Two years ago, following John Dalli’s resignation as Commissioner for Health and Consumer Affairs, Tonio Borg was appointed to that role by the Council of the European Commission. About a year ago, the title changed to Commissioner for Health. Soon he will reach the end of his term of office (31 October). Catching up with her impressive fellow Maltese during the 17th European Health Forum in Gastein, EH correspondent Moira Mizzi asked for his views on health in Europe today and what he believes has been achieved in recent years.

Bad Gastein in Austria is a health resort, thus the ideal setting to host the 17th European Health Forum in the first days of October this year. Heralded by the slogan Electing Health – The Europe We Want, the conference aims to reflect on opportunities and risks for health in light of the outcome of the recent European elections, and to discuss how to maintain and improve the health of European citizens.

After almost two years at the helm of the European Commission for Health, Dr Tonio Borg believes that the one main item that should feature on the conference agenda is the sustainability of our health systems. ‘Despite the marked progress in the health sector in recent decades, we cannot put our collective minds at rest about our health systems, no matter which parties, sceptical or otherwise, occupy the European Parliament,’ he insists. ‘We only have to look at the burden that chronic disease is putting on health budgets in most member states, not to mention the widening gap in equality in health care in many others, to put us in a constant state of vigilance.’

Dr Borg stresses that, in health matters, Europe still cannot be viewed as a Union unless this state of affairs is addressed. ‘We are still devoting only 3% of our expenditure to prevention, when a marginal increase in this budgetary measure could result in such an exponential improvement in our health statistics especially in the low socio-economic groups,’ he asserts emphatically. He also stresses the importance of pushing further the cross-border healthcare strategy including the second eHealth Action Plan 2012-2020, which focuses, amongst other issues, on supporting research, promoting international cooperation and achieving wider interoperability of e-health services.

According to Dr Borg, one of the major hurdles he faces is his lack of power to change trends. ‘My main strategies lie in the use of soft law options and political pressure to raise awareness and get things moving,’ he explains. ‘While I’m all for allowing subsidiarity to the Member States to give them more freedom to take care of their health systems, I believe that some issues, such as certain cross-border health threats, should be coordinated at a central level.’

Another bone to contend with in the Commissioner’s agenda is the migration of healthcare professionals both within and outside the perimeter of the European zone. The Commissioner, however, is clear in his stand where freedom of movement is concerned. ‘In my opinion full freedom of movement in the EU should be allowed, namely for people, goods, capital and services; it is after all, a core principle, enshrined in the EU treaties,’ he asserts.

A law graduate, Dr Tonio Borg’s many titles have included EU Commissioner for Health, Deputy Prime Minister of Malta, Minister for Foreign Affairs, Minister of Home Affairs, Minister of Justice, EU Commissioner for Malta, Deputy Leader of the Nationalist Party, member of the Barrosa Commission and lecturer in public law at the University of Malta.
**Chicago’s AACC 2014 highlights**

**Never-before-seen breakthroughs in diagnosing research and technology** were revealed during July’s American Association for Clinical Chemistry meeting in Chicago, where up to 20,000 people packed in for research updates. In the news - Abstracts included research on a portable blood test that detects low levels of Ebola – and the closely related Sudan virus – in 10 minutes. With technology found in home pregnancy tests, testing is possible in resource-limited settings prone to Ebola outbreaks and by people without extensive medical training. Early testing to identify, isolate, and treat Ebola cases quickly would be vital as preventing future outbreaks as huge as in West Africa.

**Obesity** – Jeffrey Friedman MD PhD, presented his research on the role leptin (the hormone he discovered) plays in obesity and the importance of approaching obesity as a medical issue, i.e. not driven by environmental factors or weak willpower.

**Alzheimer’s testing** – Exciting research that could lead to a treatment to halt or slow Alzheimer’s disease was revealed by Amrita Chereva PhD, one of the co-developers of an early blood test for this widespread disease.

**Big Data** – Viktor Mayer-Schönberger, co-author of Big Data: A Revolution That Will Transform How We Live, Work, and Think, offered actual examples to demonstrate the predictive power of big data and how it improves care by enabling researchers to analyse thousands of medical data points at once, rather than limiting their focus to a single question.

Following this, Mayo Clinic researcher Piero Rinaldo MD PhD examined how big data can help to avoid false positives in newborn screening, thus preventing unnecessary or even harmful medical treatment.

**Patient power** – Eric Topol MD, winner of the AACC’s 2014 Wallace H. Coulter Lectureship Award and director of the Scripps Translational Science Institute, pointed out that patients are now more empowered due to smartphone and other mobile health apps that enable them to collect their own health data.

Among the 650 exhibitors’ innovations were examples of lab-on-a-chip technology, including the very first human papillomavirus DNA test approved by the US FDA for primary cervical cancer screening, and the newest tests in reproductive health, infectious diseases, drug testing, and more.

---

**continued from page 1**

Despite this clear-cut position, Dr Borg admits that he cannot ignore the hunch this migration causes in a number of health systems, especially those where the health inequality gap is at its widest. ‘We have estimated that, by 2020, we would need around one million healthcare professionals if we aim to run our health systems efficiently, and the number doubles if old people’s homes are added to the equation,’ he explains. ‘As a result, we need to ask the collective question of whether the citizen actually wants to work in the health sector and then gear up the educational system to prepare and guide them accordingly.’ He also agreed that there should be a harmonised minimum requirements system to facilitate, yet regulate the integration of foreign doctors within different European states.

In the Clinical Trials Regulation, and the Clinical Trials Regulation, and the implementation of the cross-border healthcare Directive and the joint procurement agreement on vaccines, by far meet his greatest satisfaction – not to mention the various awareness campaigns on inequality and discrimination, and chronic disease prevention.

Despite this, he acknowledges that there is still a lot to be achieved in the way of making healthy food more accessible by decreasing its price and possibly by taxing the unhealthy alternative.

He also regrets not having more time to raise greater awareness and implementing more measures in the battle against anti-microbial resistance, although some awareness on the problem has been achieved and the subject will assume more importance politically in the very near future.

With his deadline of 2020 looming at an ominously close range (31 October), Dr Borg – and we – can only hope that his successor will choose to follow in his footsteps to guarantee that our health is safeguarded at all times.

---

**The Europe we want**

EH correspondent Moira Mizzi meeting with EU Commissioner for Health Dr Ionio Borg
Tackling tough bacteria, arenaviruses and bunyaviruses

**A breakthrough in antibiotic resistance**

**Tackling tough bacteria, arenaviruses and bunyaviruses**

**Report: Mark Nicholls**

An ‘Achilles heel’ in the defensive barrier surrounding drug-resistant bacterial cells has been identified by a team of scientists at the University of East Anglia (UEA) in Norwich, UK. The researchers believe their findings pave the way for a new wave of drugs that kill superbugs by bringing down their defensive walls rather than attacking the bacteria themselves.

Group leader Changjiang Dong, Professor of Molecular Medicine at UEA’s Norwich Medical School, says that potentially, in the future, bacteria may not develop drug-resistance at all. The discovery coincides with a warning from the World Health Organization that antibiotic-resistance in bacteria is spreading globally amid fears that even common infections, which have been treatable for many years, may once again have the potential to prove fatal.

The research team investigated Gram-negative bacteria, a class particularly resistant to antibiotics because of the cell’s impermeable lipid-based outer membrane, which acts as a defensive barrier against attacks from the human immune system and antibiotics. Thus the pathogenic bacteria can survive, but removing that barrier increases vulnerability and they die. Up to now little has been known about exactly how the defensive barrier is constructed but, Dong explained: ‘We have identified the path and gate used by the bacteria to transport the barrier building blocks, called lipopolysaccharides, to the outer surface. Importantly, we have demonstrated that the bacteria would die if the gate were locked.

The number of superbugs is increasing at an unexpected rate. This research provides the platform for urgently needed new generation drugs,’ he added.

Published in the journal Nature in June, the study, ‘Structural basis for outer membrane lipopolysaccharide insertion’ was funded by the Wellcome Trust, with research colleagues including the University of St Andrews, Dr Neil Paterson of Diamond Light Source (UK), Dr Phillip Mansfield at the University of Oxford, and Professor Wenjian Wang of Sun Yat-sen University, China. Lead author, PhD student Haohao Dong, said: ‘The really exciting thing about this research is that new drugs will specifically target the protective barrier around the bacteria, rather than the bacteria itself. Because new drugs will not need to enter the bacteria itself, we hope that the bacteria will not be able to develop drug-resistance in future.’

