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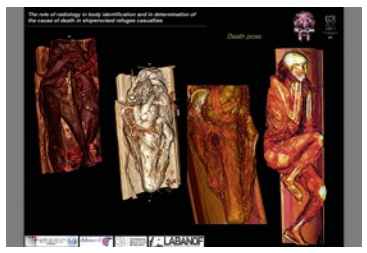

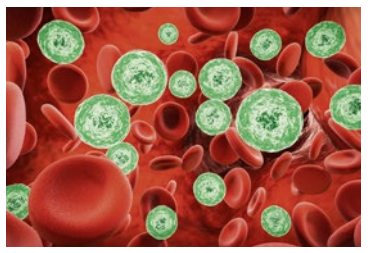

Social freezing on demand in the future

Ludwig Kiesel MD PhD studied medicine at Ruprecht Karl University, Germany, and the Royal Free Hospital Medical School, London, UK. In 1981-82 he was a research fellow in Maryland, at the National Institutes of Health. After residency at Heidelberg University he joined Tübingen University and then chaired Obstetrics & Gynaecology at Münster University.

Kiesel is also a board member of the World Endometriosis Society, German Society of Gynaecological Endocrinology and German Society of Obstetrics and Gynaecology.

Report: Brigitte Dinkloh

Since 2006 around 100 centres that offer fertility preservation for cancer and non-cancer patients in Austria, Germany and Switzerland have joined forces to form the FertiPROTEKT network. This is affiliated with the FertiPROTEKT register, which documents the measures implemented to preserve fertility and the respective results achieved. Medical freezing, i.e. freezing of human germ cells or tissue, plays an important role in bringing the dream come true of having a baby at a later stage.

A liquid nitrogen bank containing suspension of stem cells cell culture

Medical freezing beats social freezing

About two years ago, when Apple and Facebook in the USA promised their female employees to cover the costs of literally putting their desire to have children on ice, this also started a heated discussion against the pros and cons of 'social freezing' (meaning freezing one's own eggs for insemination later in life) on this side of the Atlantic. Fact: Social freezing is now also possible in Europe, but the figures are a lot lower than for medical freezing. According to the register for Germany, Austria and Switzerland, there were 406 consultations for non-medical indications with 257 treatment cycles, with an average of 9.4 eggs per cycle being cryopreserved. This compares with 1,059 consultations carried out in 76 centres in the context of fertility protection for medical reasons, with 801 patients opting for treatment.

'Medical freezing in Germany is carried out in the context of FertiPROTEKT, whilst social freezing is clearly more controversial,' explains Professor Ludwig Kiesel MD, Director of the Department for Gynaecology and Obstetrics at Münster University Hospital and representative of the division of Reproductive Biology and Medicine at the German Society for Endocrinology, which held its 60th congress in Würzburg this March.

Indications for medical freezing

The most common indication for cryopreservation is breast cancer, followed by Hodgkin's lymphoma, leukaemia, and other cancers. Benign diseases, such as rheumatism or Turner syndrome play a subordinate role. A new guideline, which Kiesel helped to develop, therefore recommends that all oncology patients up to the age of 35 should receive advice on options for fertility protection. Currently there are many more cases of disease compared to the number of consultations and measures implemented for fertility preservation. 'The problem is that tumour treatment must often start at fairly short notice, and many colleagues literally forget to offer their patients advice. Egg harvesting can only be carried out once the patient has been receiving hormonal stimulation for two weeks, in the same way as is done in the context of assisted reproduction.

With cancer treatment imminent, there is little time and decisions must be made quickly. Most patients who do not yet have children, or only one child, express an interest in fertility preservation', the gynaecologist explains. According to the new guidelines, all oncology centres will now have to offer advice on fertility preservation based on clearly defined standards. In Germany there are around 100 of these centres and, if a medical professional does not have the required competence, the guidelines ensure that the patient receives advice through a cooperation partner – a procedure already implemented at Münster University Hospital. 'After all, cancer treatment is carried out in many medical fields and not just in gynaecology and urology,' the professor points out.

Vitrification

Cryopreservation provides the opportunity to harvest eggs as well as ovarian tissue, with around half the tissue from one ovary being removed at Münster University Hospital for this purpose. The tissue is flash frozen in the same way as fertilised or unfertilised eggs. Vitrification, i.e. flash freezing is particularly sensitive and durable procedure and better than its predecessors. Once the tumour has been treated successfully, and the patient would like to become pregnant, the cells or tissue can then be re-implanted.

'The patient should either have been free of the disease for a certain period of time or should be very apt at managing it. The tissue is re-implanted where it was removed. This should enable the patient to become pregnant naturally,' Kiesel explains. There are other measures for protecting the reproductive glands apart from cryopreservation. Medication can be administered, or the ovaries can be transposed. Even though these procedures may be more likely to attract funding from health insurers, Kiesel believes that cryopreservation is the safer method. However, whether or not

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Disease research: preprocessed or raw data?

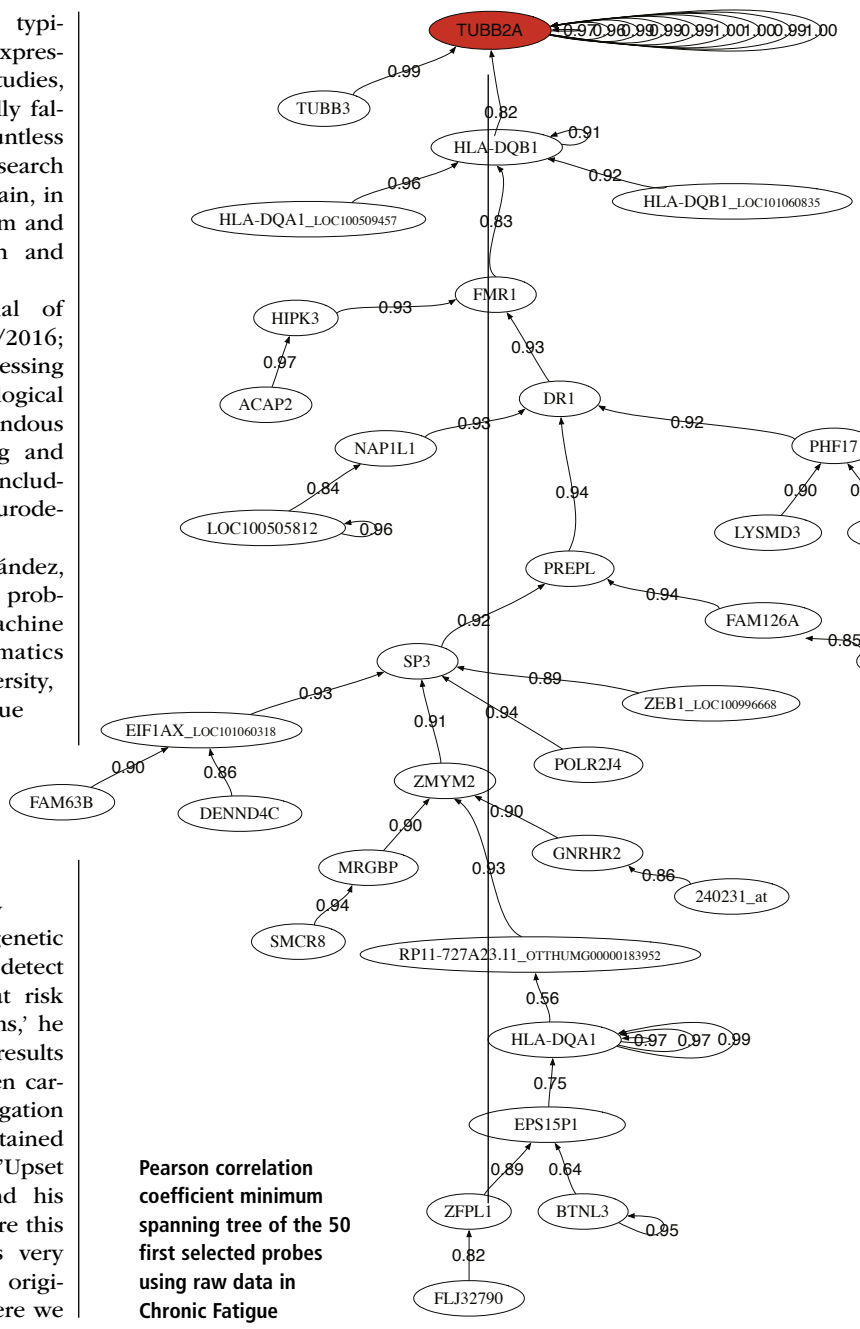
Falsified genetic pathways may explain poor results

Spanish researchers are challenging the validity of many past and ongoing clinical trials and stress the importance of working with raw or preprocessed data in genetic information study, Mélisande Rouger reports

Preprocessed data, which are typically used to decipher gene expression in a large number of studies, modified and sometimes totally falsified genetic pathways in countless scenarios, according to a research team at Oviedo University, Spain, in collaboration with the Brigham and Women's Hospital in Boston and NIH in Washington, USA.

The results (Pub: Journal of Computational Biology 8/2016; Impact of Microarray Preprocessing Techniques in Unravelling Biological Pathways) may have a tremendous impact on the understanding and prediction of many diseases, including cancer and rare and neurodegenerative disorders.

Professor Juan Luis Fernández, head of the group of inverse problems, optimisation and machine learning in the Mathematics Department at Oviedo University, was working on chronic fatigue in patients with prostate cancer undergoing radiotherapy when he found some discrepancy between results from the same measurements. 'We found those results quite by chance when looking at genetic pathways before treatment, to detect which patients were more at risk of developing those symptoms,' he said. 'We published our first results in 2014, but a year later, when carrying out the same investigation with another data set, we obtained completely different results.'Upset but intrigued, Fernández and his team began to search for where this difference arose. 'That was very disappointing; what we had originally done wasn't bad and there we ended up with very different results. That's when we noticed we'd been working with preprocessed data the second time. So we started processing raw data and realised the data we obtained was very different.'



Pearson correlation coefficient minimum spanning tree of the 50 first selected probes using raw data in Chronic Fatigue

Raw or preprocessed data?

Now enthralled, the researchers subsequently launched an investigation to find out which data was more accurate: raw or preprocessed?

Preprocessing has the benefit of reducing the size of huge genetic data, which in turn makes data analysis easier to handle. To process genetic data, researchers most commonly use RMA (Robust Mean Average) a technique that enables noise reduction during data evaluation and a boost to the signal.

Working with raw data, Fernández and his team found they obtained less precise results in prediction. However, when working with preprocessed data, they could not locate the probes as reliably. While RMA enables amplification of signal-to-noise ratio, it also modifies genetic pathways. So, in the end, it is quite challenging to know which dataset is better to use, Fernández pointed out. 'It's almost a philosophical problem; if you mix up signal with noise, you interpret part of the noise as signal - and part of the signal as noise.'

Genetic pathways deduced from preprocessed data are different to those deduced with raw data. But, with raw data, one would coincide more with real biology than with preprocessed data, according to the engineer.

A lot of researchers are only working with preprocessed data, but he believes there should be more studies based on raw data: 'In principle it's more convenient to work with raw data than preprocessed data when looking for genetic pathways.'

Currently, many genes are considered as therapy targets when possibly they are not even involved in the disease process. 'Preprocessing may totally or partially falsify genetic pathways involved in disease development. This has serious impact on therapy targets investigation because, if you are looking in the wrong direction, your treatment or diagnosis will be mistaken.'

Current research is failing

Fernández believes the absence of results in research speaks for itself. 'Hundreds of billions of dollars are poured into disease research, and, to be honest, advances are very mediocre. So we must be doing something wrong.'

Furthermore, inadequately cataloguing samples in biomedical data analysis in expression pathways could have devastating consequences. 'The worst case scenario is a physician doing false predictions and, for instance, telling his or her patients they won't have metastasis – and then they do, all of this due to an error in genetic pathways analysis.'

Fernández said he had already obtained impacting results in pancreatic cancer and multiple sclerosis. He is finishing his work on inclusion body myositis (IBM), an inflammatory muscle disease characterised by slowly progressive weakness and wasting of both distal and proximal muscles.

'We have demonstrated which genetic pathways are defective and, with a set of independent data, which pathways can fully predict phenotype. We have showed that the most important pathway is linked with viral and bacterial infection types, and we have possibly identified which infections.'

He said more results would soon be available in rare and neurodegenerative diseases.

'With our analysis techniques we

Advances in vocal pathology diagnoses

New voice app to detect diseases

A new app measuring the biomechanics of the voice could impact the market of ENT and speech pathology products, Mélisande Rouger reports from Madrid

Acoustic tools that provide glottal source analysis, which are traditionally used in the diagnosis of vocal chords pathology, could soon become obsolete due to a recently launched app that has introduced a highly reliable and entirely mobile technology.

Called Voice Clinical Systems, the new device uses the self designed Wave Tracking technology, which focuses on the signal emitted from the patient's lips. The patient only has to speak for three seconds, directly into a tablet or smartphone, and a diagnosis follows within minutes.

The app is likely to resonate in the vocal chords pathology world, as its correlation with the clinic is unheard of, according to Dr Carlos Ramirez, a Madrid-based ENT physician, who co-developed the app.

'The information we are extracting has nothing to do with what we've used previously. Until now, the analysis we have used had very little clinical correlation; these tools were not describing the pathology the patient might have been suffering. Our app offers information that has a far better correlation with the clinic than the previously used technologies,' he pointed out.

As reported, Voice Clinical Systems works by taking a sample of the patient's voice fed directly into a tablet or smartphone. The recording is then sent directly to an online server, for analysis. The information extracted is then returned shortly to the sender in the shape of a record, which is tailored to the on-going investigation.

This mobile approach enables physicians to record samples anywhere without the heavy, costly equipment usually needed for voice analysis. 'Voice analysis systems currently used require hardware and a computer, which is only available at the healthcare facilities,' Ramirez said. 'Mobility offers flexibility and brings advanced voice analysis technology to places which may not have had the necessary infrastructure before.'

The app offers three types of medical reports, which can differentiate between organic and functional pathology. All patient data are anonymized and the reports only feature the age and gender of the patient.

The one-page long basic report is called the clinical screening; this can be used by primary care professionals and general practitioners to help them refer patients to specialists. It includes straightforward colour-coded graphs, in which red is pathology and green normal.

