VOL 24 ISSUE 4/15 • AUGUST/SEPTEMBER 2015

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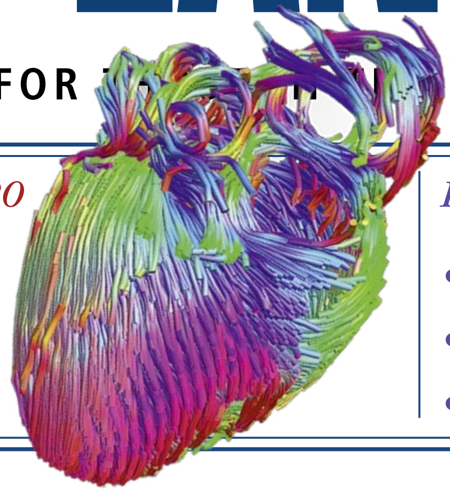

The future for big data in medicine

With registration about to begin for the Oxford-based *Big Data Science in Medicine Symposium*, we asked Professor Christoph Meinel, President of Germany's Hasso-Plattner-Institute, about the potential of big data in medicine and medical research

'In IT we often casually say that Big Data is exactly what we can't do yet,' computer science expert Professor Christoph Meinel said ruefully. 'Big Data are huge volumes of data of very different heterogeneity, origin, quality and size – and it's exactly these characteristics that pose a big challenge for evaluation, analysis and calculation because we are better versed at handling more uniformly structured data.'

Asked to about the term Big Data he pointed out that there are many examples, including human genome data, data in hospital information systems, cancer registers, clinical studies, medical sensor data, image data, acoustic data and ultrasound data, as well as medical publications. 'We are now trying to intelligently link these data sources to facilitate conclusions that can advance our medical research and therefore the treatment of diseases.'

'For example, the success rate of radio- and chemotherapy in cancer treatment is below 25%, meaning 75% of patients undergo agonising treatment for nothing. If the likelihood of determining the effectiveness of treatment based on findings of a patient's respective genetic or molecular structure was higher, we could exclude certain types of treatment right from the start because they are not appropriate, and we could spare the patient this torturous treatment. Previously this required analyses that could sometimes take several months. Now, with the In-Memory-Technology, which we developed together with SAP, we can reduce the time these evaluations take to mere seconds.

Source: Shutterstock/wk1003mike

'The first product based on this technology is the SAP HANA Database. This type of database is ten thousand times faster than traditional ones. Why? The RAM of computers is becoming ever cheaper, and new computer architecture is now possible with huge RAMs. Entire databases can be stored in the RAM, meaning that data can be analysed immediately without time intensive transport of data from external data storage. This means the factor can be calculated ten thousand times faster and data from very different sources can be linked in real time.'

The 2nd Big Data Science in Medicine Symposium, organised by the Biogerontology Research Foundation (BGRF) and Oxford Biotech, with Deep Knowledge Ventures and InSilico Medicine, is bringing to Oxford international experts in artificial intelligence, biomedical science and regenerative medicine for discussions that aim to accelerate research in preventive medicine. 'When cutting edge biomedical research meets state-of-the-art big data technologies, the extraordinary seems possible,' the organisers state. 'At the forefront of scientific innovation is the recognition that the diseases of ageing are not inevitable facts of life; instead they are biological challenges with real solutions. It is widely recognised that prevention is better than a cure – this event is an endorsement of that idea.'
Details: http://www.bigdatamed.org

A maths and computer sciences graduate from Humboldt University, Berlin, **Christoph Meinel** is president and CEO of the Hasso-Plattner-Institute, and professor for Internet Technologies and Systems at the University of Potsdam (Germany). He is a member of acatech, the national German academy of science and engineering, Chairman of the German IPv6 council, and of HPI-Stanford Design Thinking Research Programme. He heads the steering committee of HPI Future SOC Lab, and serves on various advisory boards, e.g. SAP. His research focuses on IT and systems, and Design Thinking research.

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www.healthcare-in-europe.com

Recruitment and retention of Europe's medics

Following a tender by the European Commission (EAHC/2013/Health/08), the European Health Management Association (EHMA) organised an expert consortium to carry out a study to identify and analyse effective strategies for recruiting and retaining health professionals in Europe.

The study has highlighted that many EU countries have difficulties in retaining and recruiting health staff. These problems are frequently allied with the challenge of balancing the right number of healthcare staff with the right skills in the right geographical areas to meet the changing needs of populations and health systems. These difficulties in retaining and recruiting health staff need to be addressed by policy-makers, healthcare managers and healthcare workers because they are becoming increasingly urgent. As healthcare demands increase, the health workforce shrinks – with many workers reaching retirement age – risking the future sustainability of Europe's health systems. Whilst no 'one size fits all' solution can be found to these problems, there a number of success factors like education opportunities, financial incentives and professional and personal support could help to attract and retain healthcare staff.

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French fear for the f

Excellent service but acc

An online survey of 1001 French adults, which aimed to reveal public opinion on healthcare access and other perceptions regarding public hospitals, has been carried out by IPOS for the French Hospital Federation (Fédération Hospitalière de France- FHF).

Happily, analysis of results has shown that, regardless of political affiliation, age, gender or social status the vast majority (91%) of those polled consider that the public hospital system provides excellent healthcare.

Scoring nearly as highly were the efficiency and performance of the public hospital system, which 84% of respondents think is a model worthy of introduction in other countries. They believe it to be adaptable, innovative and offering the latest in healthcare technology.

However, despite a strong sense of pride in the system, almost all these supporters, 89%, are realistic enough to be wary of the continuation of such a high quality service in the current economic situation with, in their opinion, an increasingly marked lack of trained personnel. This concern is slightly greater in the older age group (>35 years old) and also in respondents coming from lower socio-economic groups. Equal access to healthcare lies among areas for improvement in a public healthcare system that has consistently been judged as one of the world's best. Geographical inequality is apparent from analysis of the results. While 64% of the French have a general practitioner less than 5 km from their home, nearly 70% of the respondents claim to have faced difficulty in finding a healthcare professional available within an acceptable period. A similar number felt that there were not enough hospitals in France. This was more marked in rural than urban areas, where 21% of respondents had turned down a proposed healthcare option because it was 'too far from home'. Overall only 33% of those questioned felt that healthcare was equally represented over the whole country.

The cost of healthcare is also suggested as a barrier to its access. Amongst those polled, 95% have direct access to the social security system with a 'Carte Vitale' and 87% have additional private insurance (mutuelle). However, 46% think that

Reaching into the core of process rationalisation

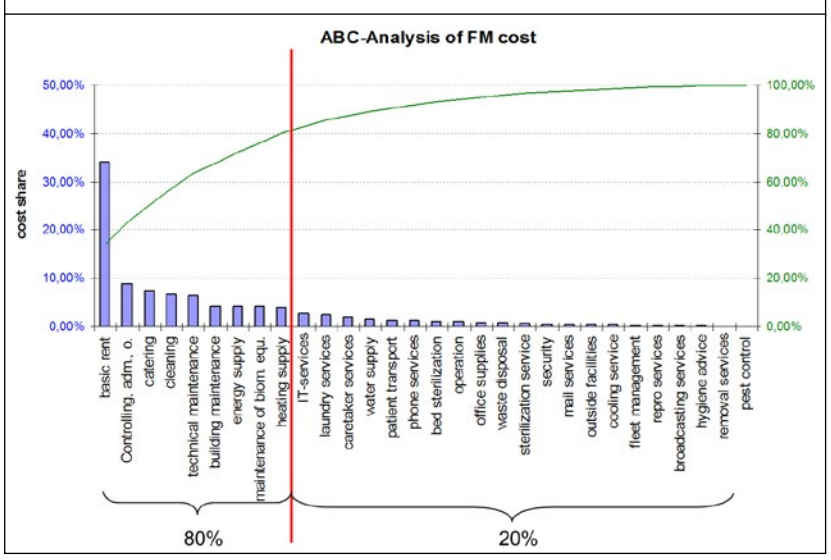
Facility Management

Report: Anja Behringer

'Facilities management is the integration of processes within an organisation to maintain and develop the agreed services that support and improve the effectiveness of its primary activities.' According to the European DIN-Norm (DIN EN 15221), this defines facility management (FM). As a control tool, FM encompasses all supportive processes within a company, in this case referring to a hospital and its core business – caring for patients.

As in a commercial company, it also includes service and maintenance of premises and all administrative tasks and services. All services generated by the hospital alongside the key healthcare business are reflected in data, which are administered with transparency in a FM-system for all cost centres. From catering staff wages to cleaning products used by cleaners, from the occupancy to the IT infrastructure, all departments are covered by the system – provided that it has been professionally developed and is continuously updated (see graphics). This results in clear findings as to opportunities for rationalisation and thus, in turn, in clear cost benefits.

In theory, anyway; in practice, many problems can arise because FM is not usually implemented right from the point of building design and construction. Introducing FM to existing premises is unlikely to be successful all across the board, and hospitals are so complex that even 'old hands' at FM only attempt partial introductions.



One of these experts is Professor Kunibert Lennerts of the Institute for Technology and Management in Construction in Karlsruhe. For a long time this facility management specialist was responsible for one of the most heterogeneous and comprehensive property portfolio in Germany – assets owned by Deutsche Bahn.

European Hospital sought answers to three questions from the professor, first asking how FM could save running costs in the hospitals.

'The ideal scenario is for FM to be incorporated during design and construction,' Lennerts advised. 'This facilitates primary as well as secondary process-oriented planning. However, this is extremely difficult because architects tend to lack the knowledge and the individual processes are extremely varied, and hospital operators who are striving to build exemplary hospitals and provide the opportunity for the integration of FM into the design and construction of a new building, right from the beginning, are very limited in numbers.

'Therefore, the strategy revolves mostly around upgrading individual, particularly cost-intensive areas of the process with modern IT tools (see graphics). The so-called 'Building Information Modelling (BIM) is a new tool that can also help with the design of virtual building models.'

Which hospital cost driver particularly suits FM introduction?

'Space Management is very effective – as documented by some compelling figures from the Charité Hospital in Berlin. No other buildings are utilised so continuously, intensively and differently as hospitals are, making under-occupancy or inappropriate occupation particularly costly. Some of the services that are closely linked with one another do have inherent savings potentials of around 10 to 30 percent – without causing any negative impact on the primary processes of healing and caring. 'Energy consumption is obviously a good starting point, with BIM also helping to achieve cost optimisation.'

'The IFHE Europe, i.e. the European branch of the International

The future of big data in medicine

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Are those data sets to be analysed actually Big Data?

'Yes, we can now access these different "pots" of data stored in different silos and look for connections with the help of modern procedures, such as 'Deep Machine Learning' and neuronal networks, or respectively we can detect presumed links. This can lead to the discovery of connections that we hadn't even imagined. It also means we are turning our backs on the natural scientific principle, i.e. the establishing of a theory and proving it with experiments. Now we throw large amounts of data into a pot and leave it to high performance computers to look for patterns and connections, often with surprising results. For example, if the analysis shows that many people suffering a certain illness benefit from one particular medication out of a number of comparable drugs, then a doctor can most probably help his patient by prescribing this medication – even though he may not understand exactly why.'

Could texts and images be correlated in the context of Big Data Analyses?

'This seems possible indeed; Ii is about attempting to bring images and texts together, i.e. mechanical recognition of semantics. Texts are now quite easy to understand, but how can I detect something in a video? You can describe the video with text, but we are looking for procedures that automatically recognise what happens in a video at what point in time, to make retrieval of this information possible at a later stage.'

If this goes well, where will we be with Big Data in five years' time? What will we be able to find out then which we can't do now?

'We will certainly know a lot more about the structural design of humans, i.e. gene analysis, protein analysis, molecular analysis, and also about processes in the body, what triggers what and how. This will result in improved opportunities to diagnose individual constitutions and in more appropriate treatment of diseases, i.e. personalised medicine. However, this will also require quite large financial investments. For the pharmaceutical industry this means the development of individualised medications, which will revolutionise the industry - bearing in mind that the strategy, so far, has been all about developing blockbuster drugs that help as many people as possible.

Data protection

'This is a key topic. Data obviously has to be protected, particularly where it is possible to draw conclusions as to personal information. However, neither the German data protection law, nor the proposed European data protection regulation, meet the level of data protection required in the age of Big Data. Historically, the philosophical principle has been one of thriftiness with data. However, if we say that Big Data is the shape of the future this will be at odds with the principle of data thriftiness.

'Additionally, there is the issue that data collection is only allowed for a previously defined, specific purpose, which may be even more problematic because it contradicts the Big Data approach where we initially just have a look and see what we can find, and then make the best of it without prior knowledge of the purpose.

'Therefore, we need at least the opportunity for special dispensation within the law to account for this, and the definition of a procedure on how to achieve special dispensation - otherwise Europe will turn into a digital colony.'

future of healthcare

ess is unequal

they pay too much for their insurance by comparison with how they use it and, worryingly, 48% say they have refused further consultation or treatment because of the costs involved.

The survey also looked at attitudes to a potential restructuring of the current healthcare system to provide more equal care. Sixty% consider healthcare as a priority for government spending another 39% consider it very important, but not the most pressing. The respondents were split 50:50 as to whether the health service could undergo financial reform without reducing the quality of care given. However, they are not resistant to change.

One area that has almost unanimous support is adoption of a geographical quota system for newly qualified doctors, which restricts choice as to where they can set up practice and bases it on the particular needs of a region. This is considered as a practical way of reducing the geographical inequality in access to care. Other positively received solutions to improve the financial burden on healthcare include charging a flat-rate fee to patients who use A&E services instead of visiting their family doctor; encouraging home hospitalisation for those with chronic illness, and reducing hospital stays by increasing the amount of day-surgery. Likewise, the adoption of new e-medicine technologies is considered a way to improve access and control costs. Many of the respondents (72%) are happy to be permanently satellite-tracked if they should have a chronic illness in order to receive rapid emergency care and 55% would consider sharing their medical data with, and receiving care/advice from their doctors via mobile telephone apps or similar e-health programmes.

Other reforms generally considered inevitable in order to maintain high quality healthcare under financial constraint were to increase the number of minor/routine procedures performed by nurses, giving more responsibility to pharmacists and bringing an end to reimbursement for medicines available without a prescription.

Conversely, any suggestion of changing the proportion of healthcare paid for by the social security and increasing the amount from private insurance is firmly resisted. However, despite this strong desire, in the long term many feel it is inevitable if high quality healthcare is to remain a feature in France.

Reference: Observatoire de l'égalité d'accès aux soins - Vague 2 – Mai 2015

FM expert Kunibert Lennerts is aprofessor at Karlsruhe Technology and Management in Construction Institute

Federation of Hospital Engineering (IFHE) and its member organisations from twelve countries is currently financing an energy research project.'

'Up to 30% of hospital costs arise from secondary services, i.e. facility management services. By comparing FM processes in different hospitals it is possible to identify factors affecting cost, to uncover weaknesses and define optimisation measures. The OPIK research project (Analysis and Optimisation of Facility Management Processes in Hospitals) has been investigating comprehensive benchmarking and optimisation potential since 2001, together with partners in industry, science and specialist associations, but particularly with a growing group of hospitals partners. The overriding objective is the best possible, efficient support of the key processes, i.e. Healing and Care in the Hospital. The group also includes hospitals from Switzerland, Luxembourg and Austria.'

"With research partners, the Institute has developed a comprehensive database of costs and services for all hospital facility management processes. The operating expenses and personnel expenditure are documented on an annual basis from an FM perspective. The database is continuously updated.

'New hospital partners can join at any time. The hospital partners receive an evaluation of their data compared to the average benchmark. Two workshops are held every year.'

Sensory-enhanced leg prosthesis sends messages from sole to brain

Just like a healthy foot

Report: Michael Krassnitzer

'It's like a new lease on life,' says Wolfgang R, 'I can feel the difference between grass and concrete again.' Eight years ago the Austrian teacher's lower leg had to be amputated following thrombosis. Today, he is the first leg amputee, worldwide, to sport a sensory-enhanced prosthesis. 'For the wearer the prosthesis is not a numb object, but a part of the body,' says Dr Hubert Egger, who developed this unique and highly advanced device in the Department of Medical Engineering at the University of Applied Sciences, Upper Austria.

Just like a healthy leg, the sensory-enhanced prosthesis sends information from the sole to the brain.

The new prosthesis is based on a commercially available high-tech prosthetic foot with auto-adaptive joint and a carbon sole by British manufacturer Blatchford. 'The moment the wearer's sole touches the ground the sensors register the pressure,' Dr Egger explains. The electric signals are transmitted to the prosthetic shaft where actuators – similar to those we know from smartphones – start to vibrate. The vibrations are detected by receptors in the stump, converted into electrical signals and transmitted to the brain via sensory nerves.

However, the transmission process requires the stump to be surgically reinnervated. During an amputation, usually the nerves are severed for protection purposes deep inside the residual limb's soft tissue. For the sensory-enhanced prosthesis to function these nerves are reactivated so they can transmit sensory information again, a procedure called Targeted Sensory Reinnervation (TSR). Severed residual sensory nerves are brought back to the stump's skin to establish connections with the body's receptors. In this particular case connections are realised at six points in the stump – where the prosthesis sensors are located.

Source: FH Oberösterreich

With the new prosthesis the leg amputee can even go climbing.

Six sensors were fitted to the foot sole of the lightweight prosthesies and these were then linked to stimulators inside the shaft where the amputee's stump sits.

The brain quickly learns to link the vibrations in the prosthesis with the sole. 'We assume a new representation of the sole is created in the brain,' explains Dr Eva Maria Baur, the senior physician at the University Clinic for Reconstructive Plastic and Aesthetic Surgery in Innsbruck, who performed the TSR.

A major benefit for the amputee: phantom pain subsides! 'Scientists think post-amputation phantom pain is caused by the brain overcompensating the lack of sensory information in the cortical representation of the missing limb. The brain becomes increasingly sensitive up to the point where it creates signals autonomously,' Dr Egger explains. When the brain receives information from the foot via the sensory-enhanced prosthesis it no longer has to overcompensate. The phantom pain disappears – as Wolfgang R. confirms. Before his new prosthesis was fitted he had to take opiates intravenously to manage the pain.

The inventor of the limb, presented in Vienna as a prototype, would like to see widespread use soon. 'We are morally obliged to make this new technology available to as many people as possible,' he underlines. He therefore offers his knowledge to technology companies free of charge and hopes that a start up will take this opportunity to enter the market and begin large-scale production of the sensory-enhanced limb.

An electrical engineering graduate from the Technical University, Vienna, **Hubert Egger** gained his doctorate in Biomedical Technology and Physics there and at the Medical University Vienna and the Seibersdorf Research Centre.
From 2000 to 2011, this native South Tyrolean worked for Otto Bock Healthcare Products, a Viennese-based manufacturer of prosthesis, where he developed a mind-controlled arm prosthesis (presented in 2007). The device is controlled by nerve impulses, transmitted via electrodes to enable intuitive and simultaneous movements. In 2012 Dr Egger became Professor of Prosthetics at the Upper Austrian University of Applied Sciences in Linz.

On the wrist is better than in a mobile

Smart watch promises smarter medication

While Swatch and Rolex count the hours until their smart watches overwhelm the time market, medical informatics researchers have already been working on solutions to improve healthcare. Some demonstrated their work on a medication reminder application during the Medical Informatics Europe conference in Madrid.

Report: Mélisande Rouger

Successful therapy depends on various factors and the patient's adherence to treatment is key. However, everyone knows it's just as easy to swallow a pill as to forget doing so; and the more pills needed, the higher the probability is to not remember when and which pill to take, and how many.

The smart phone industry tackled the issue first and several apps have been designed for this purpose. However, research shows that those tools are not as effective as they should be, said research associate at the medical informatics department at Heilbronn University, Monika Pobiruchin, when presenting her team's work on a multiple medication reminder solution during the conference. 'People simply forget to look at their phones or to put the alarm on,' she said. 'They sometimes miss the alarm, especially when their phone is at the bottom of their bags, and so on.'

Source: Samsung

In addition, smart phones are not appropriate for the digitally illiterate and many elderly people. Smart phones are complex, multi-purpose devices and readability and interaction concepts can become technological barriers for the non-initiated, such as the elderly, who are more likely to consume pills than any other population group.

On the contrary, wristband watches have been increasingly used since WWII and the elderly tend to wear such devices; smart watch-based solutions are therefore an ideal option for this group, according to Pobiruchin, whose work targets a large group of patients regardless of age or technical affinity.

She and her colleagues evaluated several smart watch models, some of which are already on sale, such as Androidly, Neptune Pine, Exetech XS-3, qOne Smart Watch, Omate TrueSmart, LG GD910 and Samsung Gear S.

They looked at whether the operating systems of the devices were open and whether apps could be developed, and they also checked the watches' battery capacity, autonomy, weight and size. 'It doesn't make sense to have to recharge your watch every six hours, nor does it make sense to have an 18-hour-long autonomy only, as is the case for the Apple Watch. The smart watch shouldn't be bulky, but light to wear around your wrist,' Martin Wiesner, Pobiruchin's colleague, pointed out.

They singled the Samsung Gear S out as particularly handy because it works on a stand-alone mode, i.e. it doesn't need to be connected to a computer or phone constantly. 'The advantage is that you don't need to pair it with a smartphone via a Bluetooth connection, so no extra device needs to be carried around,' Wiesner explained.

A multiple medication reminder solution for the elderly is only the beginning, as smart watch-based applications could also be developed for diabetics to measure their blood glucose level, or as a simple reminder for women to take their contraceptive pill. A discrete alarm could also remind users that they need to take a medicine when for instance they have to deal with hypertension, Pobiruchin suggested. Wristband watches are associated with allergies and the smart versions are no exception. 'I heard of some issues with the Apple Watch and that some people already had itching and rashes,' she said. 'The smart watches we assessed are not labelled "allergy-proof" either.'

Monika Pobiruchin received her Diploma in Medical Informatics (comparable with the MSc degree) at the University of Heidelberg in 2010. Currently she is a research associate at the GECKO Institute for Medicine, Informatics and Economics at Heilbronn University. She is also a fellow of the Nachwuchsakademie Baden-Württemberg programme, and, has been a PhD student at the Medical Faculty of the University of Heidelberg since 2012. For her doctoral thesis she investigates the automatic generation of health economic disease models based upon real-world clinical data. Pobiruchin co-founded the project group Consumer Health Informatics within the German Association for Medical Informatics, Biometry and Epidemiology (GMDS) in 2014.

A five-point roadmap to success

The German IT security act

German hospitals, having 'critical infrastructure' components, are granted a two-year transition period to comply with the IT security act (ITSiG) the German Parliament adopted in June. Many hospitals are already bellyaching about the financial burden being too high with transition period too short. According to the recently published Hospital Rating Report 2015, every sixth hospital in the country faces insolvency. Is a hospital infarction imminent? Frederik Humpert-Vrielink, Managing Director of CETUS Consulting, believes misguided investment decisions are the real cause of the financial plight of many. He has developed a five-point plan to make compliance with ITSiG less painful.

Tighten the organisation – The first point in Vrielink's five-point plan is tightening of the organisation of the IT environment and structures to ensure secure operations. 'There are still many hospital IT departments that operate on an ad hoc basis without clearly defined responsibilities. Tightening organisation here means spreading the IT tasks across the team in such a way that each team member is assigned tasks that fit their qualifications and competencies,' he explains, adding that he is increasingly seeing facilities where the IT team leaders and their deputies carry 90 percent of the operational responsibilities with the entire rest of the team carrying only 10 percent of the weight. This, he claims, is not only a waste of security resources; it wastes of economic resources.

Needs to focus on own role

Vrielink suggests creating different IT sub-teams based on department size, which are in charge of defined applications (HIS, RIS, PACS, etc.) or network in respect of infrastructure. Additionally, he underlines, 'responsibilities of department or division heads must be adjusted: management has to manage more and leave operations to their staff'.