Changjiang Dong is Professor of Molecular Medicine at Norwich Medical School of University of East Anglia, UK. He was a senior scientist at the University of St Andrews (2003-2008) before setting up his research group as a Wellcome Trust career development fellow. Since 2012 he has chaired medical medicine at Norwich Medical School, where his research focuses on emerging infection pathogens, particularly multidrug resistant Gram-negative bacteria, arenaviruses and bunyaviruses, of which his group is interested in the outer membrane biogenesis and virulent outer membrane proteins. By combining protein crystallography, in vitro and in vivo assays, fragment chemical screening and chemical probes, his group is trying to understand the biological processes and helping towards novel drug discoveries.

---

**Test patients, not your patience.**

With the CLINITEK Novus analyzer, Siemens answers the need for faster, more reliable urinalysis testing.

siemens.com/novus

SOON TO BE RELEASED

Be prepared for the new blockbuster from the publishers of European Hospital. This aims to become the industry guide to laboratory diagnostics. Curious? Grab a free copy at DGKL in Mannheim or SIBIOC congress in Rome, or send an e-mail (info@european-hospital.com) to request one.

---

Most would agree that urinalysis testing is labor intensive and time consuming. When labs are overworked, testing accuracy may be compromised. The CLINITEK Novus® analyzer is changing that by addressing the relationship between the two.

Building on the technology of our CLINITEK Atlas® system, the CLINITEK Novus analyzer improves workflow with cassette-based test loading and increases throughput. A color touch screen features intuitive navigation along with customizable menu options. Plus, a new optical system enhances clinical accuracy. Faster throughput. Improved workflow. Optimal patient care. When labs are under pressure, the CLINITEK Novus analyzer is up to the test. Take a self-guided tour at siemens.com/novus or contact your Siemens representative.

---

Answers for life.
Viktor Mayer-Schönberger is a visionary author of the book Big Data, which, as its subtitle suggests, defines the debate over the ‘Revolution That Will Transform How We Live, Work, and Think.’ Yet, in his speech on ‘Understanding Big Data and its Impact on Your Laboratory,’ at the AACC this July, he stepped up to the status of a prophet. Less than a week later the Centers for Disease Control and Prevention (CDC) in Atlanta were wrestling with precisely the situation he had described as the agency confronted the rapidly spreading Ebola haemorrhagic fever virus.

Mayer-Schönberger, Professor of Internet Governance and Regulation at Oxford, told a story at AACC about a different, earlier virus where public health experts could only hope to slow the spread of the epidemic. For that, they needed to track occurrences of the virus. Using a traditional method of relying upon physician reports they created a picture that was a week behind the actual incidence of the disease. ‘This is an eternity for an epidemic that’s underway,’ he stressed. Meanwhile, the internet search giant Google developed an alternative method of predicting the spread of the disease by plotting queries among the five billion requests it handles each day. Google servers are not selective, storing every request they noted, including the geographic origin of the request. ‘They struck gold,’ said Mayer-Schönberger, producing a map plotting the requests that were later validated by CDC data as being coincident with reportings of flu.

According to Mayer-Schönberger, Google identified a correlation between incidence of flu and data requests that, while not accurate, should not be discounted. Big Data correlations can sometimes be ‘good enough,’ he cited the observation made by the grocery store giant Walmart that, in the days following a hurricane warning, customers stocked up on a breakfast product called Pop Tarts. ‘The committee wanted to know why people did that until someone cried: ‘Who cares?’ he wrote.

Big Data can be made by the grocery store giant Walmart that, in the days following a hurricane warning, customers stocked up on a breakfast product called Pop Tarts. ’The committee wanted to know why people did that until someone cried: ‘Who cares?’ he wrote. Mayer-Schönberger queried. The epicentre for an epidemic that’s underway, he noted, including the geographic origin of the request. ‘They struck gold,’ said Mayer-Schönberger, producing a map plotting the requests that were later validated by CDC data as being coincident with reportings of flu. As an example of how Big Data handled each day. Google servers are not selective, storing every request they noted, including the geographic origin of the request. ‘They struck gold,’ said Mayer-Schönberger, producing a map plotting the requests that were later validated by CDC data as being coincident with reportings of flu. As an example of how Big Data

As an example of how Big Data the tremendous cost of more complete data collection. ‘What happens when collecting data becomes cheap?’ Mayer-Schönberger queried. The economics of data collection, data storage and data analysis have changed. The Sloan Digital Sky Survey collected more astronomical information in its first week of operation than scientists had gathered in the entire history of astronomy. Closer to home, he said, the cost of DNA sequencing has fallen from billions of dollars in 2003 to a few thousand, while the time for sequencing has dropped from years to a single day.

Small Data requires a researcher to choose a focus for investigation. Big Data invites inquiries on everything with tools enabling a researcher to zoom in or zoom out, ‘to let the data speak,’ said Mayer-Schönberger. ‘Today we are drowning in information, terabytes and petabytes of information.

The rate of data accumulation has exploded 100 times in just 20 years and, during this time, we moved from an analogue world to a digital world making information easier to store, to access. How will we shift from a quantity of data to a quality of data in Big Data?’

Clinical laboratories are data mines yielding massive, important information and Big Data will redefine expertise within the labs.

‘No one today expects decisions to be based in hunches, on the intuition of experts. Evidence-based medicine has already moved us in this direction. Mayer-Schönberger added, and concluded: ‘We will need statisticians who will become members of research teams with a greater role as quantification rises.’

Respect it, don’t fear it

WHO alerts physicians generally on Ebola

The current ebola outbreak in West Africa, which began in December 2013 in Guinea and has since spread to Liberia, Sierra Leone and Nigeria and Congo. As in the past, modern medicine is unable to prevent or cure the disease. However, the disease can be treated in the early stages.

Physicians should consider an ebola infection in patients presenting with fever who returned from the affected regions within the past 21 days and who might have had contact with ebola patients, the body of deceased ebola victims, with their bodily fluids, or with animals carrying the virus.

Guinea, Guékédou: Staff of the ‘Doctors without Borders‘ carry the body of a person killed by viral haemorrhagic fever.
A case of the tortoise and the hare

If you were lucky – or unlucky – enough to have visited a medical central lab 20, 30 or even 40 years ago and know how such a facility looks today, you will probably think you are in some kind of time warp. Indeed, not a few but many of generations have passed. Automation of medical procedures, particularly in diagnostics, has seen lightning progress to the extent that many systems, inconceivable a few years back, are already in their third generation. For example, the Brömer system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his old microscope to verify the results. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system is a small unit, frequently integrated into a line of automation and machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system is a small unit, frequently integrated into a line of automation and machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system is a small unit, frequently integrated into a line of automation and machine data.

Not only haematology was revolutionised by automation, the same approach holds true for clinical chemistry and many other central lab functions with photometers and huge clinical chemical analysers now illustrating the third generation automation.

By comparison, a pathology department appears to be almost archaic. Automation has been slow to take hold. Why is that? Are staff members less automation-prone or less automation-capable? Most certainly. 30 years ago, for example, a lab technician would manually place a slide to be stained on a rack in the slide staining system. Before that he had to ‘programme’ the slide, and punch – much like a train conductor – punch a ticket – an aluminium disk. Admittedly, the machine looked rather clumsy, but it was able to process up to 24 trays and could be connected to the water supply. Not very different from a modern slide staining system, but which is smaller, looks smarter than its predecessors and is programmed digitally rather than punched manually. Even today, however, the slides or racks must be ‘programmed’ manually. Many other routine steps in a pathology department are still done largely by hand, such as paraffin embedding, removal and sectioning. Sections of only a few microns are cut by the ‘microtome’ or cryotome.

Automation in pathology is much more difficult to realise, not only due to the many individual steps, but also because pathologists work with a wide variety of materials, from tiny biopsy specimens to entire extremities. In the 1960s, a chair at the University of Tübingen was dedicated to optimise microscope blades, which cut sections as thin as 2 to 5 μm. A British company even developed – and built – a device to sharpen microscope blades right in the lab, to avoid the time-consuming and expensive procedure of having to send the blades to specialised services. The device was called a microtome sharpening machine but it was far from what we today would consider ‘automation’ since it required a highly skilled and experienced operator, as well as time and patience: a single sharpening operation could take hours. Disposable microscope blades had not yet been invented, at least not for routine use – another reason why automation in this field was much slower than in the clinical lab.

Obviously automation did work in pathology, but it was far from what we read today: a haematology or general practitioners, then use the results, in some kind of time warp. Indeed, not a few but many of generations have passed. Automation of medical procedures, particularly in diagnostics, has seen lightning progress to the extent that many systems, inconceivable a few years back, are already in their third generation. For example, the Brömer system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data. Today, the same system was the size of a closet and equipped with a separate console. An experienced pathologist would question well over ten percent of the system’s results, take the specimens and examine it under his good old microscope to verify the machine data.
A pathologist in your pocket

Digitising individual health data will bring 'creative destruction' to medicine as we know it today

We live in a connected world, a very different world than it was a decade ago. Medical devices, wearable devices are driving a creative revolution, reducing costs, health care is going in the other direction, constantly increasing because, we haven’t begun to use the technologies yet that’s available in digital form, Topol pointed out.