For patients in need of follow-up, specialists may use the intermediate report, which provides them with an alteration index. Information contained in this report may be particularly useful in patients who have received polyp surgery or are undergoing rehabilitation to correct a functional defect.

The three-page report is a more complete document, and will help ENT and speech therapists to help diagnose pathology with a high degree of subtlety. Because voice can be an indication of neurologic disorders before any other symptoms develop, neurologists may also use the app for the early detection of Parkinson's disease.

The app only targets HC professionals for the moment, but it may become available to patients within two years, Ramirez said. 'In that case doctors will still have to interpret the report, but,' he surmises, 'patients could definitely go visit a specialist with their report in hand.'

The cost of the report ranges between €10 and 20.

Launched in English and Spanish in December, the app has been used in two private institutions in Madrid and has already received positive feedback from physicians who have tested it at various institutions across Spain. Ramirez: 'Voice Clinical Systems has been tested to check its correspondence with clinical diagnosis in 2,000 cases; the correspondence with the clinic has been higher in 99% of the cases.'

The app (Android and iOS) can be downloaded here:
http://www.voicecs.com

Carlos Ramírez Calvo MD co-directs the ENT department at Vithas Nuestra Señora de América Hospital and is co-director of the Pablo Iglesias ENT Clinic in Madrid. He is a founding member of IFMEC, a company dedicated to innovation and training in medicine and surgery. He is also a founding member of Voice Clinical Systems.

Trained as a petroleum engineer in Paris (1988) and London (1989), and following years as an IT software engineer in France, in 1994 **Juan Luis Fernández-Martínez** gained a PhD in mining engineering from the University of Oviedo, in Spain. He joined the university's mathematics department and became Professor of applied mathematics. During 2008-2010 he was a visiting and research professor at UC Berkeley-Lawrence Berkeley Laboratories and Stanford University. His expertise includes cooperative global optimisation methods, with applications in oil and gas, biometry, finance and biomedicine – in which he aims to design biomedical robots in translational medicine for diagnosis, prognosis, and treatment optimisation. The Finisterrae project particularly aims to find effective solutions for rare and neurodegenerative diseases, as well as various types of cancer.

Artificial intelligence is the rocket, big data is the rocket fuel

Watson can review a case in eight minutes

Report: Cornelia Wels-Maug

In her keynote speech at this year's Healthcare Information and Management Systems Society (HIMSS) gathering Ginni Rometty, Chairman, President, and CEO IBM, endorsed cognitive computing and its potential: 'Cognitive is an era that could usher into a golden age if we shape it wisely.' She also clarified that Artificial Intelligence (AI) 'is mainstream and real. This idea, cognitive healthcare, '… is here and can change everything about healthcare.' Indeed, Rometty left no doubt as to why AI is important: 'We need something that augments the intelligence of everyone in healthcare.'

That AI was real at this year's HIMSS in Orlando, is beyond any doubt. Its diverse applications were exhibited across the trade show floor. However, how 'real' is AI beyond the walls of Orlando's Convention Centre? Despite the reality of the digital transformation of healthcare, how mainstream is AI already on a day-to-day basis?

With healthcare and consumer-centric data being generated in unprecedented volumes, the need to transform data into actionable knowledge is a pressing concern. The development of applications based on AI and cognitive computing is advancing fast, at the pinnacle of this trend are commercial technologies such as IBM's Watson and Google's DeepMind. These accelerate the speed and accuracy with which insights are generated and increasingly find their way into healthcare delivery.

James Golden, Managing Director, PricewaterCoopers, encapsulates the challenge at hand: 'We generate an awful lot of data, some is information, just very little is intelligence. How do I generate and test hypothesis with my data?'

Golden is also very clear about the power of AI as an enabler: 'If AI is the rocket, big data is the rocket fuel.' For the time being, AI is particularly deployed in those sectors that are data rich and where cost efficiencies can be particularly leveraged, such as oncology, clinical trial recruitment, patient care management and population health.

Medical knowledge duplicates in 75 days

So, what are some of the actual use cases of AI? Tufia C Haddad MD is a medical oncologist at Mayo Clinic's Breast Diagnostic Clinic in Rochester, USA, where she is also involved in drug discovery in oncology. For her, using AI and cognitive computing skills are a means to keep abreast of medical knowledge. 'It is increasingly challenging to keep up with medical knowledge as it doubles exponentially. In 1950, it took 50 years for medical knowledge to double, now it duplicates in 75 days. By the time a medical student starts practicing medicine, she only knows 6% of the current knowledge.'

For Haddad, AI is also an important part of speeding up the drug delivery process by helping to identify eligible clients for clinical trials: 'IBM Watson understands the inclusion criteria for clinical trials, it has read all trials and all literature on oncology. With its help, it now takes eight minutes to review a medical case, down from 30 minutes. The trial coordinator can spend the time gained to convince an eligible patient to partake in a trial. The number one reason clients don't partake in clinical trials is because no one asked them!'

However, deploying AI for making decisions requires transparency on how the decision was taken in the first place.

Haddad recognises how important it is 'to know where the data came from. How was the system trained to build trust in the information you see?'

Many questions remain

AI is still a nascent technology in the healthcare field with many issues needing to be addressed. IBM acknowledged quite frankly that Watson was still a toddler who had found good parenting skills at MD Anderson and the Mayo Clinic.

As far as AI is concerned, there is still a lot of learning needed when it comes to issues such as mapping problems to AI approaches, creating a talent pool for AI within the healthcare organisations, developing proofs-of-concept or realising returns on investments. Currently, AI tools only work by giving them sufficiently deep databases to plough through and identify relationships. That is a limitation indeed.

There is also the question of scalability, which is closely related to the financial viability of the approach. Does AI always need to be a big investment? 'Watson is an aircraft carrier when we just need a hand gun', Golden observes.

Ginni Rometty BSc, gained a computer science and electrical engineering degree with high honours from Northwestern University, and became IBM's President and CEO in January 2012 and Chairman of the Board of Directors from October 2012. She joined IBM in 1981 in Detroit, Michigan, taking a series of leadership roles, including Senior Vice President and Group Executive, IBM Sales, Marketing and Strategy, responsible for business results in IBM's 170 global markets; she pioneered the firm's rapid expansion in the world's emerging economies. As Senior Vice President for IBM Global Business Services, she led the integration of PricewaterhouseCoopers Consulting – the largest acquisition in professional services history, creating a global team of over 100,000 business consultants and services experts. For her leadership in the professional services industry, Rometty received the Carl Sloane Award 2006.

are able to validate blindly. We take an independent database and select the genes, then we take another dataset and get it right in almost 100% of cases.'

Raw data, rather than pre-processed, will offer more

Scientists must now urgently reach a consensus on which pathways they must consider in which scenario, knowing that raw data will probably give more information than preprocessed data, he added. 'We have to perform retrospective analysis and be coherent. We may use raw or preprocessed data or both, depending on the situation. But we have to decide now. Some of the data you will obtain will completely change your understanding of disease.'

Pearson correlation coefficient minimum spanning tree of the 50 first selected probes using raw data in Chronic Fatigue.

Social freezing on demand …

Continued from page 1

the costs, of at least €2,500, will be reimbursed always depends on the individual case.

Chances of success

Be it social freezing or medical freezing, the younger a woman is at the point of harvesting/removal the higher the chances of success for a successful pregnancy will be. Kiesel: 'This is not a law as such, but we generally recommend egg harvesting up until the age of 35. After that the quality of the cells becomes more unfavourable. However, particularly in the case of social freezing, many women above this age opt for the procedure, because they often only face up to the issue of family planning once they are caught between the priorities of continuing a successful career and the desire to start a family.' Kiesel therefore believes that the trend towards fertility planning will become inevitable. 'I foresee that these services will be offered to both women and men. And there will also be European employers who will offer it. As Carl Djerassi has predicted: Social freezing will become standard in the future.'

POCT all round benefits in emergency units

Speeding up treatment decisions

Report: Mark Nicholls

Point-of-care testing (POCT) is speeding up diagnoses in emergency departments by almost instant delivery of laboratory quality results. In cardiac and blood gas testing, for example, POCT leads to quicker decision making, earlier treatment, and improved patient outcomes.

Erick Froede, Global Product Manager for Siemens Healthineers' Critical Care portfolio, is convinced that POCT in the emergency department (ED) is a 'win-win' scenario for hospitals. 'Essentially, we are trying to deliver accurate, actionable intelligence to clinicians – where and when they need it. This, combined with rapid results, leads to better treatment decisions and patient outcomes. We have done some studies on this and, with cardiac testing, for example, we found that the faster turnaround times can reduce mortality and bed stay, ultimately saving the hospital money while increasing patient satisfaction.'

Throughout Europe, both the Stratus CS 200 Acute Care Analyzer for cardiac testing as well as the RAPIDPoint 500 Analyzer for blood gas testing are available. The instruments deliver results to clinicians within 14 minutes and 60 seconds, respectively. Froede confirms that the instruments are easy to use, cost-effective, and have a low overhead in terms of training requirements. 'When a patient goes into the ED it is a really stressful experience,' he said. 'They don't know if they are having a heart attack or another major issue. To have that result in hand and a decision made more quickly is a significant benefit to the patient and their family.'

In the era of smart phones and information at our fingertips, POCT

technology in the ED is leading the way in meeting patient and doctor expectations, he pointed out.

With cardiovascular disease, a major cause of death globally, the ability to use POCT in the ED means quicker diagnoses and treatment. When a patient has a myocardial infarction, or heart attack, with each passing moment heart muscle dies and loses function. Being able to diagnose and treat patients sooner helps minimize further damage from occurring.

The Stratus CS 200 Acute Care Analyser offers an extensive panel of cardiac tests, which include measuring levels of Troponin I – the protein released when the heart muscle has suffered damage during a heart attack – and NT-proBNP to indicate if a patient is experiencing heart failure. Additionally, the instrument offers the D-dimer test to check for blood clotting issues and to exclude pulmonary embolism at the point-of-care.

The instrument is being used by a number of leading hospital EDs across Europe, including Addenbrooke's Hospital, near Cambridge, UK, where it is available 24/7 to ensure rapid turnaround times for diagnostic tests.

In terms of blood gas testing, the RAPIDPoint 500 Analyzer covers pH and blood gases, electrolytes, metabolites, glucose, lactate, neonatal bilirubin, total hemoglobin, as well as full CO-oximetry.

Froede explained that, with a key indicator of sepsis being lactate levels, the instrument's fast turnaround time enables early detection and treatment of this condition, reducing mortality of patients in the emergency department.

In addition, Siemens Healthineers offers several point-of-care IT solutions. One, called PEP Administrator, is a web-based platform that facilitates all aspects of instrument

As Global Product Manager for Point of Care Diagnostics for Siemens Healthineers, **Erick Froede MSc** is responsible for supply, quality and product innovation across the company's Critical Care portfolio internationally. He gained his Bachelor and Master of Science degrees in Mechanical Engineering from The Pennsylvania State University.

training, from basic operation through advanced maintenance. The RAPIDComm Data Management System is also available, which takes results from the instruments and integrates them into the hospital's Laboratory Information System and ultimately the Hospital Information System. It also has additional functionality to help Point of Care Coordinators manage and control their POCT – instrument status, quality control and operator lockout, operator competency, and compliance management.

Finally, Siemens Healthineers recently acquired an open POC informatics company called Conworx. 'With our new POCcelerator software,' Froede added, 'we can connect more than 150 POCT devices from over 40 manufacturers, simplifying POCT workflows and reducing staff workload – especially important in an ED. The power of an open POC Ecosystem with our point-of-care informatics solution is that it can electronically send test results from all connected POCT devices directly to electronic patient records, and can centrally manage all instruments, patient results, operators, reagents and quality control materials.'

Alongside cardiac and blood gas testing, Siemens Healthineers also has POCT capabilities and platforms covering diabetes, urinalysis, and coagulation.

Prudenc corners

Report: Mark Nicholls

Following a top level EU report showing antimicrobial resistance (AMR) remains high, Professor Mike Catchpole, Chief Scientist at the European Centre for Disease Prevention and Control (ECDC), has warned that stricter use of antibiotics is critical.

The document on AMR in bacteria by the European Food Safety Authority (EFSA) and ECDC revealed that bacteria found in humans, animals and food continue to show resistance to widely used antimicrobials, posing a serious threat to public and animal health, with related infections causing around 25,000 deaths in the EU annually.

So concerned is the European Commission that later this summer it intends to launch an Action Plan presenting a new framework for future coordinated actions to reduce the spread of antimicrobial resistance.

'Treating infections due to resistant bacteria is a challenge: antibiotics commonly used are no longer effective and doctors have to choose other antibiotics,' Catchpole said. 'This may delay getting the right treatment to patients and may result in complications, including death. Also, a patient may need more care as well as alternative and more expensive antibiotics, which may have more severe side-effects.

'The situation is getting worse with the emergence of new bacterial strains resistant to several antibiotics at the same time. A major antibiotic resistance problem, especially in hospitals, is the emergence of bacteria that are resistant to last-line antibiotics, which therefore severely limits treatment options for infected patients. Such bacteria may eventu-

Evaluating the capillary blood collection system

Small tubes, great impact

Imagine a few drops of blood could be sufficient to analyse a wide range of parameters. If blood testing could be quick and easy, without searching for veins, staunching or using unnecessary equipment. Thanks to some clever innovations, a small tube is now making daily life a lot easier for users and patients.

Sometimes less is more. In some situations, only low quantities of blood can be taken in order to ensure that patients are as safe and comfortable as possible. The system not only benefits geriatric patients or those who need to have blood taken on a regular basis, but also burns victims, for example. Above all, a particularly gentle approach is required when it comes to our youngest patients. With this in mind, the Austrian firm Greiner Bio-One has developed and optimized the MiniCollect capillary blood collection system.

Capillary not the vein

It's not always possible to take venous blood from a patient, often due to difficult vein conditions, sometimes the case with geriatric patients, for example. The situation is different for burns victims: infections resulting from unnecessarily large puncture wounds present an additional risk to them.

The volumes of blood samples taken from patients with long-term illnesses, who need to have blood taken on a regular basis, should also be kept to a minimum. The MiniCollect capillary blood collection system offers a suitable alternative for these situations as, for the most part, capillary blood samples can be taken quickly and easily, even in difficult situations.