Documentation is another important issue. All activities should be documented following unambiguous standards so as to trace and manage changes. Vrielink favours role-specific task definitions with clearly defined qualifications because, 'This ensures each team member has or acquires appropriate qualifications and that new staff can be recruited according to actual need'. Investments in competent staff with

THE FIVE-POINT PLAN:

1. Increase the degree of organisation in the IT department and create structures that allow safe and secure operations
2. Define responsibilities for documentation, operations and applications
3. Invest in competent staff with an adequate professional background
4. Quantify the resources required for secure IT operations
5. Re-assess building and medical technology to identify new security risks

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Martin Wiesner is with the department of Medical Informatics of Heilbronn University. He received the Diploma in Medical Informatics (comparable with a MSc degree) at the University of Heidelberg in 2007. Since then he has been teaching database and information systems at the joint Medical Informatics study programme of the two partner universities. His research on health recommender systems is closely related to the PhD thesis he is currently developing at Heidelberg University's Medical Faculty. In 2013 Wiesner received the Certificate of Medical Informatics by the German Association for Medical Informatics, Biometry and Epidemiology (GMDS), in which he co-founded, in 2014, the national working group for Consumer Health Informatics.

As a next step an evaluation of the prototype is planned in public partner hospitals to investigate on usability aspects and other effects related to the age of patients.

Another problem the researchers found with some smart watches and third-party apps that collect vital data is a conflict with data safety and privacy. 'Sensitive questions, such as where are collected data transferred to, and who has access to these data, must be discussed.'

Mathematical graphs and networks seek answers

Discovering what causes di

Systems biology allows the mathematical visualisation through graphs and networks of complex body processes such as disease development. The aim is to improve understanding processes and triggers of diseases, so as to access and repair a damaged network. 'We are still approaching this issue with a lot of naivety and underestimate the complexity of biological systems, and therefore of diseases,' says Professor Rudi Balling, Director of the Luxembourg Centre for Systems Biomedicine at Luxembourg University.

Report: Marcel Rasch

'Network Science in a biomedical context is derived from the concept of a system,' Professor Rudi Balling explains. 'If you look at any system you will find certain similarities that will occur over and over again. There are components that react with one another and we can look at this interaction over time and observe the dynamics. All of this can be described mathematically with graph theory as a network.

'Transferred into the world of biological systems, organs and cells, and lastly also diseases, this means that we can also record the different cell types and different relations between the cell types as graphs or networks respectively. 'If we, for instance, look at a liver tumour or inflammation, we can see where the relationships between the different components change. These changes can then also be visualised as graphs and be compared with one another mathematically. We try to describe and understand diseases as changes in networks.'

Challenges

'In the world of medicine and biosciences this is our first attempt at systematically and (almost) completely capturing all components. The main challenge currently is of a purely technical nature. Currently, capturing the genome sequence is no longer a problem; but capturing all proteins quantitatively is still a big challenge. Each organ produces its own, different set of proteins, and therefore the genome is read organ-specifically. Measuring this is very difficult.

'There is also a kind of "background noise" in the body that fluctuates from hour to hour, minute to minute and from person to person. Unfortunately at the moment, we don't understand what level of fluctuation is "normal" and what level may be an indication of disease, which is gene-controlled in respect of the adaptation of a certain organ. Even more important is the understanding of control cycles, such as blood pressure and blood glucose. Why does the body change the control variable of blood glucose, which makes obese people more prone to developing diabetes? We need to do more research here.'

'The human body has around 20,000 genes that can probably code 100,000 to 300,000 different proteins. The possible combinations are therefore almost infinite and we have not yet discovered which combinations nature actually utilises and under which conditions. Our ultimate objective is to intervene in a damaged network to repair it.'

An ideal approach

'It would be ideal to carry out family studies. On average, we would have to examine 30,000 to 40,000 patients to obtain relevant data that could point to a disease or its development. However, if we examine families with known hereditary diseases, then it suffices to sequence just one family to find the path of inheritance and the responsible gene. We need to get to the depths of things.

'We are also currently developing Spatial Systems Biology where, in addition to temporal systems biology, we are looking at the spatial resolution. Thanks to modern imaging procedures and new, high-resolution microscopes we can see how a cell works, when, where and which proteins move in, which way and what they do exactly. We try to model and predict these dynamics.'

The objective

'We want to observe what happens when mutations occur, or what changes when we change different parameters. In the future, we will work mainly with non-invasive imaging procedures that have an ever-improving resolution. This allows the combination of different procedures, which is very interesting. However, in doing this we always produce an enormous volume of data – in future likely to be in the region of terabytes of data per second. Therefore, we either need better storage solutions or we'll have to analyse in a more sophisticated way.'

More to come

'We'll have to have in-depth discussions around the issue of data pro-

Systems medicine

IT is a resource just like water or energy

Systems medicine – the interdisciplinary field incorporating biochemical, physiological and environmental interactions in the study of human body systems as part of an integrated whole – draws heavily on the technological advances in information technology (IT). New ways to use data impact on healthcare and society, says Professor Dr Heyo Kroemer, Dean of the Medical School, Georg August University, in Göttingen, Germany. 'We live in times when many things undergo fundamental changes. New possibilities to use data may well herald the beginning of a new era in medicine.'

Interview: Sascha Keutel

Dr Heyo Kroemer: 'Today, new analytical technologies allow us to collect highly complex data on diseases – and consequently to understand these diseases better. For example, it's no longer particularly expensive to sequence a genome and identify genetic variants that may or might be disease-relevant. Similarly, we can have a comprehensive look at epigenetics, the modifications of all DNS structures; or, proteome technology allows us to view all proteins. When we use these new analytical procedures and combine them with bio-informatics, we will be able to understand diseases and processes to an extent that allows us to intervene far better.'

Exactly who or what drives systems medicine forward?

'Many of my colleagues are convinced that the new technology is the driver but, frankly, I don't think so. As far as I'm concerned it's the demographic change that prompts us to act. Our ageing population, which naturally means people are sick more frequently, and immense medical progress, create a pressure towards the development of affordable and feasible solutions. 'What we'll see in the future is a triangle of many patients, few payers and a wide array of services made possible by medical progress. This triangle is a wellnigh insurmountable challenge for a healthcare system financed through solidarity-based mechanisms – if we don't use modern technologies. One of these options is the system medicine approach, which will lead to physicians being able to predict individual courses of disease better. Medicine will become much more precise and much more specific.'

Thus the importance of constant exchange between clinicians, IT people, physicists and mathematicians…

'Exactly. The systems medicine approach requires cooperation between physicians, specialists in analytical procedures, such as proteome analyses, and experts who mediate between physicians and analysts, who basically process data – the bio-informatics specialists. The success of systems medicine relies on the cooperation of these groups. Moreover, we need experts who deal with healthcare-related issues that cannot be solved within healthcare itself, such as legal or ethical issues regarding huge data volumes.'

'Potentially, systems medicine also has significant social relevance. On the one hand it creates the preconditions for broad segments of the ageing population to be able to participate in medical progress. On the other, we already see today how Big Data can change our lives. Point in case: the availability of huge amounts of personal data on smartphones. 'We know from the USA that the integration of these data into the patient record has already begun. This will allow people to be health-monitored around the clock and to analyse the data. The interaction between patients and Big Data and the impact this has on diagnostics and therapy has the potential to change our healthcare system fundamentally.'

The German IT security act

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a proper professional background are crucial. 'Learning by doing or learning by reading is insufficient to keep you abreast of the developments and to become really familiar with the applications being used,' he says, contradicting the proponents of Blended Learning, who consider this method to be the future of knowledge acquisition. 'When day-to-day business makes concentrating on other issues difficult and when interruptions are part of the work day, a focused seminar away from the office hustle and bustle is clearly the better choice.'

Quantify resources

To be able to operate the IT infrastructure safely hospitals have to know how many members of staff are needed for the task. Therefore quantifying the resource requirements is unavoidable, says Vrielink. Does that mean hospitals, many of which are already operating on a tight budget, have to hire more staff? 'There is no clear-cut answer to that question,' Vrielink says, 'but indeed some of them will have to do that. If, as mentioned above, the costs are correctly calculated these human resource investments will be worthwhile. That is a management task, not a consequence of the IT security act. Additional costs should be within reasonable limits.'

Fill future security needs now

In the course of the next few years, building and medical technology must be reviewed from the IT perspective, since both areas will continue to increase the network density; but what to do with the data flood – where to store all the data? 'This question, no doubt, will keep us busy in the next few years,' Vrielink concedes. 'There will be efforts to make the data collected in the hospital available for research purposes, or to turn dead data into revenue-generating data by making them available for analysis. This will create new security issues. Well-known problems such as interfaces to open networks, or the security of remote maintenance access for building and medical technology, will intensify.'

Frederik Humpert-Vrielink, Managing Director of CETUS Consulting and specialist in data security and risk management, has comprehensive experience in the implementation of DIN 80001 – Risk Management for healthcare IT networks. He has been advising hospital groups on the development and successful implementation of IT security management systems for over a decade.

Management has to re-assess the IT strategy

Does that mean hospital management has to rethink its strategy and re-assess IT? The answer is 'Yes, but'… 'The re-assessment provides the opportunity to examine the entire facility and to identify black holes that gobble up money. Purchasing, redundancies, hidden double work, inefficiencies – these are but a few areas where targeted process optimation based on secure and confidential IT will reduce costs.

Implementing a security management system always involves close scrutiny of all business processes. For hospital managers who moan about the financial burden, Vrielink offers a recommendation: 'Facilities that face insolvency should ask themselves whether their current situation is not the result of the 'Ghost of Christmas Past' – of misguided decisions. No hospital will have to shut down because of sensible investments in IT and IT security. It is wrong investments and omitted process and IT optimation that exacerbate financial pressure.'

seases

tection. In the era of social media, is the data protection law not actually well beyond what is required? As a society, we don't yet know how to deal with this, but we'll have to find a way.

'The discussion around data protection is anyway a lot more intensive in Germany than in other countries. Unfortunately, this data protection law is a hindrance in certain ways, not only for research but for patients as well.

'The discussion around utilisation of the Cloud should also be carried out in a different way. In the future we will have few alternatives to the use of the Cloud, because we won't be able to efficiently store and transport data in another way.

'Institutes can no longer cover the storage costs of our own data on internal servers. It might work up to the terabyte and petabyte level, but from the exabyte-level onwards it will no longer be possible.

'The real question should therefore be: Do we stop research or will we get secure Clouds?

'This development will have a dramatic impact on the next generation because biomedicine cannot work without mathematics – it will therefore have to work safely with IT and large data volumes.'

Rudi Balling studied nutrition at the University of Bonn and Washington State University (USA) and gained a PhD in Human Nutrition from the University of Bonn in 1984. After several research posts, in 1993 he was appointed Director of the Institute of Mammalian Genetics at the GSF National Research Centre for Environment and Health in Munich. Then, in 2001, he joined the Helmholtz Centre for Infection Research in Braunschweig as its Scientific Director. Eight years later, Prof. Balling became the founding director of the Luxembourg Centre for Systems Biomedicine (LCSB).

How do you explain 'Big Data'?

'Big Data refers to data sets that are either too large or too complex to be analysed by conventional means. Note that complexity here is even more of an issue than size. I personally would classify Big Data in healthcare in three categories:

1. Conventional Big Data, meaning information from genome or transcription analyses
2. Unused Big Data, meaning information that is being stored for regular healthcare purpose
3. Private Big Data, meaning data, such as those generated by smartphones, which potentially could be used for health monitoring purposes.

In my opinion Big Data in healthcare is a potential research, and therefore knowledge, resource that is currently not being used and which we urgently have to tap.'

Is there European cooperation for this?

'Many ideas are being discussed worldwide with regard to standardisation. The USA's government has created massive incentives and invested significantly in electronic patient records and is now in the process of ensuring interoperability. While there is a lively international debate on standards, in Germany, unfortunately, we are lagging miles behind. In healthcare IT, be it with regard to research or provision of care, there are only very few cooperation projects. We hope there will be an increasing awareness of this issue, since I am utterly convinced that without these technologies we will not be able to master the demographic change in the healthcare system.'

'We must change our idea of information technology. IT is a basic resource, just like water or energy. Thus it should not be an item we have to apply for in our individual project applications. IT should be available anywhere and there has to be the will to use or to be allowed to use untapped resources.'

Professor Heyo Kroemer studied pharmacy at Braunschweig Technical University and, in 1992, received his postdoctoral lecture qualification (habilitation) in pharmacy and toxicology at Eberhard Karls University Tubingen. He was professor of pharmacology and toxicology at Ernst Moritz Arndt University Greifswald (1998-2012), Dean of the Medical School at University Hospital Greifswald (2000-2012) and is currently Dean, Chairman for Research and Teaching and Chairman of the Managing Board at the University Medical Centre Göttingen. Dr Kroemer is also President of the German Medical Faculty Association.

Do patient rights come into play in this context?

'That's a crucial issue. As mentioned before, in modern healthcare there are a number of problems that concern healthcare but cannot be solved by healthcare alone, for example legal, ethical and participation issues. We absolutely must deal with these questions. For example: when I, as a patient, transfer my data via a smartphone to a certain system, such as an EPR in a hospital, it has to be clear beforehand who the owner of these data is.'

Are you afraid we will become 'transparent patients'?

'I recommend we don't approach the issue driven by fear, but that we do a sensible and factual risk assessment: we recognise the positive potential, the risks and the potential for abuse, and we look at them carefully.
At the end of the day it is a cost-benefit analysis. I think the benefits of using Big Data far outweigh potential drawbacks.'

Beating the clock in disease surveillance

Big Data may streamline epidemic control

Report: Sascha Keutel

It's a race against the clock; every hour counts in efforts to halt the spread of a disease, but identifying anyone with whom the infected patient has had contact is time-consuming, with Contact Officers generally collecting data on paper.

Now, however, scientists from the Nigerian Field Epidemiology Laboratory & Training Programme, the Helmholtz Centre for Infection Research, the Hasso Plattner Institute (HPI), Robert Koch Institute and Bernhard Nocht Institute for Tropical Medicine are developing a system to support reporting, communication and management of infectious diseases outbreaks including Ebola, Measles, Avian Flu and Cholera with the help of a mobile app and Big Data technology.

The prototype from the Surveillance and Outbreak Response Management System (SORMAS) is currently being tested in Nigeria. The system was designed to offer real-time and interactive capabilities to manage outbreak management procedures, analyse data and generate reports. 'SORMAS covers surveillance as well as containment functionalities,' explains Professor Gérard Krause, head of the Epidemiology Department at Helmholtz Centre for Infection Research and the project coordinator.

Mobile technology

The system supports the different parties involved in epidemic surveillance, e.g. Contact Officers (Cos) who visit those who may have had contact with infected persons. Whilst the COs previously collected data on a hard copy questionnaire, with SORMAS they enter detailed case data directly on to the mobile device and transfer these in real-time to the relevant authorities. The data are stored in a cloud to be accessed by all other authorized participants in the process. 'Involvement' is a key issue for the epidemiologists: 'From the outset, we designed SORMAS to integrate fully into existing national and international information processes and to comply with statutory requirements. We did not want to develop an additional and separate system but provide a tool to make the existing systems more efficient.'

SORMAS is based on in-memory database technology developed at HPI. It combines Big Data technologies with smart applications. Commercially available smartphones and tablet PCs, which can be used even in remote rural areas, are equipped with specialised apps for mobile data collection in the field. In the background, complex processes run on cloud technology working with SAP's HANA database structure, which can handle information processes on Big Data level.

Epidemiologists and a Surveillance Officer testing SORMAS in Nigeria

An ebola exercise with SORMAS

A medical graduate from the University of Mainz, with a research doctorate in tropical hygiene from the University of Heidelberg, **Gérard Krause** worked as a physician and research associate in tropical hygiene, internal medicine and hospital hygiene in different hospitals and universities. He was epidemic intelligence service officer at the Centres for Disease Control and Prevention in Atlanta, USA, before moving to the Robert Koch Institute (RKI), in 2000, and there became director of the infectious disease epidemiology department (2005-13). In 2011 Dr Krause became chair for infecious disease epidemiology at the Hannover Medical School and head of the epidemiology department at the Helmholtz Centre for Infection Research, Braunschweig.

Pilot phase ends

After returning from a site visit during the field pilot in Nigeria, Krause reports, 'fortunately there are no Ebola cases in Nigeria currently. So we had to design a complex virtual environment in which we simulated an Ebola outbreak, but we carried out the simulation under field conditions in the close to 100 localities and staff that would normally have to cope with the outbreak.'

The current funding of this research project from the German Ministry for Research and Education is scheduled for completion soon. In late August the data will be evaluated. Based on the results, the project partners will decide whether this approach will be persued for further development and expansion. Summarising his initial impressions, Krause said: 'SORMAS definitely has an enormeous potential. People in the field want such a system and, as far as the technology is concerned, it's feasible. The concept offers several advantages compared to other current approaches using mobile devicest.'

Electronic medical records

Patients wholly embrace EMR access

When real medical records go live more than eight in ten users seeking information are patients, not their caregivers.

Who really uses electronic medical records? At most European hospitals, even the physicians and nurses have trouble accessing the hodge-podge collections of mismatched data. Yet, once a hospital installs an EMR system that is truly robust and capable of reporting up-to-date information about patients, it turns out that the patients are looking at their records more than their medical carers – by a ratio of 8 to 2.

The report comes from the software firm Epic, which has surged ahead over the past five years as the preferred provider for e-health systems at major hospitals in the United States. Among the firm's 354 customers are prestigious medical centres such as the Mayo Clinic, Johns Hopkins, the Cleveland Clinic, and Kaiser Permanente, to name just a few. The company claims that 56% of the American population has a digital record on one of its systems.

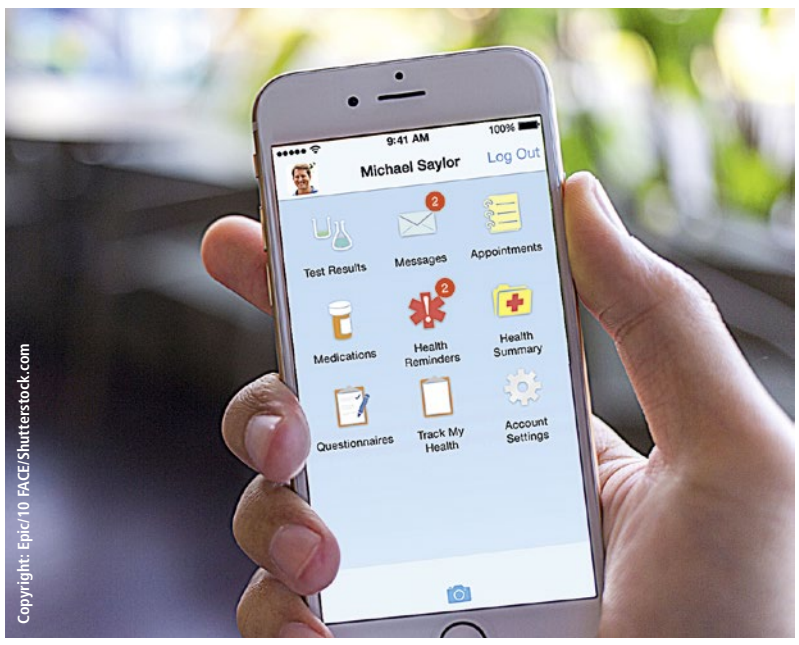
To gain a better understanding of patient portal usage patterns, Epic monitored the online traffic during 30 days among 12 of its participating medical centres. The results were staggering, according to Martijn Antonius, Vice President of informatics in the Netherlands. 'We saw something like 150,000 caregivers using the records, but when we looked at how many patients were accessing records, we saw there were 680,000,' he said. 'We learned that, through the patient portal, patients are doing all kinds of things to participate in their treatment and to become more responsible for their health. We think this is extremely important, and so do our customers, because patients not only embrace their role in healthcare but also, once they can be integrated into their healthcare, they become engaged in that care.

'Looking at Europe as a whole, this is an area where there is potential for considerable growth,' the Vice President said.

Earlier this year the first European hospital to go live with a full Epic system for managing EMRs achieved the highest ranking for its ability to share complete patient records in real time among physicians and care-givers. Radboud University Medical Centre in Nijmegen, the Netherlands became only the third in Europe to receive a Stage Seven Certification from HIMSS Analytics, based in Leipzig, Germany, a branch of the Healthcare Information and Management Systems Society based in Chicago.

Radboud University Medical Centre, shares this distinction of meeting the highest requirements for the European EMR Adoption Model with the University Medical Centre Hamburg-Eppendorf in Germany, which runs a system developed in-house, and the Hospital de Dénia-Marina Salud in the Alicante Province of Spain that runs an EMR system from Cerner, another American health IT company. Nine years ago, after landing in Europe with a Dutch team, Epic won deployments for its system with the Amsterdam Medical Centre and Vrije Universiteit Medisch Centrum (VUMC; Free University Medical Centre), also in Amsterdam.

Epic MyChart gives patients controlled access to the same Epic medical records their doctors use, via browser or mobile app



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The company's track record in the USA, and the increasing importance of opening EMR to patient access, have fuelled its recent success. Leading centres that are ahead of this curve are discovering they need to rip out pieces of their homegrown health IT systems and turn to an established, proven system.

In the United Kingdom Epic has installed a system with the Cambridge University Hospitals foundation trust. In Denmark, Epic won the contract to install its systems in the Copenhagen and Zealand regions, covering more than 20 hospitals with 44,000 caregivers. That contract specifically assures the hospitals receive the most advanced EMR features developed by Epic.

'The patient portal is more than a nice touch; it becomes an important tool for hospitals. It is much more than being patient friendly; it's about making the patient part of the treatment team, and it can mean much greater efficiency,' said Antonius. He cites examples where patients can schedule visits themselves, and can complete questionnaires to provide essential information in advance and online. The patient portal giving access to an EMR is going to become even more important in the near future, he suggested.

Martijn Antonius, Vice President of informatics at Epic in the Netherlands

When Apple, Inc. wanted to develop the HealthKit, it turned to the Mayo Clinic and Epic as its leading partners. That system has now gone live. Antonius: 'It can gather patient information from the iPhone, is now fully integrated into the patient portal, and is opening a vast new area of possibilities.'

He cites the example of a patient who has recently had a prosthetic knee implanted with the recommendation from the surgeon to be more active. The iPhone can push results from step-counting to the EMR. For a patient for whom the cardiologist is concerned about weight gain, the daily results from a weight scale can be pushed into the EMR for later review. 'With rising costs, hospitals understand now that demands for higher quality and greater patient engagement they can only deliver great healthcare if they are a data-driven organisation,' he pointed out. 'To do this, they really need to have their act together in terms of the infrastructure supporting a patient portal and the EMR. This is the challenge right now.'

UK hospital reaches Stage 6 of EMRAM

Applause for digital maturity

Report: Mark Nicholls

A senior consultant spearheading a UK hospital's drive to become paper-free has stressed the importance of seeing the process as a clinical transformation, rather than merely an IT project.

St George's University Hospitals NHS Foundation Trust, London, has been recognised for the significant progress made towards paperless-ness and has been validated by the Healthcare Information and Management Systems Society (HIMSS) at Stage 6 of the Electronic Medical Record Adoption Model (EMRAM).

However, Dr Martin Gray, the Chief Clinical Information Officer at St George's, said it was critical that clinicians were seen as being a key part of the process of the hospital becoming 'digitally mature'.

Gray, who is also a paediatric intensive care consultant, said: 'There are a large number of clinicians from this organisation without whom this project would not have succeeded. It does help having clinicians from varying roles bridging the gap between IT and change management, and the clinical "shop floor".'

St George's, which has more than 1,000 beds and serves a population of two million, has become the second and largest trust in the UK to be validated at EMRAM Stage 6.

It is paperless in the paediatric intensive care unit – apart from consent and child safeguarding forms. In the renal, cardiac and neurosciences wards it is almost paper-free.

However, on general medical and surgical wards while patient administration and ordering of tests is paperless, much of the patient's journey is still on paper.

'For us, as a hospital, this accreditation puts us on the map,' Gray added. 'There has been a lot of hard work over a number of years by both clinical and non-clinical personnel within the organisation working to develop an Electronic Medical Record and digitise the hospital.

