for private sponsors because the federal government no longer finances this campaign!'

The symposium in Munich also featured discussions about HAP (hospital acquired pneumonia) and the American programme 'zero VAP', aimed at reducing the number of ventilator associated pneumonia cases to zero. Says Welte: 'The Americans have now realised that this measure is absurd: with a patho-mechanism that causes such complex cases of pneumonia you can only influence some individual factors, but not patient-inherent ones. As yet, there are no significant procedures for this.'

A lot has been invested over the last few years to accelerate infection diagnosis. This has two major implications, says the pulmonologist: 'The classic, microbiological diagnosis has become much faster; resistant pathogens can now be isolated and identified in just a day.

Additionally, modern PCR systems help to gain another few hours. However, the disadvantage is that these staff and equipment intensive procedures are based on amplification, meaning they can only detect what is coded on the chip.

'That's easier for gram-positive pathogens with their fairly preserved, standard resistance mechanisms, than for gram-negative pathogens, where we basically observe new resistance mechanisms emerge almost every week. In my view it will be hard for PCR procedures to become established in the hospital. There also will be no way around classic microbiology in the future.'

Could the rise in resistances be contained? Welte is optimistic: 'Thankfully there is finally a little more happening with regards to the development of new substances. At the beginning of October a new cephalosporin* was introduced to the German market that's also effective against MRSA. Some other substances are also currently going through the licensing procedures, so we should be able to move on from the very low point – i.e. 10 years without new antibiotics.

'However, the problem remains that the development of resistances occurs much faster than that of the new substances. Too many factors come into play here, including the misuse of antibiotics itself, their widespread use in mass farming and the globalisation of resistances through tourism.

'Ultimately, the much-needed support from politicians is not forthcoming: All (preventative) measures are labour-intensive. In high-risk areas, such as intensive care units, the staff cover in many places is already insufficient. If staff numbers keep being reduced further for economic reasons all well-meant infection prevention and control programmes will be of no benefit – and incidentally, neither are standards and guidelines implemented on their own, without repetitive teaching and monitoring!'

* A group of broad-spectrum antibiotics that prevent the rebuilding of the cell walls in bacteria that divide and therefore have a bactericidal effect. Penicillin falls within this group.

Tobias Welte MD is a specialist in internal medicine, pulmonology, critical care and infectology. Early on in his career he was a house officer and registrar in Lehrte and Hanover, before spending a decade as head of the Pulmonology and Critical Care Medicine Division, at Otto-von-Guericke University, Magdeburg. The professor has directed the Department of Pulmonology at Hannover Medical School since 2004 and is the current president of the German Respiratory Society.

Immune marker identifies children's nosocomial infection risk

New for paediatric intensive care

Critically ill children hospitalised with traumatic injuries have a high risk of acquiring nosocomial infections, especially if their immune function is impaired. A nosocomial infection, such as sepsis, can become as deadly as a traumatic injury, the leading cause of death in children. Nosocomial infections also contribute to longer stays in paediatric intensive care units (PICU) and thousands more in medical costs, Cynthia E Keen reports

Clinical scientists at Nationwide Children's Hospital in Columbus, Ohio, have identified an immune marker that predicts the risk of a paediatric patient developing a nosocomial infection. Physicians can more closely monitor these highly susceptible patients and more rapidly perform immune function tests.

Immune system impairment is measurable and characterised by a reduced ability of whole blood to produce the pro-inflammatory cytokine tumour necrosis factor alpha (TNF-alpha) that fights infection. Lower TNF-alpha production capacity has also been associated with adverse outcomes for children with influenza, cardiopulmonary bypass, and organ dysfunction syndrome.

Principal investigator Dr Mark W Hall, chief of the critical care medicine division and director of the Immune Surveillance Laboratory, and colleagues, have spent more than a decade studying the immune systems of critically ill children, including collaborative work with Dr Hans-Dieter Volk of the Department of Medical Immunology at Charité University Medicine Berlin.

Their most recent study (pub. online 21/6/2014 in Shock) analysed the immune systems of 21 healthy children and 76 critically injured children admitted to the PICU. Sixteen critically injured patients (21%) developed nosocomial infections within 14 days of admission. All had lower TNF-alpha production capability (< 520 pg/ml compared to a median 1297 pg/ml measured in the healthy control group).

The Nationwide Children's hospital in Columbus, Ohio

Half the patients also received at least one red blood cell transfusion. The researchers also discovered that children who had a transfusion with blood stored for more than two weeks demonstrated a lower level of TNF-alpha production than children who received blood stored for 1-13 days. Potentially, this finding could change blood selection for transfusions in patients identified at high risk for infection. 'It's not yet clear if blood transfusions are immunosuppressive, but our work so far suggests that blood may become more immunosuppressive the longer it sits on a shelf,' Dr Hall explained. Currently, ABC PICU, an international clinical trial being conducted by the other investigators comparing the clinical consequences of red blood cell storage duration (NCT01977547), is recruiting paediatric patients to determine if fresher blood will help improve outcomes.

Additionally, Dr Oliver Karam, attending physician at Geneva University Hospital's neonatal and paediatric critical care unit, heads a clinical trial that started in April 2014 to assess the effect of plasma transfusions on critically ill children. This international initiative has enrolled more than 100 hospitals in 22 countries, and will be the largest paediatric study on transfusion medicine ever undertaken, Dr Karam told *European Hospital*. Patients are still being recruited, with information at *http://www.plasmatransfusion.org/'www.plasmatransfusion.org*.

These are among several activities of members of the Paediatric Critical Care Blood Research Network *(http://www.bloodnetresearch.org www.bloodnetresearch.org)*, a coalition of predominantly Canadian and U.S. researchers, but which is intended to have a global reach.

'Continuing research is so important,' Dr Hall stressed. 'Paediatric hospitals have made headway in reducing preventable infections; but what we learned from our study is that it's important to consider each individual patient's immune system and how well the patient can fight off infection. We believe that critical illness- and injury-related immune suppression may be reversible and help our patients recover more rapidly.'

Paediatrician Mark W Hall MD heads the Immune Surveillance Laboratory, Columbus, Ohio

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