Accessories are no longer needed

The cumbersome process of transferring the drop of blood using capillary tubes or funnels is now a thing of the past, thanks to the MiniCollect

System. The special feature here is the blood collection scoop integrated into the wide tube opening. In this way, the drop of blood can be transferred to the MiniCollect primary tube quickly and easily, minimising adhesion. The sample comes into contact with the additive immediately.

The caps are completely sealed, meet the highest standards and can easily be sent via pneumatic dispatch or other transport systems without losing any sample material.

Carrier tubes and combined filling volumes simplify use

For centrifugation, the MiniCollect tubes can be screwed into a premium carrier tube using a simple rotational movement. When combined, the dimensions correspond to a standard 13 x 75 mm tube format and can easily be placed in a standard rack or standard centrifuge.

Combined filling volumes for the EDTA and serum tubes, make the preparation of samples more straightforward. Two easily visible filling marks on the tube provide greater flexibility for use. It is no longer necessary to decide on a certain volume in advance, which reduces logistical efforts.

Avoid unnecessary agitation

When taking a blood sample is unavoidable, tears and anxiety do not affect just the little ones, but also their parents, and should be kept to a minimum.

However, the sight of a puncture needle often does cause fear in children. 'One of the main advantages for our young patients is that the safety mechanism of the MiniCollect safety lancets means that no needle is visible at any point before or after the puncture. This makes the situation more relaxing for all involved,' explains Petra Langmayr, former paediatric nurse and product specialist at Greiner Bio-One.

The puncture can either be carried out by pressing the Lancelino safety lancet down on the puncture site (contact-activated safety lancet), or by pressing down the release button (pressure-activated safety lancet).

After the puncture, the needle retracts automatically and is safely enclosed within plastic casing. Thus the risk of needlestick injuries is prevented.

EU reports antimicrobial resistance remains high

ce is the tone of prevention

ally become resistant to all existing antibiotics.'

That, he warned, could lead to a return to the 'pre-antibiotic era' when organ transplants, cancer chemotherapy, intensive care and other medical procedures would no longer be possible.

In terms of action needed and next steps, he said the ECDC has identified three main strategies to address antibiotic resistance: prudent use of antibiotics is the cornerstone of preventing the emergence and spread of resistance, since antibiotic resistance reported across Europe is directly linked to antibiotic use; implementation of good infection control practices, including hand hygiene as well as the screening and isolation of infected patients in hospitals, in order to prevent the spread of resistant bacteria; promoting the development of new antibiotics with novel mechanisms of action.

'Prudent use of antibiotics in human and veterinary medicine is extremely important to address the challenge posed by antimicrobial resistance,' he underline. 'We all have a responsibility to ensure that antibiotics keep working.'

ECDC has recently completed an expert consultation to develop proposals for EU Guidelines on the prudent use of antimicrobials in humans.

Salmonella is highly multi-drug resistant in EU

The latest report also showed that multi-drug resistance in Salmonella bacteria is high across the EU, though experts note that resistance to critically important antimicrobials used to treat severe human cases of Salmonella infection remains low.

Salmonellosis is the second most commonly reported food-borne disease in the EU and it is of particular concern, Catchpole said, that some common types of Salmonella in humans, such as monophasic Salmonella Typhimurium, are exhibiting extremely high multi-drug resistance.

The report also highlighted how antimicrobial resistance levels in Europe continue to vary by geographical region, with countries in Northern and Western Europe tending to show lower resistance levels than those in Southern and Eastern Europe.

The EFSA suggest the geographic variations could be related to differences in antimicrobial use across the EU.

According to Marta Hugas, Head of EFSA's Biological Hazards and Contaminants unit, 'Countries where actions have been taken to reduce, replace and re-think the use of antimicrobials in animals show lower levels of antimicrobial resistance and decreasing trends.'

Other concerns of the report's author include the discovery that resistance to carbapenem antibiotics - usually the last remaining treatment option for patients infected with multidrug resistant bacteria to other available antibiotics - has been detected for the first time, while extended-spectrum beta-lactamase (ESBL)-producing E. coli has been detected in beef, pork, pigs and calves.

The report also noted that more than 10% of the tested Campylobacter coli bacteria in humans (the most commonly reported foodborne disease in the EU) showed resistance to two critically-important antimicrobials (fluoroquinolones and macrolides), which are used to treat severe cases of Campylobacter infections in humans.

Professor Mike Catchpole has worked in infectious disease epidemiology and response at national and international levels since 1991. A former Director of Public Health at England's national Centre for Infectious Disease Surveillance, his primary research interests have included HIV and other sexually transmitted infections, the wider health effects of major incidents, and public health information systems development. Prior to joining the European Centre for Disease Prevention and Control (ECDC) as Chief Scientist in 2014, he was the United Kingdom representative on the Centre's Advisory Forum.

International experts highlight gaps in pandemic planning

The world is underprepared for infectious diseases

Report: Mark Nicholls

A team of international experts has highlighted how the world remains 'grossly underprepared' for infectious disease outbreaks, which are likely to become more frequent in future decades.

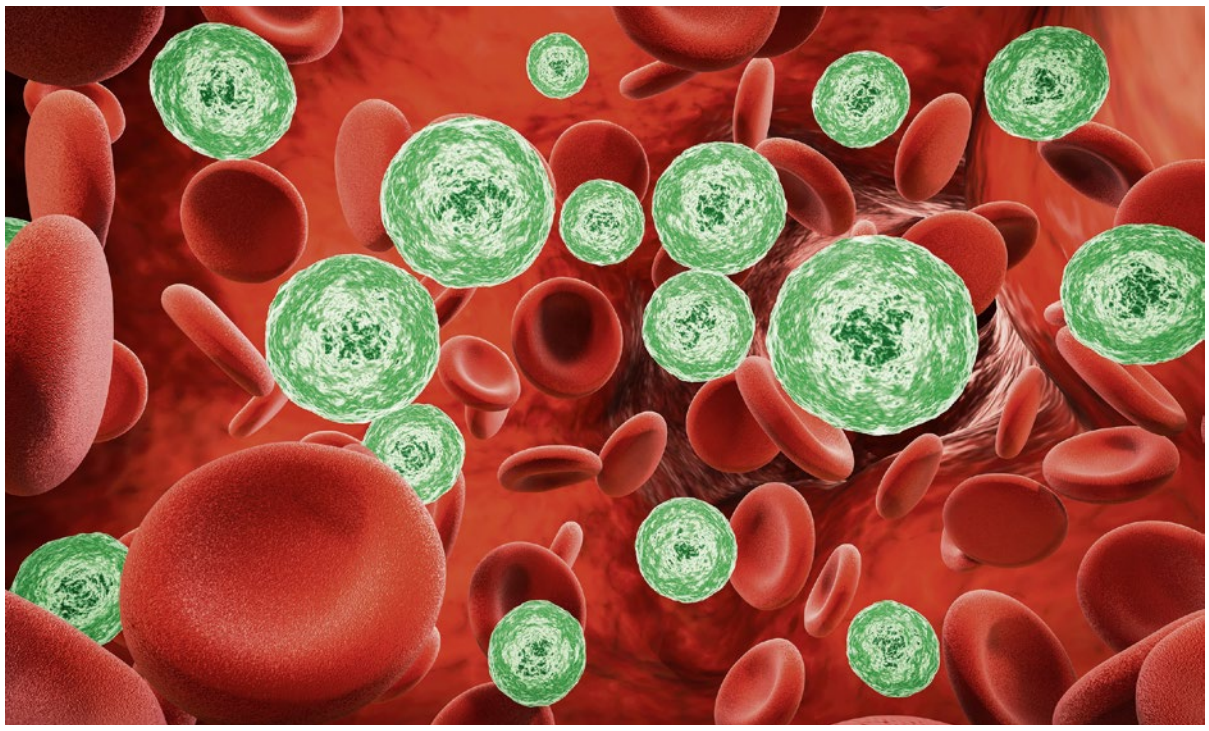
Led by Professor Suerie Moon at the Graduate Institute of International and Development Studies in Geneva, the researchers looked at progress and gaps in actions and concluded: 'Ebola and, more recently, Zika and yellow fever, have demonstrated that we do not yet have a reliable or robust global system for preventing, detecting, and responding to disease outbreaks.'

The warning came after the team reviewed reports on the recent Ebola virus outbreak in West Africa and say better preparedness and a faster, more coordinated response could have prevented most of the 11,000 deaths directly attributed to Ebola and also the broader economic, social, and health crises that ensued.

In August 2014, the World Health Organisation (WHO) declared the Ebola outbreak in West Africa a Public Health Emergency of International Concern (PHEIC).

In the aftermath, several reports were published reviewing what went wrong and how infectious disease outbreaks should be better managed.

However, a lack of clarity in terms of the main priorities and proposed reforms, led the researchers to look closer, synthesising seven major post-Ebola reports to assess recommendations and progress.



3D-rendering red blood cells infection with bacteria and virus

Their findings recognised that the reports differed in scope and diagnosis of the key problems and recommendations for action converged in three critical areas: strengthening compliance with the International Health Regulations (IHR); improving outbreak-related research and knowledge sharing; reforming the World Health Organisation (WHO) and the broader humanitarian response system.

According to the team, so far progress has been mixed in addressing the issues raised. Key problems include the fact that investments in country capacity building have been inadequate and difficult to track; arrangements for fair and timely sharing of patient samples remain weak, and reform efforts at the WHO have focused on operational issues but have neglected to address deeper institutional shortcomings.

The analysis authors say they found 'remarkable consensus on what went wrong with the Ebola response' and what is needed to address the deficiencies but so far 'not nearly enough has been done'.

Warning: prepare or face significant threats

Moon has warned that being underprepared for infectious disease is one of the most significant threats facing the global community: 'The risk of emerging infectious diseases is increasing due to environmental degradation, increased human-animal interaction, urbanisation, intensified trade and travel, and inadequate investment in health systems.

'It poses risks to all countries - the richest, poorest and all countries in between. The losses in human lives, health, and economic activity would be devastating. Estimates based on the risk of a major pandemic over the next century have found annualised losses in the range of between $60-$570 billion.'

In terms of next steps to avert crisis, Moon acknowledges that there has been significant progress since the 2014 Ebola outbreak. 'But the glass is still half-empty, maybe even less than half,' she warned. 'Many different organisations need to take action to improve preparedness - local and national governments, intergovernmental organisations, companies, NGOs, academic institutions, and others.

'I'd say three ingredients are especially crucial now: political leadership to keep the issue on the global agenda, financing from richer and poorer countries alike, and a system to monitor what is and isn't being done in order to achieve mutual accountability.'

The researchers urge the global community 'to mobilise greater resources and put in place monitoring and accountability mechanisms to ensure we are better prepared for the next pandemic'.

Failure to do so, they conclude, could mean the world will not be prepared for the next outbreak.

Dr Suerie Moon is Director of Research at the Global Health Centre, Graduate Institute of International and Development Studies in Geneva and adjunct Lecturer on Global Health at the Harvard T.H. Chan School of Public Health. She was also Study Director of the Harvard-LSHTM Independent Panel on the Global Response to Ebola and co-founded and led the Forum on Global Governance for Health, a focal point at Harvard University for research, debate and strategic convening on issues at the intersection of global governance and health. Her research and teaching focus on global governance and the political economy of global health, focusing on areas such as outbreak preparedness and response.

England's first dedicated emergency unit Sepsis Team

Rapid sepsis recognition saves lives

Report: Mark Nicholls

The UK's first dedicated emergency department sepsis team has been set up in one of the country's leading hospitals.

Leicester Hospital's created the team to recognise and manage sepsis. The key aim is to strengthen the response, in a timely manner, to sepsis cases admitted to the emergency department or to identify rapidly any patients who deteriorate within the unit.

The team of medical professionals from various backgrounds includes personnel from intensive and critical care, emergency medicine and operating theatres and is headed by consultant anaesthetist Dr John Parker, Lead Consultant for Leicester's Hospital. Parker explained that the initiative follows 'Time to Act', the Parliamentary and Health Service Ombudsman report of 2013, which observed patient deaths in the NHS after failure to diagnose and rapidly treat severe sepsis.

The document focused on 10 cases in which patients did not receive urgently needed treatment. The care failings appeared to occur mainly in the first few hours, when rapid diagnosis and simple treatment is critical for patient survival.

From that, Leicester Hospital's began a project in early 2014 and formed a 'Sepsis Awareness' group, bringing together the mentioned healthcare professionals, led by Dr Parker and Sepsis Lead Specialist Nurse Sarah Odams.

A sepsis improvement project was put in place to raise staff awareness of sepsis, recognising that this is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs and leads to shock, multiple organ failure and death if not recognised early and treated promptly.

The trust also implemented measures at that time to improve the management of septic patients across the Trust's hospitals.

Dr John Parker (centre) with the new emergency sepsis team

Since then, the response to sepsis has evolved in a number of ways. The Trust has written a bespoke 'Sepsis Adult Screening & Immediate Action' pathway, which has been shared with staff across hospitals in line with NICE (National Institute for Health and Care Excellence) and the UK Sepsis Trust protocols.

'We have developed a range of training for our staff, primarily face-to-face,' Parker explained. 'We will also soon have an e-learning package available. Sepsis Awareness training is now mandatory for our staff. We have also carried out regular surveillance audits to make sure that staff are compliant with the care pathway.'

This has seen an improvement in the number of patients being given IV antibiotics and fluids within an hour, as recommended by NHS England, and recognition of sepsis across the Trust is now at 95-100%.

'With funding from the NHS Litigation Authority, our new dedicated Sepsis Team will be in our Emergency Department, where two thirds of our patients present with the symptoms of sepsis,' Parker pointed out. 'On an average day there could be between five and 10 people coming into the Emergency Department with potentially life threatening sepsis.

'The team will support the emergency team to recognise and immediately treat anyone who we suspect has sepsis. They will then help to make sure that patient gets the right care from emergency surgery to intensive care support.'

Aiming for the earliest diagnosis of hepatocellular carcinoma

Biomarkers are decisive

For almost three quarters of hepatocellular carcinoma (HCC) patients in Europe it is too late for curative treatment because the disease is often only diagnosed at a very advanced stage. Ralf Mateblowski interviewed Professor Guido Gerken MD, Director of the Department for Gastroenterology and Hepatology at University Hospital Essen, about improved and timelier diagnostic capabilities that have already been established elsewhere.