'The recognition by an internationally-accredited body that we have reached that level of digital maturity is important; but it also helps to set the agenda for what we have to do to reach the next level.'

The next phase sees the further extension of digitisation of health throughout the hospital.

'It's also about opening up the digital records to enable patients to access their own electronic files and allowing cross agency working with GPs, community health, social services and with our network hospitals in South West London through inter-operability,' said Gray.

With consent forms, however, third party documents and referral documents still in paper format, the goal of becoming wholly paperless remains some time away.

He explained that the journey towards a paperless NHS is not about implementing software but about a clinical transformation. 'It's about changing the way people work, looking at processes and systems and how you build a digital workflow for the delivery of care within the healthcare ecosystem.'

Gray admits there were challenges with clinical engagement, communication about the project and bringing all departments on board with the project, which began in 2010 with the implementation of the Cerner patient administration system.

Ordering and reporting diagnostic tests followed in 2012 and, in 2014, St George's moved to electronic prescribing, medicines administration, and clinical documentation.

Care digitisation has proved particularly effective with the Cerner Millennium closed loop medication management system; when medication is ordered electronically for a patient it is verified in the pharmacy by a clinical pharmacist, then dispensed automatically by robot and delivered to the ward and, at the point of administration, the right patient and right drug are identified by barcode scanning.

The solution has resulted in increased accuracy of prescribing, fewer missed doses, and savings in time to complete the drug rounds.

'One of the softer benefits is that nurses now have more time to explain to patients about the drug they are about to take,' Martin Gray gladly underlined.

Dr Martin Gray is a Consultant Paediatric Intensivist at St George's University Hospitals NHS Trust in London and its Chief Clinical Information Officer.
Trained in the UK, Australia and Canada, his role is in clinical governance and collaborative research, with a strong interest in healthcare IT solutions and commissioning and contracts.
Within the Paediatric Intensive Care Unit, his interests lie in traumatic brain injury and neuro-critical care.

The system has also improved the efficiency of patient flow by cutting down the time patients spend waiting for drugs before discharge.

The centralised Electronic Patient Record system now has more than 5,500 users including nurses, consultants, doctors and administrators, and means access to documentation and notes is possible from anywhere in the hospital, or even remotely.

Gray's conclusion: 'While it's still in the very early days in the process, we are starting to see efficiency savings and quality improvements.'

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LONDON • GREAT BRITAIN 29 AUG - 02 SEP 2015

Diffusion tensor MRI

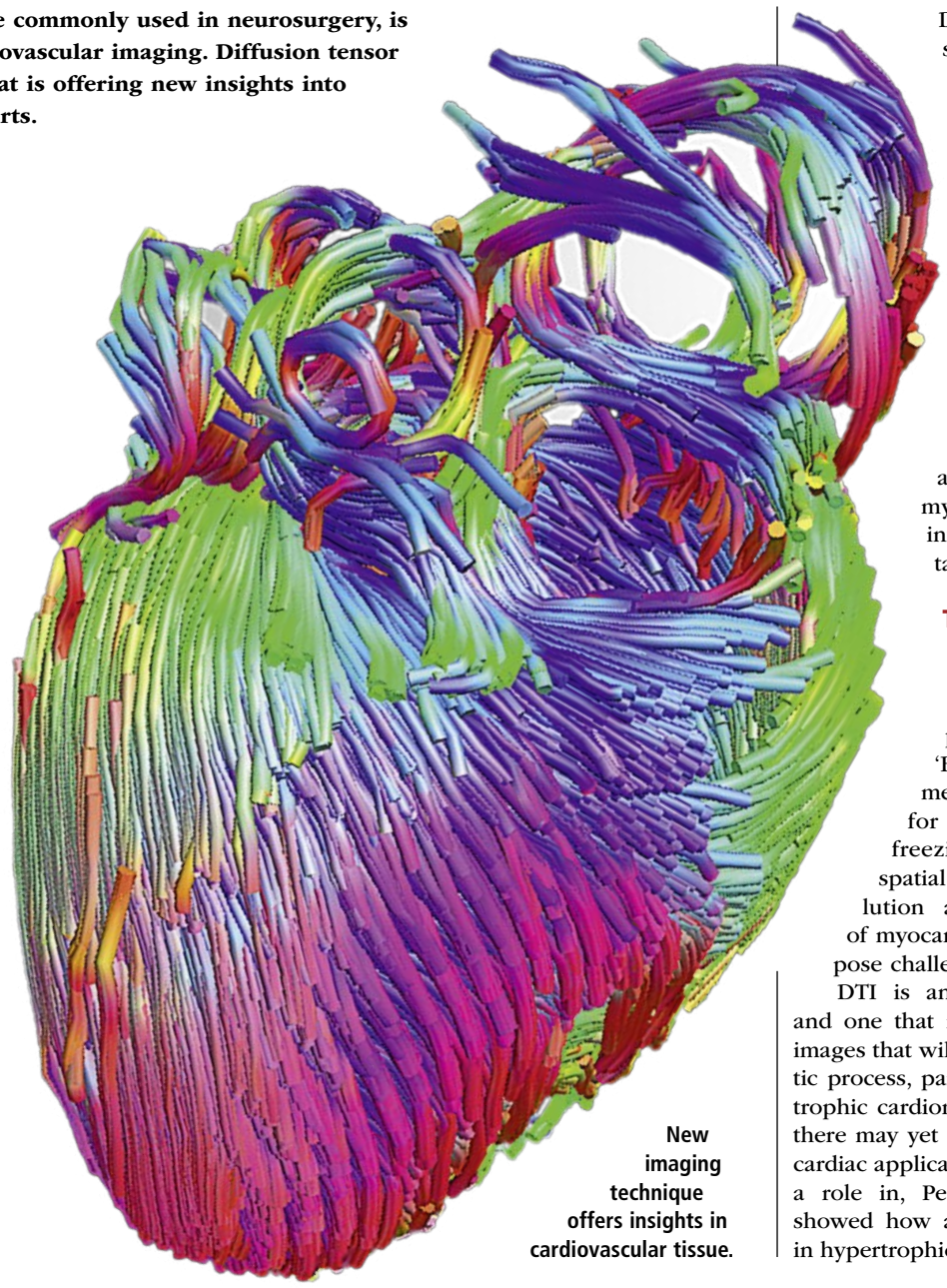
An innovative imaging technique, more commonly used in neurosurgery, is finding fresh applications within cardiovascular imaging. Diffusion tensor MRI is an evolving form of imaging that is offering new insights into tissue architecture, Mark Nicholls reports.

During a session focused on innovations in cardiovascular imaging, at the British Cardiovascular Society annual conference (Manchester in June), Professor Dudley Pennell, Director of the Cardiovascular Magnetic Resonance (CMR) Unit, and Director of Non-Invasive Cardiology at Royal Brompton and Harefield NHS Foundation Trust, outlined the background to diffusion tensor imaging (DTI). He explained how the technology yields information on water diffusion in tissue and is widely used by neurologists. It allows the mapping of the diffusion process of water molecules in biological tissues, in vivo and non-invasively, with the water molecule diffusion patterns revealing microscopic details about tissue architecture, either normal or in a diseased state.

Tractography

Through seven individual measurements taken by MRI, the DTI can map out the path of neurons and myocytes using an image processing technique called tractography.

'With brain tractography, the images are colour-coded for direction and it reveals amazing details in 3-D and is used by neurologists to map where the neurons are going,' Pennell explained. 'It also has an application for the heart and can image the organisation of myocardial cells.'



New imaging technique offers insights in cardiovascular tissue.

DTI has been around since the mid-1990s but until recently has been a slowly evolving technology.

It has taken huge steps forward with the use of accelerated imaging, advanced technology, and high field magnets (3-Tesla). Within cardiology, it has an application for cardiomyopathy, myocardial infarction and congenital heart disease.

The challenges

'There are, however, major challenges for cardiac DTI,' the professor added. 'Because of the movement, there is a need for advanced motion freezing techniques, for spatial and temporal resolution and the complexity of myocardial architecture also pose challenges.'

DTI is an evolving discipline and one that is revealing stunning images that will help in the diagnostic process, particularly with hypertrophic cardiomyopathy (HCM) and there may yet be a range of further cardiac applications that it may have a role in, Pennell suggested. He showed how abnormal contraction in hypertrophic cardiomyopathy has been shown to result from abnormally reduced rotation of blocks of myocytes, called sheetlets, which are organised contractile structures in the heart consisting of many myocytes.

Dudley Pennell is Professor of Cardiology at the National Heart and Lung Institute, Director of the National Institutes of Health Research Cardiovascular Biomedical Research Unit located at Royal Brompton Hospital, and additionally he directs the Cardiovascular Magnetic Resonance (CMR) Unit.

'With Cardiac DTI the current approaches appear promising and it is improving our understanding of normal cardiac structure,' he concluded.

During the same session, Derek Hausenloy, Professor of Cardiovascular Medicine at University College London and Duke-National University of Singapore, outlined the role of Hybrid PET/MR imaging in cardiac disease.

A technology that has only been available since 2011, he said it had the advantage in that the PET element images the biological process and MR the tissue characteristics. Hausenloy: 'Through that, we are gaining new pathophysiological insights into cardiac disease.'

Improved soft tissue definition and contrast

PET/MR is promising

PET/MR has long been studied for oncology but the technique also holds promise in cardiovascular applications, according to a panel of experts at the recent International Conference on Nuclear Cardiology and Cardiac CT (ICNCT), Mélisande Rouger reports.

A new kid on the block, PET/MR enables the acquisition of soft tissues definition and contrast unseen in PET/CT. The new hybrid combines both PET and MR strengths – excellent spatial resolution with molecular data – an alliance that has begun to tickle the interest of the cardiology community.

'What are we going to get when we put PET and MR together?' asks Bristol-based cardiologist Dr Chiara Bucciarelli-Ducci, who has used MR extensively in her work. 'Potentially a lot,' she added, 'but we still don't know because it's early days.' Cardiac imaging, she believes, is still very much a niche for PET/MR, but its potential in myocardial function makes it an attractive option. 'Although these machines were not developed for cardiac imaging, but rather oncology, their potential in myocardial infarction assessment represents an opportunity. Acute myocardial infarction is the nearer development and this is where cardiac MRI has really been worked on, to find some constraints that hopefully now, adding PET, we'll be able to understand better.' MR pictures of recent myocardial damage usually show a large scar with micro vascular structure on top. Adding PET to the formula, cardiologists can not only see a lack of metabolism in the damaged area itself, but also in surrounding segments.

'What it means is still a bit unclear, but it offers unprecedented pathophysiological opportunities to understand these complex processes,' Bucciarelli-Ducci said.

For the last few years, MR has been an exciting tool for interventional radiologists in myocardial salvage after primary percutaneous coronary intervention (PPCI) in acute ST-segment elevation myocardial infarction, to show the area at risk as end point for successful PPCI. Simply put, MR is increasingly used because it allows a reduction of miscalculation.

Stress MRI is excellent to image induced myocardial ischemia; combining it with PET could also increase diagnostic accuracy.

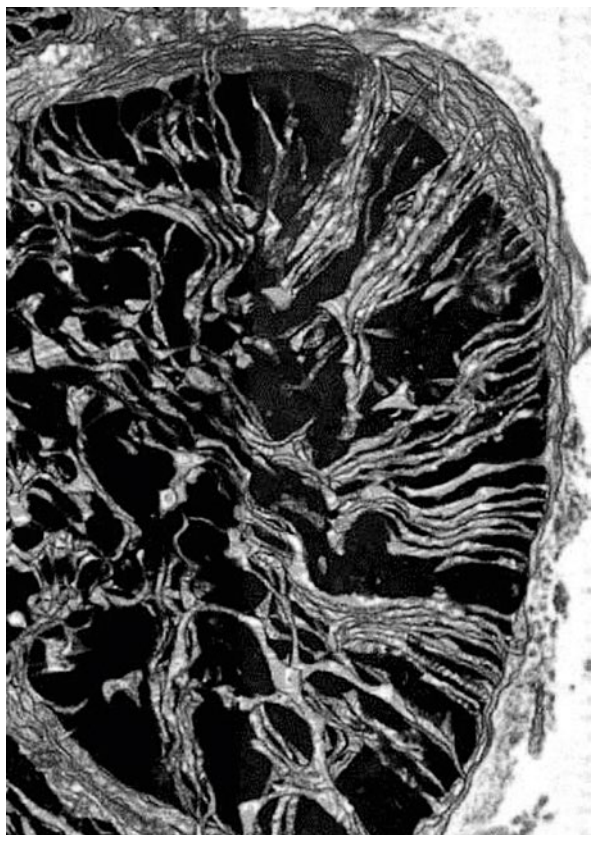
PET/MR also holds promise in sarcoidosis and acute myocarditis, an acute inflammatory disease of the heart. 'The potential here is really immense. The question is really how do we combine the information and how do we want to use these techniques,' she added.

A consultant cardiologist and lecturer at the UK's Bristol Heart Institute, **Dr Chiara Bucciarelli-Ducci** also co-directs the Clinical Research and Imaging Centre (CRICBristol) and leads creative medical research (CMR) at the Bristol National Institute of Health Research (NIHR) Biomedical Research Unit (BRU).

Continued on page 10

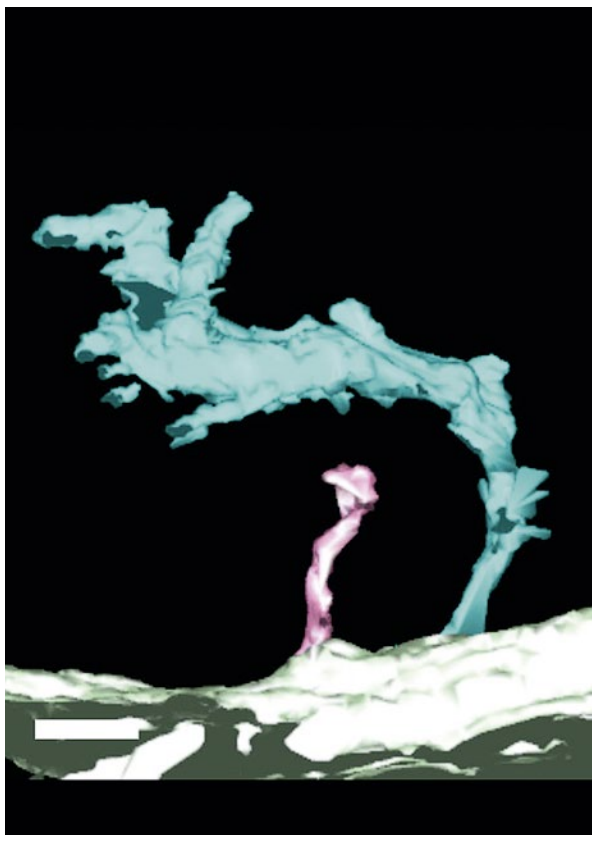
Brilliant 'bicycle spoke' images may hold clues to myocardial infarction

Advanced imaging techniques reveal T-tubules



Part of a healthy heart cell with a T-tubule 'bicycle spoke' structure

Part of a heart cell following a heart attack, where T-tubules have been lost.



A 'super-tubule' (cyan) compared with healthy T-tubule (pink)

Report: Mark Nicholls

Images revealing the 'bicycle spoke' structure of a heart cell may hold key clues to reducing damage from a heart attack.

Research conducted by Dr Ashraf Kitmitto and colleagues at the University of Manchester provides new information as to why some cells do not work properly following a heart attack. Their findings – illustrated with striking 3-D nano-images – were presented at the British Cardiovascular Society (BCS) Conference in Manchester in June in the session 'Unravelling the structural basis of cardiovascular disease through the application of advanced imaging techniques'.

Using serial block face scanning electron microscopy (SBF-SEM), Kitmitto and her team produced the 3-D images of a healthy heart cell at nanoscopic scale, which shows that part of their structure is arranged like spokes on a wheel.

During her talk, '3-D views of myocyte remodelling in heart failure and MI', Ashraf Kitmitto discussed how the spoke-like structures, called T-tubules, carry an electrical signal from the outside the cell to the inside and are necessary for the coordinated transmission of the electrical impulse through the cell, enabling cardiac cells to contract and thus the heart to pump blood around the body.

However, following myocardial infarction, the T-tubules are lost in many areas and the electrical signal cannot be carried properly through the cells. The cardiac myocyte death triggers a healing response or remodelling with extracellular matrix, fibrous tissue deposition within the surviving myocardium.

The remaining T-tubules appear to fuse and clump together forming very large, but distorted, 'super-tubules'.

Funded by the British Heart Foundation (BHF), the research has offered what Kitmitto described as 'the most detailed images of the T-tubule network to date' – promising new insights into the structural changes that may contribute towards the development of heart failure and dangerous irregular heartbeats. The next step is to find out why this process happens following a heart attack and develop strategies to intervene to stop it from happening, for improved outcomes.

With an estimated 550,000 people in the UK living with heart failure following a heart attack, Kitmitto said: 'We've made major advances in treating people following a heart attack, so more people are surviving, but the treatments don't address changes to the structure of the heart.' For the first time, we've been

PET/MR is promising in cardiology

Continued from page 9

Researchers hope they will be able to use PET/MR in many more applications. Bucciarelli-Ducci: 'The ambition for PET/MR is that it represents a one-stop shop where you can measure precisely myocardial function, but also viability assessment with FDG, which is the gold standard on top of tissue revascularisation and weak cardiac MR.'

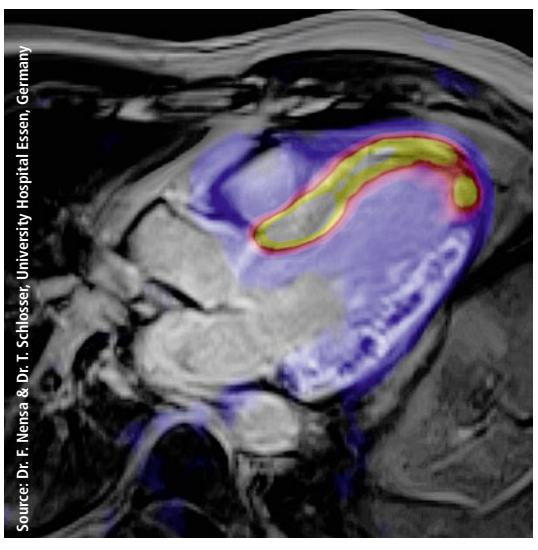
Simultaneous acquisition by PET/MR studies is another advantage, since it facilitates workflow and image registration significantly.

Choosing PET/MR over PET/CT leads to a dose reduction of 80% by leaving CT alone – a strong argument in they system's favour, especially in child imaging.

Although data on PET/CT or PET/MR for cardiac applications is almost non-existent, a paper published by Catalano et al. in Radiology in 2013, can be used as a reference. The study compared the use of the two hybrids in cancer patients and concluded that data found by PET/MR revealed additional findings not similar to PET/CT in 41% of the patients. 'It's very relevant because it did impact on clinical management in about 18% of patients, and influenced decisions on whether they should receive additional chemotherapy and surgery or not' she points out.

Despite numerous promises, a series of very real weaknesses continue to restrain development of the new hybrid. First, the price of the modality is dissuasive and means doctors will have to justify the cost. Then, PET/MR equipment is scarce, and only very few centres worldwide do cardiac PET/MR. Siemens recently published a map of its Biograph mMR (which enables to do 3-T) global distribution; Even if they were present on four continents as of January 2015, they only had about 60 machines in total.

Additionally, the level of expertise demanded by the modality is very high and remains an obstacle to its widespread use among cardiologists. 'Once you do PET/CT, it's



Siemens' Biograph mMR provides MR and PET data as one dataset – molecular MR acquisition data. Although this machine was not developed for cardiac imaging, but rather oncology, its potential in the cardiac field represents an opportunity

Dr Ashraf Kitmitto is a Reader in the Institute of Cardiovascular Sciences, University of Manchester. Having established her own research group she worked on structural studies of proteins mediating excitation-contraction coupling, leading to the determination of the first 3-D structure for the L-type voltage-gated calcium channel. This research has now developed to encompass the morphological changes that occur to the cellular structure of the heart as cardiac failure develops, using state-of-the art 3-D electron microscopy imaging methods.

able to look, in 3-D, at the nano-architecture of the cells around the damaged area of the heart and see the changes following a heart attack.

'The regular pattern of T-tubules – like spokes on a wheel – is really important because it means the whole heart cell can receive the same information and it can contract together. But, following a heart attack that regular structure is lost, so some parts of the cell will get the signal and other parts won't.

'Now, we can see what's going on; the next step is to find out why and how we can intervene to prevent heart failure development.'

BHF Associate Medical Director Dr Mike Knapton said: 'This interesting research and the beautiful images may hold key clues to reducing the permanent damage caused by a heart attack.'

Other talks in the session included clinical imaging for vulnerable plaques: VH-IVUS, CT and OCT by Professor Martin Bennett; Materials Science in Cardiovascular Research: a new perspective (Dr Sergio Bertazzo); and how SICM microscopy/FRET reveals molecular and cellular basis of heart failure (Professor Julia Gorelik).

not so much trouble. But for me, if I want to learn about PET/MR, I have a lot of work to do to understand the PET part. The opportunity is there to have a lot of data, but what can you do without the skills?' Bucciarelli-Ducci underlines.

Last, but not least, a number of issues come up with 3-T cardiac MR: artefacts can ruin pictures and patients with non MRI-conditional devices or metallic cerebral clips cannot be screened with 3-T.

Robert Gropler from St Louis, USA, who also spoke during the session, summed up the situation and outlined the perspectives for the near future. 'PET MR is slowly being introduced in the clinic and it will remain slow for a while. It's challenging but strategies are coming. We have to keep the industry involved. The most money is going to oncology, so we need to make it shift to cardiac.

'Finally, radiation exposure is not trivia. CT strategies are reducing radiation but, in the US, you can see that risk areas, such as vaccines, food, etc. are getting pushed back. I could see that for radiation exposure as well,' Gropler warned.

Stable chest pain and suspected CAD

Seeking CT's role

Coronary artery disease (CAD) is the major killer worldwide. Its early detection can save the lives of many. Computed tomography (CT) has shown tremendous results in this area, but its advantage over more invasive techniques remains to be demonstrated, especially in patients with low to moderate risk. Across Europe, a large team of investigators decided to do just that through the new DISCHARGE study. Mélisande Rouger interviewed team member Marc Dewey, Professor of Radiology at the Charité University Hospital in Berlin, about the study's aims and design.

'DISCHARGE is a large multicentre randomised trial that aims to determine whether CTA helps to reduce myocardial infarction, stroke and cardiovascular death,' explained Professor Marc Dewey, a team mem-

Continued on page 12

From the International Conference on

Dose reduction strategies

World-renowned cardiologists reviewed the latest trends and dose reduction strategies in cardiac CT during the International Conference on Nuclear Cardiology and Cardiac CT (ICNC) that unfolded in Madrid in May. Mélisande Rouger reports.

During this year's International Conference on Nuclear Cardiology and Cardiac CT, Dr Marcio Bittencourt, from Sao Paulo, Brazil, offered an overview of the newest available technology, namely GE Healthcare's Revolution, Siemens Force, Toshiba's Aquilion ONE ViSION, and Philips' Brilliance and IQon Spectral Detector CT scanners.

New scanners must do four things: improve image quality, acquisition speed and coverage, and reduce radiation dose, Bittencourt explained.

Temporal resolution – the time needed to acquire one image – should be <15% of the cardiac cycle to minimise motion artefacts. Thus, acquisition time, a challenge in the cardiac setting, must be as low as possible. Faster rotation is one way to achieve that, and most new scanners have indeed increased speed up to 0.25s per rotation. Other options are dual source CT and multi segment reconstruction.

To improve spatial resolution, users can either do sharper reconstruction, although some recent changes in detector technology and flying or dynamic focus spot have also improved spatial resolution.

For z-axis coverage, cardiac imaging usually required about 14 cm. Some new scanners now allow this to be performed in a single heartbeat, though this technology is not available for all vendors, Bittencourt pointed out.