Topol pointed out. We have not been able to do better up to this point, but that is changing, and clinical labs need to adjust to the technological and societal trends. Today we can digitise the individual, and this is extraordinary.

In a recently published article in Cell, entitled, ‘Individualized Medicine: From pre- to post-genomics,’ Topol suggests that through an individual’s digital data we can understand their medical essence, take a panonomic view of each individual and learn what makes him or her tick.

Medical metrics have moved beyond the established genomic or proteomic information about the individual, growing to a family of up to 10-omics, as well as a study of an individual’s environment, or e-omics.

Progressively, he said, this data will enable the delivery of preventive care and far better medical outcomes in the future. It will take medicine to a much higher, more precise level. Google, Apple, and Samsung are all companies positioning to aggregate this data, though it is not yet medical-grade data.

Blood pressure and glucose measures are today well established with mobile devices. Recently cardiograms have come into the digital picture. Cardiograms have been read by algorithms for decades. Now they can be read at the consumer level, stated Topol. ‘Smart watches pre-empt the need to get to a smartphone, sending all kinds of stored information to other devices that monitor vital signs continuously. All of this needs to be validated through rigorous study, but, it has been called a Trillion Dollar Cure for the healthcare system, to have individualised healthcare, rather than the increasing cost of Population-Based Healthcare.’

Lab testing is pivotal to medicine, he noted, but at a cost that is among the top drivers of increasing medical costs.

Today, innovation is starting to rethink the role of laboratory medicine, he said. Increasingly, both patients and providers are able to read lab results. Why shouldn’t they have access to their lab results. Why shouldn’t they have access? Why do we even ask this question? Because the lab results are the bedrock of the audience of lab clinicians. ‘We have a new model that is going forward, with diagnostics by patients, in the years ahead. This will be a big shake up enabled by all this technology.’

Medical imaging is being revisited, the cardiologist believes, thanks to pocket tools made possible with new technologies. Patients will soon be able to do selfsies of a joint, or a bone. ‘On the other hand, today can already be done with the EyePhone at a fraction of the cost of the usual visit. ‘The stethoscope is out,’ he confirmed. ‘Havard is asking doctors, why would you listen to the heart, when you can see it in seconds?’

Topol pointed out. The changing landscape in France is identified by many new and ongoing processes, such as the open data initiative that was rolled-out to run from July 2014 onwards (data.gouv.fr).

This will also have an effect on laboratory medicine, in addition to more direct legislation, which includes the necessity for laboratory accreditation by 2020 and medicalisation of laboratory reports.

German laws have been passed to restrict the number of specialists relating to laboratory medicine has changed recently in both countries’ said Professor M Klouche. Therefore, each speaker will present in their own native languages with simultaneous translation provided.

It is impossible to discuss laboratory medicine without considering the political implications and governmental influence. The law relating to laboratory medicine has changed recently in both countries’ said Professor M Klouche. Both governments are expecting significant changes in laboratory medicine provision over the next five to 10 years.

German law expects some very knowlegeable and well placed speakers and also lose masses in translation because although some organisations have similar or overlapping functions, these are not strictly comparable and therefore the Haute Autorité de Santé in France cannot be easily translated to the German Bundesärztekammer, which is the guideline-producing self-organising Federal Chamber of Medicine in Germany explained Professor M Klouche. Therefore, each speaker will present in their own native languages with simultaneous translation provided.

It is impossible to discuss laboratory medicine without considering the political implications and governmental influence. The law relating to laboratory medicine has changed recently in both countries’ said Professor M Klouche.

New France-Germany Forum will compare structures, training, tests and costs.

Originally, the idea was that the forum should be English, but on reflection, it was decided this would perhaps exclude some very knowledgeable and well placed speakers and also lose masses in translation because although some organisations have similar or overlapping functions, these are not strictly comparable and therefore the Haute Autorité de Santé in France cannot be easily translated to the German Bundesärztekammer, which is the guideline-producing self-organising Federal Chamber of Medicine in Germany explained Professor M Klouche. Therefore, each speaker will present in their own native languages with simultaneous translation provided.

It is impossible to discuss laboratory medicine without considering the political implications and governmental influence. The law relating to laboratory medicine has changed recently in both countries’ said Professor M Klouche.

Both governments are expecting significant changes in laboratory medicine provision over the next five to 10 years.

German law expects some very knowledgeable and well placed speakers and also lose masses in translation because although some organisations have similar or overlapping functions, these are not strictly comparable and therefore the Haute Autorité de Santé in France cannot be easily translated to the German Bundesärztekammer, which is the guideline-producing self-organising Federal Chamber of Medicine in Germany explained Professor M Klouche. Therefore, each speaker will present in their own native languages with simultaneous translation provided.

It is impossible to discuss laboratory medicine without considering the political implications and governmental influence. The law relating to laboratory medicine has changed recently in both countries’ said Professor M Klouche.

Both governments are expecting significant changes in laboratory medicine provision over the next five to 10 years.

German law expects some very knowledgeable and well placed speakers and also lose masses in translation because although some organisations have similar or overlapping functions, these are not strictly comparable and therefore the Haute Autorité de Santé in France cannot be easily translated to the German Bundesärztekammer, which is the guideline-producing self-organising Federal Chamber of Medicine in Germany explained Professor M Klouche. Therefore, each speaker will present in their own native languages with simultaneous translation provided.

It is impossible to discuss laboratory medicine without considering the political implications and governmental influence. The law relating to laboratory medicine has changed recently in both countries’ said Professor M Klouche.
PET-MRI, according to many experts, is the best clinical procedure to confirm coronary heart disease (CHD). Prof. Markus Schwaiger begs to differ: ‘We can learn a lot from this type of set-up,’ says the Director of the Clinic of Nuclear Medicine at Klinikum rechts der Isar in Munich, Germany, who nevertheless is convinced that hybrid imaging can help clinicians make better use of positron emission tomography (PET) and magnetic resonance imaging (MRI) for coronary revascularisation.

Overall, the professor agrees that cardiac imaging has developed extremely quickly over the past few years. While clinicians continue to struggle with the diagnosis of many diseases today, they can choose among a whole slew of procedures to diagnose CHD early and to track the course of the disease.

However, the wide range of available diagnostic imaging techniques and modalities has a downside: it has become difficult to develop recommendations for an integrative diagnostic workflow. Part of the problem is that the fact experts are divided into different camps as Prof. Schwaiger explains: ‘There are those who are convinced that a fast CT scan is ideal, others consider perfusion imaging more important.’

Schwaiger supports a different approach: ‘The imaging procedure should be selected depending on the probability of a coronary heart disease. If CHD needs to be excluded, fast CT or CT-Angio are the methods with the highest negative predictive value. For patients with confirmed calcifications, however, the combination with a perfusion marker makes sense,’ he explains, since the marker shows the area that is compromised under physiological or pharmacological stress—the so-called ischaemic burden can be evaluated. Today, the relevant guidelines demand a pre-interventional ischaemia test. ‘The literature on single photon emission tomography, also called SPECT, indicates that an intervention is useful when more than ten percent of the left ventricular myocardium is ischaemic,’ Schwaiger underlines.

Modalities such as PET, SPECT and MRI are well suited to evaluate myocardial perfusion. ‘PET allows rather precise quantitative perfusion measurement,’ he points out, adding that in this context the so-called coronary flow reserve is not only of diagnostic but also of prognostic value: ‘Limited coronary flow reserve is associated with poor survival rates, or with a high risk of cardiovascular complications.’

Although quantitative measurements with PET and increasingly with MRI might present an alternative to the invasive measurement of the fractional flow reserve (FFR), they cannot entirely replace it due to their complex and thus expensive material requirements.

The clinical value of hybrid imaging is, according to Schwaiger, rather low: ‘I consider PET-MRI a research tool rather than a method to be used everywhere for coronary diagnostic purposes—it is much too expensive. The Formula 1 of imaging so to speak.’

PET-MRI is useful for validation capacity and prognostic outcome. PET/CT with the radiotracer FDG is highly sensitive in the detection of residual myocardial viability in areas of infarction, while MRI with delayed-imaging of gadolinium trapping in the myocardium can reliably detect old scar tissue and/or fibrosis with specific T1-weighted sequences. In this respect, cardiac MRI provides more specific information on potential recovery of heart function after coronary revascularisation.