Asked about necessary improvements in hepatocellular carcinoma (HCC) diagnoses, gastroenterology expert Professor Guido Gerken explained: 'Basically we need to identify and diagnose HCC patients earlier and faster and clearly to achieve a better prognosis for treatment and for the course of the disease. HCC is one of the most common primary tumours in humans, ranking among the "top five" for morbidity and amongst the "top three" for mortality. We are looking at a growing problem, as the number of HCC cases is on the increase. We need to intervene to reduce the overall mortality.'

How do AFP-L3 and DCP biomarkers help?

'Let's ask ourselves what the current standard for HCC diagnosis is, and what is wishful thinking. In Europe, diagnostic imaging is the gold standard – the only accepted procedure for early diagnosis. Guidelines state that patients with suspected HCC should be monitored, using ultrasound, CT or MRI scans. In Japan, however, there is clear evidence that biomarkers are important, or even decisive, for early detection. China also utilises biomarkers to improve early diagnosis.

'In any case, clarification of the causes of liver cirrhosis is indispensable, i.e. establishing whether there are viral causes, a non-alcoholic steatohepatitis or genetic factors. Conventional laboratory diagnosis with alpha-fetoproteins (AFP), the biomarkers typical for HCC, has now been enhanced with subtypes such as AFP-L3 (lectin-reactive AFP) and DCP (des-gamma-carboxy prothrombin): The three-way combination of AFP, AFP-L3 and DCP now also allows us to confirm HCC with significantly higher sensitivity and specificity in Europe.'

Tab: Sensitivities and Specificities for various markers (combinations) in early stage HCC (BCLC 0/A) and total cohorts

Markers/combinations	Sensitivity (ratio of correct positive markers in HCC) in %	Specificity (ratio of correct negative markers in non-HCC) in %
AFP, AFP-L3 or DCP alone	30-60 %	90-95 %
AFP and DCP	55-75 %	90 %
AFP and AFP-L3	62-82 %	85 %
AFP, AFP-L3 and DCP	72-85 %	85 %
GALAD-Score	67-85 %	93 %

What is the GALAD-Score?

'The above-mentioned markers have been known for a decade and a half. They have been established in Japan for years, but have not been accepted in Europe. The GALAD-Score will hopefully initiate a new evaluation of these markers as this new diagnosis algorithm links biological patient data (gender and age) with laboratory data AFP-L3, AFP and DCP.

'We carried out a prospective study in Essen that was published in December [Best J., Bilgi H. et al. The GALAD scoring algorithm based on AFP, AFP-L3, and DCP significantly improves detection of BCLC early stage hepatocellular carcinoma. Z Gastroenterol 2016; 54(12): 1296-1305]. The data presented clearly speak for the GALAD-Score. Our investigation was carried out over a period of several years and has shown that the individual markers improve the early HCC detection substantially, but the most significant improvement was seen with the combination of all three markers: It achieves a sensitivity of 85% and a specificity of 93%!

'Improved early detection, as seen with the GALAD-Score, cannot be achieved with dynamic imaging because it has limitations. The significance of ultrasound depends on the patient and examiner and varies according to the standard of equipment used. In turn, cross-sectional imaging procedures have economic aspects, because diagnosis via MRI or contrast enhanced CT has very different financial dimensions compared to biomarkers.

As a young internal medicine specialist in the 1980s, and funded with a research grant, **Guido Gerken MD** carried out research into hepatitis B virus-associated liver disease at the Pasteur Institute in Paris. A recognised expert in gastroenterology, Gerken has been Director of the Department for Gastroenterology and Hepatology for 20 years, and Managing Director of the Centre for Internal Medicine at the University Hospital Essen since 2005. The 64-year-old professor's treatment focus ranges from acute and chronic liver disease to transplantation. Some of his scientific questions centre around molecular-biological pathomechanisms in acute liver failure and also on the establishment of biomarkers in gastroenterology.

'The feasibility is also questionable: Can we really carry out diagnostic imaging procedures for a patient every three or six months? For a large country such as ours this is not practicable, and it is also far too expensive for the healthcare system.'

How is GALAD used in Essen?

'Thanks to the GALAD-Score, we can detect the early stages of HCC earlier and can therefore start the appropriate treatment earlier. The score is established in our central laboratory, CE marked and implemented in the laboratory information system (LIMS). We also offer the determination of AFP-L3 and DCP to other providers nationally, as a service, including Professor Michael Manns in Hannover and Dr Thomas Rasenack in Berlin/Potsdam. We'd like to see the procedure become established so that optimised early detection of HCC, combined with diagnostic imaging, becomes accessible to all.'

Global warming causes vectors for emerging diseases to spread far further north

Science can only react

The 'Transmission, Prevention, and Reporting of Emerging Infectious Diseases' program for the International Conference IMED 2016 in Vienna, this November, reflected events in the field of emerging diseases that have occurred over the last two years. Therefore, key congress topics included the Zika virus, the effects of global warming and the unusually high number of hospital-acquired infections (HAIs) caused by MERS-CoV. 'With all emerging diseases, science can only ever react to them,' Austrian virologist Professor Norbert Nowotny, a local scientific organiser and member of the scientific committee at IMED, told EH during the event.

Infections caused by the Zika virus present a very broad clinical picture. In 2015, when problems in the unborn babies of infected pregnant women were first observed, the cardinal symptom was microcephaly. However, it has since been discovered that the typical cerebral anomalies (reduced volume, calcifications or malformations of the cortex) can also occur in children whose heads are of normal size. The clinical picture has also been significantly extended, with malposition of the hands and legs now also frequently diagnosed. Furthermore, there are indications that an infection with the Zika virus can also lead to severe clinical symptoms in adults.

Considerable research is needed

'The diagnosis of the Zika virus, along with all other types of Flavivirus, is still a big problem,' Nowotny points out. With Flaviviruses, the time span in which the virus itself, or its molecular footprints (e.g. via polymerase chain reaction) can be detected is relatively short, and the serological tests available (Zika Virus Immunoglobulin-G and M) cause massive cross reactions with other Flaviviruses, such as with the pathogens causing Dengue fever, Yellow fever or West Nile fever. Considerable research is still needed, Nowotny explains.

Global warming causes the vectors for emerging diseases to spread further and further North. Although Aedes aegypti, the transmitter of Dengue fever and Chikungunya fever, has not yet managed a breakthrough into Europe, Aedes albopictus, a type of mosquito and close relative, has now spread across the entire Mediterranean, and can also function as a transmitter for both those diseases.

The international threat from holiday makers

Spread via infected holidaymakers bitten by this species of mosquito, there has already been a local Dengue fever outbreak in Dubrovnik, Croatia, and around 200 people developed Chikungunya fever in Ravenna, Italy. These outbreaks were only contained with the help of a massive chemical fight against the transmitters. 'This shows how important monitoring systems are,' Nowotny emphasises. This is not only important in the Mediterranean countries: 'Aedes albopictus is on the brink of crossing the Alps,' this leading virologist warns.

A problem from the Arabian Peninsula

'For hospitals, MERS-CoV is a big problem,' he stresses. There has been an unusual increase in hospital infections through this viral agent, which originates in the Arabian Peninsula. Only 5% of those infected had direct contact with dromedaries, which act as vectors for this infection, and the remaining 95% of infections were transmitted from human to human – within the family, in the community and frequently also in hospitals.

The hospital acquired infections were initially limited to Saudi Arabia but, in mid-2015, at least 186 people became infected in South Korea (of whom 36 died) after an infected traveller who had returned home from a trip to the Arabian Peninsula had sought help in several hospitals. 'There is not yet sufficient research into the problem of why there are so many hospital-acquired infections from MERS-CoV,' Nowotny reports.

Although travellers have now spread the virus throughout many countries there have not yet been any cases of hospital acquired infections involving the MERS Corona virus outside the Arabian Peninsula and Korea.

Norbert Nowotny PhD is a Professor at the Institute of Virology in the University of Veterinary Medicine, Vienna, and Professor for Virology at the Mohammed Bin Rashid University of Medicine and Health Sciences in Dubai, United Arab Emirates. The virologist researches all aspects of infectious diseases (particularly viral related) in humans plus domestic, zoo and wild animals. He also specialises in medical and veterinary medical entomology, viral infections spread by mosquitoes and ticks, emerging infectious diseases and zoonoses. His work as local scientific organiser and member of the scientific committee at the IMED 2016 is a role he has held at five previous IMED congresses.

Radiologist highlights imaging values

Identifying shipwrecked refug

Interview: Mélisande Rouger

Forensic radiology was, yet again, a central theme at ECR 2017, as Italian radiologists unveiled details of their work in the investigation following the shipwreck in the Mediterranean in April 2015.

An estimated 900 people lost their lives in what proved to be the worst disaster yet involving migrants, most of them refugees from Syria and sub Saharan countries including Gambia, Sri Lanka and Ghana.

For the first time, and in an exclusive interview with European Hospital, Italian radiologists in charge of forensic imaging spoke about their challenging task of identifying corpses that had been trapped under water for more than a year.

Dr Giuseppe Lo Re, a forensic radiologist from Palermo University, said he could only start imaging corpses in July 2016 because he had to wait for the rescue team to extract the bodies from the boat, which sank about 60 miles off the Libyan coast and 120 miles south of the Italian island of Lampedusa.

'The boat was overcrowded; there were seven people per square metre. For some victims we could only identify the bone structure, so we found out which area they came from, but not which country,' he explained. 'Skin colour was no indicator either as it got washed out; all the corpses were grey.'

Lo Re and his six colleagues (seen with three, far right) were loaned a mobile CT device for just ten days, in which they managed to identify 194 casualties.

The whole benefit of forensic imaging in that context, he said, lay in the impossibility of practicing an autopsy in a decomposed corpse. 'If you cut dissolved bodies, you will not be able to recognise anything once they are open.'

CT enabled identification of the casualties' sex better and faster than any anthropological study. 'Anthropology looks at particular bone lines or angles, a long and not so reliable procedure. We know the Caucasian type, but we don't know the other types so well.

'Our first days with the CT were difficult because radiology can't see these items very well. So we changed our point of view and searched for the radiological items of sex,' he explained. 'This was a score! We could prove that all of the victims were male.'

Lo Re and his team were also able to determine the age and death pose of the casualties, both key aspects in understanding why and how people died.

'With CT we can study the bone nucleus, which enables us to determine if the victim was older or younger than 18, a key information in any legal investigation ,' he said, adding: 'The death pose is also very important in forensic science because it describes the movement immediately before death and helps to understand causes of the accident,'

A lot of the victims died because they were stuck in a lower room of the boat and because of oil residuals or water leakage during the shipwreck.

Except for the short time they had to image the bodies, Lo Re and his colleagues faced additional challenges. 'We scanned the casualties 15 minutes each, 12 hours a day for six consecutive days,' he said. 'But we had to stop a whole day because of a worm invasion. I will never forget that terrible smell.

Under the water, the rescue team was also able to find wallets and phones, which helped identify who boarded the vessel. Besides their

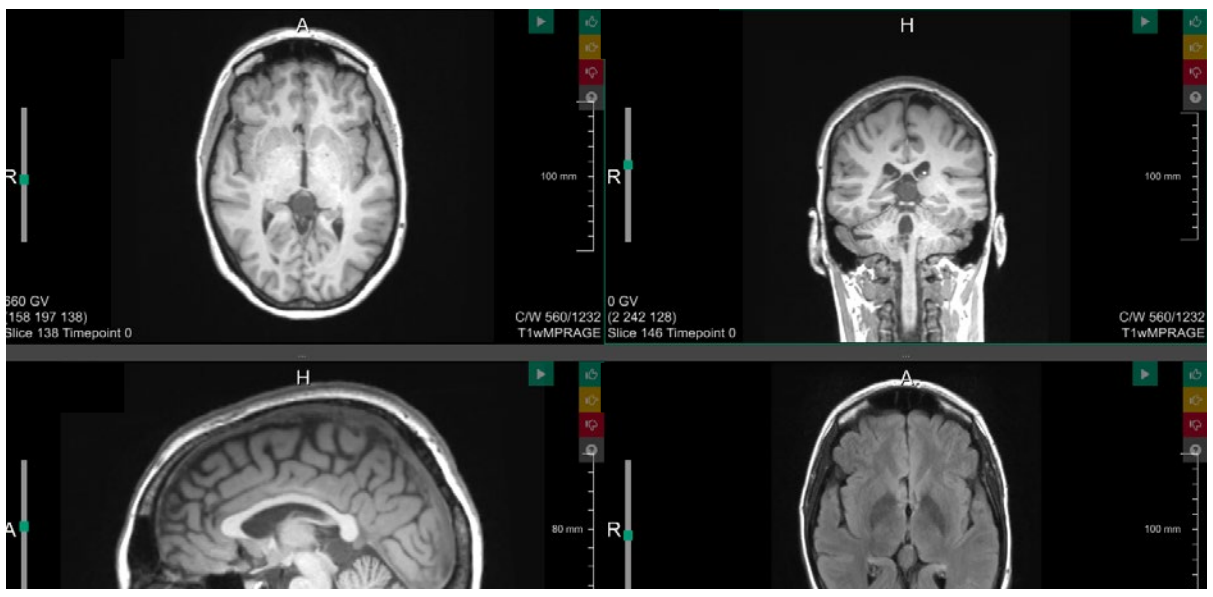
No biobank donor shortages: UK 500,000; Germany 200,000

Biobanks benefit research

Report: Michael Krassnitzer

By definition, biobanks are collections of specimens of human bodily substances, such as tissue, cells, DNA, proteins, blood or other fluids, with data on the donor attached.

They are well suited for large-scale population studies, for example to understand certain diseases better and to improve prevention, early detection and treatment. 'Biobanks should also include radiology image data,' says Professor Ritva Vanninen, at the Department of Clinic Radiology in Kuopio University Hospital, University of Eastern Finland.



Pineal gland cyst from NAKO (in most cases this type of benign cyst is clinically irrelevant) (c) NAKO

After all, these images contain quantifiable parameters with prognostic or diagnostic value. 'High quality image data and their reading by radiologists can be an important contribution to bio-medical research,' Vanninen emphasises, adding: 'vice versa, imaging biomarkers are validated by their use in research.'