New technology enables selection of the best scan mode and protocol for each individual examination, which contributes to reducing radiation dose. Besides protocols, other features, such as automated exposure control, reduced target noise and iterative reconstruction, may also lower dose significantly.

One recent technology, spectral energy imaging, has the potential to do calcium subtraction, myocardial perfusion or iodine map, and beam-hardening correction for perfusion.

However, not all these options are necessary if users are not doing top-notch research, Bittencourt believes. 'If you can't afford newer technologies, any 64 detector scanner allows adequate diagnostic image quality for most patients. Anything newer will cost more. If you ask me whether any of the new scanners better, I think they certainly have improved temporal resolution and spatial resolution, which are interesting and may allow evaluation of more complex patients. So, if you can pay for these new toys, my answer is yes, they are better. But if you ask if they are a cost effective replacement for a 64 detector scanner, from a health perspective, the answer is probably no.'

Dr Stephan Achenbach from Erlangen, Germany, focused on methods for low-dose coronary CTA. 'CT made its way into European guidelines on stable coronary disease and acute coronary syndrome, so it should really be considered in patient management,' he said.

There is tremendous potential for dose reduction. A 2007study at 50 sites across Europe compared 1,965 CTA examinations in 2,000 individuals. It showed tremendous differences in estimated radiation dose associated with CT angiography, with some sites using doses of up to 13 mSv on average and others 4.6 mSv.

Image quality, however, did not correlate to dose. 'This study from the past clearly shows that radiation dose can be lowered without sacrificing image quality, and today we

Professor Stephan Achenbach is Chairman of the Department of Cardiology at the University of Erlangen, Germany and Vice President of Global Affairs and Communication at the European Society of Cardiology (2014-2016). With major clinical interests in cardiac CT, imaging of atherosclerosis and interventional cardiology, he was president of the Society of Cardiovascular Computed Tomography between 2007 and 2009, and is currently its secretary. He is also a fellow of the European Society of Cardiology, the American College of Cardiology and the Society of Cardiovascular Computed Tomography, and a member of the European Academy of Sciences and Arts.

Dr Marcio Sommer Bittencourt is Assistant Physician at the Division of Internal Medicine, University Hospital of Sao Paulo, Brazil, where he obtained his PhD in 2014. He also gained a Masters Degree in Public Health from Harvard Medical School in 2013, and carried out a post-doctoral research fellowship in cardiovascular imaging at Brigham. His main clinical interests lie in cardiovascular disease, epidemiology, internal medicine, public health, biostatistics, medical and biomedical image processing and cardiac MRI.
He is one of the Fellow and Resident Leaders of the Society of Cardiovascular Computer Tomography SCCT and has over 100 publications to his name. Dr Bittencourt obtained a Masters in Public Health at Harvard Medical School in 2013, and gained his PhD in cardiology from Sao Paulo University in 2014.

Seeking CT's role

Continued from page 11

ber in this pan-European study. 'Procedural complications will be a secondary outcome.

'The study design was presented at the last ECR, during a late-breaking clinical trial session. The study has only just begun and is being conducted in 30 sites across Europe so far. We also plan to include large and small hospitals in the project.

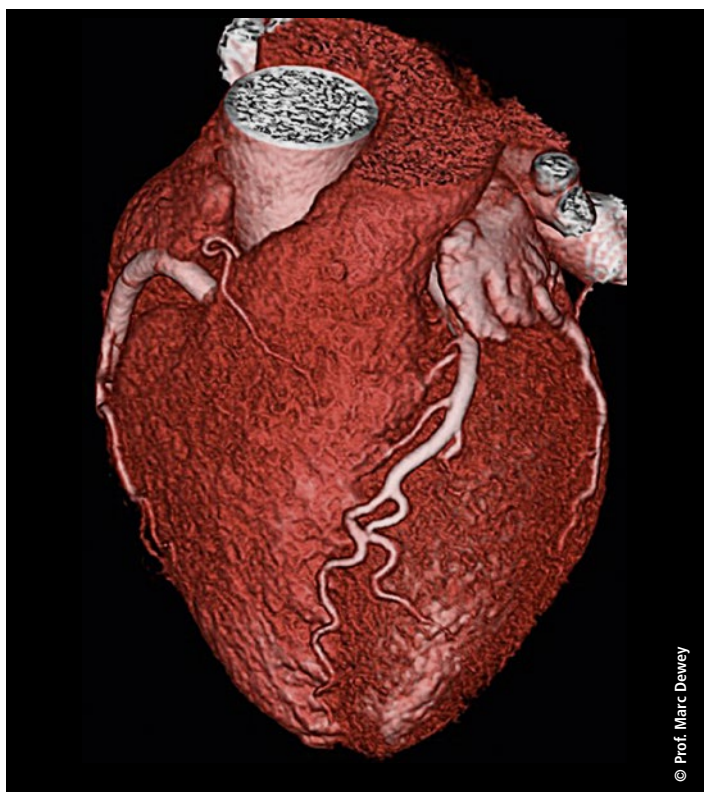
'Ultimately, DISCHARGE aims to provide the basis for new guidelines in cardiac imaging. Therefore, we are collaborating closely with clinical sites as well as non-clinical partners to optimise the impact of the study for the benefit of the different European health systems.

'This study has been granted six million euros through the 7th Framework Programme of the European Union (EC-GA 603266). It will actively recruit for two years with a maximum follow-up of four years.'

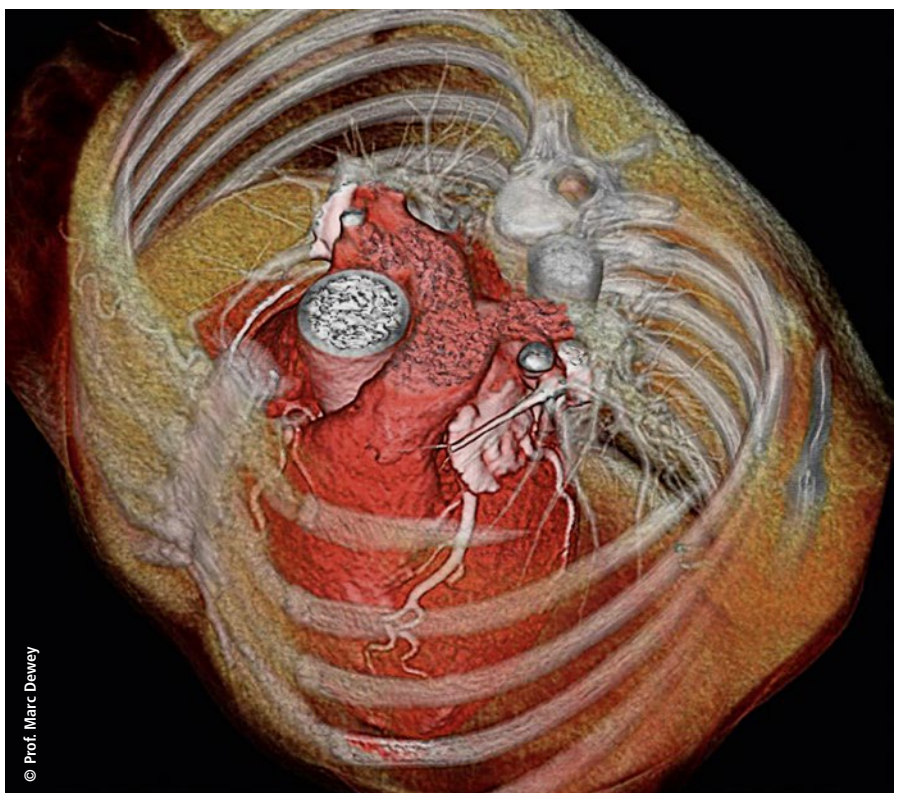
Today, where is CT placed in assessing suspected CAD?

'Currently, CT has little role and is not reimbursed for this purpose. Despite its proven high diagnostic accuracy, CT's full diagnostic potential is not being used, mainly because the comparative effectiveness of CT versus invasive coronary angiography (ICA) has not been shown in patients with stable chest pain and suspected CAD.

'In most European countries, ICA is the final reference standard to detect CAD, but it only allows minimally invasive treatment of coronary stenosis during the same procedure. However, approximately two million ICAs, done in Europe every year, do not detect CAD. It is thus the focus of our research efforts to analyse in which cases CT could replace these invasive tests.'



Cardiac CT without CAD



Cardiac CT with 3-D reconstruction of the chest

Does CT have diagnostic value in stable chest pain and suspected CAD?

'ICA is an invasive technique. As a diagnostic tool for patients with suspected CAD, especially with a low to moderate risk (10-60%), alternative tests that are non-invasive might provide a better risk/benefit ratio in favour of the patient.

'CT, because it is non-invasive, also grants potentially higher patient safety if used in appropriate clinical situations – but currently we do not know which ones.

'Early detection and improved characterisation of coronary plaques in the entire coronary artery tree is possible with CT. Certain unique high-risk plaque features have been shown to predict subsequent events and outcomes if assessed by CT. However, it's not known from a randomised trial whether such high-risk plaques should lead us to recommend intensified risk factor modification or certain medications.

'Another advantage is that CT images the tissues surrounding the heart, whilst ICA is limited to the coronary arteries. Therefore, CT has the possibility to check the lungs, oesophagus and spine, which may result in a diagnosis that explains chest pain and suggests appropriate treatment, but could be overlooked by ICA.

'In conclusion, ICA is the best way to treat known CAD; but in a situation where ruling out diagnosis of CAD is likely, CT, with its tremendously improved image quality, might prove to be the best method available.'

Other imaging modalities to rule out CAD

'We also use imaging ischemia tests, such as stress MRI, PET/CT, SPECT and stress echocardiography. These tests, while they allow the detection of CAD, are so-called functional tests and thus have a different purpose than CT.

'These perfusion-imaging tests enable a search for stress-induced ischemic myocardial areas, which play an important role in clinical decision-making in case of anatomic coronary stenosis found by CT with unclear functional relevance.'

Future promising techniques

'For all the above-mentioned non-invasive techniques (CT, MRI, PET/CT, SPECT, and echocardiography), dedicated research groups are working in Europe to further improve these diagnostic tests from a technical and clinical perspective.

'The main goal would be to develop a comprehensive imaging test that would allow accurate stenosis detection, characterisation of coronary plaques and myocardial perfusion assessment.

Due to CT's high diagnostic accuracy for stenosis detection and plaque visualisation, CT itself, which is broadly available, and more costly

s in cardiac CT

have many more options to do so,' Achenbach said.

The first strategy to limit exposure is to modify the mode of acquisition and to avoid spiral or helical scanning with continuous radiation exposure, which results in a dose in the 25-30 mSv range. 'That is really inappropriate for most patients who undergo CTA and can easily be modified because, in most cases, we want image reconstruction only in diastole. Most technology enables limitation of the full output of the X-ray tube during the diastolic segment of the cardiac cycle, thanks to ECG-correlated tube current modulation, often called ECG pulsing,' he explained.

Achenbach recommends using ECG pulsing systematically when spiral/helical acquisition is performed, as this will lead to a dose reduction of 40 to 50%.

Prospectively ECG triggered acquisition avoids spiral acquisition and combines step-wise table movements with short periods of data acquisition, typically in diastole. Therefore the dose is low, between 3 and 5 mSv.

High-pitch spiral acquisition, sometimes called Flash mode, is a combination of spiral l acquisitions and prospective ECG triggering. Thhis is only possible with dual source scanners and spends low dose, between 1.5 and 2 mSv. However, it requires low and very regular heart rates.

Lowering tube voltage also helps to reduce dose. Traditionally 120 kV were used in cardiac CT, but in many cases this can be lowered to 100 kV. Doing so will reduce the dose by 40%, even in patients who have high body mass index (BMI), according to Achenbach. '100 kV should be used in patients less than 85 to 100 kg – some say with BMI < 30 or 25, some combine the two, there are no strict guidelines,' he pointed out. By combining 100 kV tube voltage with prospectively ECG triggered axial acquisition, dose can be lowered to 2-3 mSv, and to as little as 0.9 mSv with high-pitch acquisition. 80 kVp work in very thin patients (<70 kg), and can lower dose to 0.6 mSv.

Some studies have combined all possible modes for dose reduction and performed coronary CTA with doses as low as 0.1 mSv. However, image quality can be seriously hampered in such an approach.

'Very low doses are possible, but I have to say I am not a fan for continuing this race for lower doses because we really risk sacrificing image quality and makinf misdiagnosis if we put too much weight on dose. Cardiac CT imaging is not a race to achieve the lowest possible dose; you always have to make sure you retain image quality to evaluate even those patients who have complex situations such as calcified plaque, etc.

hybrid imaging techniques such as PET/CT, are most promising to comprehensively assess CAD.'

For further information please go to:
DISCHARGE Trial
www.dischargetrial.eu

Department of Radiology
http://radiologie.charite.de

Prof. Marc Dewey MD
www.marcdewey.de

EU-Project DISCHARGE
http://ec.europa.eu/research/health/medical-research/cardiovascular-diseases/projects/discharge_en.html

Marc Dewey MD is the Heisenberg Professor of Radiology and Vice Chair of the Department of Radiology at Charité University Hospital, Berlin, Germany. He studied medicine at Charité and Johns Hopkins universities.
His research focused on non-invasive cardiovascular imaging, cardiac MRI and CT, radiation dose, experimental radiology, meta-analyses, cost-effectiveness and patient-centred imaging. Publications number over 150 and he has produced 65 original papers as first or last author, and given more than 70 invited lectures, including at the RSNA and ECR.

Hypertrophic cardiomyopathy

Experts: Echocardiography is an invaluable tool

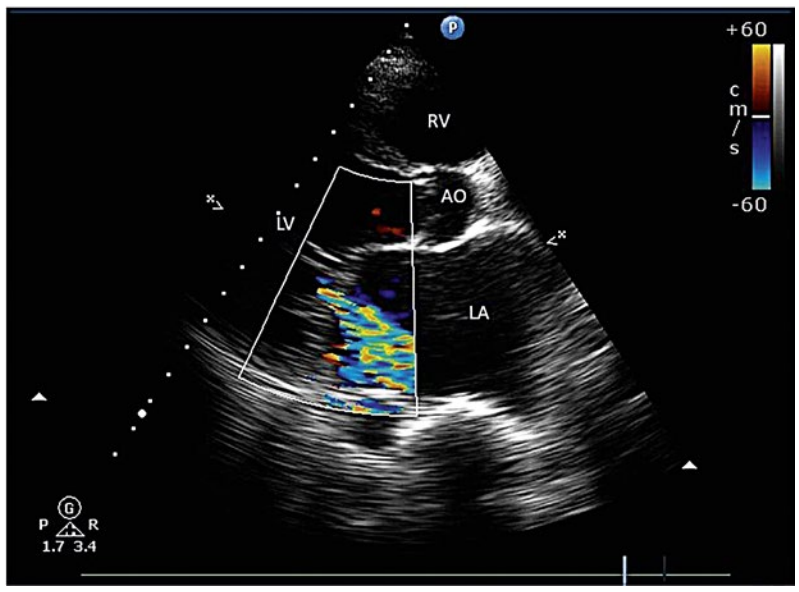
The challenges and advantages of using echocardiography as an invaluable tool in the assessment of Hypertrophic Cardiomyopathy have been highlighted at a major UK cardiology conference. A key benefit of echocardiography is its ability to accurately measure important aspects of cardiac structure and function related to hypertrophic cardiomyopathy (HCM), explained cardiac physiologist Dr Martin Stout.

Speaking at the British Cardiovascular Society Conference, held in Manchester this June, during a session that examined the use of cardiac ultrasound in diagnosis, Dr Stout looked at the advantages, challenges and factors in using echocardiography to assess HCM.

A primary disease of the myocardium, where a portion becomes abnormally thickened and fibrosed, HCM has a prevalence of 0.02-0.23% in adults and, in children, prevalence estimates are 0.3-0.5 per 1,000 – although data is more limited in this population.

Dr Stout: 'Diagnosis in adults is a wall thickness of 15mm or above in one or more myocardial segments. Echocardiography plays a central role in diagnosis but both cardiac MR and cardiac CT may also be relevant.'

Giving examples of different phenotypic patterns of HCM, Stout explained the importance of using contrast media in patients where diagnosis with echocardiography alone was difficult, particularly for a better view of the apex in potential apical HCM. 'It's very important in these cases to use contrast to aid diagnosis and there's real benefit in patients with apical HCM,' he added.



Echocardiography: Ultrasound examination of the heart

Viewing from different imaging planes

Working with current ESC 2014 guidelines on HCM, he stressed the importance of viewing from different imaging planes and the particular need to assess for right ventricle (RV) involvement and measure left atrial (LA) dimensions /volume (a particularly powerful indictor of prognosis).

With echocardiography in HCM, he pointed out, factors also to be aware of include mitral valve abnormalities and left ventricular outflow tract obstruction (LVOTO). He also added the importance of assessing LVOTO at rest, during valsalva manoeuvre (exhalation against a closed airway), and during exercise.

'The problem,' Stout warned, 'is that not everyone will have outflow tract obstruction at rest: only one third of patients with HCM will have outflow obstruction at rest, and another third will have obstruction during provocative manoeuvres.' However, he stressed that not only SAM (systolic anterior motion) might result in LVOTO in HCM. Other factors to consider are papillary muscle abnormalities and MV leaflet or apparatus abnormalities; so it remains important to rule out other causes of LVOTO.

According to Stoute, there are additional challenges in using echocardiography for HCM.

'Monitoring LV diastolic function in HCM is not always that straightforward either, it's difficult because of the phenotypic variation of hypertrophy and fibrosis. You must use all available technologies including LA volume and assessment of PA systolic pressure.'

LV systolic function in HCM can be monitored using advanced strain technology to look at subtle aspects of LV mechanics, which he said was particularly important when ejection fraction is usually normal or supranormal in these patients.

'Strain imaging can help in the clinical management of a patient and is also useful in patients with apical HCM,' he said. His Echo HCM "checklist" includes: assess presence and distribution of hypertrophy; think about use of contrast agents; assess for RV involvement; assess LV systolic function in detail; LV diastolic function; LA volume; PA systolic pressure; LVOTO, MV, and the extent of MR and papillary evaluation.

The session also heard from Paediatric Echo Cardiographer Dr Saleha Kabir, from the Evelina London Children's Hospital, who highlighted the role of echocardiography in inherited conditions, in particular left ventricular noncompaction, which, although rare, is increasingly recognised primarily through advances in imaging technology.

Dr David Oxborough, reader in cardiovascular physiology at John Moores University, in Liverpool, discussed echocardiographic assessment of ARVC, a genetically determined heart disease. He said ECG is crucial for this diagnosis and stressed the importance of multi-angle views.

Dr Martin Stout is Clinical Researcher in Cardiac Physiology at University Hospital South Manchester Cardiology Department and at the Manchester Metropolitan University School of Healthcare Science, where he performs advanced echocardiography techniques, physiologist-led exercises and dobutamine stress echo services for routine and more complex cases. He is also programme director for the modernisation of scientific careers, academic pathways in cardiac, critical care, vascular and respiratory and sleep sciences. An active member of the British Society of Echocardiography Education and Research he also takes part in Audit committees and is a regular presenter at national and international conferences.

The British Cardiovascular Society Conference

Music reaches the heart

British Cardiovascular Society

Report: Mark Nicholls

Innovative presentations, groundbreaking science and inspirational lectures underlined the diversity of sessions at the British Cardiovascular Society 2015 conference held in Manchester this June.

Professor Cliff Garratt, the conference programme committee chair, pointed to an evolving programme as key in the event's success. 'From my point of view it has been very exciting and energising to see so many people in the cardiovascular community involved in various ways in the meeting.'

Renowned scientist and TV personality Professor Robert Winston set the tone during the opening ceremony, with his presentation 'Where are we going with molecular medicine?'

With the conference theme "Hearts to Genes" a number of sessions focused on new genetic tests for cardiac disease and how these are being applied.

Among research presented was the discovery of a faulty gene that can cause fatal abnormal heart rhythms that are brought on by exercise, while another session suggested that fat surrounding blood vessels may actually help fight heart disease to reduce the risk of a cardiac attack.

The conference also offered unusual sessions, notably one by Professor Peter Sleight, from the University of Oxford, on music and the cardiovascular system, highlighting the therapeutic potential of music on the heart rate, blood pressure and wider well-being. This session attracted widespread national media interest in the UK.

Cliff Garratt is Professor of Cardiology at the Institute of Cardiovascular Sciences, Professor of Cardiology at Manchester University and Hon Consultant Cardiologist at Central Manchester University Foundation Trust. His research and clinical interests focus on the mechanisms and management of atrial fibrillation and familial sudden cardiac death syndromes. He is co-chair of the Heart Rhythm UK Working group on Clinical Management of Familial Sudden Death syndromes and Vice-President (Education and Research) of the British Cardiovascular Society

Professor Garratt, who is also BCS vice president (education and research), said the increasing involvement of the British Heart Foundation (BHF) in the meeting was pivotal in its success and development: 'The BHF is a key supporter of the meeting and had a number of sessions devoted to research that it funds,' he pointed out.

This included a highlight session of hypertrophic cardiomyopathy, which focused on research from a single clinical research department, showing how it works in terms of vision and scope. 'For that reason we were keen that the cardiology trainees who attend the meeting went along because soon they will be looking to see whether they are interested in cardiovascular research as a career, or part of their career, and the session gave them an insight into what might be involved," Garratt added.

The UK Genetic Testing Network (UKGTN) was involved in a session on the new genetic tests for cardiovascular disease that helps cardiologists to treat inherited conditions more effectively while the Strickland Goodall Lecture, topic "wellness and its causes", was given by Sir Harry Burns, professor of global public health at the University of Strathclyde and former Chief Medical Officer for Scotland.

Other highlight lectures covered issues such as the transplant cycle, the medico-legal minefield. There were also hands-on interactive training, popular hot topic sessions, a strong focus on cardiac imaging and exhibitors.

One of the more popular sessions, said Professor Garratt, was the 2015 hypertension update for cardiologists, which drew a large audience with discussions outlining why cardiologists should be interested in hypertension.

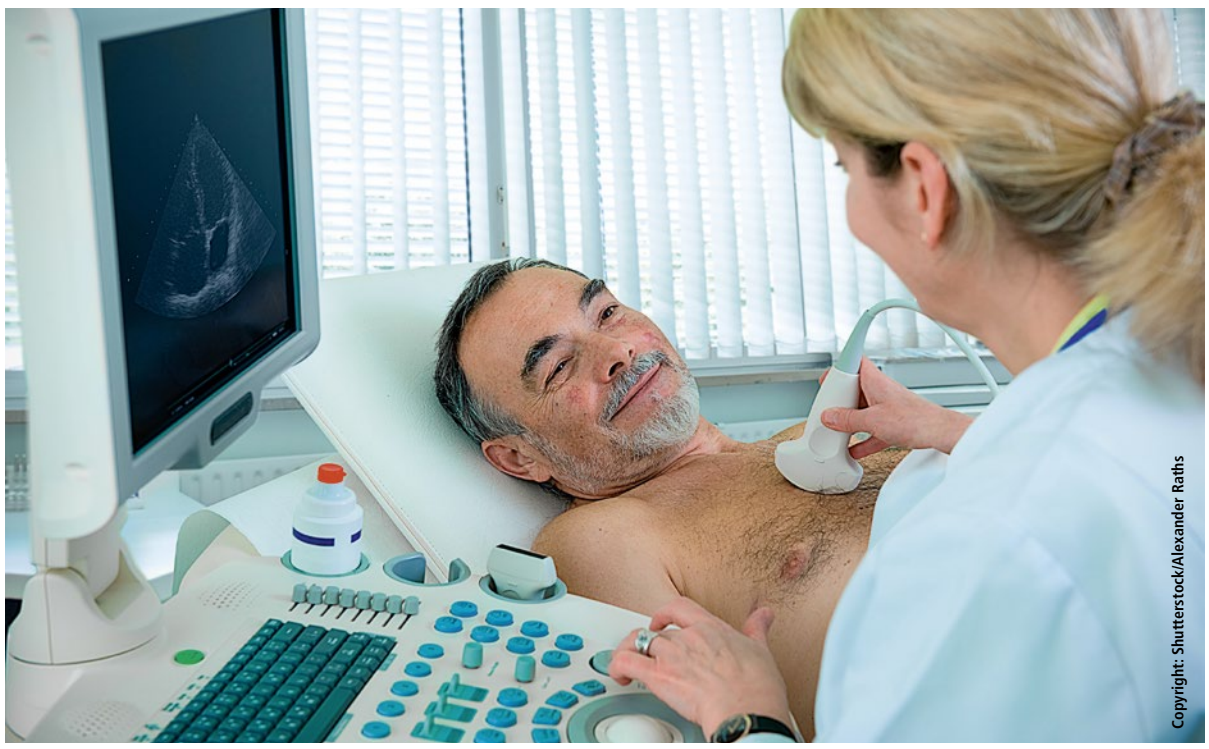
'The aim of the British Cardiovascular Society Conference is to deliver the best basic and clinical science sessions in such a way that is relevant to everyone,' Garratte concluded. 'We think we have achieved it, but will continue to build on that for 2016*.'