There are heart centres using primarily PET, and centres that use MRI, he said, and each modality comes with a certain bias.

Clinical tests to confirm coronary heart disease

PET-MRI, according to many experts, is the best clinical procedure to confirm coronary heart disease (CHD). Prof. Markus Schwaiger begs to differ: ‘We can learn a lot from this type of set-up,’ says the Director of the Clinic of Nuclear Medicine at Klinikum rechts der Isar in Munich, Germany, who nevertheless is convinced that hybrid imaging can help clinicians make better use of positron emission tomography (PET) and magnetic resonance imaging (MRI) for coronary revascularisation.

Overall, the professor agrees that cardiac imaging has developed extremely quickly over the past few years. While clinicians continue to struggle with the diagnosis of many diseases today, they can choose among a whole slew of procedures to diagnose CHD early and to track the course of the disease.

However, the wide range of available diagnostic imaging techniques and modalities has a downside: it has become difficult to develop recommendations for an integrative diagnostic workflow. Part of the problem is the fact experts are divided into different camps as Prof. Schwaiger explains: ‘There are those who are convinced that a fast CT scan is ideal, others consider perfusion imaging more important.’

Schwaiger supports a different approach: ‘The imaging procedure should be selected depending on the probability of a coronary heart disease. If CHD needs to be excluded, fast CT or CT-Angio are the methods with the highest negative predictive value. For patients with confirmed calcifications, however, the combination with a perfusion marker makes sense,’ he explains, since the marker shows the area that is compromised under physiological or pharmacological stress—the so-called ischaemic burden can be evaluated. Today, the relevant guidelines demand a pre-interventional ischaemia test. ‘The literature on single photon emission tomography, also called SPECT, indicates that an intervention is useful when more than ten percent of the left ventricular myocardium is ischaemic,’ Schwaiger underlines.

Modalities such as PET, SPECT and MRI are well suited to evaluate myocardial perfusion. ‘PET allows rather precise quantitative perfusion measurement,’ he points out, adding that in this context the so-called coronary flow reserve is not only of diagnostic but also of prognostic value: ‘Limited coronary flow reserve is associated with poor survival rates, or with a high risk of cardiovascular complications.’

Although quantitative measurements with PET and increasingly with MRI might present an alternative to the invasive measurement of the fractional flow reserve (FFR), they cannot entirely replace it due to their complex and thus expensive material requirements.

The clinical value of hybrid imaging is, according to Schwaiger, rather low: ‘I consider PET-MRI a research tool rather than a method to be used everywhere for coronary diagnostic purposes—it is much too expensive. The Formula 1 of imaging so to speak.’

PET-MRI is useful for validation
Looking for the perfect modality

Today there is no method available to detect vulnerable plaque

Continued from page 7

Combing the two modalities creates the potential for more objective information for the decision-making process and can lead to a more highly individualised therapy decision for interventional and medical treatment options in patients with ischaemic cardiomyopathy.

He hopes his present study – not even at the department of cardiovascular imaging at Heidelberg's University Hospital, which is headed by Prof. Korosoglou. Coronary angiography shows stenoses and is the current gold standard in the diagnosis of coronary heart disease. But there is no modality that can tell us which plaque is unstable and thus a potential source of a future cardiac event such as a myocardial infarction. 

Currently, interventional or surgical therapy for patients with coro-
nary heart disease (CHD) is geared towards obstructive lesions: only those lesions are treated which significantly narrow the coronary artery lumen. 'But today we know that a myocardial infarction is not necessarily caused by these lesions,' Prof. Korosoglou explains, 'but by those which were not considered significant in angiography.'

While certain diagnostic procedures can identify potentially dangerous plaque based on plaque morphology, most of these techniques are 'not clinically established,' Prof. Korosoglou underlines, 'such as intravascular ultrasound, known as IVUS. This invasive procedure is based on virtual histology to identify plaque with a large necrotic core and spotty calcifications. Studies have indicated that a large necrotic core correlates with plaque at risk of rupture.'

Cardiac CT is used routinely to classify patients with suspect-
ed CHD and is considered by the European Society of Cardiology to be a modality that will play an increasingly significant role. Cardiac CT is particularly useful because it not only visualises stenosis but also allows the characterisation of the coronary artery walls and the composition of atherosclerotic plaque. Recent CT studies have indicated that patients with a high number of non-calcified so-called low attenuation plaques have a significantly higher risk for future cardiac events, such as a myocardial infarction or sudden cardiac death.

Magnetic resonance imaging (MRI) is another modality which might offer the possibility to iden-
tify vulnerable plaque but it also is, as the Heidelberg-based cardiologist explains, still in the experimen-
tial stage. There is for example the attempt to use iron-containing nanoparticles in MRI to visualise inflammation-related plaques. Plaque macrophages take up the intraveno-
sously applied nanoparticles. Thus MRI provides information on the accumulation of macrophages in the plaque which is considered a surro-
gate parameter for plaque instability and by extension unstable cardio-
vascular disease. MRI, however, still has certain limitations. The spatial resolution of the MRI scans is not yet sufficient to provide detailed images of the coronary plaques.

There is another high potential among the imaging modalities, as Prof. Korosoglou points out: Fluorine-18 positron emission tomography combined with com-
pared tomography, known as PET-CT, might become clinically rel-
evant. Fluorine-18 is a radioisotope that was previously used to visualise bone formation. Recent clinical studies with acute myocardial infarction patients have shown increased fluorine uptake in ruptured plaques. Moreover increased fluorine uptake was recently found in patients with seemingly stable CHD – exactly those plaques that had been classified as particularly at risk of rupture according to the IVUS scores.

Thus PET-CT might be a non-
invasive modality to detect plaques at risk of rupture or even the early stages of the rupture before the cardiac event – the infarction – hap-
pens. Not all plaques, however, take up fluorine-18 particularly patients with a high degree of calcification seem to be metabolically inactive with regard to fluorine-18.

These very different approaches show that there are many aspects of atherosclerosis which we have not yet understood. We used to think, for example, that the degree of cal-
lication correlates directly with the risk of future coronary event. Today we know that it might be possible that only metabolically calcified and metabolically active plaques are those with the high risk of rupture,' he summarises. Conclusion in a nutshell: There is much work to be done in atherosclerosis research.
Cardiac resynchronisation

Newly implanted defibrillators enable MRI scanning

This summer the world’s first implantations of Biotronik’s new CRT-D (implantable cardioverter-defibrillator) series and their ProMRI quadripolar leads took place at the Spedali Civili Hospital, Brescia, Italy. "My ICD and heart failure patients are frequently indicated for MRI scans to diagnose potential comorbidities," said Dr Antonio Curnis. The researcher had implanted the firm’s ProMRI Inventra HF-T and Sentus quadripolar lead in a 73-year-old patient with congestive heart failure. "With the Biotronik devices, I know I can give my patients high-quality therapy and broad access to diagnostics," Curnis explained.

With Sentus quadripolar leads and the Inventra series, the manufacturer confirms that it is the first and only company to produce cardiac resynchronisation devices and leads for heart failure (HF) patients that are approved for MRI scans. As patients age, they may develop comorbidities, and MRI scans can be critical in diagnosing conditions such as stroke, brain tumours or orthopaedic conditions. "The quadripolar Sentus lead eases the implantation process by giving physicians access to challenging vessels. With CE approval in early July, Biotronik’s new implantable defibrillator series includes the industry’s first quadripolar left-ventricular leads to be approved for MRI use."

In addition to ProMRI technology, the firm’s new ICDs and CRT-Ds reduce inappropriate shocks with MorphMatch morphology detection criteria and anti-tachycardia pacing (ATP) optimisation. "While delivering shocks at the right time can save patients’ lives, shocks should be minimised to appropriately control arrhythmias, improve patients’ quality of life and increase device longevity," Biotronik point out.

Dr Werner Jung, at the Schwarzwald-Baar Clinic, Villingen Schwenningen, Germany, successfully implanted a 72-year-old HF patient with a new ProMRI CRT-D from this bio-tech manufacturer. Speaking of the ‘exceptional quality of Biotronik products, the surgeon said: ‘Many heart failure patients are very ill and shocks put stress on the body and mind. By choosing a device with unique algorithms that reduce shocks, I can give my patients peace of mind and restore their sense of safety.’ The company has included its Closed Loop Stimulation (CLS) technology in ICDs for the first time: ‘CLS helps patients experience the most natural rate adaptation possible by utilising their neurological information,’ the company explains. It’s the only system that allows pacemakers, and now ICDs, to react naturally to patients’ physical as well as mental activity or stress.”

www.siemens.com/cardiology

CARDIOLOGY

It is amazing what cardiovascular medicine can accomplish today. And how challenging it can be to accomplish it. At Siemens, sustainable cardiovascular care is all about pushing back clinical boundaries and pulling down operational barriers. In other words, it’s about helping you deliver more cardiology with less heartache.