Biobanks do not lack numbers

As of 2014, the member states of the European Society of Radiology (ESR) have been operating 27 biobanks with imaging content. The British UK Biobank, with 500,000 donors, and the German NAKO Health Study collection, with 200,000 donors, are among the largest of these biobanks. Smaller ones were established inter alia in the context of the Dutch Rotterdam Study (approx. 15,000 donors) or the German SHIP study (approximately 8,700 donors). Upon request, both UK Biobank as well as NAKO make their data available for research purposes; these data are thus the foundation of many a research project. Modern digital methods to gain data, radiomics and machine learning, the buzzwords here, may at some point in the future contribute to the analysis of biobank content.

However, biobanks are not only a source of knowledge; they also raise a number of ethical issues: when collecting data that originally are meant to clarify the relationships between risk factors and diseases and the course of diseases, quite frequently incidental findings show up. How to deal with such data? Professor Sabine Weckbach, Consultant at the Clinic of Diagnostic and Interventional Radiology at University Hospital Heidelberg, offered the answer last March, during a session at the 29th European Congress of Radiology (ECR 2017), in Vienna, Austria.

Weckbach is among the radiologists who analyse MR images acquired for NAKO. The so-called incidental findings, however, are neither incidental nor unexpected.

Invariably unplanned findings

Examinations with a 3-Tesla system, as prescribed for NAKO, will invariably yield unplanned findings. These may relate to acute diseases but also to diagnoses that are clinically irrelevant. 'This raises a number of ethical issues,' Weckbach points out. Which findings should be relayed

gee casualties

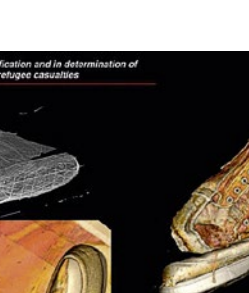
identification documents, many of the victims were carrying their university degrees with them. 'A lot of them were engineers or medical doctors; they travelled with their certificates in order to find work in Europe,' Lo Re explained.

The Italian anthropologists and pathologists in charge of the investigation are now faced with the complicated task of sorting out and identifying over 400 body bags, some of which, according to Lo Re, may contain as many as seven skulls. 'It's very hard to understand what you are seeing,' he said, describing the dilemma.

Even though he demonstrated that radiological assistance in mass disasters is possible when cooperating with anthropology and pathology, Lo Re is not sure his experience can be applied to further mass casualties, especially if there is no international cooperation to support the investigation.

'It was important to understand how people died. But this kind of work is too big; it requires a lot of money and time,' he pointed out.

Nonetheless this kind of work is crucial and must be carried out, he believes. 'The Italian government said it would give a name to each person who died. To quote anthropologist Professor Christina Cattaneo, from Milan University, who is coordinating the investigation, identification of the bodies is fundamental not only for the dignity of the dead but also the living.'



Radiologist **Sabine Weckbach**, studied medicine at Ludwig Maximilian University (LMU) in Munich, and today is Professor of Radiology and a consultant at the Clinic of Diagnostic and Interventional Radiology, in Heidelberg University Hospital. She specialises in musculoskeletal imaging, heads the Imaging Core Incidental Findings of Germany's massive NAKO Health Study, and is a member of the European Society of Radiology (ESR) Leadership Institutes.

to the donor and which of them should not be mentioned at all? How should these findings be conveyed, since physicians don't want to scare donors with false positives? Each biobank and each large-scale population study approaches these issues differently. NAKO donors for example are informed in writing; if the incidental findings point at acute conditions they are contacted by telephone. NAKO clearly defined which kinds of diagnoses will be passed on to the donor and which will not.

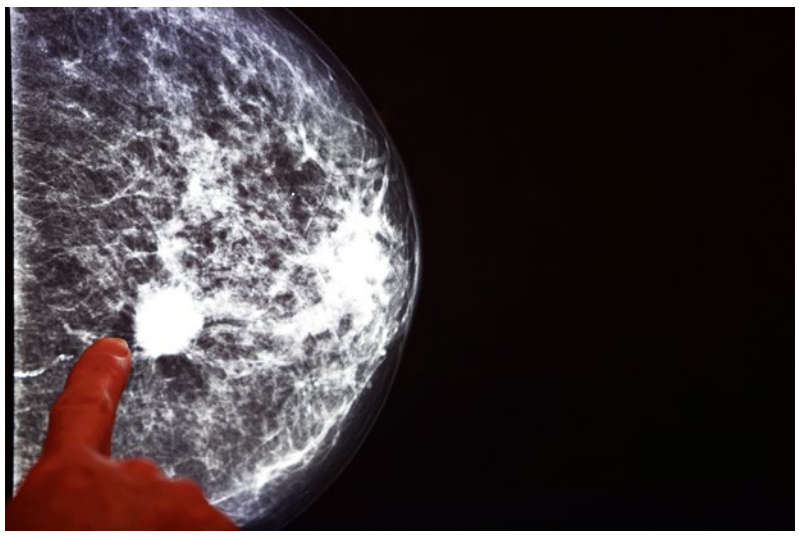
Demanding more research

In view of the fact that there are so many different approaches to incidental findings, inevitably Weckbach demands more research: 'Unfortunately, there is not yet a gold standard for handling incidental findings,' the radiologist point out. We have to work on drafting harmonised guidance and recommendations for dealing with incidental findings in population-based studies.'

Breast cancer screening programs

Benefits must outweigh risks

Report: Mélisande Rouger



Biannual mammography can help to reduce breast cancer mortality by 40% in women aged 50-69, but the benefits for women under 35 years old are questionable, eminent Spanish radiologists highlighted during a session held by SERAM, their national society of radiology, last November, during the International Radiology Day.

'Mammography today is the only method that has demonstrated capacity to reduce breast cancer mortality. Only in high-risk patients is MRI a proven screening method,' said Dr Marina Álvarez Benito, President of the Spanish Breast Diagnostic Imaging Society and a radiologist at the Reina Sofía Hospital in Córdoba.

Biannual screening reduces mortality by 40%

A study recently published in European Radiology showed that early detection through biannual mammography in a screening program reduces mortality by 40% in women aged 50-69. But there is less evidence for women aged 40-49 and over 70. 'Actually, for women between 35 and 40 there is very little evidence regarding associated risk factors or patient specific situations,' explained conference speaker Dr Carmen Carreira, a radiologist at Fuenlabrada University Hospital, in Madrid, and a member of the executive committee of SEDIM.

Cancer incidence is very low in a breast cancer screening program – on average five per thousand, Álvarez estimates. This means it is crucial to weight the benefits of screening against the potential risks, she added.

Benefits must outweigh potential risks

'The women who take part in a screening program are healthy and most of them will not develop cancer; it's very important to remember that benefits must outweigh potential risks.'

Both radiologists' comments came a month after the Spanish Society of Gynaecology and Obstetrics issued recommendations advising women to undergo their first clinical exploration together with a mammography as early as 35 years of age, to determine their breast type and morphology, an indication on their potential predisposition to develop cancer (http://www.efesalud.com/noticias/primera-mamografia-los-35-anos/).

The SERAM asked all parties involved to avoid sending confused messages on breast cancer screening program, which was initiated in the early 1990s in Spain; instead, women should be informed in a clear and transparent manner.

'The chance of saving a life thanks to early breast cancer detection is 100% superior to the possibility of death caused by the radiation used in the examination,' the society wrote in a release.

Benefits of mammography include mortality reduction and the possibility of conservative treatment. Most common potential risks would be false positives, over diagnosis, overtreatment and the detection of harmless lesions that will trigger useless biopsies and anxiety in the patient.

'Benefits will only affect a small part of the women whereas potential risks will affect all women who take part in a screening program,' Álvarez pointed out.

The possibility for false positives in a woman who has taken part in 10 screening programs, i.e. during 20 years of her life, is around twenty percent.

The only way to improve screening efficiency is to have quality controls at every stage of the program, Álvarez believes.

The European guidelines offer a wide range of indicators to evaluate false positives, including the number of recalls. 'To have what we call a good false positive rate, recall rates should not rise over 7%. For a program to be efficient, 70% of the women should participate on a regular basis, and not just one time,' Álvarez said.

Know the route from primary to secondary care

Adherence to the program is key and doctors must follow their patients between primary and secondary care to guarantee the proper chain of actions. 'It's relevant to know a woman's circuit from the detection of a lesion in primary care to her management in secondary care,' she said. 'One key element here is to communicate screening results within 15 days of the examination.'

Radiologists and radiographers should also undergo dedicated training in breast imaging. Technicians must know how to position and compress the breast, and be able to assess examination quality.

'For radiologists the learning curve is extremely long,' she emphasised. 'They need to dedicate a very significant amount of their time to training and practice.'

Marina Alvarez Benito is Director of the Clinical Management Unit of Radiology and Breast Cancer at Reina Sofía University Hospital in Córdoba, Spain. She is also the current President of the Spanish Society of Diagnostic Breast Imaging. The expert received a bachelor degree and doctorate in medicine and surgery from Córdoba University.

A former member of the Board of SERAM, she currently works in partnership with the society.

The core of patient satisfaction & workflow efficiency

Communication is vital

Dr Massimo Calabrese, head of the Complex Operative Unit of Diagnostic Senology in Genoa's San Martino Hospital, examines aspects of stereotactic breast biopsy procedures and workflow and the need for improvements in certain areas of breast diagnostics.

Healthcare administrators constantly seek investments to drive up revenue. When making such decisions, two primary aspects to consider include workflow efficiency and patient satisfaction.

These important factors share a common thread that is equally necessary for decision makers to keep uppermost in mind: At the core of advancing any workflow scenario, and patient experience, comes a useful examination of communication.

This certainly holds true in radiology, particularly when it comes to the stereotactic breast biopsy procedure. As head of the Complex Operative Unit of Diagnostic Senology in San Martino Hospital, in Genoa, Italy, I have performed numerous breast biopsies, observing both the wonderful advancements in breast screening and biopsy technology, as well as areas where advancements can still be made. I do believe there is significant room for improvement when it comes to communication throughout the stereotactic breast biopsy process, and I have witnessed how this current gap ties directly to workflow efficiency and patient satisfaction.

The lightweight Affirm system integrates with the Hologic tomosynthesis system in under a minute

Forms of communication

Communication comes in all forms throughout the breast biopsy procedure.

Technologists and radiologists, and patients— and even the informatics systems— one way or another, all communicate with each other. This is especially true for the sample verification process during a biopsy.

Once the suspicious breast tissue is extracted from the patient, the technologist must verify the appropriate samples were gathered on a tomosynthesis unit, which is sometimes already in use by another colleague, who is simultaneously screening a patient for a regular mammogram exam appointment, in a different room.

As such, radiologists and technologists must constantly communicate with one another—taking turns, waiting and sharing equipment for their respective patients, which is time consuming. This can become particularly cumbersome if the initial breast biopsy samples are not verifiable, in which case the process of extracting, waiting and verifying repeats, until the acquired samples prove positive on the tomosynthesis unit.

With each repetition, the technologist travels back and forth between the biopsy procedure room and the area with the sample verification technology, which may interrupt the workflow of those who are using the equipment for breast screening patients. The additional time spent travelling to and from the verification technology can take an average of five to 10 minutes per biopsy, which accumulates throughout a day of procedures.

Furthermore, each time technologists must take the time to separate the tissue samples into smaller specimens for pathology to properly communicate results.

The entire sample verification process—from beginning to end—can contribute to a significant delay in scheduling for radiologists. This may drive radiologists and technologists to be in more of a rush to catch up on their next patient, leaving less time to really connect, and communicate, with their current patient, creating a less personal patient experience and underwhelming patient satisfaction scores.

Open the lines of communication

While breast imaging technology has come a long way, it is clear that the stereotactic breast biopsy procedure can still be improved, particularly when observing the overall communication issues throughout the process. As healthcare administrators search to make worthwhile investments for their companies that improve workflow efficiency and patient experience, they should consider their current states of communication: Does their equipment read and communicate information in an efficient way with other systems, or are extra steps involved? Does the radiologist have enough time to communicate with patients in detail, ensuring they feel as comfortable as possible and essentially to understand what they are experiencing along the way?

The answers to these questions are very telling and, in this case, demonstrate that even medical device manufacturers should be considering communication issues because they develop products to appeal to administrators who demand superior workflows and more satisfied patients.

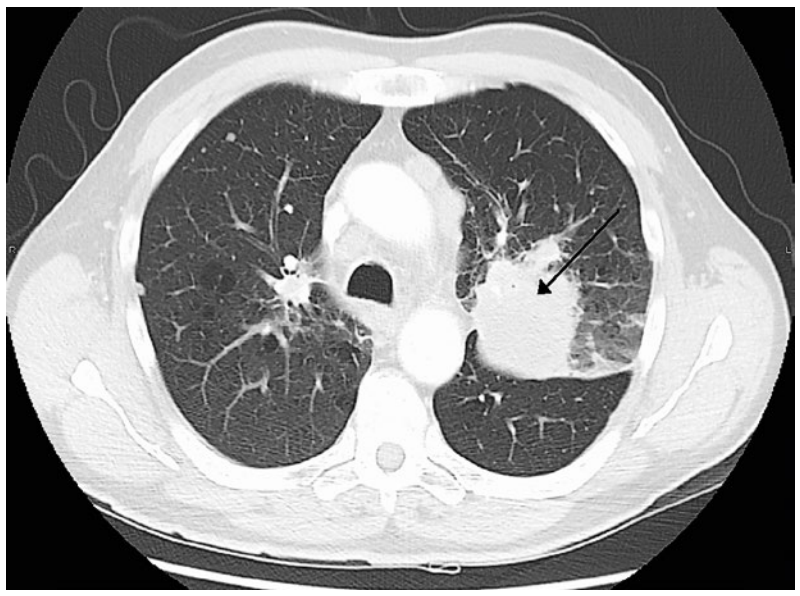
Once administrators are fully in tune with how their facility's components are communicating with one another, they will be able to make the right investment decisions to lead to prosperity.

Dr Massimo Calabrese is the Chief of the Complex Operative Unit of Diagnostic Senology at San Martino Hospital in Genoa, Italy, a national institute for research and treatment of cancer (IRCCS). IRCSS A.O.U. San Martino is a reference site for a volume of two million people. Every year the institute receives 45,000 women and performs 500 tomography guided vacuum assisted breast biopsies (VABB), 800 ultrasound breast biopsies and 50 VABBs under RM.