*For the diary: 6-8 June 2016
BCS conference. Manchester, UK

When should this procedure be performed?

Transthoracic echocardiography

The role transthoracic echocardiography plays in a number of common clinical scenarios was discussed by leading cardiac imaging experts at this year's British Cardiovascular Society Conference, Mark Nicholls reports.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Posing the question of when transthoracic echocardiography should be used, four senior figures in cardiac imagery examined its value in atrial fibrillation, chemotherapy, hypertension and stroke.

Speaking in this session, Dr Dipak Kotecha, a clinician scientist in cardiovascular medicine at the University of Birmingham and consultant cardiologist specialising in cardiac imaging, said transthoracic echocardiography had a significant role to play in atrial fibrillation (AF). 'AF,' he said, 'is becoming more prevalent and echo is important and essential in the patient management pathway. Incidence is expected to double in the next 20 years and by 2030 there will be 15-20 million people in Europe with AF. 'We have to do echo in AF for ejection fraction but it is important for choosing what rhythm control drug you may use or whether it's safe to use rhythm control in the first place.

'Echo should be considered for all AF patients, as we are looking for LV function, risk of stroke, safety of rhythm control drugs and interventional support.'

Within hypertension Professor Jamil Mayet – who heads the Surgery, Cardiovascular and Cancer clinical, educational and research programmes at Imperial College Healthcare NHS Trust in London – outlined how transthoracic echocardiography can be used to try to support patients, to decide which ones receive treatment and for risk stratification.

He explained that it can be used to assess whether there is left ventricular hypertrophy (LVH), diastolic dysfunction, LV systolic dysfunction, aortic valve issues or to assess myocardial ischemia.

Concluding that transthoracic echocardiography has a role to play in hypertension, he said: 'With patients who have stage one hypertension, we need to decide whether to treat the risk factors, lifestyle, or with drugs, and we can use echo if we are going to change the management of patients.

'Patients who will benefit from referral for routine echocardiograph are those with borderline blood pressure, where LVH may have an influence on the decision to treat; possibility of white coat hypertension; risk stratification in patients with multiple risk factors or routine reasons for echo, such as shortness of breath.'

Dr Leonard Shapiro, consultant structural interventionist at Papworth Hospital, Cambridge, suggested that the use of transthoracic echocardiography was not critical in all cases of stroke, but had value if it made a contribution to the management of patients.

Dr Thomas Mathew, consultant cardiologist at Nottingham University Hospitals NHS Trust discussed the role of transthoracic echocardiography in patients undergoing chemotherapy in the context of cardio-toxicity. With patients suffering cellular destruction, biopsy changes, cumulative dose-related effects and permanent damage as a result of chemotherapy, echocardiography had a role in their assessment.

'We should use the best form of echocardiography available and, on the evidence it is 3-DE as 2-DE fails to detect small changes in contractility. If 2-DE has to be used, it should be with GLS or Troponin, which is the best biomarker in this context.'

Mathew is concerned that all heart failure trials have excluded patients with cancer and there are no proper studies in this evaluation group. 'Using echocardiography is important,' he underlined. 'The main purpose is to decide whether to continue or stop chemotherapy because of the risk.

Dr Dipak Kotecha MD is a clinician/scientist in cardiovascular medicine at the University of Birmingham and a Consultant Cardiologist at Queen Elizabeth Hospital, Birmingham, specialising in cardiac imaging. An Honorary Research Fellow at the Royal Brompton Hospital, London, and the Monash University Centre of Cardiovascular Research & Education, Melbourne, he is a Task Force member for the European Society of Cardiology Guidelines on Atrial Fibrillation, and is currently writing the next set of practice guidelines that will be published in 2016. His main research interests are heart failure and atrial fibrillation.

Dr Thomas Mathew is the clinical lead for cardiac imaging at Nottingham University Hospitals and specialises in echocardiography, cardiovascular magnetic resonance imaging and nuclear cardiology. He is also the training programme director for East Midlands North Deanery and a member of the BCS training committee. An elected council member of the British Society of Echocardiography and a member of the BSE educational committee, he is also an editorial board member of the British Journal of Echocardiography. With more than fifteen years' experience in cardiovascular imaging, his interests include non-invasive imaging of ischaemic heart disease, valve assessments and cardiomyopathies.

Test predicts myocardial infarction outcome

Researchers have identified a new test that can be used to predict the likelihood of a patient developing heart failure, or even dying following a heart attack, Mark Nichols reports.

Known as the index of microvascular resistance – or IMR – a new test to predict myocardial infarction outcome uses a pressure-sensitive and temperature-sensitive wire that can be used to accurately work out the extent of injury in a blood vessel supplying blood to the heart.

Findings from a study from the University of Glasgow and funded by the British Heart Foundation (BHF) were presented at the British Cardiovascular Society (BCS) Conference, held in Manchester this June. The researchers showed that a wire inserted into the coronary artery, after someone has a heart attack, can predict if they will go on to develop heart failure.

Professor Colin Berry, lead researcher and cardiologist from the University of Glasgow and Golden Jubilee National Hospital, said: 'Heart attacks lead to heart failure, which is a big problem in the UK, and has a huge impact not only on the individual, but on the families and carers of those suffering – affecting whole communities.

'Thanks in large part to the work of the British Heart Foundation, 70% of people who have a heart attack now survive, but this means we now see an increased number of people surviving but left with damaged hearts and heart failure.

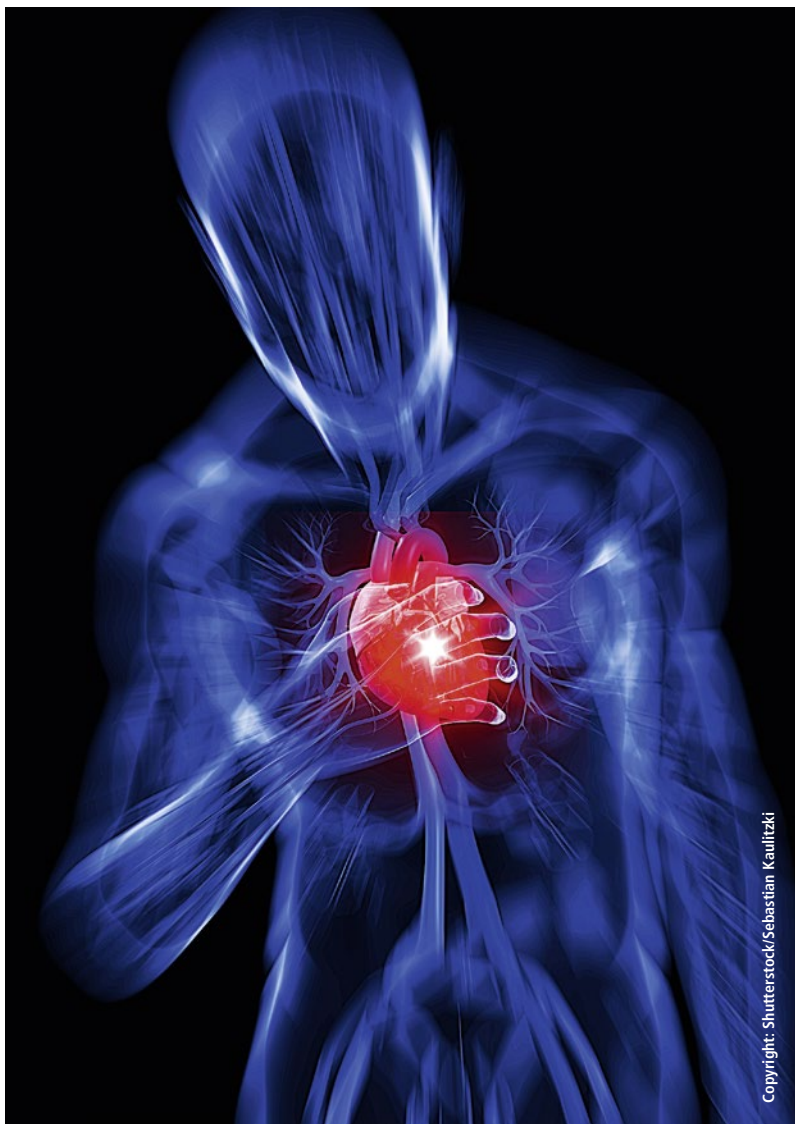
'We want to improve the outlook for people after they have a heart attack and develop new treatments to limit heart damage, reducing the burden of heart failure.'

Around 175,000 heart attacks occur in the UK each year; survivors could find the heart has been damaged and could lead to heart failure (HF). As is known, early treatment after a heart attack can reduce the chance of HF.

After a suspected myocardial infarction a patient is routinely given a coronary angiogram to identify any narrowed blood vessels – but although this can identify narrowed vessels, it cannot show if, or how much, cardiac blood vessel damage has occurred.

The Glasgow researchers now say the new wire technique can be used to work out the level of arterial damage, enabling doctors to quickly identify patients at a high risk of HF after their heart attack, based on damage to the arteries.

Patients were enrolled in this new research at the Golden Jubilee National Hospital in Glasgow. All will have life-long follow-up to check whether the IMR result predicts survival in the long term.



Professor Colin Berry is Chair of Cardiology and Imaging in the University of Glasgow and academic lead in cardiology and consultant cardiologist at the Golden Jubilee National Hospital and Western Infirmary, Glasgow. With specialist interests lie in interventional cardiology and imaging, and research focus on injury and repair pathways in coronary heart disease, Berry is a committee member of the British Cardiovascular Society Academic & Research Committee, the British Society of Cardiovascular Research and the British Society of Cardiovascular Magnetic Resonance. He is also a Fellow of the Royal College of Physicians and Surgeons of Glasgow, the Royal College of Physicians of Edinburgh and the American College of Cardiology

Cardiac exploration gains tool to access hidden areas

New mobile ECG gives 360-degree view

The conventional 12-lead ECG has certainly proved its worth in displaying rhythm disorders or ischemia. Nevertheless, as the display possibilities of a 12-lead ECG are limited to only about 110 degrees of the heart, an exact location of a cardiac event often cannot be determined.

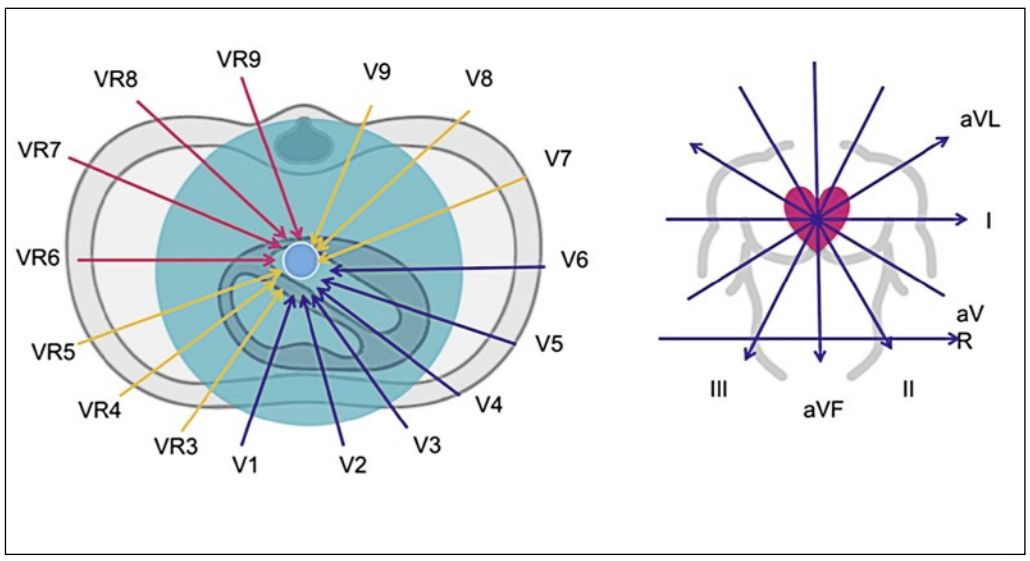
Personal MedSystems has produced a brand new combination of smartphone, or tablet PC, and ECG technology to reveal a significantly greater area of the heart. This is the next generation of ECG devices. A broader display is gained via ten supplementary leads, calculated for a 360-degree view. Combined with the free CardioSecur pro app – and using only four electrodes – the mobile 22-lead ECG shows V7-V9 as well as VR3-VR9, in addition to all 12 standard leads. Thus it allows diagnosis of the left and right lateral as well as posterior cardiac wall.

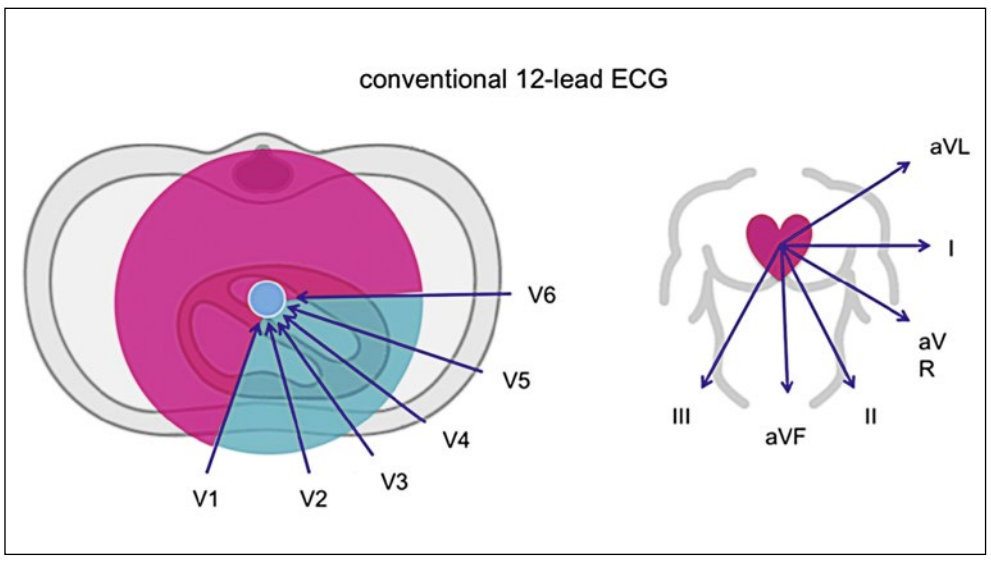
CardioSecur pro also provides unrivalled communication and mobility options, the manufacturer points out.

Faster precise diagnosis

Distinguished in the Best Medical App contest at MEDICA 2014, CardioSecur pro ECG technology is a reduced electrodes system based on the EASI standard first developed in the 1960s and described by Dower in the 1980s. Numerous publications scientifically acknowledge that EASI is a highly precise alternative to conventional ECG systems, the maker reports. 'The outstanding quality and accuracy of CardioSecur pro has been validated in numerous clinical studies against conventional 12-lead ECG systems with 10 electrodes, and evidences a 99% plus match regarding specificity on the heart's activity.

'Using only the four electrodes mitigates artefacts to a bare minimum ensuring maximum signal quality and exceptionally stable lead depiction. As the four electrodes are placed on very marked positions of the thorax lead misplacement, often consequential to highly diverse anatomies, is eradicated.' The originality of the professional mobile ECG system lies in its mobility and simple communication system, the firm adds. 'Due to its small size and light weight (50 grams), it can be taken anywhere easily, without taking up much space. Time saving is significant due to swift electrode application and intuitive ECG report export options in PDF format via email, iMessage or AirPrint. ECG reports can be easily e-mailed to fellow professionals or attached to the patient's electronic records, serving the increased need of efficiency.'





ECG readings with CardioSecur pro do not take up much space on a mobile device, as 10,000 minutes of ECG can be recorded per 1GB. Optionally, Personal MedSystems offers an automatic interpretation.

Details: www.mobile-ecg.com
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Ultrasound is at the heart of Spanish strategy

Chest pain units

Imaging modality complements a stress test in diagnosing the aetiology of chest pain, according to an expert speaking at the International Conference on Nuclear Cardiology and Cardiac CT (ICNC) held this May in Madrid.

Report: Mélisande Rouger

Chest Pain Units (CPUs) have spread through Europe, and Spain is no exception. Almost every large hospital offers this service to rule out acute coronary syndrome and diagnose unspecific chest pain, according to Professor Ivan Nuñez, a cardiologist at the San Carlos Hospital in Madrid and Chairperson of the Ischemic Cardiopathy and Acute Cardiovascular Care Section of the Spanish Society of Cardiology.

'CPUs can either be physical or virtual, i.e. work with dedicated personnel or on-call physicians – the latter being the most common scenario. Services offered within the units are heterogeneous and depend mainly on the hospital and region,' Nuñez explained. A stress test, highly available and reproducible, remains the most widely used examination in Spain's CPU setting.

When the aetiology of chest pain is unclear and the patient doesn't come for cardiac trauma, ultrasound (US) can be a powerful ally, according to Daniel Rodriguez-Muñoz, a cardiologist at the Hospital Ramon y Cajal in Madrid, and a speaker at the International Conference on Nuclear Cardiology and Cardiac CT (ICNC).

'Our main strategies are CT; nuclear cardiology following either exercise test or stress test with drugs; and exercise or stress dobutamine test using alterations in wall motion with echo detection,' he continued. 'In general, we choose echo when we have to use drug-induced stress. When the patient is obese, or a heavy smoker, the acoustic window may be bad and alter image quality, so you would rather use nuclear tests or CT".

Do we need to run?

In his presentation Rodriguez-Muñoz tried to answer the main questions a cardiologist faces in the CPU setting, the first and foremost being: 'Do we need to run?'

Patients in shock, or presenting with myocardial infarction, or pulmonary embolism, are all situations in which physicians must act immediately: 'We need to run whenever we believe that clinical symptoms and the ECG are suggestive of acute coronary syndrome.'

Echo will help to show whether the patient is suffering from hypovolemic, cardiogenic or septic shock. Rodriguez-Muñoz recommends using echo when the suspicion of pulmonary embolism is high and the patient presents with shock or hypotension, or when CT can't be performed.

Echo will also work for distinguishing cardiac vs. non-cardiac aetiology of dyspnoea when clinical and lab clues are ambiguous, and for guiding therapeutic option in patients with intermediate risk.

The next step is to determine whether the patient has angina or acute coronary syndrome, or not, by focusing on the negative predictive value of echo, i.e. by looking at regional wall motion abnormalities, depressed LV function, and other data. When the symptoms are atypical, a common situation in this setting, echo will also help to confirm or take decisions about where to refer the patient next. 'We rely on echo to make the final call. In on-call shifts, we see many patients with chest pain that is non suggestive of acute coronary syndrome based on the symptoms alone. Echo helps us to discharge patients when we have doubts – for example when the patient is a 75 year-old hypertensive, diabetic and obese man, so the likelihood for coronary disease is high, but the symptoms are atypical and the ECG is normal.'

An increasing number of emergency physicians use US to assess patients in the emergency department, especially in small hospitals that may not have on-call cardiologists. Ramon y Cajal is one of Madrid's largest hospitals, with 1,000 beds, including 50 in cardiology and 14 in the acute coronary unit. The CPU has an average two patients per on-call shift, amounting to 700 to 800 patients per year, Rodriguez-Muñoz estimates.

'The number of patients referred for additional cardiac examination from the CPU is not very high. When it's clear that it's acute coronary syndrome, patients go directly to the cath lab. Patients presenting with heart failure or other associated clinical problems that require further treatment, go directly to the cardiology ward – and, when there is highly suggestive clinical evidence that it's not acute coronary syndrome, patients will undergo other tests in the emergency department.'

Spanish are unique

At the ICNC the panel concluded that most CPU strategies of detection of ischemia or coronary artery disease eventually include patients with very low probability of having acute coronary syndrome; around 95% of the tests are usually negative.

Spanish CPU organisation is unique. Spain has not one but several public healthcare systems managed by the comunidades autonomas, or regions. Protocols are not always the same and they may impact on patient care differently.

'Each region's network, resources and mortality rates are different. Studies on infarction showed that the mortality rate in Valencia was higher than in Madrid or Barcelona. This was relayed in the media and pushed the national government to issue measures to improve infarction prognosis. However, apart from that, the national Health Ministry has very little power,' Nuñez pointed out.

'There is a very different prevalence of coronary artery disease between Japan and the USA, so it makes sense to have different approaches there; but it doesn't seem to make much sense to have different approaches in Andalusia, Madrid or Catalonia. It's really an administrative and political issue,' Muñoz believes.

However, Spanish hospitals tend to follow the European recommendations, which smoothes out differences, experts suggested.

In 2009 **Daniel Rodriguez-Muñoz** qualified in medicine at the University of Málaga and later (2015) completed his residency at the Department of Cardiology, Ramón y Cajal University Hospital, in Madrid. Now a medical doctor at the Unit of Electrophysiology and Arrhythmias, at the same department, he is completing his work towards a Masters degree in medical education at the University of Barcelona and PhD on Intra-cardiac Flow Parameters to guide Atrio-Ventricular Delay Optimisation in Resynchronisation Therapy at the University of Alcalá de Henares, Madrid. With his experience in peer-education, formal/non-formal training, and design of training programmes, Rodriguez-Muñoz's main interests are the design and development of projects and publications, and medical education.

An extra asset in the diagnostic toolkit

New cardiac genetic testing panels

Cliff Garratt is Professor of Cardiology at the Institute of Cardiovascular Sciences, Professor of Cardiology at Manchester University and Hon Consultant Cardiologist at Central Manchester University Foundation Trust. (See profile on page 14)

Report: Mark Nicholls

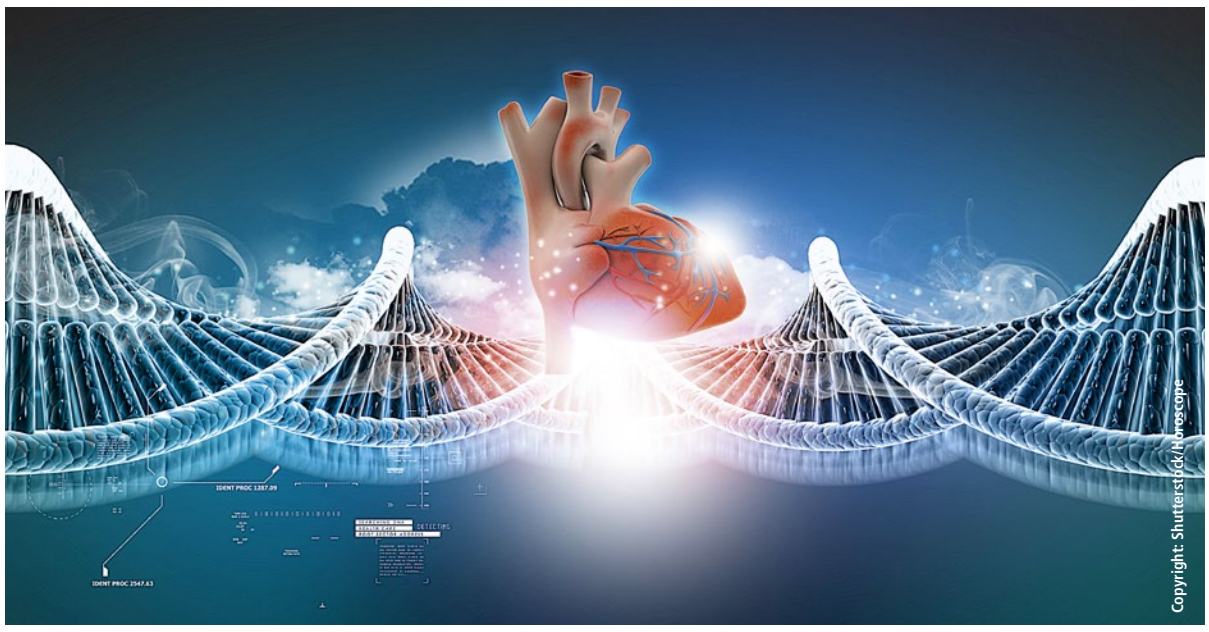
As new cardiac genetic testing panels become available, cardiologists have been warned not to lose sight of the importance of comprehensive clinical evaluation. While genetic testing is helping to identify more people at risk of inherited conditions, experts stress they are only part of the diagnostic toolkit.