Less heartache means improving patient outcomes by reducing time-to-diagnosis, offering new therapeutic options, and getting better guidance during advanced procedures. Less heartache also means performing safer procedures with higher operational efficiency – on the way to a more personalized care.

Innovation brought us here. At Siemens, innovation continues. Advancing cardiovascular care, with less heartache, sustainably.

www.european-hospital.com
When cardiac catheterisation delivers no result...

radiologists diagnose the causes of non-specific chest pain using MRI

Complementary cardiac imaging

CT angiography combined with PET perfusion measuring becomes gold standard

The significant benefits of cardiac catheterisation remain undisputed. However, cross-sectional imaging modalities are serious competitors when it comes to arriving at the right diagnosis.

Recently, during the German Radiological Society Congress, Dr Tilmann Emrich presented the results of his study on the diagnostic importance of cardiac MRI (CMR) for patients suffering acute chest pain, elevated levels of cardiac enzymes and a negative coronary angiography.

A 25-year-old male without a known pre-existing illness, and a 45-year-old female who had recently suffered a severe blow, were admitted to AEK at Mainz University Hospital and treated in the specialist chest pain department. The ECG showed no abnormalities but blood tests showed elevated troponin levels. Independent of the patients’ age and sex everything pointed towards myocardial infarction. As per the established guidelines for these cases, the patients are therefore taken to the cardiac catheter laboratory. However, the cardiologist could find no evidence of a myocardial infarction. In this case, the cardiologist is faced with a dilemma. What should he do – send the patient home and continue treatment without a diagnosis? asked Dr Tilmann Emrich of the Clinic for Diagnostic and Interventional Radiology at Mainz University Hospital. His answer: In this situation, a heart MRI can be helpful as it enables an examination of the functionality together with the anatomy and analyses of the tissue. The clinical and laboratory results suggested an undiagnosed heart problem for both patients.

Studies published to date have documented the field of application, i.e. CT angiography plus PET perfusion measuring. ‘Both procedures, i.e. CT angiography plus PET perfusion measuring, can be used to calculate the coronary calcium score. The best discipline is the CT angiography, i.e. the visualisation of the contrast medium-filled coronary vessels and the quantification of the grade of stenosis,’ Hacker emphasises, and confirms: ‘The opinion now tends to be that if you have PET/CT available you should run the entire range of procedures, i.e. CT angiography plus PET perfusion measuring. Both procedures complement one another and thus deliver benefit.

Although PET perfusion measuring – with specificity and sensitivity of more than 90% – achieves a very high accuracy on its own compared to the more invasive coronary angiography, a simultaneous CT angiography additionally facilitates the attribution of any perfusion defects detected to the respective coronary stenosis that actually cause them. With PET alone, this can only be achieved in around 30% of cases. This makes it possible to plan revascularisation measures,’ Hacker explains. Furthermore, first studies show that CT angiography also has an additional benefit regarding individuation of cardiovascular MRI in these cases, although there is as yet no study on a case where a patient’s radiological diagnosis was cross-checked with the cardiologist’s final reference diagnosis in the context of clinical proceedings.

Back in 2007, this prompted Emrich, then still in specialist radiology training, to carry out a cardiac MRI in 125 patients whose cardiac catheter examination did not have any indicator results, and to compare both diagnoses.

His work was overseen by Professor Karl-Friedrich Kreiter and the study was carried out between 2007 and 2010 – with a satisfactory result. The MRI scan showed multiple cardiac pathologies and in nine out of ten cases the MRI diagnosis concurred with the cardiologist’s final reference diagnosis.

The five most common indications were myocarditis, dilated cardiomyopathy, acute myocardial infarction, Takotsubo cardiomyopathy (Broken-Heart Syndrome) and hypertensive heart disease; explains Emrich. The MRI scan helped to make the right diagnosis for all cases of myocardial infarction and Takotsubo cardiomyopathy; in the other cases there were only slight variances.

In the case of four patients, the cardiologists were not able to make a final diagnosis at all.

Example: Takotsubo Cardiomyopathy – 45-year-old female, with no abnormalities, seen during the cardiac catheter examination. However, with limited pumping function, the patient’s life was in danger. MRI scanning shows left ventricular apical ballooning and a corresponding oedema in the tissue without significant abnormalities seen in the late enhancement sequence – typical for Broken Heart Syndrome. This type of cardiomyopathy can be caused by stress without the presence of a vascular obstruction. After three months the problem had completely disappeared (right).

Example: Myocarditis – 23-year-old male with no abnormalities is seen in pumping function during an echocardiographic and MRI examination. After contrast medium administration, inflamed necrosis in the sub-epicardial myocardium becomes visible in the late enhancement sequence. All the information available, such as normal pumping function, no wall motion abnormalities, oedematous changes and the late enhancement sequence pattern, make a myocarditis diagnosis highly likely.

In this case, the cardiologist is faced with a dilemma. What should he do – send the patient home and continue treatment without a diagnosis? asked Dr Tilmann Emrich of the Clinic for Diagnostic and Interventional Radiology at Mainz University Hospital. His answer: ‘In this situation, a heart MRI can be helpful as it enables an examination of the functionality together with the anatomy and analyses of the tissue. The clinical and laboratory results suggested an undiagnosed heart problem for both patients.’

Studies published to date have documented the field of application, i.e. CT angiography plus PET perfusion measuring. ‘Both procedures, i.e. CT angiography plus PET perfusion measuring, can be used to calculate the coronary calcium score. The best discipline is the CT angiography, i.e. the visualisation of the contrast medium-filled coronary vessels and the quantification of the grade of stenosis,’ Hacker emphasises, and confirms: ‘The opinion now tends to be that if you have PET/CT available you should run the entire range of procedures, i.e. CT angiography plus PET perfusion measuring. Both procedures complement one another and thus deliver benefit.

Although PET perfusion measuring – with specificity and sensitivity of more than 90% – achieves a very high accuracy on its own compared to the more invasive coronary angiography, a simultaneous CT angiography additionally facilitates the attribution of any perfusion defects detected to the respective coronary stenosis that actually cause them. With PET alone, this can only be achieved in around 30% of cases. This makes it possible to plan revascularisation measures,’ Hacker explains. Furthermore, first studies show that CT angiography also has an additional benefit regarding individuation of cardiovascular MRI in these cases, although there is as yet no study on a case where a patient’s radiological diagnosis was cross-checked with the cardiologist’s final reference diagnosis in the context of clinical proceedings.

Back in 2007, this prompted Emrich, then still in specialist radiology training, to carry out a cardiac MRI in 125 patients whose cardiac catheter examination did not have any indicator results, and to compare both diagnoses.

His work was overseen by Professor Karl-Friedrich Kreiter and the study was carried out between 2007 and 2010 – with a satisfactory result. The MRI scan showed multiple cardiac pathologies and in nine out of ten cases the MRI diagnosis concurred with the cardiologist’s final reference diagnosis.

The five most common indications were myocarditis, dilated cardiomyopathy, acute myocardial infarction, Takotsubo cardiomyopathy (Broken-Heart Syndrome) and hypertensive heart disease; explains Emrich. The MRI scan helped to make the right diagnosis for all cases of myocardial infarction and Takotsubo cardiomyopathy; in the other cases there were only slight variances.

In the case of four patients, the cardiologists were not able to make a final diagnosis at all.

Example: Takotsubo Cardiomyopathy – 45-year-old female, with no abnormalities, seen during the cardiac catheter examination. However, with limited pumping function, the patient’s life was in danger. MRI scanning shows left ventricular apical ballooning and a corresponding oedema in the tissue without significant abnormalities seen in the late enhancement sequence – typical for Broken Heart Syndrome. This type of cardiomyopathy can be caused by stress without the presence of a vascular obstruction. After three months the problem had completely disappeared (right).
Three artificial hearts to be implanted

French authorities have given the green light for continuing the clinical trial for the first fully implantable mechanical heart after a four-month review of the device and the causes of death of the first patient to receive the prosthesis.

The manufacturer, Carmat, can now continue its recruitment of three other patients authorised for this first trial to test device safety and feasibility. All implantations will be performed in France.

Congratulating participants on the quality of their work in collecting and analysing the data from this first implantation, Carmat CEO Marcello Conviti said in a company announcement that ‘complementary measures’ have been put in place to continue the trial in order to assure the best conditions for safety.

In an e-mail response to European Hospital, the company said the measures ‘concern notably manufacturing processes or protocols which the company does not wish to discuss.’