Controversy: lung cancer screening

High costs prevent programmed scans

Report: Michael Krassnitzer



CT image of a non-small-cell lung carcinoma in the upper lobe of the left lung

Lung cancer is the cancer that causes the highest mortality worldwide, claiming an estimated 1.7 million patients annually, with 270,000 of those deaths in Europe. According to statistics, in 2012, 3,673 people died from lung cancer in Austria alone. Why such large numbers? The first symptoms of this disease only show up once the cancer is already at an advanced stage. The five-year survival rate is just 15%.

Thus the notion of a screening programme, such as regular CT scans for those at risk, appears to be obvious. The assumption is that it should help to diagnose and treat many cases of lung cancer at an earlier stage. 'Although, at first glance, lung cancer screening may seem an obvious concept, introducing this type of programme is controversial,' explains Professor Stefan Diederich, Senior Consultant at the Institute for Diagnostic and Interventional Radiology at the Marien Hospital Düsseldorf, and President of the International Cancer Imaging Society (ICIS). This type of screening programme and the respective recommendations are available in the USA, but not in Europe.

In the 1960s and 70s, breast cancer studies were carried out into the benefits of screening. Several randomised studies, which in those days were based on chest X-rays, showed that screening programmes significantly increased the number of cases of lung cancer being discovered at an earlier stage, but patients saw no benefits: Screening did not lower the mortality rate.

Studies carried out in the 1990s, based on CT scans, showed the same result. Although more cases of cancer were discovered at an earlier stage no effect was seen on mortality. Only in 2010, when the USA's National Lung Screening Trial (NLST) was published, was there evidence that screening lowers mortality.

However, European studies have not yet been able to confirm the respective effect. This apparently also applies to the Dutch-Belgian NELSON Study, carried out from 2003-2012, with no results yet comprehensively published. Diederich knows the reason: The NLST study participants were at a higher risk right from the start because they were older and consumed more tobacco. At the start of the NLST study the participants were aged between 55 and 74 and had been smoking for at least 30 pack years, i.e. the number of cigarette packs consumed per day multiplied by the number of years smoked, whilst the participants in the Nelson study, as well as other European studies, were aged between 50 and 74 at the beginning and were included from 15 pack years upwards.

The consequences of the NLST study in the USA were acknowledged and lung cancer screening for those with more than 30 pack years was introduced. Not so in Europe. 'There is not a single screening programme in Europe and no efforts to introduce one either,' Diederich points out. Ostensibly, this is because not one European study has yet been able to demonstrate the benefit of lung cancer screening. However, the truth is probably somewhat different. 'The real issue is around the costs involved,' the radiologist believes. 'Each case of lung cancer, discovered in the context of screening, results in additional costs for the healthcare system.'

If suspicious lesions are discovered during screening this leads to further diagnostic steps, all of which cost money. In addition, the cost of cancer drugs has literally soared over the last few years. 'Screening may have its benefits for the individual,' Diederich concludes, 'but society as a whole is faced with higher costs.'

Professor Stefan Diederich is Senior Consultant at the Institute for Diagnostics and Interventional Radiology at the Marien Hospital Düsseldorf. A specialist in radiological diagnostics and diagnostic radiology, he studied in Münster and Heidelberg and trained in Münster and Cambridge. He is President of the International Cancer Imaging Society (ICIS); consultant for numerous scientific publications and recipient of the Eugenie and Felix Wachsmann-Prize presented by the German Radiological Society.

Teleradiology provider wants to include pathology in the equation

Integrate technologies to upgrade reports

As the demand for imaging studies booms and digital pathology takes off, it is becoming necessary to look at the interactions between radiology and pathology in telemedicine, an expert explained during the Radiology Triangle Madrid meeting early this year.

Demand for teleradiology services is growing fast and the business is expected to generate US$3.8 billion in 2019.

'We exist because of the increasing gap between the demand for imaging work and current possibilities,' said Alexander Böhmcker, CEO of Telemedicine Clinic (TMC), a teleradiology provider with a network of 195 radiologists in Sweden, the United Kingdom and Australia. 'Small hospitals now have a huge challenge to attract talent locally.'

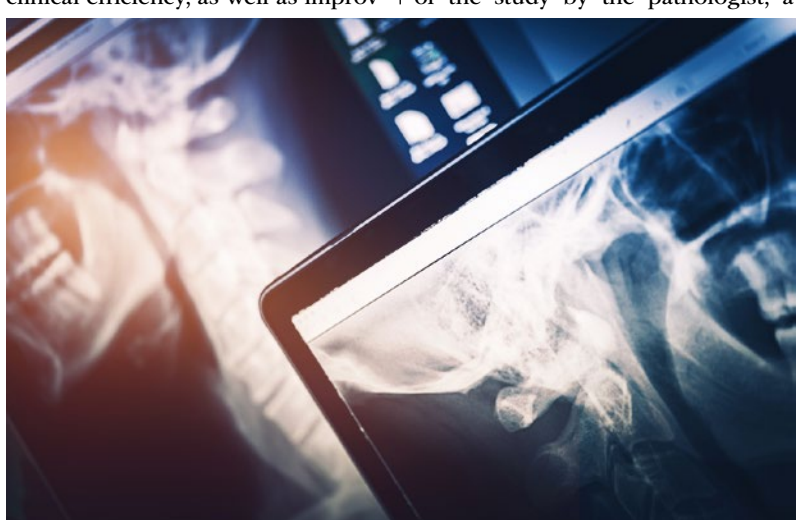
Organisational issues apart, teleradiology makes sense when there is a need for sub-specialisation, the businessman told key radiologists from Spain and overseas – all personally invited to the meeting. 'This is how we can connect many different cases from different hospitals and route them to the best available specialist. The main advantage of teleradiology is sub-specialisation, because it leads to increased effectiveness and better outcomes.'

Sub-specialisation is also relevant for telepathology, an emerging area that TMC has started developing with a network of seven pathologists, who provide reporting services, second opinion and training services.

The company has issued 40,000 digital histopathology reports so far and it is keen to develop a synergy between radiology and pathology in the future.

'When we think about the integration of teleradiology and telepathology, we also think of applied sub-specialisation to pathology,' he pointed out. Sub-specialisation may be even more important in pathology because pathologists often wonder who checks the results afterwards. Having second readings and the radiologist providing an opinion on their reports would be of tremendous help.'

In the literature there is a large amount of evidence for specific needs for radiology and pathology integration, e.g. in breast cancer, lung diseases, bone and soft tissue diseases and prostate cancer, Böhmcker argued. 'It's about using the report data in larger cohorts and clinical efficiency, as well as improving the reporting environment and the preparation of tumour boards. It can also help in data mining and research.'



Integrating pathology results into the teleradiology report makes sense from a referring clinician and patient perspective, and matches the needs of the customers, Böhmcker explained. 'There are situations in which hospitals ask for both services at the same time.' Combining teleradiology and telepathology in a single report would be relevant in areas such as mammography.

'Once the biopsy has been performed, and before the pathologist creates his or her initial report, he/she would have access to the radiology report. After the interpretation of the study by the pathologist, a final consensus report would be created.'

Pathology results could easily be added to the structured report, to evaluate discrepancies between the reports of both specialists. 'In the end,' Böhmcker said, 'we would have an integrated report combining all the available clinical data. We would have a pathology summary with key images, the same as for radiology.'

TMC is currently working with two Swedish hospitals on two reporting platforms and technical solutions to combine both pathology and radiology findings. Using common reporting platforms would enable specialists to exchange information and feedback before and after they read each other's reports. It would also grant the provider direct access to the final report and improve its adherence to outcome.

'While a teleradiology company can be very far from the outcome results, an integrated solution can bring it very close,' Böhmcker pointed out.

Developing common reporting platforms requires a lot of technical effort and the models used by TMC are locally based. The company is now working on a scalable solution.

Another challenge is that the structured report (SR) is still not very popular among radiologists, despite its benefits over free text, according to Böhmcker.

'The SR first appeared in the literature in 1922, but its application today remains limited. However, standardising information offers many opportunities, for instance better communication and the possibility to perform data mining for peer review, audit, teaching and research. And most importantly, clinicians like it.'

To help radiologists switch to the SR, TMC is working on making it user-friendlier by clearing some of its unused sections and using voice commands.

Teleradiology, on the contrary, has become more accepted ever since its introduction in 2009. 'Acceptance has grown,' he confirmed. 'The discussion is no longer on whether we want to have teleradiology or not, but rather what's the best combination – onsite and remote radiology, and when and how to best use teleradiology.'

Teleradiology still needs to overcome a number of difficulties including access to clinical information, communication with the referring physician and outcome access.

'This stresses the importance of integrated technologies and structured reports. Image transfer is not an issue anymore,' Böhmcker concluded. (MR)

Alexander Böhmcker, CEO of the Telemedicine Clinic (TMC), completed his Lic.oec. degree at the University St. Gallen, Switzerland and his MBA at ESADE in Spain. Prior to joining Telemedicine Clinic he had Business Development and Finance leadership roles in the Deutsche Bank, BMW and GFT. He joined TMC in 2008, managing in close collaboration with the co-founders. Today the firm leads European teleradiology and pathology, providing around 120 hospitals in Scandinavia and the UK with diagnostic reports, delivered by a network of over 200 sub-specialist radiologists and pathologists. He is also co-founder of the Spanish Chapter of 'Conscious Capitalism'.

PART 1: What keeps a hospital's immune system healthy?

A strong IT security system

Report: Marcel Rasch

'You can't get 100 percent security, you can't avoid all risks – but you can improve security tremendously just by considering some rules,' explains Torbjörn Kronander, Board member, CEO and President of Sectra AB. When hundreds, or even thousands, of machines and computers are connected with each other and diverse operating systems coexist with the PACS, hospitals have real IT security problems. In addition, today all imaging equipment is no longer simple machines; devices are complex computers that could become infected by a virus. The problems hospitals face and what options they have to address those challenges were discussed by European Hospital and Dr Stefan Bücken, IT safety advisor in the Medical Centre for Information and Communication Technology at Erlangen University.

IT security can be easy

Ideally, a secure system would be totally isolated and blocked but, because there has to be an internet and data has to be exchanged, this situation is unthinkable. 'We should see IT-security not as a curse, but compare it to our immune system,' suggests IT-expert Torbjörn Kronander. 'When we are born, we don't know which germs and viruses will attack us in our lives, but the immune system has a mechanism to detect infections and take care of them. This is actually what a good IT-security system does; it monitors the environment, detects infections or potential harm and applies a mechanism to get rid of those.'

Unfortunately, most hospitals still handle their IT-systems incorrectly. They connect every workstation and every computer not caring enough about potential risks. 'Hospitals must understand the seriousness of this situation and that they need to invest some time on reorganising their systems. Practically speaking, in PACS workstations, for example, never open private stuff, webpages, email and documents with attachments. Attachments can always contain contagious active elements,' Kronander points out. Although zip-files carry the biggest risk because antivirus-software often cannot detect potential harm in them, Word-documents, Excel-sheets and even pdfs can also be contagious. 'If you really want to stay safe, open and save documents only in a plain-text format like .rtf,' he advises. 'Never click "yes" to enable an active element in an attachment of a document.'

'When a hospital looks for an IT-consultant, the management should ensure somehow that this consultant evaluates the entire system, considering all potential risks. He will also tell you that no user should have administration rights on their computers. There must be some kind of user identification and authorisation to access a workstation or a computer. There always must be log-in and log-out,' Kronander points out. What sounds familiar to people who have paid attention at least to some IT-security subjects, appears to be totally new to other hospital staff members. 'You won't believe what we sometimes experience,' the IT-consultant reveals, 'In some hospitals, kids are coming to work with their parents and start playing computer games to dawdle. You never know what potential harm is on that system thereafter.'

According to Kronander 'the most common security risk today are either USB sticks which inject a code into the system (a safe computer should have all USB ports glued by epoxy) or Phishing attacks, where users are fooled by a seemlingly correct email, often appearing to come from their boss or equivalent safe sender, into clicking on webpages with malicious content that injects malware into their system. Carefully setting up a system helps to prevent infections. 'A lot of hospitals re-install their operating systems every single night to prevent potential harm on their computers. This means that documents in general cannot be saved locally. By having a completely new systems set-up every night, these hospitals avoid any risk of potential viruses that have been saved locally on a local computer during a working day.'

Medical technology comes with deeper risks

The biggest challenge, however, is medical devices such as MR and CT, because these are not simple machines anymore; they are complex computers. 'The problem here is that to receive FDA approval, the industry has to nearly freeze the version of the operating system they use. While Microsoft releases an upgrade for Windows every week, to take care of new threats, the version of a MR or CT system cannot be upgraded regularly enough without violating FDA regulations at the same time,' Kronander explains. 'This is a big problem the industry must take care about and for which we don't have an appropriate solution up to today.

'Is must also be made known that hospitals are prime targets for "Ransom ware" where the hard disks of all available computers are encrypted and the key for decryption is only made available after a very sizeable amount of money has been paid to some account somewhere. In normal companies the reaction most often is to get a backup and knowingly lose a week of work or so.

However, in hospitals, if the wrong medical devices are infected patients may even die.

Therefore several hospitals have paid, and this has lead to even more attacks. It should also be noted that these attacks are no longer the work of a 14-year-old hacker somewhere. They are made by organised crime, the IT mafia.'

With a doctorate in technology and Masters in Business Administration, **Torbjörn Kronander PhD** was the founder of the medical area, became an executive vice president of Sectra AB, and President of the company's Medical Systems business section, accounting for 88% of Sectra's sales. In 2012 he was appointed the company's CEO and President. Today he is the largest shareholder of the company.

Part 2: What keeps a hospital's immune system healthy?

The User Perspective

Report: Marcel Rasch

'From an IT perspective, medicine is now networked to a very large degree, no matter which departments you look at,' says Stefan Bücken, IT Security Officer at Erlangen University Hospital, Germany. Just a few years ago it was still possible to look at individual medical technology systems in isolation, but this is no longer possible. Medical technology systems must exchange data to make diagnoses and results available for patients' medical care,' he emphasises.