This was outlined in a session entitled 'The new cardiac genetic testing panels: implications for the clinical cardiologist' held during the British Cardiovascular Society Conference in Manchester this June.

With the emergence of new genetic tests for cardiac disease, Professor Cliff Garratt raised issues 'the cardiologist needs to know' in making the modern diagnosis.

Sanger Sequencing remains the standard to confirm a single genetic variant but new tests – next generation sequencing – which can be applied to a large number of genes, are now facilitating more testing, more cheaply and in the same timescale with panels of genes.

Garratt, who is Professor of Cardiology at the Institute of Cardiovascular Sciences, Professor of Cardiology at Manchester University and Hon Consultant Cardiologist at Central Manchester University Foundation Trust, explained: 'We can have them highly targeted at 5-15 genes for LQT, for example, or a less targeted panel for 20 genes, though the disadvantage of the panel approach is that you have the problem of background genetic noise.'



Advances in genetic and genomic technology are enabling many more patients with a rare disease to benefit from genetic tests, either to establish or confirm a diagnosis; or assess the genetic status of other family members and gene panel tests are now making it possible to test simultaneously all the genes known to be associated with a condition.

Despite having the benefits of genetic testing, Garratt issued a clear warning that, whilst genetic testing is proving valuable, it is not an alternative to making a clinical diagnosis. 'It will not solve your clinical problems but will help management of patients who you have a proper diagnosis for,' he said.

During the same session Dr Shehla Mohammed outlined the work of the UKGTN (United Kingdom Gene Testing Network) in the evaluation process for genetic tests.

The role of UKGN is strategic; it involves healthcare commissioning and evaluating new genetic tests for clinical utility and validity with screening for 698 disorders, 872 genes and 46 panel tests. 'It's about promoting equity of access of genetic tests for individuals who have, or are, at risk of genetic disorders,' Mohammed explained.

UKGTN works with 30 member laboratories across the UK, many affiliated to regional genetic centres and some linked with specialist services and follows the ACCE model process for evaluating genetic tests of: Analytic Validity; Clinical Validity; Clinical Utility; and Legal and Ethical and Social implications. 'The reasons for doing genetic testing is for diagnosis, treatment, prognosis and management, pre-symptomatic diagnostic testing and genetic risk assessment,' Mohammed added. 'The UKGTN promotes high quality, equitable and appropriately identified genetic tests.' It has the capability to deliver effective cascade testing in inherited cardiac disorders.

Dr Kay Metcalfe, NHS Consultant Clinical Geneticist at St Mary's Hospital Manchester, discussed panel testing for Sudden Cardiac Death SCD syndromes.

Underlining Garratt's point, she added: 'Family screening helps identify those at risk, but the challenges of the exome and genome sequencing approach are the large amount of data generated. Genetic testing is probabilistic and forms part of a comprehensive clinical evaluation.'

Dr Paul Clift, from Queen Elizabeth Hospital, Birmingham, spoke about genetic testing in the context of Marfan syndrome and other familial thoracic aortic aneurysm syndromes but stressed the importance of physical and clinical assessment in such conditions in association with genetic testing.

According to Clift, Marfan remains a clinical diagnosis but fibrillian-1 (FNB1) gene testing aids that diagnosis and there are advantages with panel testing giving rapid genotyping allowing a detailed management strategy for patients.

'Panel testing in aortopathy allows for early genotyping for suspected hereditary aortopathy, risk stratifies management strategy for patients and families.'

UK progresses genetic testing to identify FH

Familial hypercholesterolaemia

A ground-breaking genetic testing programme for an inherited and potentially-deadly high cholesterol condition has been extended to more United Kingdom health trusts, Mark Nicholls reports.

The faulty gene associated with Familial hypercholesterolaemia (FH) is found in an estimated one in 200 UK families – making this the country's most common genetic mutation, with possibly as many as 320,000 people affected, including around 68,000 people under 18 years old.

FH is caused by a genetic fault that leaves people with abnormally high cholesterol, which significantly increases their risk of heart disease, including a heart attack and, on average, shortens life expectancy by 20 to 30 years if untreated. If one person in a family is found with FH, on average half of their brothers and sisters and half of their children will also have the faulty gene and be at high risk of early heart disease.

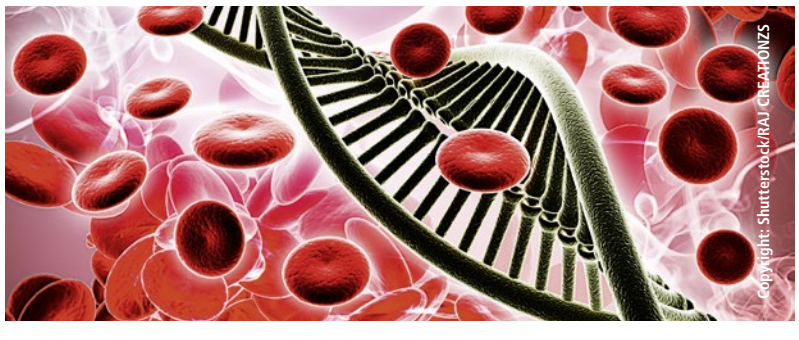
Most FH cases are never diagnosed, putting them at significantly higher risk of dying young from a heart attack. Now funding of over £900,000 from the British Heart Foundation (BHF) is enabling the availability of FH testing in five further UK areas. With a simple DNA blood test, a specialist nurse can identify whether an individual with a clinical diagnosis of FH carries the faulty gene. If discovered, they are then referred for family cascade testing with all immediate first-degree relatives also invited for testing and treatment at their local clinic.

If diagn#osed, early statin treatment, lifestyle advice and careful monitoring, mean that an individual's life expectancy goes up to match the average of the general population.

The additional FH cascade testing funding – extended to University Hospitals Birmingham, York Teaching Hospitals Foundation Trust, NHS Western Isles, Gloucestershire Hospitals NHS Foundation Trust, and the Royal Brompton & Harefield NHS Foundation Trust – was announced in June at the British Cardiovascular Society Conference.

These follow the initial roll-out across eight sites – Royal Free London NHS Foundation Trust, Guys and St Thomas National Health Service Foundation Trust, South Yorkshire Cardiothoracic Centre, Greater Manchester and Cheshire Cardiac and Stroke Network, University Hospitals Bristol NHS Foundation Trust, City Hospitals Sunderland NHS Foundation Trust, NHS Grampian / North of Scotland Cardiac Network, and University Hospital Southampton NHS Foundation Trust – which has already identified 500+ FH people.

Jo Whitmore, the FH Clinical Lead at the BHF, said: 'If high cholesterol is left unchecked, fatty materials can build up in your arteries, increasing your risk of heart disease. The problem with FH is that it dramatically increases the LDL cholesterol in the person's blood, causing a heart attack, commonly at a very young age. We know that cascade testing within families works, and the challenge is now to engage with NHS organisations and commissioners across Britain so that no family falls through the cracks.



'FH is easily treated, so no family should have to go through the pain of seeing a loved one have a heart attack that could have been prevented.'

The National Institute for Health and Care Excellence (NICE) estimates that if 50% of the predicted relatives of people with FH are diagnosed and treated, the NHS could save £1.7 million per year on healthcare for heart disease by preventing cardiovascular events.

From a clinical commissioning perspective, FH has not been on the 'radar' of general healthcare commissioners, but has not been seen as small enough to do specialist commissioning either.

However, screening is a cost effective option, Whitmore confirms: 'For the first person in the family identified the cost is about £200 for the DNA test but, once you've identified the gene you are looking for, the test comes down to £75 for other family members.'

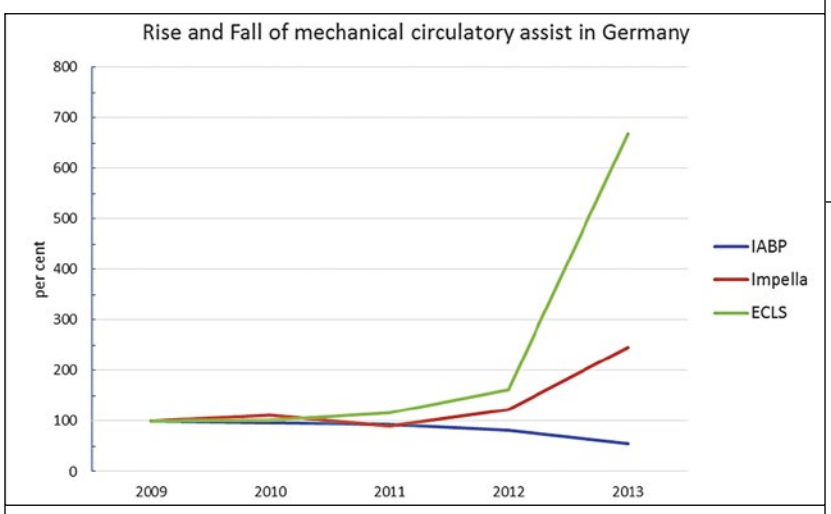
Jo Whitmore has worked within cardiovascular nursing for over 20 years in roles that include managing a Coronary Care Unit and being a specialist nurse in Cardiology involved in acute chest pain management and thrombolysis.
More recently she has been involved in a number of projects in relation to CVD, working for the British Heart Foundation Clinical Lead for Familial Hypercholesterolaemia sites. She is a member of the Primary Care CVD Leadership Forum in the UK, which works alongside Public Health England, NHS England, Royal College of General Practitioners and the British Heart Foundation.

IABP: Aortic counter-pulsation reduced hospital mortality

Evidence at last

Cardiac surgeons have finally found what cardiologists had reported missing three years ago: evidence to support the use of the oldest mechanical circulatory assist devices: IABP. Nevertheless, EH correspondent *Holger Zorn* expects the findings to have only limited impact.

A small study at the small University of Halle (Saale), Germany, triggered the most significant business kill of the current decade. Confirmed by a multi-centre study, the IABP Shock II trial, it prompted the worldwide revision of guidelines: the recommendation regarding the use of intra-aortic counter-pulsation (IABP – intra-aortic balloon pump) was downgraded from a Class I 'strong' recommendation to a simple recommendation (see European Hospital, 4/2013 p. 20-21 and EH 4/2014 p. 14-15). Why: There was no difference in 30-day and one-year mortality between patients who had received IABP in addition to conventional therapy after infarction-induced cardiogenic shock and those who had not received IABP (30d, 40% vs. 41%; 1a, 52% vs. 51%). Consequently, in Germany, the number of implantations decreased by almost one third (see figure).



Development of the use of circulatory assist devices in Germany. In 2009, 10,205 percutaneously implanted IABPs were recorded (2009 was chosen as the base year because the first patients for the IABP shock II trial were recruited in that year). In 2013, the year following the publication of the results, the figure had fallen to 5,712. In the same period the number of Impella implantations had risen from 153 to 372, and of ECLS (without purely perioperative use) from 273 to 2,268.

*** Source: own illustration, based on data provided by Statistisches Bundesamt (Destatis) and personal conversations.**

Meanwhile, the sister clinical discipline cardiac surgery, where in the early 2000s significantly more IABPs had been implanted, made renewed efforts to assess the oldest and most easily implantable mechanical circulatory assist device and published a specific S3 guideline on the use of intra-aortic counter-pulsation in cardiac surgery (S3 Leitlinie zum Einsatz der intraaortalen Ballongegenpulsation in der Herzchirurgie [Source: www.awmf.org/leitlinien/detail/ll/011-020.html, viewed 30.07.2015].

These guidelines clearly recommend the following:

For haemodynamically stable patients with high surgery risk, IABP implantation is recommended, based on the second-highest evidence category IB.

For patients with pre-surgical cardiac decompensation, implantation should be taken into consideration. This is a class B recommendation – just like the one mentioned above – however, evidence is three classes lower: class IV rather than I.

Evidence is equally weak regarding the recommendation on the point in time of implantation: early if HLM weaning of the patient is difficult or impossible.

Very strong evidence (IA) - and strong recommendation – for the operation of IABP: Pre-surgery implanted IABP is recommended for use during the actual cardiac surgery, to transform non-pulsatile flow of the HLM to pulsatile flow.

Dr Kevin Pilarczyk, cardiac surgeon and coordinator of the guideline, which was drafted in cooperation with the national professional organisations for cardiology, intensive and trauma medicine and extra corporeal techologies, sums up the recent data: 'The results of the IABP shock II trial, with patients who almost exclusively had received interventional treatment, cannot readily be applied to cardiac surgery patients.

Considering pathophysical conditions

'A patient in infarct-induced cardiogenic shock who has to undergo balloon dilatation or stent implantation in the cardiac cath lab cannot be compared to a comparatively stable non-infarction patient who has an increased perioperative risk profile due to reduced pump function. Surgery involving general anaesthesia, heart-lung machine and temporary cardiac arrest differs fundamentally from cardiac therapy.'

Such pathophysiological considerations are supported by a recent meta analysis assessing several randomised studies on preoperative IABP in high-risk cardiac surgery patients: it showed that aortic counter-pulsation is associated with reduced hospital mortality and reduced length of stay – even when limited to more recent studies [DOI: 10.1093/ejcts/ezv258]. Data regarding the continuation of IABP-induced pulsatility during HLM are equally reliable [Source: Int J Artif Organs. 2009;32:50-61]. In contrast, IABP in high-risk patients before stent implantation does not seem to have any benefits [DOI: 10.1016/j.ijcard.2012.12.027]. Dr Pilarczyk concludes: 'While there are no dedicated studies for this particular setting, we recommend considering IABP implantation in infarction-induced cardiogenic shock with surgical revascularisation due to the differences to cardiology.'

It remains to be seen to what extent these data will lead to an increase in implantations. Today, cardiologists are familiar with other, more difficult to implant systems – with remarkable results: attacked as business killers two years ago, they have now turned into business boosters. All other relevant systems – Impella, TandemHeart and ECLS – are significantly more expensive than IABP. The reimbursement a hospital receives for ECLS is at least ten times the amount reimbursed for IABP.

The implantation figures of all other systems totalled and projected into the future indicate that these other systems will overtake IABP in 2017 – despite the fact that, to date, no randomised study has demonstrated an advantage over – shown to be useless – IABP.

Following medical studies in Giessen, Essen and Houston, **Kevin Pilarczyk MD** became a researcher at the Mayo Clinic Rochester. He is now senior resident at Westdeutsches Herzzentrum, the West German heart centre in Essen, Germany. His clinical and research focus is cardio-surgical intensive care, particularly extracorporeal cardiac and pulmonary support systems. He is secretary and coordinator of the interdisciplinary S3 guideline for the use of intra-aortic balloon counter-pulsation in heart.

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Subscriptions
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Theodor-Althoff-Str. 45, 45133 Essen, Germany

Subscription rate
6 issues: 42 Euro, Single copy: 7 Euro.
Send order and cheque to:
European Hospital Subscription Dept

Printed by: WVD, Mörfelden-Walldorf, Germany
Publication frequency: bi-monthly
European Hospital ISSN 0942-9085

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The Lab2Go project

POC test detects myocardial infarction

Philips Minicare delivers rule-in/rule-out readings for heart attacks in 10 minutes. It takes a lot of hard work to make things easy, John Brosky reports.

Biomedical experts at Royal Philips have spent more than 10 years developing a simple test for the emergency department that, in less than 10 minutes, may indicate whether a patient suffering chest pains is having a heart attack.

The company's new Minicare I-20 point-of-care (POC) system is now undergoing field evaluation at six prominent European hospitals as part of Lab2Go, the three-year European Union-funded project. If successful, this handheld, bedside device would open a new pathway for rapid, reliable diagnosis that responds to a long hoped-for, critical need in emergency medicine.

Professor Volkher Scharnhorst PhD, from the Catharina Hospital in Eindhoven, the Netherlands, presented the preliminary results of the Lab2Go evaluation to colleagues at EuroMedLab 2015. According to him, Minicare Acute has the potential to support near-patient testing for people suffering acute coronary syndrome when they arrive at the Emergency Department; and therefore would enable faster diagnosis or treatment.

If it sounds simple so far, here comes the fun part – making it work. The widely accepted test for a rule-in/rule-out decision on heart attacks is the Troponin I (cTnI) assay. A physician draws a patient's blood and the sample is sent to the central lab and after 60 minutes, the answer comes back. While the patient has to wait, often distressed, until the results return and the physician can then determine what treatment to provide.

To cut that window for treatment from 60 minutes to 10 minutes, Philips had to overcome a series of technical challenges. First, the simple finger prick to draw a droplet of blood for the POC test means drawing capillary blood, which is different from venous blood used in today's lab tests. Would the results be comparable?

Philips' Minicare I-20 POC system is designed to help physicians, nurses and paramedics identify patients at high risk for acute cardiac events– right at the bedside or in pre-hospital settings.

Second, to reduce work for emergency departments, the Philips POC test needs to be user friendly and reliable by relying on microfluidics and chemistry that require no additional steps for staff.

Third, all the complexity of a laboratory instrument needs to be reduced to a hand-held device that anyone can operate without special training. To solve the miniaturisation challenge, Philips brings together an unexpected combination of nanotechnology with a compact disc player. It turns out that the optics used for reading music and film, an early Philips invention, work with a precision and reliability that can be applied to chemical testing. By mixing magnetically charged nanoparticles in the blood sample, the optics can detect and quantify the prevalence of a given biomarker – in this case, the cTnI protein indicating acute coronary syndrome.

At Philips, the potential was discovered long ago. The work to create a handheld diagnostic reader instrument began in earnest in 2009 by looking at ways to enhance the sensitivity of the detection and reduce the sample concentration required.

According to Michel Simons, Marketing Director of Philips Handheld Diagnostics in Eindhoven, 'no one else can deliver these high quality results from a finger-prick sample in less than 10 minutes.'

Jos Rijntjes, Head of Commercial Operations for Philips Handheld Diagnostics in Eindhoven

Michel Simons, Marketing Director of Philips Handheld Diagnostics, in Eindhoven

Looking beyond this first cardiac test, he sees a wider range of potential applications in the emergency department for the Minicare system. 'We will be able to measure all the different proteins in less than 10 minutes. We can do multiplexing on our device to test different parameters so that, with one drop of blood on the same cartridge with a nano-dispensing technology, we will be able to conduct up to 20 different tests at the same time.'

Jos Rijntjes, who leads Commercial Operations for Philips Handheld Diagnostics said that 'with the successful implementation of this first assay for chest pain, we can go on to apply the same technology and methodologies to additional assays. In one square millimetre we might, for example, be able to load tests for high fever, trauma, brain injury, or mental disorders – offering a series of assays to help emergency physicians understand which patient needs immediate attention and treatment when rapid results are critical.'

The second challenge for ease-of-use for the device is at the heart of the current test in the Lab2Go project. In addition to clinical results, the aim of the project is to gather evaluations of real-world use and identify where the workflow or usability can be improved. Rijntjes explains that the Minicare I-20 cartridges use dry chemistry without the liquid reagents found in central laboratories. 'The only fluid in the disposable cartridge comes from the tiny droplet of the patient's blood,' he said. 'There is no need to add agents, no need to wash, to dilute – no need for the staff to do anything but put the patient's finger on the cartridge and then insert it in the Minicare Acute reader.'

Returning to the first challenge, after all the engineering and technological marvels, the entire success for this break-through approach comes down to that finger prick and the micro droplet of blood from the patient. As one physician said, if there is not a strong correlation between results from a capillary blood sample and the traditional troponin results using venous blood, 'out go the finger-pricks and the utter simplicity.'

Scharnhorst is cautiously optimistic, reporting what he called a correlation that is 'very comparable and offers the potential to interchangeably use both capillary and venous samples.'

The full results of the evaluation from hospitals in Austria, France, Germany, Netherlands and the United Kingdom are not expected until 2016.

Meanwhile, Philips faces one more critical challenge, clinical trials that will put the Minicare Acute troponin assay up against laboratory results in a head-to-head comparison. Simons explained: 'We plan to start in Europe, but aim to have parallel trials running in the US as soon as possible. Discussions are currently underway with the FDA (Food & Drug Administration) to determine what our clinical trial needs to look like. Several sites in the U.S. have already expressed interest in joining the trial.'

Mechanical thrombectomy performs like a 'corkscrew'

Stroke is a surgical disease!

Cardiologists call for the establishment of 24/7 centres for rapid surgical interventions to remove blood clots in the brain, John Brosky reports

They did it for heart attacks. Can cardiologists now lead an effort to speed up the emergency medical response for stroke?

Over the past five years, the Stent for Life initiative organised by interventional cardiologists has pushed majors medical centres to assure 24/7 coverage and reduce the time to treatment for patients showing up with severe chest pain.

Now armed with fresh evidence that a mechanical intervention to pull out blood clots is more effective to halt devastating damage to the brain than the slower treatment with drugs to dissolve the clot, the European Association of Percutaneous Cardiovascular Interventions (EAPCI) has formally issued a call to action to mobilise its growing army of interventional cardiologists.

'We need to build healthcare systems for early intervention in stroke,' Jean Fajadet MD, the outgoing president of EAPCI.

Qualified physicians are needed

Even a quick glance at the number of interventional neuroradiologists in Europe compared to the number of stroke patients shows there are far too few qualified physicians to offer such a service everywhere, all the time.

'To offer this intervention rapidly, the question becomes whether cardiologists can help,' suggested Kenneth Snyder MD, from the State University of New York in Buffalo, who joined Fajadet at EuroPCR 2015 in calling for next-generation stroke centres.

A consensus statement issued this year by the European Stroke Organisation (ESO; Basel, Switzerland) unequivocally recommends rapid percutaneous intervention within 4.5 hours with a clot retrieval device.

ESO developed the statement with the European Society of Minimally Invasive Neurological Therapy (ESMINT; Zurich, Switzerland) and the European Society of Neuroradiology-Diagnostic and Interventional (ESNR; also Zurich).

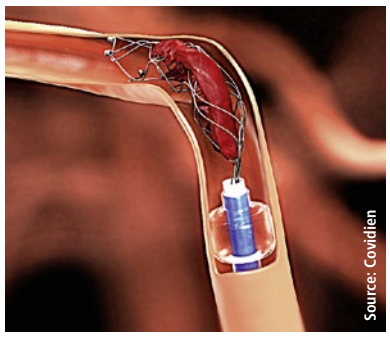
'Stroke is a surgical disease,' Snyder declared.

This bold statement challenges the current standard of care and is based on new scientific evidence from four major stroke studies presented this year at the International Stroke Conference in Nashville, USA. Those studies showed that rapid mechanical thrombectomy using a new generation of clot retrieval devices improves patient function after acute ischemic stroke.

'Five clinical trials have been halted because the new technology is better, because it works,' said Snyder. The current standard of care for stroke patients is an intravenous (IV) injection of a tissue plasminogen activator (t-PA) meant to dissolve a clot blocking blood circulation in the brain. The new procedure for mechanical thrombectomy is a surgical intervention, in which a device is used to pull out the blood clot immediately and directly. The procedure is performed without general anaesthesia as the patient is not aware of the catheter snaking through blood vessels to arrive in the brain with a device some call simply a cork-screw.

Surgeons have reported that patients in some cases have sat up on the operating table after the clot was removed and began speaking with them.