The company also said that it will not communicate any further information until the full trial for safety has been completed.

The first artificial heart that was implanted

The first patient to receive a totally implantable artificial heart died 75 days after the procedure. The cause of death on 2 March 2014 was not disclosed in a short announcement made by the Hôpital Georges-Pompidou in Paris.

Christian Latremouille MD, at the Hôpital Georges-Pompidou, noted that a survival of 74 days for the first patient with end-stage heart failure widely exceeded the 30-day endpoint for the safety study.

The 76-year-old patient was ‘fully aware of the risks and by his confidence, his courage and his willingness has made a remarkable contribution to the efforts undertaken to combat a rapidly progressing disease,’ the medical team stated.

The heart was implanted on 18 December 2013, by the surgical team led by Dr Latremouille with the participation and guidance of the inventor of the device, Alain Carpentier MD.

The artificial heart adapts blood supply

This was the first time an artificial heart requiring no external pumps had been implanted. Only two wires exited the body at the abdomen, one to supply power and a second to monitor device performance.

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

In an interview with the French weekly, Journal du Dimanche, Carpentier said the first patient’s death ‘is not linked to a complication of the patient, nor to the fundamental principles of this prosthesis.’

He said the risk of thrombosis was limited, that the patient did not demonstrate any cerebral deficiency, and that an autopsy confirmed there was not the least bit of clotting in the device nor in the circulatory system.

‘In this sense, the trial was a success,’ he concluded.

Thanks to PureECG™, SCHILLER has achieved unparalleled signal quality in Holter recordings.

With state-of-the-art amplifiers and filter technology only SCHILLER is capable of direct P wave detection and therefore makes it possible to identify in a matter of seconds the onset and offset of atrial fibrillation and atrial flutter episodes.

The more accurate your Holter ECG recording is, the less post-processing time you need.
HRV analysis is important – Functional disturbances of the autonomic nervous system are always accompanied by reduced heart rate variability (HRV). With the heart being a central target organ of autonomic regulation, heart rate is a crucial regulation parameter for many processes in the body and offers a wealth of information on the functional status of the human organism.

Usually, heart rate is analysed statistically, for example with spectral analysis, in order to filter relevant information. Conventional ECG devices compress the data and much information is lost.

However, the functional status of a highly complex system, such as our autonomic nervous system, cannot be described by a few parameters. The complete information can only be culled from the 120,000 RR intervals in 24 hours.

Schiller reports: ‘Fire of Life can present these data, which map the regulation processes of the autonomic nervous system, in a non-compressed way and in high resolution. This allows the integration of HRV analysis in many clinical specialities, such as internal medicine, cardiology, occupational medicine, psychiatry, psychosomatic medicine or sleep medicine.’

HRV in cardiology

‘In cardiology HRV is above all a risk marker: the lower the HRV, the higher the risk of cardiac events or cardiac death,’ says Dr René Hefti, senior consultant and medical director at Klinik SGM Langenthal, in Switzerland. He uses HRV analysis to record autonomic dysregulation in hypertensive patients, for example: ‘Some hypertensive patients are difficult to assess due to a number of stress factors, such as psychosocial stress, poor sleep quality, lack of physical exercise, etcetera. This hypertension ought not to be looked at as an isolated phenomenon. HRV allows us to gain a comprehensive picture of the regulation processes.’

The Fire of Life application measures HRV over a 24-hour period thus providing information on the autonomic overall balance, sleep quality, the linkage between respiration and heart rate and similar indicators to support management of the hypertensive patient. The application’s spectral images show the quality of the regulation processes while the frequency values offer quantitative data, the cardiologist explains. ‘I don’t need HRV to diagnose noise hypertension, but I do need it to understand whether and to which extent hypertension is accompanied by autonomic dysfunction.’

Individualised therapy

The results of the HRV analysis provide crucial information for an individualised therapy of the hypertensive patient. ‘If we promote sympathetic dominance, which even continues through the night and is accompanied by reduced vagal activity, we not only need drugs that block the sympathetic nerve but also immediate measures to increase vagal activity, such as regular physical exercise or deep relaxation techniques, for example based on HRV bio-feedback. At the same time, risk factors and psychosocial stress need to be reduced; he explains.

Long-term HRV measurements allow the physician to monitor the quantitative efficacy of therapeutic measures. If the sympathetic tone decreases and vagal tone increases, which indicates a better balance of the autonomic nervous system, therapeutic measures are effective.

In addition, the easy-to-understand spectral images play an important long-term role in guiding and motivating the patient. 24-hour HRV monitoring can be used in the same way to manage other cardiovascular diseases such as coronary heart disease.

The Fire of Life application measures HRV over a 24-hour period thus providing information on the autonomic overall balance, sleep quality, the linkage between respiration and heart rate and similar indicators to support management of the hypertensive patient. The application’s spectral images show the quality of the regulation processes while the frequency values offer quantitative data, the cardiologist explains. ‘I don’t need HRV to diagnose noise hypertension, but I do need it to understand whether and to which extent hypertension is accompanied by autonomic dysfunction.’

Individualised therapy

The results of the HRV analysis provide crucial information for an individualised therapy of the hypertensive patient. ‘If we promote sympathetic dominance, which even continues through the night and is accompanied by reduced vagal activity, we not only need drugs that block the sympathetic nerve but also immediate measures to increase vagal activity, such as regular physical exercise or deep relaxation techniques, for example based on HRV bio-feedback. At the same time, risk factors and psychosocial stress need to be reduced; he explains.

Long-term HRV measurements allow the physician to monitor the quantitative efficacy of therapeutic measures. If the sympathetic tone decreases and vagal tone increases, which indicates a better balance of the autonomic nervous system, therapeutic measures are effective.

In addition, the easy-to-understand spectral images play an important long-term role in guiding and motivating the patient. 24-hour HRV monitoring can be used in the same way to manage other cardiovascular diseases such as coronary heart disease.

The Fire of Life application measures HRV over a 24-hour period thus providing information on the autonomic overall balance, sleep quality, the linkage between respiration and heart rate and similar indicators to support management of the hypertensive patient. The application’s spectral images show the quality of the regulation processes while the frequency values offer quantitative data, the cardiologist explains. ‘I don’t need HRV to diagnose noise hypertension, but I do need it to understand whether and to which extent hypertension is accompanied by autonomic dysfunction.’

Individualised therapy

The results of the HRV analysis provide crucial information for an individualised therapy of the hypertensive patient. ‘If we promote sympathetic dominance, which even continues through the night and is accompanied by reduced vagal activity, we not only need drugs that block the sympathetic nerve but also immediate measures to increase vagal activity, such as regular physical exercise or deep relaxation techniques, for example based on HRV bio-feedback. At the same time, risk factors and psychosocial stress need to be reduced; he explains.

Long-term HRV measurements allow the physician to monitor the quantitative efficacy of therapeutic measures. If the sympathetic tone decreases and vagal tone increases, which indicates a better balance of the autonomic nervous system, therapeutic measures are effective.

In addition, the easy-to-understand spectral images play an important long-term role in guiding and motivating the patient. 24-hour HRV monitoring can be used in the same way to manage other cardiovascular diseases such as coronary heart disease.

The Fire of Life application measures HRV over a 24-hour period thus providing information on the autonomic overall balance, sleep quality, the linkage between respiration and heart rate and similar indicators to support management of the hypertensive patient. The application’s spectral images show the quality of the regulation processes while the frequency values offer quantitative data, the cardiologist explains. ‘I don’t need HRV to diagnose noise hypertension, but I do need it to understand whether and to which extent hypertension is accompanied by autonomic dysfunction.’

Individualised therapy

The results of the HRV analysis provide crucial information for an individualised therapy of the hypertensive patient. ‘If we promote sympathetic dominance, which even continues through the night and is accompanied by reduced vagal activity, we not only need drugs that block the sympathetic nerve but also immediate measures to increase vagal activity, such as regular physical exercise or deep relaxation techniques, for example based on HRV bio-feedback. At the same time, risk factors and psychosocial stress need to be reduced; he explains.

Long-term HRV measurements allow the physician to monitor the quantitative efficacy of therapeutic measures. If the sympathetic tone decreases and vagal tone increases, which indicates a better balance of the autonomic nervous system, therapeutic measures are effective.

In addition, the easy-to-understand spectral images play an important long-term role in guiding and motivating the patient. 24-hour HRV monitoring can be used in the same way to manage other cardiovascular diseases such as coronary heart disease.
The Lotus Valve System is a differentiated second-generation TAVI technology that consists of a pre-loaded, stent-mounted tissue valve prosthesis and catheter delivery system for guidance and percutaneous placement of the valve.