'From an IT department perspective, a hospital should be treated just like any normal company. We face the same technical problems with regards to systems networking as the automotive and other industries face. However, we do need to take into account the extended risks of medical treatments. And technical concepts for the comprehensive operation of networked systems in medical technology are still in their infancy."

The expert sees one current problem in the increasing utilisation of cloud solutions. 'Making these solutions completely secure is the great challenge we currently face.' Bücken also believes that the so-called 'Medical Device Isolation Architecture' to safeguard networked medical technology is not future proof. 'If you look at developments over the last few years, we no longer look at defined areas of IT. We can no longer run individual departments, such as radiology, with a designated MRI scanner and defined interfaces, but are moving increasingly in the direction of the utilisation of networked service structures, which go beyond individual systems limitations.

'Apart from the utilisation of cloud services, there is also the large area of systems part of the Internet of Things (IoT), which constitute a particular challenge. Data protection and data security issues here are also similar, no matter whether we are looking at networked infusion pumps or the evaluation of diagnostic data somewhere in the cloud.'

The need for discussion

How safe can we make hospitals? Complete screening blocks medical advances, but an open-door policy is no solution either, Bücken says. Any disruptions to the running of a hospital can quickly result in life-threatening effects for patients. 'We need to think very seriously about these structures in the near future,' he emphasises.

The publication of the IEC 80001-1 norm a few years ago was a first step in the direction of improved security for medical technology systems within networks. This norm describes risk management for the networked operation of medical devices. The German IT Security Law, the EU-Cyber-Security Guideline (NIS Guideline) and the EU Data Protection Law, which will be legally binding from 2018, will lead to a wider discussion around the increasing networking of IT in the healthcare sector. 'However', says Bücken, 'management systems focused on organisation are only part of the solution, as paper is often very persistent.

'We also require coherent basic technology concepts that need to be consistently applied. Although there are already some sustainable technical safeguarding procedures, all suppliers of medical technology systems are more or less working according to their own rules. In hospitals, however, these concepts must be amalgamated into a meaningful whole. It remains to be seen whether the current, diversified solutions will pass the test of time.'

A rift between users and manufacturers

So much for the users' perspective – 'the manufacturers' perspective looks very different,' Bücken points out. 'The development and distribution of medical devices is particularly regimented. Manufacturers must abide by a comprehensive set of norms, utilise risk management procedures and undergo licensing procedures. Each change to a system requires companies to carry out repeated, comprehensive control and validation processes. In the context of the innovative environment of medical technology and the background of forever changing IT threats, this is an approach unlikely to last in the medium term,' he explains.

Specifically, the orientation towards international markets often makes it difficult for manufacturers because each country has its own licensing procedure. 'It's understandable that manufacturers, once they have finally had their products approved, ideally don't want to implement any changes. If they were to do so, this might entail having to go through the entire licensing procedure again,' he points out. 'On the other hand, however, the lack of regular software updates is dangerous from an IT security point of view. A hospital network will continue to develop gaps in security that need to be adequately filled. We are currently discussing these problems with medical technology specialists because we continue to use Windows WP at Erlangen, which, as everyone knows, Microsoft officially stopped supporting in April 2014.

'Therefore, manufacturers try to resolve the problem through risk management and read-only systems; but this hasn't been thought out enough. Although the system returns to its original status after a restart it will be very vulnerable and easy to attack as long as it remains active around the clock, without any further security measures being implemented.'

'Or, imagine a hospital where all systems run on Windows 10. Depending on the system version chosen, the hospital computers, based on Microsoft's update strategy, would have to undergo operating system updates every six months. In a complex, heterogeneous IT environment, as found in hospitals, this cannot work. Manufacturers and users must engage in a much more

Driving the mhealth market for many years to come

Patient connectivity to server or cloud

Anders Frick is a Senior Analyst with a Media Technology Master's degree from Linköping University and a Technology Management MBA degree from National Chiao Tung University. His areas of expertise include IoT, smart homes and mHealth. Before being an analyst, he was a journalist for over a decade, covering technology, economy and innovation.

Over seven million people were using remote monitoring in 2016, mainly for cardiac rhythm management (CRM) and sleep apnoea therapy. The number of users will soar as they can increasingly connect to servers and clouds, Swedish analyst Anders Frick predicts.

About 7.1 million patients were enrolled in mHealth care programs, in which connected medical devices are used as part of the care regimen to monitor patients remotely, as of 31 December 2016, according to a recent report from the Sweden based M2M/IoT market research firm Berg Insight.

The firm also estimated that the number of remotely monitored patients would grow at a compound annual growth rate (CAGR) of 50 percent to reach 50.2 million by 2021.

mHealth is growing fast, but these figures are still a long way from what the market could look like if every potential patient were using the available technology, according to Anders Frick, senior analyst at Berg Insight. 'We have estimated that more than 200 million people around the globe would benefit from remote monitoring, so seven million is actually still a pretty small number,' Frick told European Hospital.

Most commonly used remote monitoring solutions are currently focusing on CRM and sleep apnoea therapy. In terms of revenue, these areas generated €5.1bn in 2016, and names like Medtronic or ResMed have become references. All areas included, remote monitoring generated €7.6 billion in 2016.

Profits are expected to quadruple over the next five years, as opportunities for remote monitoring multiply. 'We expect revenue to rise to €32.4 billion in 2021, boosted mainly by CRM and sleep therapy, but also medical adherence, glucose level, telehealth and other monitoring devices,' Frick predicted.

Patients with chronic welfare diseases such as obesity, diabetes and hypertension represent the core of remote monitoring users and could potentially use the technology for other diseases related to their condition.

The elderly are also increasingly using monitoring devices, as the world population grows older. However, since many of this group have never owned or used tablets or mobile phones, companies should worry about developing appropriate strategies, Frick pointed out. 'Technology and user interfaces are becoming better and better. Companies that want to be, and stay, on top need to provide good user interface and user experience,' he said. Non-prescribed monitoring and healthcare consumerism could also help boost sales in this sector, he predicted. 'People today use equipment that could track their activities, their weight, their blood pressure, etc. Because of this, when people, by any reason, become patients, they are already pretty used to track and measure themselves, and the threshold for using medical graded tracking equipment is much lower than otherwise.'

The market should continue to grow under the impulse of clinical trials requiring increased monitoring, incentives from insurance companies and payers, national health systems supporting remote monitoring and new clinical evidence based on cost effectiveness.

The biggest trend in the market now is connectivity: meaning equipment used by the patients is connected to a server or the cloud. The patients are also likely to use more and more their own tablet or phone for remote monitoring. 'The trend that we see is that more and more equipment will use the patient's own cellphone, tablet, etc. to connect the medical equipment to the server or cloud,' he said.

As health-related apps and devices generate potentially huge amounts of data, and this data becomes increasingly shared with third parties like clouds, privacy and protection will remain major concerns for the industry.

'When the line between medical devices and health gadgets becomes blurred, traditional companies and start-ups try to position themselves as important stakeholders in the mHealth data ecosystem. National personal health records systems; device manufacturing companies, and independent app producers and tech giants such as Google, Apple and Microsoft are common options for data storage.

'One trend is to share data in third party clouds. It's important,' Frick concluded, 'for end-users, doctors and care giving institutions to choose a place where as many standards as possible are respected, and where it is as easy as possible to export the data.'

Formerly head of the Systems Technology Department at Erlangen University Hospital for eight years, a role that included coordinating operational IT security, **Dr Stefan Bücken** became the hospital's IT Security Officer in 2015. He is a qualified hospital manager and member of the UP KRITIS 'Medical Care' working group. Along with his medical IT skills Bücken also has a professional background in environmental and laboratory IT and in bioinformatics.

intensive dialogue in the future.'

The liability issue remains unresolved

As is so often the case, the devil is in the detail. 'The issue of liability is very interesting. The hospital obviously has a duty of care. The Act on Medical Devices, however, states that manufacturers must take responsibility for their products and must clearly define how they can be used safely. But a hospital integrates such medical devices into a heterogeneous IT environment. Competing specifications issued by different manufacturers can quickly lead to mutually exclusive configuration requirements. Making the technology required for the provision of excellent medical care available to medical staff is a real challenge,' Bücken confirms.

One certainty exists. In this time of highly networked technologies, hospitals – with their inevitable constraints and security needs – will be unable to run alongside faster paced technological developments.

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Procedure may establish liver as alternative access in catheterisation

NEW: Pulmonary valve placement via a child's liver

A Spanish team has, for the first time, successfully placed a pulmonary valve using catheterisation through the hepatic vein in a paediatric patient. Specialists believe this type of intervention could become an interesting alternative when traditional access points are not available.

Report: Mélisande Rouger

In what will probably pave the way for further similar interventions, a team at Virgen del Rocío Hospital in Seville has just successfully placed a valve inside the pulmonary artery of a child with congenital heart disease, by entering a catheter in the hepatic vein.

Only the second procedure to be performed

This is the first time this type of intervention has been carried out in a paediatric patient in the world and the first time it has been performed in a patient in Europe. Before that, only one adult patient had undergone this procedure in the USA.

Dr Álvaro Iglesias López has worked as a vascular and interventional radiologist at Virgen del Rocío Hospital since 2004. He performs diagnostic and therapeutic studies in peripheral vascular, hepatic and renal pathology, and procedures involving the placement of central and peripheral venous accesses. He also serves as a general radiologist and carries out CT, MR and ultrasound examinations.

Dr José Félix Coserria Sanchéz, a paediatrician who specialises in cardiology and haemodynamics at Virgen del Rocío Hospital, coordinated the intervention.

He explained the challenges his team had to face for this type of catheterisation, which is traditionally performed from the femoral or jugular artery. 'It's very rare to use liver access for this kind of intervention,' he explained during our European Hospital interview.

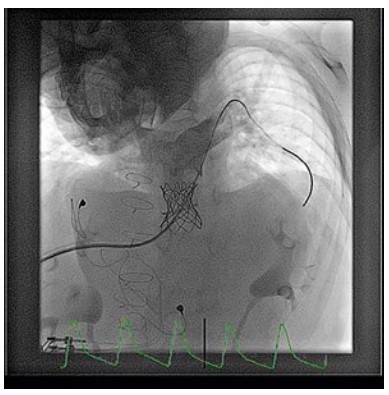
Doctors chose to place the valve through the hepatic vein because the eight-year-old patient, whose implant was failing and needed urgent replacement, had already received multiple surgeries to treat a complex heart disease he had been suffering since birth, called Tetralogy of Fallot (TOF).

The haemodynamics team unit benefits from two years' experience

Opening the patient again with traditional surgery simply presented too many risks, Coserria explained. 'The child had problems in his trachea and oesophagus. Traditional access points were thrombosed, so they were not viable.'

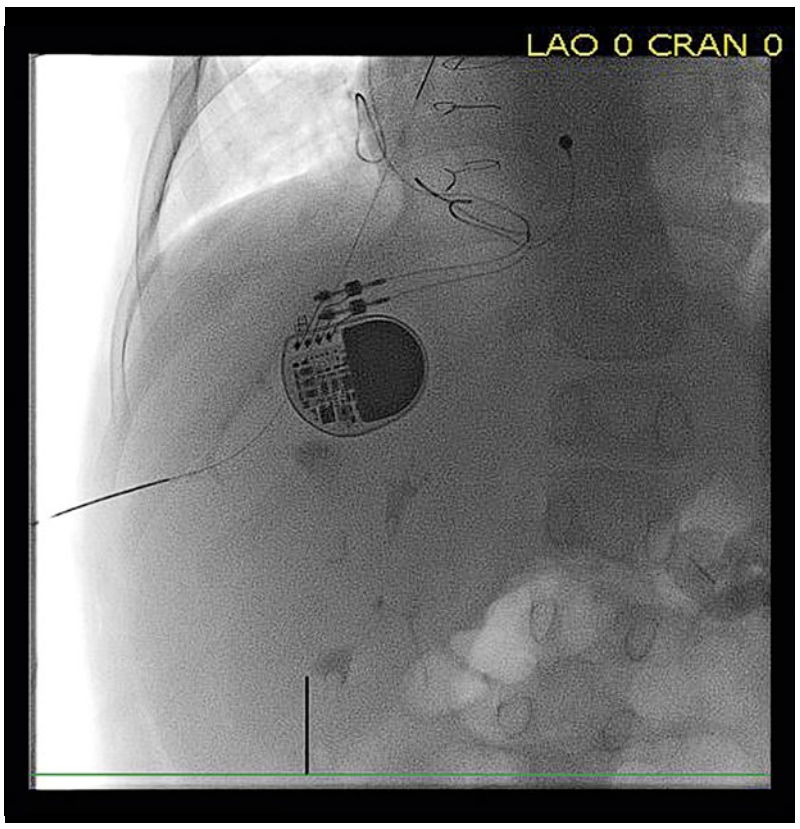
Catheterisation has been widely used since 2001 to replace cardiac valves when surgery proved inefficient. The haemodynamics unit at Virgen del Rocío Children Hospital has been using this technique for the past two years and performs three to five interventions a year to replace valves through the pulmonary artery.

Contrast injection performed in pulmonary trunk, in which previous dysfunctioning pulmonary valve shows severe regurgitation towards the right ventricle



Contrast injection performed in the pulmonary trunk, in which correct function of implanted valve with catheterisation inside the stent is observed

Liver access is sometimes used in catheterisation for congenital heart disease, but in these interventions physicians usually insert a small catheter through the liver and up to the heart. However, this time, due to the large valve size, doctors had to by-pass the organ so as not to damage it. 'We could have torn the liver or caused important bleeding had we touched the organ,' Coserria explained.



Access wire to right atrium by transhepatic puncture

This is unique in that a child with a congential heart condition is involved

To ensure a successful outcome, Coserria performed the intervention with another haemodynamist, Dr Zunuzegui from Gregorio Marañon Hospital in Madrid, and vascular radiologist, Dr Álvaro Iglesias from Vigen del Rocío, who provided image guidance with fluoroscopy at the time of placing the catheter inside the hepatic vein.

Iglesias has performed many liver catheterisations in his career. He also stressed the uniqueness of the procedure in the context of a paediatric patient with congenital heart disease.