Catheter operators trained through EAPCI have the basic skill set needed for the procedure, and with additional training could maintain the 24/7 coverage for this time-critical procedure, according to Fajadet.



Solitaire is a mechanical thrombectomy device used to retrieve a clot in patients experiencing acute ischemic stroke

Membership in EAPCI has grown rapidly since it was founded in 2006. In the first five years 2,700 cardiologists joined to train for angioplasty and stenting procedures. That number nearly doubled again so that, in 2014, there were 5,500 members. There are almost 13,000 interventional cardiologists attending EuroPCR events in 2015.

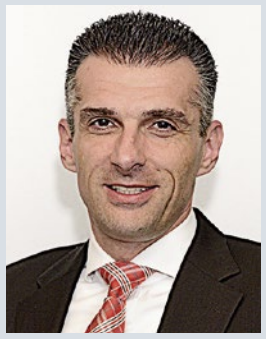
New devices that are generating the excitement surrounding this procedure include the Solitaire revascularisation device from Covidien and the Trevo from Stryker Neurovascular.

European hygiene standards differ from country to country

A case for better safety guidelines

In recent years a number of hygiene incidents concerning medical practices or hospitals have worried patients across Europe. However, every incident has become a learning experience and heightened awareness of the importance of thorough hygiene.

Henry Schein, the world's largest provider of healthcare products and services to more than one million dental, medical and animal health practitioners, is No 1 on FORTUNE's list of the World's Most Admired Companies in healthcare (wholesalers category). The company offers integrated consulting for efficient medical practice management, with hygiene among the focus topics. A unified hygiene standard, however, is by no means easy to achieve, as illustrated during a discussion, with Markus Bappert, Regional Director for Austria and Eastern Europe, Otto Wiechert, Sales Manager for Germany for Hygiene and QM, and Juan Molina, Managing Director of Henry Schein in Spain and Portugal, to take a comparative look at Spain, Austria and Germany.



Markus Bappert joined the Henry Schein Dental division in January 2014 as Regional Director for Austria and Eastern Europe. In February this year he took on additional responsibilities in Germany as Director of Henry Schein Dental Germany Business Operations. In this role, Markus Bappert is a member of the Senior Leadership Team for the firm's full-service business in Germany.

Otto Wiechert has been Sales Manager in Germany for Hygiene and QM at Henry Schein since 2013; before assuming his current role Otto Wiechert had founded different expert groups on hygiene and quality management with physicians, organisations, government agencies, manufacturers and associations.

With more than 25 years' experience in the technology information field, and eight in the dental-medical industry, **Juan Molina** is Managing Director of Henry Schein in Spain and Portugal. He is a member of AED, the Spanish Federation of Health Technology Companies and the Spanish Academy of Historical Stomatology and Odontology Studies.

Focusing on the importance of hygiene and infection prevention:

Bappert: 'In Europe you have to look at each country individually. As far as Henry Schein is concerned, hygiene is very important – in any country. Since there are different standards in different countries, implementation of a unified standard is a major issue. Due to extensive media coverage, and attention the issue receives from patients, hygiene and everything related to it have gained importance.'

Wiechert: 'We increasingly notice that medical practices are using hygiene as a marketing tool to underscore the quality of their facilities. It's cool to portray one's practice as "green" and as hygiene-conscious. Before, hygiene measures were more or less considered a burden, something imposed by the regulator in order to protect patients and staff. This view is changing as patients themselves are becoming aware of the issue.'

Molina: 'In Spain, the issue of hygiene is as important as in any other country. As a company we consider it our task to increase awareness and knowledge of hygiene issues along the entire healthcare economy chain, since studies have shown that healthcare-associated infections in Spain cost 700 million euros each year – that's one million euros per larger hospital.'

To what extent do hygiene standards differ between one country and another?

Bappert: 'In Austria there is a guideline published by the Austrian Society of Hygiene in Dentistry, the ÖGHZ. However, this guideline cannot be compared with a law as it exists for example in Germany, and it's not as strict as a law, meaning the guidelines do not prescribe the products the physician has to invest in to establish a certain hygiene standard.

'Much is happening right now. Last summer we initiated a round table with leading experts and we launched an initiative that aims to put the spotlight on hygiene. In this context, ÖGHZ and Schein jointly organised a series of events that drew more than 1,200 participants.

'This led to several companies expressing a strong interest in cooperating with us as well as supporting us with their expert hygiene knowledge.'

Wiechert: 'In Germany, the situation is somewhat more complex. Whilst there is a national law, implementation and standards differ in the individual German federal states. A multitude of government agencies audit medical practices, such as the healthcare authority, the trade inspection authority and regional government, with the latter sometimes "outsourcing" the audit to the German Medical Association, or the Regional Dental Chamber. In short: there is no unified national standard. As far as implementation is concerned this means that each agency or authority which audits a practice has a different focus. 'Moreover the term "consultant" is unfortunately not a protected designation and consultants indeed apply different approaches to the implementation of hygiene measures. Consequently, a professional training event, such as the series that was organised in Austria, might make little sense on a national level in Germany; a presentation given in North Rhine Westphalia might not be valid in a different federal state.'

Molina: 'In Spain, there are currently different initiatives, some launched by the government, others by professional associations. The most important one is arguably an initiative by the Spanish Federation of Health Technology Companies, which aims to reduce the number of healthcare-associated infections by 30 percent by the year 2020.

'We do have to raise awareness on all aspects of hygiene and infections in all healthcare facilities and we need to establish a hygiene control system and quality audit. Moreover, we need constant monitoring of all hygiene and disinfection measures in all facilities in order to effectively prevent infections.'

Should European countries all establish unified standards and require medical practices to use certain products?

Bappert: 'Whilst indeed there are hygiene and non-hygiene products and systems, it's not the products that are crucial, but the processes. On the one hand you can create sterility without equipment, using a manual procedure; the equipment simply facilitates the task. On the other hand, if you have top of the line equipment but no adequate procedures, you do have a hygiene risk right there. Vice versa: simple equipment and the right process can be immensely effective in assuring superior hygiene without major capital investments.'

Wiechert: 'In my opinion, it should be exactly the other way round: there should be a certain financial incentive for certain services that are to be guided by the health insurers. As the manager of a medical practice, for example, I'd have to obtain a "green light" label, which shows that I implemented certain measures – and only those practices that have obtained the label would be eligible for reimbursement by the health insurers. That would be the easiest approach for all parties concerned.'

Molina: 'Spain has a very well developed network of public and private hospitals. We are currently working to make all facilities implement identical control mechanisms and protocols because we have to be even more effective in identifying potential problems with regard to hygiene and disinfection quality. This, as far as I am concerned, requires a unified quality assurance process and identical use of technology.

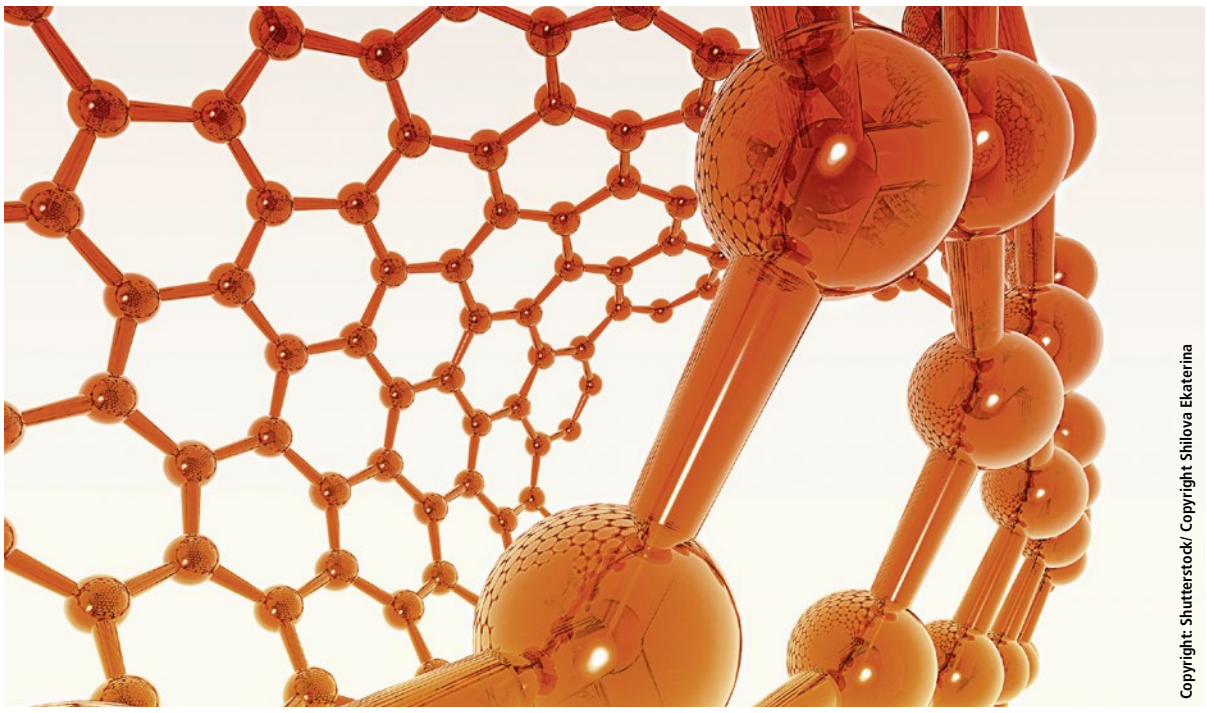
'A recently published European study indicated that, in Spain, the level of out-dated equipment is slightly above the European average. Therefore, I consider it very important for the decision makers in healthcare, and in government, to invest in adequate technology in order to ensure the required level of hygiene and infection prevention.

'One of Spain's strengths is clearly the quality of our excellently trained physicians. They play a crucial role in the assessment of the hygiene situation and can initiate improvements. I'm convinced we need a balance between professional training and the quality of the technology we use. We need safety guidelines and concrete work instructions and we have to further improve communication with the patients.'

Technology against infectious diseases

Developing vaccines and r

Mélisande Rouger reports on expert reviews of vaccines in the pipeline and the potential of nanomedicine given during the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) annual meeting in Seville.



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Vaccination remains one of the most efficient strategies against infectious diseases, often being the best protection against infections such as hepatitis B, or influenza.

Vaccine science has evolved greatly over the past few years, according to Dr Carlos Martín from the Medical Faculty, University of Zaragoza: 'There's been a huge advance not only preventing infectious diseases but also chronic diseases such as cancer. The hepatitis B vaccine, for instance, has significantly lowered the incidence of liver carcinoma and, with the papilloma vaccine, we will see less and less cases of cervical cancer in the coming years.'

Clinic trials

Most commonly, new vaccines in development use viruses or new generation of adjuvants to improve immunisation. They can use adenoviruses such as MVA, virus-like particles, purified proteins or nanoparticles.

It is essential to conduct efficacy clinical trials and new technologies, such as transcriptomics, could be used as potential correlates of protection to accelerate the development of a new vaccine, Martín explained. 'We usually have to wait 25 years for a vaccine to be developed and bringing it to the market costs between 500 and 800 million euros. In the 80s, the discovery phase was extremely long and clinical trials lasted about five years,' he said. 'We should be able to reduce the time of clinical trials with new technologies.'

Combined vaccines reduce HIV

HIV is an important but complex area of innovation. Researchers have worked for the past 20 years on a prevention cure for AIDS, first with inactivated viruses, and then with vaccines trying to improve T-cell response by using Adenovirus and Poxvirus. According to Martín, recent studies have shown that combining those two vaccines reduced HIV infection by 30%.

Over 100 of malaria vaccine candidates, studied in animals, and dozens of clinical trials exist for malaria. Adjuvants are just as important in the equation. A study conducted in more than 15,000 infants and young children showed that malaria vaccine RTS S candidate reduced disease over four years of follow-up. Protection is low – only in about 30% of the vaccinated – and reduces within a year, but approval is under study. 'That would be the first time that a protection vaccine against malaria would be brought to the market,' he said. Due to the human challenge, the context of vaccine development for malaria has changed tremendously.

TB: Respiratory transmission route

Things are also changing for TB, a disease responsible for 1,000,000,000 deaths in the past two centuries, according to an article recently mentioned in Nature.

The BCG candidate has been around for over 100 years and is used worldwide. The problem is that TB's main route of transmission is respiratory, which BCG does not cover. In 1993 a mycobacterium bovis triggered a very resistant TB epidemic in Spain. The strain showed an increased expression of the phoP gene. The unusual outbreak killed 114 individuals and was highly transmissible by aerosol route. This spurred the creation of the MTBVAC candidate, following recommendations by the 2005 Geneva consensus criteria that two stable independent mutations (phoP and fadD26) should be used for live vaccines.

Some of the newest developments include vaccines against cytomegalovirus, dengue and Japanese encephalitis, RSV and, last but not least, Ebola. The latter actually serves as a model of accelerated vaccine development, according to Martín. 'This epidemic caught us by surprised because of its scale. But there were already candidates in macaques, so things went quickly.'

The rVSV-ZEBOV – recombinant vesicular stomatitis virus and the ChAd3-ZEBOV – chimpanzee adenovirus 3 had already been used in clinical trials in Switzerland, the USA and Germany before December 2014. There are now Vaccine Phase 3 efficacy trial designs in Liberia and Sierra Leone. 'By comparison, we've been in the developing process of a malaria vaccine for over 25 years; and in Ebola we've shorten this period to one year!' Martín said.

The multidisciplinary plan to tackle antibiotics resistance

Spain's response to EU dire

Increasingly resistant bacteria are a global problem and require innovative action from all parties concerned, says Jesús Rodriguez-Baño, President of the Scientific Committee of the annual meeting of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), which unfolded last May in Seville. Mélisande Rouger asked him why the creation of a national plan has become necessary to tackle antibiotics resistance.

'The plan is a consequence of a directive of the European Union and is coordinated by every country; in Spain, the Spanish FDA is responsible for its management,' explains Jesús Rodriguez-Baño. 'It follows the concept of one health and includes a multidisciplinary plan involving doctors and pharmaceuticals. The idea is to regroup all our actions because the problem is multifactorial; therefore the solution must be factorial as well. 'We aim to find a common solution to a global problem.

'There are currently very important changes in our society. People travel more than any time of human history, not only for holidays or living, but also to receive healthcare. These migrations increase the risk of spreading bacteria. 'Of course, bacteria are present in our food. Antibiotics are used in animals to increase their weight and make them larger. This technique is banned, but it is hard to control. Antibiotics are also used as a prophylactic technique to make sure one sick animal doesn't infect the others. Resistance develops here as well and the meat becomes contaminated. Importing food from a country where resistance is strong can bring this problem to other countries. Bacteria are also present in the water, which can contaminate vegetable and plants.

Jesús Rodríguez-Baño, Head of the Infectious Diseases and Clinical Microbiology Interhospital Department at Hospital Universitario Virgen Macarena, Sevilla, Spain and SEIMC 2015 President.

'Furthermore, the global population is growing older; people need more care and the number of nursing homes is rising. These environments are highly favourable to the spread of bacteria. 'It's no coincidence that resistance is coming now. It is a consequence of antibiotics use in humans and animals, the fast-paced development of many countries and ageing population. In a nutshell, it's a consequence of globalisation. 'We have to think of all these aspects and find new ways to address them. There's no answer right now, we have to think outside the box.'

What measures will Spain take?

'Surveillance will be central to the plan. Surveillance is a complex task because resistance is not homogeneously spread. If you do something superficially, you will not realise that an outbreak is occurring somewhere and you might not be able to contain it. We need to be able to detect outbreaks anywhere to prevent them from spreading.

'We are working towards having reference labs in different areas of Spain so that every single lab can rapidly isolate the bacteria and send results to obtain an answer within 48 hours. In Andalusia, for example, one hospital receives alarms from everywhere else in the region and provides answers quickly to control transmission as early as possible.

'As you know, Spain is very heterogeneous and this is why harmonising surveillance is an important part of the plan. The problem with having different communities is that management differs from one region to another.'

Do you expect improvements after November's general election?

'We have a very interesting situation right now in Spain. There

nanotechnology

Dr Eduard Torrents from the Catalan Bioengineering Institute observed the potential role of nanomedicine, which applies nanotechnology tools such as atomic force microscopy, scanning tunnelling microscopy and dip pen nanolithography to infectious diseases.

Nano-delivery products are helpful

Nanoparticles (NPs) are particularly helpful in drug delivery because they are soluble and bio available, and decrease immunological reactions, Torrents explained: 'They deliver a predetermined dose while decreasing the frequency of administration, enabling drugs delivery locally and precisely, and minimise secondary effects, and liberate two or more components in combined therapies.'

There are currently 44 nano-delivery products on the market, including some for fungal infections and oral and perioral infections, as well as 18 pharmaceutical products, one of which is designed for fungal infections.

This figure is expected to grow as labs express an increased interest in the field. The nanotechnology market represented 73 billion dollars in 2011 and is expected to grow to 131 billion in 2016, at a rate of +12.5% a year. In 2016 nano products will represent 10% of all sales in pharma industry.

To advance NPs use, Torrents recommended that nano scientists should get away from the evidence concept, understand that pharmacokinetic concepts in NPs are different and conduct infection trials in animal models. There should be functional and safety studies, which shouldn't follow the patterns of classical pharmacology studies.

'Challenges remain in the detection of infectious agents, penetration of the hematoencephalic barrier and antibiotics resistance. Metallic NPs are very promising,' he concluded, 'and we hope to be able to use them for vaccination, and open the oral and pulmonary routes for drug delivery.'

Carlos Martín is Professor of Microbiology at the Faculty of Medicine, University of Zaragoza, and a member of the Advisory Committee of Tuberculosis Vaccine Initiative (TBVI). With more than 25 years of experience in mycobacterial genetics he, and his team, aim to develop novel TB vaccines and vaccination strategies to improve protection against pulmonary TB. He is currently working in collaborative TB research projects with research groups in Europe and Latin America. Previously, Martín worked as permanent researcher at the Pasteur Institute in Paris, and he has published more than 100 international publications on TB. Since 1992 his TB research has continuously received national and European Union funding. The professor also belongs to CIBERES, a research network on respiratory diseases of the Spanish Ministry of Health (Instituto de Salud Carlos III).

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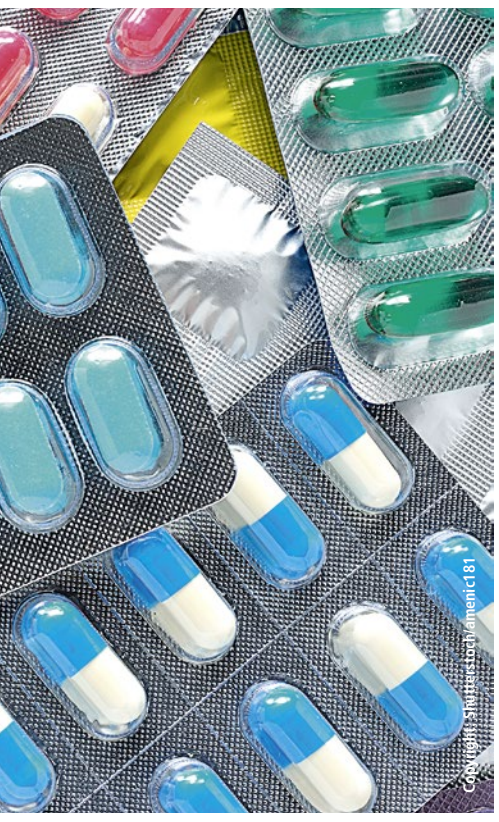


have already been many changes following local elections earlier in May. I expect it will be challenging, because every time politicians change you have to start from scratch to convince them. However, at this point the work is very visible, so I'm rather optimistic.'

Increasingly presenting a potential role

CAD in pathology

Report: Mark Nicholls

Computer-aided diagnosis could soon play a greater role in digital pathology. Dr Jeroen van der Laak, an Assistant Professor in Digital Pathology at Radboud University, believes a breakthrough that would increase the speed and accuracy of diagnoses and prognoses is closer than many observers think.

Van der Laak has been leading studies in the use of computer aided diagnosis (CAD) in pathology and will outline the 'progress on the introduction of these promising techniques' at the Digital Pathology Conference in London at the end of this year (3-4 December).

In his presentation 'CAD in Pathology: Closer than You Think' he will argue that, while the introduction of digital pathology in primary diagnostics is still hampered by high costs, CAD techniques will be the tipping point, leading to large scale introduction of digital scanning of histopathological slides.

The introduction of CAD in pathology will make digitisation of tissue sections a worthwhile step, he believes. 'As it is now, many pathologists doubt this transition to "digital pathology" because the required investment is large, and benefits are not fully clear,' he said. 'If we can really take some of the workload off a pathologist - by pre-screening sections for certain tedious tasks, for example - the business case will become much more favourable.'


Source: Huron

Significant steps are achieved

Research in his department – undertaken mainly using a Pannoramic P250 scanner from Budapest-based firm 3DHistech with all pattern recognition software developed by the group – has achieved significant steps in the last couple of years in developing advanced pattern recognition algorithms that can work on entire 'whole slide images' (WSI), in contrast to much research still being conducted on small image regions.

'We also aim to use standard H&E staining whenever possible. This means that the software we develop will work in any lab, without special adjustments, and with hardly any user interaction.'

However, although the introduction of CAD in pathology is much closer than many people realise, he acknowledges that the availability of algorithms is only a new beginning and further research is needed to bring the algorithms into the pathologists' workplace. 'If we succeed in seamless integration in to daily pathology routine,' he said, 'and can prove that the software really aids the diagnostic process, large scale introduction may happen.'

Such a step would see pathologists become more efficient in certain routine tasks, and it could improve the accuracy and reproducibility of diagnosis, he suggested.

'Future applications may add valuable information from tissue sections that is currently not available. Advanced pattern recognition may enable extraction of strongly prognostic, sub-visual information,' van der Laak pointed out. 'CAD in pathology has the promise to radically change the way we examine tissue sections.

'We are at a stage in which we have availability of pattern recognition techniques more powerful than ever before. What is needed now is availability of material from large cohorts of patients with treatment and follow-up data.

'Trained pathologists are also needed to help identify regions of interest and to study how we can best include our algorithms in the diagnostic workflow.

'These requirements are challenging because pathologists frequently suffer high workload, and well-defined cohorts are often hard to acquire.' A next step is for his group to study the benefit of developed algorithms in a routine diagnostic setting.

Dr Jeroen van de Laak is Assistant Professor in Digital Pathology at the Department of Pathology at Radboud University Nijmegen Medical Centre, The Netherlands, where he leads a research group on CAD in pathology. Currently numbering eight, the group is set to expand in 2016. Covering diverse disciplines – computer science, medicine, lab technology, the group is embedded in the pathology department, and included in the radiology department's diagnostic image analysis group (DIAG) at Radboud University Medical Centre.

Yet, if implemented, CAD in pathology could have benefits for pathologists in making routine tasks easier. Advanced quantification of histopathological patterns will add valuable information to the diagnostic process, he said.

Patients will benefit because the diagnostic process may be more accurate and personalised, and surgeons and oncologists may also benefit from increased speed and accuracy of diagnostics and prognostics.

Learning from the Danish experience

A national digital pathology system

A national digital pathology system across Denmark has helped to significantly improve efficiency and raise levels of patient safety, Mark Nicholls reports.

Denmark has used advanced computer software systems and created a countrywide database to optimise the assessment of patients' specimens. The development and success of the system will be highlighted at the Digital Pathology Conference in London (3-4 December) where Professor Ben Vainer will lead the session 'How Digitisation Can Improve Pathology Service – The Danish Experience'.

Vainer, a consultant in the Pathology Department at Rigshospitalet, University of Copenhagen, will focus on the Danish civil registry database and other national databases connected to this, and the use of the same LIS in all pathology departments in the entire country with access to the national pathology database of all pathology reports in Denmark since at least 1998.

He will also discuss the important links between LIS and patient medical records in hospitals and in private practice (e.g. general practitioners), and how computerisation of the entire laboratory flow, from ordering the pathology service to specimen presentation to the ordering physician, has helped ensure patient safety and eliminate time-consuming manual steps.