Glenfield Hospital. We are now into our eighth year of the TAVI programme and the first UK TAVI patient is still fine, seven years after implant, which itself is remarkable.

The Leicester programme is constantly evolving as Dr Kovac’s team endeavour to tailor treatment to individual patients with as many as possible having the least invasive procedures. “We are constantly looking for newer designs coming to mainstream,” he said. “The Lotus release was chosen with these in mind as initial data suggested very good sealing, non-disruption of cardiac output during implant and the option of repetitive repositioning.”

Jane Healy, vice president of Medical Affairs at Boston Scientific, added: “The Lotus Valve System offers a unique and effective new treatment alternative for patients with severe aortic stenosis at high risk with surgical valve replacement. This is the first commercial implant of the valve in the UK, following our CE mark approval in October 2013.”

The repair of a dysfunctional heart valve by using the Lotus Valve System to treat aortic stenosis sits among a line of surgical ‘firsts’ for the Glenfield unit, which treats local patients as well as those from much-further afield. Others have included the congenital interventional team performing the first closure of septal defects in 1996, the EP team pioneering robotic AF ablation, and Dr Kovac’s first TAVI in the UK in 2007, the first of several hundreds providing better functional effect and long-term outcome along with shorter hospital stays.
Bringing surgical quality to TAVR valves

**Report: John Brosky**

A cardiac surgeon, Wolfgang Goetz MD once stitched together custom aortic valves in the operating room. Today he is CEO of Transcatheter Technologies in Regensburg, Germany, a firm bringing to market a novel design for a next-generation aortic valve that he believes solves key issues challenging the current models for transcatheter aortic valve replacement (TAVR), specifically paravalvular leakage, improper positioning, durability of leaflets, and a high rate of pacemaker implantation.

In July 2014, ahead of print, the journal EuroIntervention published results from the first-human implantation of the TRINITY heart valve from Transcatheter Technologies, emphasizing the unique ability to both reposition, and where necessary, retrieve the device.

The lack of these capabilities in first- and second-generation TAVR devices leads to suboptimal positioning of valves in many cases, the abstract text notes, which ‘may result in paravalvular regurgitation, AV conduction delay, or compromise of coronary perfusion’. In the highlighted case, repositioning was required during the procedure and ‘repositioning of the Trinity resulted in optimal position without paravalvular leakage and with perfect function,’ according to the EuroIntervention abstract.

‘The reposition-ability for the Trinity valve that we provide is not perfect function,’ according to the out paravalvular leakage and with resulting in optimal position with-repositioning of the Trinity was required during the procedure the highlighted case, repositioning promise of coronary perfusion’. In the abstract text notes, which ‘may solution of valves in many cases, the abstract text notes, which ‘may result in paravalvular regurgitation, AV conduction delay, or compromise of coronary perfusion’. In the highlighted case, repositioning was required during the procedure and ‘repositioning of the Trinity resulted in optimal position without paravalvular leakage and with perfect function,’ according to the EuroIntervention abstract.

‘The reposition-ability for the Trinity valve that we provide is not perfect function,’ according to the out paravalvular leakage and with resulting in optimal position with-repositioning of the Trinity was required during the procedure the highlighted case, repositioning promise of coronary perfusion’. In the abstract text notes, which ‘may solution of valves in many cases, the abstract text notes, which ‘may result in paravalvular regurgitation, AV conduction delay, or compromise of coronary perfusion’. In the highlighted case, repositioning was required during the procedure and ‘repositioning of the Trinity resulted in optimal position without paravalvular leakage and with perfect function,’ according to the EuroIntervention abstract.

‘The reposition-ability for the Trinity valve that we provide is not perfect function,’ according to the out paravalvular leakage and with resulting in optimal position with-repositioning of the Trinity was required during the procedure the highlighted case, repositioning promise of coronary perfusion’. In the abstract text notes, which ‘may solution of valves in many cases, the abstract text notes, which ‘may result in paravalvular regurgitation, AV conduction delay, or compromise of coronary perfusion’. In the highlighted case, repositioning was required during the procedure and ‘repositioning of the Trinity resulted in optimal position without paravalvular leakage and with perfect function,’ according to the EuroIntervention abstract.

The Trinity valve is pre-mounted on a detachable tip. The expanded valve and leaflets are packaged in a liquid. Before implantation, the valve prosthesis is folded and the leaflets are stored in a ‘garage’ in which the leaflets are not crushed. Once the valve is in position, a sleeve slides back and then the valved stent is expanded. Now the valve can be released or folded again if repositioning is needed. The leaflets are only folded but not crushed, the sheath is protecting the prosthesis but does NOT fold the valve

If Goetz is proud of the success achieved in addressing these well-known challenges, he reserves his real passion for the little-discussed issue of durability of valve leaflets in current generation TAVR devices.

‘What about durability?’ he asks. ‘I am not talking about the durability you need to receive CE mark approval, which is 200 million cycles mechanical testing. You won’t get to the market unless you have this. Trinity has now reached 600 million cycles. The mechanical durability of our leaflets is incomparable.

‘Our objective is to demonstrate the same durability performance as a surgical valve. The big problem with TAVR devices is the crimping. No matter if you have a self-expanding or a balloon-expandable model, you have to crush the valve leaflets,’ Goetz explains. ‘As a cardiac surgeon my first question was to see what they are doing to these leaflets. The leading valve producers can show you how they produce surgical heart valves with very special technologies to ensure they never crush the valve leaflets, to prevent any damage to the integrity of the material. They avoid damage to the surface of the very fragile material they are using for leaflets.

‘As a surgeon you are told to be very gentle and be careful to never to touch the leaflet, because where you have touched or damaged the integrity of the material, it will start to deteriorate faster.

‘Now TAVR comes along and they are crushing these leaflets to squeeze them into the catheters and, for sure, they are damaging the leaflets. You break collagen fibers, and you cause disruption of leaflet surface, which was already shown in several studies. It is very well known that this can cause damage to the integrity of the leaflets. The proof will only come once TAVI is performed in patients with a longer life expectancy’ he said.

‘What we do is offer a valve that is pre-mounted on a detachable tip,’ he explained. ‘The expanded valve and leaflets are packaged in a liquid. Before implantation, the valve prosthesis is folded and the leaflets are stored in a ‘garage’ in which the leaflets are not crushed. Once the valve is in position, a sleeve slides back and then the valved stent is expanded. Now you can release the valve or you can stepwise fold the valve again if you need to repossession. We have quality control with a pre-mounted valve and we save time in the operating room because assembly is faster, that will

Remote monitoring of undiagnosed cardiac conditions

CardioSecure, a personalised mobile 12-lead ECG system with four electrodes for iPhone and iPad, allows patients to monitor their symptoms and transmit the data to their physicians in less than a minute. The system is reported to be ideal for patients with intermittent, difficult to diagnose cardiac symptoms and those who are still symptomatic post-intervention. This also could be use as a tool to monitor drug safety, the manufacturer points out.

‘The patient records a reference ECG reading while sitting calmly with no symptoms. When symptoms occur, the patient takes a control ECG reading for 10 seconds, which is compared to the reference reading. An instant assessment of rhythm, heart rate and perfusion status is performed, see image 2.

The ECG data is uploaded to a database accessible by the patient’s physician immediately, so that viewing the 12-lead ECG data is at the exact moment of the cardiac event (image 1).

In the REDUCE-Trial (Revealing Undesirable Cardiac Events-Trial) by ZNA Middelheim, Belgium, 51 patients were given the mobile 12-lead ECG system for a period of three months to record their experienced symptoms. Medical conditions included: recurrent palpitations of unknown origin (41.2%), atypical chest pain (33.3%), angina pectoris (15.7%) and tachycardias of unknown origin (11.8%).

1,237 ECG readings were recorded and CardioSecure diagnosed a new or undiagnosed condition in 10% of the patients. Four were diagnosed with arrhythmias: two with atrial fibrillation; one with monofocal ventricular premature beats with his- and trigemina; one with AV nodal re-entry tachycardia.

Depending on the discrepancies between these two readings, the patient receives an instant message based on a traffic light system: no change to baseline (white); make material they are using for leaflets.

No changes compared to original ECG

Performance

Surface (yellow) and contact a doctor immediately (red)

Using the system, the attending physician is able to access the patient’s uploaded 12-lead ECG data at the exact moment of the cardiac event and take action
To pulse or not to pulse

Whether mechanical, temporary cardiac assist systems should pulsate in the same way as a biological heart is a discussion topic, which raises the pulse rates amongst all those involved within the industry and in hospitals. The latest developments confirm this, reports Holger Zorn.