'Catheters we traditionally use in liver access interventions are in the 8 Fr. range. This time we had to use a 22 Fr. diameter, so about

Long-term home monitoring system reduces risk of all-cause mor

Success for pacemaker r

Biotronik Home Monitoring is an award-winning remote cardiac monitoring system that automatically collects data from a patient's cardiac device, enabling the physician to review cardiac function independently of in-office visits. According to results presented at last year's ESC from the TRUECOIN randomised controlled trial, the system reduced the risk of all-cause mortality by 38 percent in ICD patients after one year, and there was a 36 percent reduction in the combined risk of all-cause mortality and hospitalisation for worsening heart failure.

The meta-study pooled the results of 2,405 patients from the TRUST, ECOST and IN-TIME trials.

Trust included 1,339 ICD patients randomised 2:1 to remote monitoring or conventional follow-up at 102 centres, concluding that Biotronik Home Monitoring reduced in-office visits by 45 percent.

Ecost showed how continuous monitoring reduced the rate of patients who experienced inappropriate shocks by 52%.

In-Time researchers evaluated heart failure (HF) patients with the remote monitoring system, demonstrating a 50 percent decrease in all-cause mortality in ICD and CRT-D patients with symptomatic HF. This is the first randomised trial to demonstrate a benefit in terms of all-cause mortality in remote monitoring. Based on these results, the European Society of Cardiology recommends remote monitoring according to the In-Time approach for this patient group in its latest heart failure guidelines.

Dr. Gerhard Hindricks, Director of the Electrophysiology Department at University of Leipzig Heart Centre, Germany; President of the European Heart Rhythm Association and lead investigator of Truecoin and In-Time said: 'Both studies' results show that Biotronik Home Monitoring leads to improved clinical outcomes for patients. I believe this is due to differences in manufacturers' technology, the data collected and clinic workflow.'

'The system is the only remote

monitoring system on sale that is clinically proven to notably reduce risk of all-cause mortality in ICD patients,' Biotronik points out.

'To ensure efficacy of remote monitoring,' Hindricks emphasised, 'frequent data transmission, quality data, and appropriate responsive treatment pathways from physicians are essential.'

José Félix Coserria Sánchez MD is a paediatrician who specialises in cardiology and haemodynamics. In 2014 he became coordinator of paediatric cardiology at the Virgen del Rocío Children's Hospital in Seville, Spain. His experience, in all aspects of paediatrics and paediatric cardiology, includes acute admissions and interventional catheterisation, PICU, intra-operative cardiovascular imaging and transoesophageal echocardiography.

6 mm and a half, which is very big for a patient this young,' he told European Hospital.

Once they placed the tube in the hepatic vein, doctors reached the heart very quickly. The whole intervention lasted less than two hours, about an hour less than when accessing through the neck or groin. 'We have significantly reduced the duration of the procedure and it was much easier to place the valve inside the pulmonary artery than when using traditional access,' Coserria said, adding that the patient had fully recovered and significantly improved his quality of life.

Entry via the liver could be used to place a new large valve

These benefits could help establish the liver as an alternative access in pulmonary catheterisation when no other access is available or damaged, or in small patients who need a large cardiac valve, the paediatrician believes.

'We could,' he pointed out, 'use the liver when we need to place a new valve, especially in the case of a large implant that may not fit through the jugular or femoral artery.

'The liver can definitely be an interesting option in this case,' Coserria confirmed

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Resembling a smartphone, and designed for mobile and stationary use, the CardioMessenger Smart can be used for up to 48 hours when on the move, or on a night stand, can receive data from an implanted device while patients sleep

Aiming for constructive teamwork between two disciplines

Amalgamating cardiac expertise

A formerly bitter competition between cardiology and cardiac surgery is increasingly replaced by constructive cooperation. The Austrian Society of Cardiology (ÖKG) even held its annual congress along with the Austrian Society of Thoracic and Cardiovascular Surgery this year. 'There should be no competition between the two different disciplines; to the contrary, the entire heart team needs to find appropriate solutions for individual patients,' emphasises Franz Xaver Roithinger MD, President of the ÖKG. 'The future belongs to the heart team.'

These multi-professional teams include cardiologists, cardiac surgeons and other specialists, such as anaesthetists if required, who make the relevant treatment decisions together - decisions such as whether a patient should undergo open heart surgery supported by a heart-lung machine or whether they should receive less invasive treatment using cardiac catheterisation. 'The lines are already a little blurred,' Roithinger explains. 'Minimally invasive procedures are increasingly used in heart surgery whilst there are catheter interventions that involve the heart being tapped.'

Both disciplines offer different solutions for numerous problems. In interventional cardiology, blocked coronary vessels, for instance, are treated with stents that are inserted via cardiac catheters and moved into the required position in previously dilated vessels. Heart surgery solves this problem with bypass surgery. The occluded vessel is bypassed with a venous graft taken from a patient's leg. 'Both procedures have their special features, advantages and disadvantages. The heart team discusses these cases and selects the best solution for each individual patient,' Roithinger points out.

Patients with several coronary occlusions, who would alternatively require the insertion of numerous stents to ensure adequate blood supply to the heart, are typical candidates for bypass surgery. 'Studies have also shown that diabetics with heart disease experience more benefits from bypass surgery than from the insertion of stents,' he adds. 'In contrast, the stent is preferable for all patients who do not suffer from any other complications because the implantation is significantly less invasive than heart surgery.'

Implantation of artificial heart valves, particularly aortic valves, is a further interface between interventional cardiology and heart surgery. For some years transcatheter aortic valve implantation (TAVI) has been an increasingly popular alternative to heart valve surgery.

Inoperable or high risk cases benefit from TAVI

'TAVI is now an established procedure to treat aortic valve stenosis for inoperable patients and particularly high risk patients,' Roithinger says. 'According to figures from the AQUA register (the German Institute for Applied Quality Improvement and Research in Health Care GmbH), TAVI also has a lower mortality risk than conventional surgery for patients at medium risk. However, whether TAVI should generally be recommended for medium risk patients needs to be confirmed by large-scale, randomised studies.'

This is another area where the heart team seeks the right solution for individual patients. Roithinger banks on the rule of thumb: Older patients and patients in worse health are more likely to be treated with TAVI to avoid the risks of open heart surgery. Younger, healthier patients are more likely to undergo heart valve surgery because they can still anticipate a longer life expectancy and because there is no long-term data available on TAVI yet. 'However, Roithinger pointed out, 'the heart valves implanted via TAVI are increasingly more durable so,' he adds, 'in all likelihood, the procedure will also see more use for younger patients in future.' (MK)

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Austrian cardiologist **Franz Xaver Roithinger MD, MSc, Prim. Univ.-Doz**, is President of the Austrian Society of Cardiology (ÖKG) and Head of the Internal Medicine II Department at Landesklinikum Wiener Neustadt. Having trained in medicine in Vienna and Wels, he completed a two-year specialist course on electrophysiology (arrhythmia treatment) in San Francisco. When heading the Internal Medicine Department, at Landesklinikum Mödling, he helped to set up a cardiac catheterisation laboratory.

Robotic-assisted visceral surgery

The advantages are obvious

Report: Brigitte Dinkloh

The implementation of minimally invasive technology in the 1990s was a milestone for visceral surgery. A further chapter of innovation began about five years ago with advances in robotics, which were able to address certain technological shortcomings of minimally invasive surgery in the fields of optics, instrument technology and reconstruction.

If nothing else, pancreatic surgery has benefitted from these developments. 'It ranks amongst the most complex interventions in abdominal surgery and opens up an important perspective to be able to offer these complicated and very time consuming interventions, which have been carried out almost exclusively with conventional surgery, with an assistance system and minimal invasion,' explains Colin M Krüger MD, Dipl.oec, Senior Consultant at the Department for Surgery, in Immanuel Hospital Rüdersdorf, near Berlin.

A lower rate of complications

First studies and analyses confirm that the quality of organ removal and partial removal is more or less comparable for both procedures, but also that the rate of complications associated with the intervention is significantly lower for minimally invasive procedures than for open surgery. Therefore, minimally invasive surgery, whilst achieving the same surgical outcome, has clear advantages.

But, which patients and indications are suitable for robotic surgery? 'Basically, all patients who are operable and fulfil the surgical entry criteria,' Krüger responds. 'If the diagnosis confirms that a patient is likely to benefit from surgery, then this can also be done with minimally invasive procedures, or, in the best case, with robotic surgery, such as the da Vinci Surgical System.'

Krüger does not foresee a considerably better perspective for patients with pancreatic cancer as 70-80% of them are only diagnosed once the tumour has already spread and is considered inoperable.

However, there are other pancreatic diseases with a less negative prognosis, where surgical intervention is worthwhile. These include hormone producing tumours, as well as all types of chronic pancreatitis such as those that may develop due to chronic alcohol abuse or as a result of autoimmune diseases, where the body tries to fight its own pancreatic tissue. The resulting inflammatory changes can cause jaundice, gastroparesis and, most importantly, chronic pain. This is an area of application for robot-assisted surgery.

Colin Krüger is establishing the first centre for robotic-assisted, visceral surgery in Rüdersdorf, near Berlin

Improved optics and a higher degree of freedom

One essential advantage of the da Vinci Surgical System is the improved visibility over the operating area. 'Unlike conventional laparoscopy, which only offers 2-D visualisation, it facilitates 3-D HD visualisation in the same way as open surgery does. The surgical structures can be enlarged up to tenfold, which means more precision during preparation,' the Berlin-based surgeon emphases.

The same applies to handling, with much more freedom when guiding the instruments in the abdomen compared to conventional laparoscopic surgery. "The instruments have up to seven degrees of freedom,' Krüger points out. 'When you work with double-joint technology the instruments carry out their own hand movements. This is the principle of the surgical robot – it controls the manipulators, and the hand movements carried out outside of the operating area are implemented 1:1 to the instrument working inside the abdomen. You sew externally, with the manipulator in your hands, and the robot sews with the needle, which you hold in the external needle holder, but inside the abdomen. This is brilliant.'

More 'radicality'

A further advantage of robot-assisted surgery in oncology is immunofluorescence. These fluorescent dyes, injected by the anaesthetist, can stain the lymphoid tissue or other vessels and structures during surgery, either to protect them or remove them even more precisely with the respective radicality. The prescribed number of lymph nodes to be removed for certain types of tumour surgery can be significantly increased with the da Vinci system. 'During open surgery, the dyeing is very complex because there isn't normally a camera system available, which is why it's not usually done.

'For a long time, it was quite controversial whether tumour surgery should actually be carried out with the minimally invasive procedure at all,' Krüger points out. 'There was always the claim that it is not sufficiently radical. However, this has been scientifically refuted. It obviously always depends on the expertise of the surgeon, but the procedure achieves at least the same, and sometimes even more radicality, and at the same time allows the patient to benefit from the advantages of minimally invasive surgery.'

Costs and viability

Only a few patients in Germany currently benefit from robotics in pancreatic surgery. Last year, 43 surgical departments had access to one of the 87 systems currently available in that country. The number of departments for visceral surgery and centres that treat a noteworthy number of patients with robotics is considerably lower still; Krüger estimates it to be around 10-15 centres.

This can most probably be attributed to the increased costs of the procedure, which are €1,000-€1,500 higher than the costs of conventional surgery and therefore still not always viable, despite shorter in-patient stays.

The discussion as to whether these systems are really required, or not, is still very heated and affected by jealousy. On the other hand, there are currently almost exclusively only studies that confirm the feasibility, and only very few studies that confirm a clinical advantage of robotics compared to minimally invasive surgery. 'However, this is to be expected at the moment, as we require a critical number of users and data to confirm clinical superiority. Method studies are difficult to carry out anyway, and often only individual parameters are examined. We don't generally compare the minimally invasive procedure with robotics, so it is difficult to evaluate this,' he explains.

Krüger is establishing the first centre for robotic-assisted visceral surgery in Brandenburg, and plans to carry out his own studies. With gynaecological and urological colleagues he aims to achieve full capacity for the da Vinci-SI with around 500-600 interventions annually in one to two years' time.

Financial easing could occur from 2018/19 when large manufacturers will break the current monopoly held by Intuitive by releasing their own equipment, and when competition will regulate the prices for acquisition and maintenance. Krüger is sure that 'in five years' time the costs will settle down around the level of those currently expected for a complex laparoscopy'.

In April 2017, **Dr Colin M Krüger MBA, Dipl.oec**, became a senior consultant at the Department for Surgery at the Immanuel Hospital, Rüdersdorf, near Berlin since April 2017. Earlier, as a specialist for general, visceral and vascular surgery and emergency medicine at Vivantes GmbH, he also headed the visceral surgery programme for 'Robot-assisted, minimally invasive Surgery (Da Vinci)'. From October 2016, he was senior consultant at the Centre for Robotics and Minimally Invasive Surgery in the Department for Surgery, Vivantes Humboldt Hospital, Berlin. Krüger also holds a Master of Business Administration in Health Economics, is a medical advisor at Intuitive Europe and is currently writing his habilitation at the University of Greifswald on the risk stratification in pancreatic surgery.

Led lamp to meet surgeon's needs

The right lighting of a surgical site is critical. Bologna-based lighting specialist firm ACEM confirms that the special optics of its LEDS in the firm's STARLED5 NX surgical lamp 'generate a shadowless, clear and homogeneous light, assuring visual comfort and best working conditions both for the surgeon and medical staff. Thanks to its next generation LEDs, the lamp can produce a perfect illumination under every condition generating an IR-free light, an excellent colour temperature and a practically endless life cycle at low consumptions.

'The 43 LEDs,' Acem continues, 'are circularly positioned and divided into five reflectors (with seven LEDs each) and another eight LEDs are radially placed around the handle. In this way, the lamp produces a high illumination level of 130.000 lux (160.000 lux optional) for a steady life cycle of about 50,000 hours.'

The firm's system ACRIS, with microprocessor, is reported to ensure control of electrical curves typical of LEDs to remain unaltered over the time, but maintaining a long life cycle.

'The colour rendering index of Starled5 NX is 95 and its colour temperature is 4,500 °K,' Acem adds. To meet various surgical needs, the system can produce focused and ambient light, with a 'light field focusing system adjusting the light spot diameter accurately assuring an excellent sharpness of details in the operating area'.

** Acem Medical Company is based in Bologna, Italy. www.acem.it e-contact and queries: Info@acem.it*

The Starled5 NX surgical lamp with LEDs provides surgical teams with shadowless, clear and homogenous light in the operation and surrounding area