Vainer: 'Pathology departments in Denmark have, through close collaboration, been able to build a national pathology system, where each individual pathology department serves as a sort of "branch office".'

'All steps of the specimens are followed through the pathology department, which gives a good global view of the departmental activities and the possibility to trace individual specimens. For the managers this also provides good measures of operational objectives.' The "users" – ordering physicians – are provided with a clear overview of their patients' specimens during the assessment process, and patients have full access to reports on their own tissue, he added.

Ben Vainer is Professor of Pathology at the University of Copenhagen and consultant pathologist at the Department of Pathology of Rigshospitalet, Copenhagen University's main teaching hospital.
His primary interest is in the digitisation of pathology for education, research and diagnoses.

Digitisation of laboratory processes and the link to the pathology LIS, plus national pathology database, opens up the opportunity for image automation, including digital image analysis and transfer of whole slide images, in cases where a second opinion is needed without compromising either patient safety or the international data acts.

Vainer believes other countries can learn several points from this system: 'In large pathology labs the large number of specimens is often a hindrance to efficient handling and ensuring patient safety without time-consuming steps. Such steps can be turned digital, releasing valuable staff resources. However, most important is that digitisation opens up for the implementation of new imaging techniques, which are necessary to provide each patient with the correct assessment of diagnosis and biomarker expression profile.'

The system is fully implemented, with automated image analysis and the option for second opinions using whole slide images currently being tested.

There are also a number of patient benefits from the Danish system. Vainer: 'The risk of specimen mix-ups are minimised, and application of national pathology databases linked to national person-identification databases ensures that the pathologist always has access to previous tests performed on the patient. This increases the quality of the pathology assessment and hence the final diagnosis.'

Denmark's next step is to introduce new digitisation procedures such as automated image analysis and substitution of conventional light microscopies with whole slide images, including possibilities to perform a second opinion without the delays when using shipment of glass slides by postal services.

Vainer: 'Automated image analysis will further increase the pathology assessment quality by eliminating subjective readings of biomarker expression, for example, in addition to elimination of the risk of patient case mix-up.'

Big data histopathology

Unlocking imaging potential

Dr Peter Caie is a Senior Research Fellow in Digital and Systems Pathology, at the University of St Andrews, and he leads the Systems and Quantitative Pathology team alongside Professor David Harrison. His scientific expertise lies in cellular and tissue imaging, and his special interest is systems, quantitative and digital pathology.

Report: Mark Nicholls

Automated image analysis shows significant potential within histopathology to help identify novel and subtle prognostic features.

UK expert Dr Peter Caie also believes such image analysis can turn aspects of histopathology from a traditionally semi-quantitative field into a fully quantifiable and standardised science. However, he also points out that challenges remain before the full potential is seen within digital pathology.

During the Digital Pathology Conference to be held this December in London, Caie will outline the advances in the 'Profiling Big Data Histopathology through Image Analysis' session.

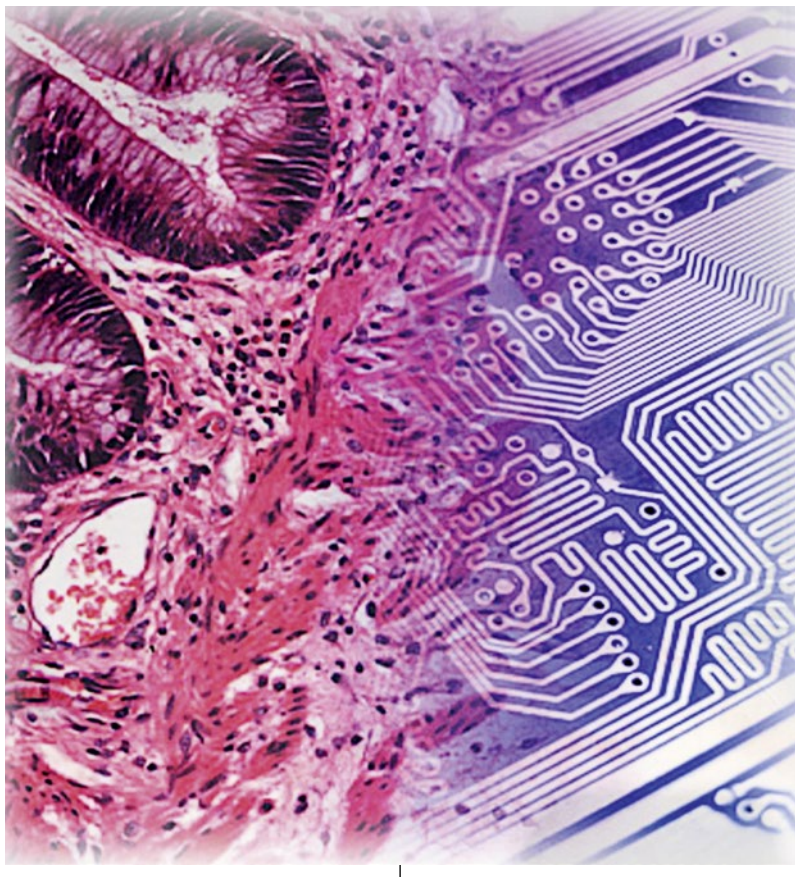
As a Senior Research Fellow working on Digital and Systems Pathology at the University of St Andrews in Scotland, Dr Caie's aim is to demonstrate how complex image analysis of digital pathology specimens can now create robust hierarchical 'big data'.

Ahead of the conference, he told European Hospital: 'I will be outlining how automated image analysis can not only quantify set histopathological features in a standardised and reproducible manner - such as tumour buds, lympho-vascular invasion, lymphatic vessel density and tumour nuclear morphometry - but also can be utilised as an investigative tool to identify novel prognostic or predictive features that have previously gone unnoticed or unreported.'

Caie explained that modern image analysis of digital pathology slides can now also create big data sets associated with multiple export parameters from computer segmented and classified objects within the digital tissue section.

These can be parameters associated with set histopathological features - such as their shape and extent - or features captured in an unbiased manner, where every segmentable and visible object is captured and morphometric, texture, number of objects and spatial information (such as heterogeneity, distribution, location, neighbouring to other objects) is extracted.

'That big data must then be mined with appropriate bioinformatics to identify the significant prognostic or predictive parameters, or combination of parameters, to stratify the patient population in question,' he pointed out.



This emerging field is termed 'Tissue Phenomics', a phrase first coined by Gerd Binnig, Nobel Prize winner and founder of the image analysis software company Definiens. However, Caie acknowledges that there are multiple challenges in digital pathology and image analysis. Reproducibility and validation are key to standardised quality big data histopathology, he said, and stressed that the image analysis algorithms themselves must be of a high enough quality to deal with complex and heterogeneous tissue, whereas simple algorithms may report back false results or classifications due to heterogeneous cell populations.

'Similarly when quantifying histopathological features in the complex tumour microenvironment, image analysis may also report false positives or inaccurate parameters due to non-specific staining or autofluorescence within the tissue,' he added.

Other challenges include the need for fast IT infrastructure to enable digital pathology to be routinely used, as well as large and secure data stores to archive the digital specimens and their associated analysis.

Another challenge, he said, is for the traditional field of pathology to accept the novel field of image analysis and 'tissue phenomics' and allow it to be implemented into routine clinical use.

Big data pathology has a range of benefits for clinicians and patients. Caie: "Image analysis allows reproducible and standardised reporting of biomarkers or histopathological features that negate observer variability. It can also free up a pathologists time to concentrate on complex cases if the quantification of histopathological features in more routine cases becomes automated.'

Image analysis can quantify fluorescence in situ hybridisation (FISH) and proteins across a dynamic range with the application of fluorescence, leading to more accurate patient results, as big data pathology can identify subtle or complex patterns within the tissue section which may be difficult to reproducibly identify by eye.

'Therefore,' Caie pointed out, ' it can provide the clinician with novel and significant new biomarkers to aid in clinical decision making, and the patient can receive a more personalised and informed answer to their individual case.'

The next step in big data histopathology, he suggests, is to validate the technology in large retrospective and prospective clinical trials to demonstrate its full potential.

Big data histopathology will increase in power as technology evolves. This includes multiplexing many biomarkers, which can be used to map entire pathways within a single cell.

Caie concludes: 'Co-registering multi-omics, such as single cell transcriptomics, genomics and histopathological data, with protein biomarkers onto the same tissue section will also make for a more informative and powerful big data pathology, which again will provide insight into disease progression and biomarkers for predictive studies and drug trials.'

Date for the diary

25-28 May. Berlin, Germany

13th European Congress on Digital Pathology

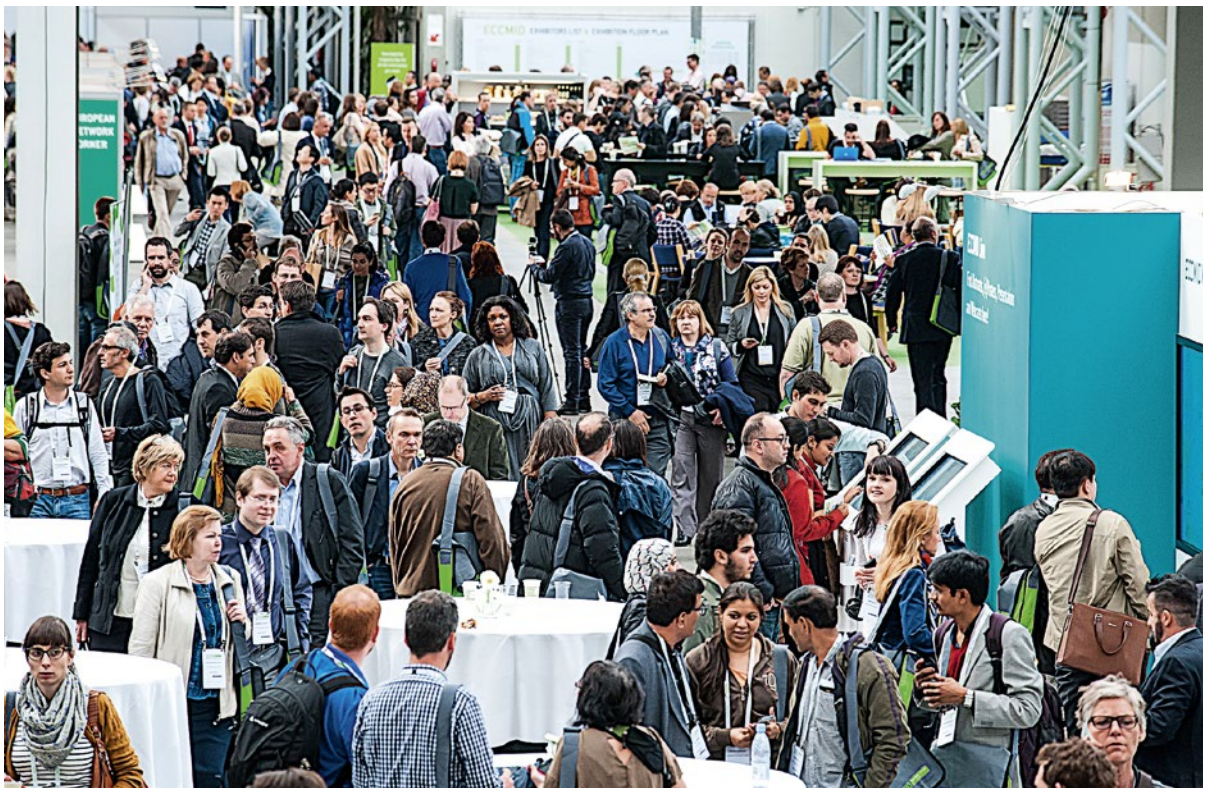
www.digitalpathology2016.org

Methodological Changes in microscopic techniques, imaging, molecular pathology, genetics and bioinformatics are the drivers of digital pathology. The programm of the ECDP in Paris last year with insights in several new technologies will find its continuation in Berlin.

The European Congress of Clinical Microbiology and Infectious Diseases

The world's largest microbiology event

The European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), the largest conference of its kind, drew 10,697 specialists and companies from around 110 countries to Copenhagen for its 25th annual event. Over 200 sessions were delivered, including an in-the-pipeline gathering, keynote lectures, symposia, oral sessions, educational workshops, meeting with experts, and around 2,500 poster presentations – plus some 3,000 abstracts presented by international experts.



Inevitably, antimicrobial resistance continues to lead the agenda of the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), with a general consensus among delegates that big pharma will provide answers to antimicrobial resistance, but the keys to finding the solution will be found by universities and small medium enterprises (SMEs).

A new addition to the congress is the pipeline corner, which gave SMEs a chance to present what they have in terms of new mechanisms and approaches.

An interesting, recurrent theme was the search for a very narrow spectrum of pathogen-specific antibiotics, working on the premise that it is promising to exploit specific differences in physiology, or virulence mechanisms – an approach that might contribute to personalised treatments and one drug for one bug. A key theme for ECCMID is the importance of innovation and new discoveries – for example, for the late-breaker session more than 50 abstracts are submitted annually; the society selects only the top five for presentation.

2015's late-breakers included evidence on the efficacy of a new herpes zoster vaccine, a study on renal failure rates, as well as advances on the treatments of bacterial pneumonia urinary tract and intra-abdominal infections.

A possible threat from Ebola engendered considerable international discussions – and also medical heroics. At ECCMID the organisation Médecins Sans Frontières was honoured with a special excellence award in recognition of their recent work against this disease in Africa, as well as decades of international efforts to treat people in other areas of disaster.

As mentioned, ECCMID is now the world's largest scientific event in clinical microbiology and infectious diseases. Over the last decade, attendance numbers have doubled and are expected to rise again at ECCMID 2016 in Istanbul.

Diagnostics and life sciences firm gains ID/AST gold standard

Giant aims to inflate microbiology

At Europe's largest meeting for clinical laboratories, Beckman Coulter stepped forward to welcome a new class of customers looking for familiar and reliable instruments, John Brosky reports.

In January this year, Beckman Coulter acquired the entire microbiology business of Siemens, including the world-leading line of MicroScan analysers for microbial identification and antibiotic sensitivity testing (ID/AST). With an installed base of over 6,000 instruments worldwide the company enters this segment of clinical laboratories for the first time, yet already as the undisputed global leader.

At EuroMedLab in Paris, at the front and centre on the Beckman Coulter stand was the fourth generation MicroScan WalkAway *plus* system freshly dressed with the company's logo, and backed by the same experts, including Senior Marketing Manager for the business unit in Europe, Philippe Arowas. 'The MicroScan system is the key test for identifying and controlling, and potentially reducing the prescription of antibiotics, he told *European Hospital*.

The quantitative measures of a bacteria's resistance with the analyser helps physicians to know which specific antibiotics they might use to treat a patient and, perhaps more importantly, which ones they should not use.

There are some 300 types of bacteria, with new ones appearing suddenly. He cites the example of the New Delhi Metallo (NDM) that showed up in 2008 and spread so quickly that a year later it was found in India, Pakistan, the UK, USA, Canada and Japan. NDM proved to be highly resistant to a broad range of antibiotics, including an entire family of drugs designed specifically for the treatment of antibiotic-resistant bacterial infections.

MicroScan WalkAway plus

Capturing the results of MicroScan analysis with Beckman Coulter's LabPro Information Manager and LabPro Connect helps clinical labs share data for epidemiology studies to identify trends in pathogen resistance and to track the spread of such infections better.

'Patients can also share resistance to a bacteria as well as the bacterial infection itself,' Arowas pointed out.

The patient samples to be tested might come from any infected part of the body, he said, whether it is an organ, skin, hair, or bone. After creating a culture, the MicroScan panel is inoculated by introducing the bacteria to the array of wells, each containing different concentrations of an antibiotic.

The technician can literally walk away from the instrument, returning after an overnight analysis that will show where the bacteria continued to flourish or where a specific concentration of antibiotic was effective in killing the pathogen.

Beckman Coulter takes over what Arowas estimates to be a 40% of the market share in the world for ID/AST. In some countries, such as Japan, the installed base accounts for 70% of the market, in Spain it is 60%, he said. The main competitor in this segment is bioMérieux, while Becton Dickinson holds a less significant footprint.

Testing for infectious disease is a steadily growing area in clinical laboratory, he said, and the former Siemens group now makes up a new core business for Beckman Coulter.

'The company acquired these products because it intends to invest in the science and develop new products,' Arowas added. 'MicroScan is a first step, but we will see more and more product solutions developed for microbiology. Already we have seen how strong this interest is, though we just started in January.'

This combination, he suggested, means that Beckman Coulter is not only well-positioned to maintain its lead position in microbiology, but holds unique capabilities for advancing its portfolio of products.

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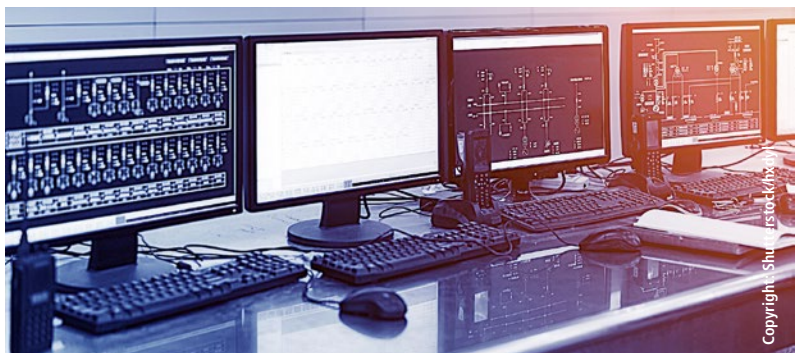
New standards speed data sharing between devices

The LAW of the Lab

First they fixed the cables to hard-wire a faster data transfers from laboratory instruments. Now a coalition of the largest manufacturers of lab equipment for patient diagnostic tests have agreed on shared protocols for how software should report results. This is the first update to international standards in 20 years.

'Past standards left too much room for interpretation and had a Baskin-Robbins 31 Flavours outcome, where each vendor had a different implementation,' said Serge Jonnaert, from the sponsoring organisation the IVD Industry Connectivity Consortium (IICC).

The resulting set of standards, called the Laboratory Analytical Workflow (LAW), has been documented and published by the non-profit, open platform association Integrating the Healthcare Enterprise (IHE). The new LAW integration profiles were recently tested for true interoperability of data sets among diverse vendors at the IHE Connectathon 2015 held in Chicago. Lab vendors who have certified their equipment conforms



to the new standards include Abbott Diagnostics, Beckman Coulter, Impeco, Omnilab, Orchard Software, and Siemens Healthcare.

'We expect more vendors to come online as customers demand conformance to the IHE LAW profile,' Jonnaert said.

Members of the consortium who will test IVD analysers at upcoming Connectathons in Europe, Japan or North American include Becton Dickinson, bioMérieux, Data Innovations, Hitachi, Ortho Clinical Diagnostics, Roche Diagnostics, Samsung, Sunquest Information Systems, and Systelab Technologies.

After grinding its way through five years of arcane processes with IT engineers, the new lab standards promise a new era of open exchanges of data with plug-and-play connectivity among analysers, middleware and laboratory information systems.

A key piece in this puzzle was the first milestone marked by the ICC, at the European Connectathon 2012 in Bern, Switzerland, when companies demonstrated a successful switch from serial cables for transmitting data to a transmission control protocol (TCP) internet protocol (IP) communication port.

Most lab instruments to that point, and many still today, were running on what some may remember as the clunky 9-pin printer cables that had to be screwed onto the back of a computer. In most cases laboratory results were being communicated at the extremely low-bandwidth rate of 9600 baud, for those who remember what a 'baud' is. Now instruments can send data at the blistering speeds that TCP/IP allows.

Thanks to the successful testing of the interoperability profile at the Connectathon 2015, in July, 2015 the Clinical and Laboratory Standards Institute (CLSI) said it had begun development of a standard on next generation in vitro diagnostic (IVD) instrument interface.

The new standard, to be called AUTO16, based on the IICC/IHE work around the LAW profile, will improve IVD instrument connectivity by defining an interface that is more consistent across instruments and leverages the faster connectivity protocols and network technologies.

The Institute specifically highlighted the deep work undertaken by the consortium of manufacturers with IHE to develop the necessary use cases, transactions, data flows, and Health Level Seven (HL7) messaging conventions and definitions.

Additionally in July, the IICC work was boosted by an endorsement from the European Commission that selected 27 IHE Integration Profiles to be part of the eHealth European Interoperability Framework that can be referenced in public procurement tenders in Europe.

Among the 27 is the LAW profile, and the specification of conformance to the LAW is one of the key endpoints among manufacturers for the work of the jointly sponsored IICC. According to Jonnaert, 'LAW substantially reduces connectivity installation cost and time, improves integrity of patient data, and standardises the data flow of IVD, which have been key pain points for laboratory customers for many years.'

'Using LAW for specifications in requests for proposals is certainly our expectation. It benefits the customer to do so, reducing complexity and unpredictability as it comes to large, multi-vendor laboratory projects,' he said. 'The plug-and-play dimension to this assures that connectivity and interoperability will become a negligible cost component.'

High-res image of 20,000 cells speeds far more than blood count…

Bloodhound approaches fully digitised analysis

A fully integrated haematology analyser with novel digital scanning capabilities – the cobas m 511 – can transform the work of lab technologists, John Brosky reports.

With its innovative Bloodhound technology, Roche Diagnostics is hot on the trail leading to full digitisation of laboratory analysis.

Instead of the conventional technique of smearing blood on a glass slide for analysis, the cobas m 511 uses a one-microlitre droplet to print a patient's sample on the slide to a thickness of one cell using a principle comparable to ink jet technology, and then stain the sample for study.

Imaging the slide using four LED sources, the bloods cells are individually assessed. There can be more than three million individual cells automatically counted on the slide and the digital assistant on-board the cobas m511 presents a high resolution snapshot of each of 20,000 of them, images that can then be identified as platelets, red or white blood cells, counted, classified and categorise

The results are produced in less than six minutes and presented on a Viewing Station for the technologist in a standard format showing all complete blood count (CBC) parameters, a traditional five-part differential display and a reticulocyte count. Results for additional samples are produced at a rate of one per minute.

The system also measures the mean corpuscular volume (MCV), the mean corpuscular haemoglobin (MCH) and uses multiple measurements to determine total haemoglobin concentration.

Whenever the system detects cells that it cannot clearly identify, they are highlighted on the system's viewing station for subsequent reclassification by the medical technologist.

Sorting is as rapid and familiar as working with any data worksheet and, according to Jan Hoogendijk, the International Business Leader for Haematology in the Roche Diagnostics division, the cobas m 511 algorithms can single out a subset of just a few individual cells from among the 20,000-cell sample to show, for example, cells with an inclusion. This could include cells that are infected with malaria.

The new system integrates three instruments into one compact solution, combining a digital morphologic analyser, cell counter and classifier for a complete haematology result including morphology assessment. Requiring the mentioned low blood volume of just 30 microliters, it can perform a complete analysis of white blood cells, red blood cells and platelets.

Every third tube moving through the central lab is a haematology sample, said Hoogendijk, and the cobas m 511 with Bloodhound is designed to allow medical technologists to increase efficiency while processing a higher volume of tests and only highlighting for the technologists cells of interest in a next-generation digital format.

Presenting results comparing the analysis of the cobas m 511 with an established haematology system, Roche Diagnostics Chief Science Officer for Haematology, David Zahniser, showed a strong correlation and noted that the cobas m511 Bloodhound technology demonstrated 'excellent repeatability with equal-to-or-better-than the published percentage of coefficient of variation (CV) of automated haematology analysers.'The new all-digital Bloodhound technology is

Using Bloodhound technology, the cobas m 511 combines a digital morphology analyzer, cell counter and classifier into one streamlined instrument preparing, staining and analyzing microscopy blood smears.

transformative for haematology with capabilities for multispectral imaging at low and high-powered magnification and computing power to differentiate and assess size, shape, colour, and optical density for final morphology assessment.

Imagine then, the potential, said Zahniser, who posed an open question for lab technologists:

'What else can we learn from the morphologic analysis of each cell on the slide, and what will be the clinical value?'