It happened in Orlando, Florida on 14 November 2011: Dr Timothy J. Gardner, Medical Director of Christiana Care’s Centres for Heart and Vascular Health and Past President of the American Heart Association, reignited the debate surrounding pulsing after around two decades of relative calm on this topic. Gardner talked about the development of a synchronised cardiac assist device.

This would be as small as an ECG and was to detect the patient’s ECG signal. Connected to the subclavian artery, it was going to generate a stroke volume of 30 cc – in the counter-pulsation known from the IABP. That was predicted to take the strain off the heart, improve coronary circulation and improve the supply of the peripheral organs.

One weak point was the limited frequency: The device only pulsates to 100 bpm; above that it would pulse continuously and the physiological advantage would be gone. However, Gardner encouraged everyone to trial the device and amongst ‘plenty of good reasons’ included the ‘current need for an activity-friendly IABP’. At the end of January 2012, again in Florida – but now in Fort Lauderdale – Dr Renzo Cecere, Director of the Mechanical Assist Programme at McGill University Health Centre in Montreal, Quebec, reported on his first two implantations of the new assist devices in humans. He was pleased with the recovery potential, which the new product from Abiomed called Symphony offered for 28 days up to the point of its scheduled explantation, and expressed hope that the comparatively simple intervention would soon make it possible to not only treat patients with congestive heart failure with a conventional IVAAD at the therapy-refractory terminal stage when they no longer respond to medication, but to slow down the progress of the disease at a relatively early point, thus significantly increasing quality of life.

The concept of a minimally invasive implantable pump for patients in chronic heart failure; coupled with the ability to remodel the heart, is unique and ground-breaking, and we are very pleased with the initial findings of Symphony,’ said Cecere.

From the USA to Germany

Although this study is not yet finished, contrary to the initial plans, another pulsatile cardiac assist device was recently trialled in Germany for the first time. On 25 June, his 56th birthday, Kurt-Josef M. was the first patient worldwide to have the Heartmate III by Thoratec implanted at Hanover Medical School.

One of the innovations of this type of device is an artificial pulse. To achieve this, the revolutions of the pump are slowed down and then sped up again every two seconds. However, this does not work under stress. ‘We can’t yet do this ECG-triggered,’ explains Dr Jan Schmitto, who implanted the device. It is also not yet quite clear what the optimum pulse frequency should be. Whether a pulse beat is even necessary is currently the subject of scientific discussion.

Schmitto cites physiological arguments. ‘In older patients in particular we may be able to reduce complications from gastrointestinal bleeding as the long term by generating a little pulsatility.’ Moreover, with a lacking pulse there is a danger that the media, the muscular layer of cells in the arteries, atrophies if it is no longer activated – which probably increases the risk of capillary ruptures in the gastrointestinal tract.

Around three months before (25 March 2014), Dr Ulrich Laufs, Professor for Clinical-Experimental Medicine at Saarland University in Homburg, had given a much-regarded lecture. Using the i-cor manufactured by Novaulag, the first pulsatile circulatory assist device for interventional cardiology (image) which actively pumps blood, he managed to measure coronary flow, which was around 500% higher than conventional, non-pulsatile perfusion in animal experiments (o/w) with a fibrillating pig heart. As the device also has an ECG trigger, this makes heart-rate-pulsated extracorporeal circulation with diastolic augmentation possible.

It also eliminates the main disadvantage of conventional extra-corporeal life support (ECLS): the bloodstream no longer continuously pumped against the weakened heart. This lowers the cardiac afterload and the need for oxygen. At the same time, coronary perfusion increases and therefore the amount of oxygen available. Last, but not least, the circulation in the end organs improves – as Timothy Gardner put it, ‘plenty of good reasons’ for the i-cor, which can even pulsate up to a heart frequency of 150 bpm.
**Streamlining non-invasive cardiology diagnostics**

**Partnership optimises uniform processes**

By recognition and early intervention against the most significant risk factors, many heart diseases can be prevented. At the 32 health centres of Charlottenburg, Fennpfuhl and Friedenau, in Berlin, state-of-the-art medical technology is used for a reliable cardiovascular diagnosis.

A partnership between Henry Schein Medical and the Polikum has restructured the non-invasive cardiology diagnostics area by establishing uniform processes so that doctors can take advantage of synergies and a fluid internal workflow.

The healthcare centres, CardiSoft from GE Healthcare is fully integrated into the workflow. Combined with Turbomed, this enables reliable data collection – the absolute key to determining the root causes of cardiovascular disease.

The CardiSoft system records the ECG, runs ergonomic tests, and measures long-term blood pressure and the long-term ECG. Spirometric data and even data from spirometry (cardiopulmonary exercise testing) diagnostic tools can be captured, providing high quality results for the physicians. Thanks to the ‘TurboMed’ billing programme, twice the size it should be.

In turn, the findings are centrally stored in a single computer system and can be viewed by doctors at the Polikum health centres, depending on activation of access regulations (ensuring patient data protection), even if the patient has been examined at another site or treated by another doctor.

Working with the mod-tech network, Dr Marc Oliver Grad, cardiologist and Head of Cardiology at Polikum Berlin, said: ‘The benefits of medical diagnosis systems and of incorporating electronically captured data in the patient file are used every day and represent a genuine advancement in quality and functionality.’

He added that, in addition to options in the follow-up survey, he uses one application in particular – a stored ECG and pre-ECG can easily be displayed one above the other, channel-by-channel, to reveal minor differences – for example, in the final stages analysis.

‘In just a few minutes findings can be made available to external medical colleagues for the entire period during which the patient was in the Polikum, without having to make bothersome requests for files from the archive. Particularly in cardiological emergencies, this lets us pass on valuable information without delay.’

Henry Schein’s nationwide network includes 350 technical staff so service and support is very quick, according to Jürgen Hahn, President of the European Medical Group Henry Schein. For medical staff he pointed out, the automated IT processes are easily learned, and give a clear structure for better work transparency through one procedure followed by all the medics and patient. Finally, he added: ‘This is a paperless system that is always up to date.’

His observations are backed up by Sabine Baerwolf, Chief Technology Officer and Manager at the Polikum, who said the need for a fully-integrated system, run with the highest reliability, has been met and added that the partnership with Henry Schein supports the health centres in ‘breaking new ground’.

---

**ECMO’s role in a world’s first cardiac procedure**

ECMO’s role in a world’s first cardiac procedure

The Polikum health centres in Berlin

Cardiologist Dr Marc Oliver Grad using Vscan, a handheld, pocket-sized ultrasound tool by GE Healthcare

---

**Report: Mark Nichols**

Cardiac specialists in the UK have performed a world’s first operation on a 14-year-old boy suffering a severe heart condition. The patient had a Tetralogy of Fallot - a congenital heart defect with four abnormalities inside the heart – and underwent the procedure at the East Midlands Congenital Heart Centre at Glenfield Hospital, Leicester, earlier this year.

The teenager has now made a complete recovery.

What set this procedure apart as a world first was the way the surgical team worked alongside the ECMO (Extracorporeal Membrane Oxygenation) system. That helped ensure that the complex keyhole stent and valve insertion procedure to cure the congenital heart defect was able to go ahead, because of the ECMO unit being on standby to minimise the risk of damaging the patient’s heart muscle and provide instant cardiac support if needed.

Consultant congenital cardiologist Dr Frances Bu’Lock, who led the diagnosis and was involved in the planning for the surgery, explained that the patient had a recurrent right ventricular outflow tract obstruction caused by a bar of muscle that contained a branch of the right coronary. It required urgent urgent treatment because narrowing had caused the right side of the heart to swell to twice the size it should be.

After three previous operations had not resulted in a satisfactory outcome, Dr Bu’Lock said surgeons were running out of options to tackle what had become a very severe obstruction.

Due to the associated risks, the Glenfield team consulted other European cardiologists – there was the possibility the patient may have an acute infant during the procedure and might become electrically and haemodynamically unstable, or could develop arrhythmias, which would make the procedure impossible to complete.

Their contact led to the decision to use ECMO with a team of more than 20 doctors, nurses and physiologists assembled to perform the procedure, and with the ECMO specialist on hand to support the patient’s circulation if he suffered a heart attack during the procedure, with a full life support circuit prepared and ready for use at a moment’s notice. ‘We did it as a combined procedure,’ Dr Bu’Lock explained. 

With the surgeons and the ECMO team in the lab suite, if the patient did go into ventricular fibrillation or cardiac arrest when we inflated the stent and compressed the coronary, we would go on to ECMO and complete the procedure.

Deliberately sacrificing the coronary as part of that procedure, with the involvement of the ECMO team, was the first time this type of procedure had been performed this way anywhere in the world. The cardiac and surgical teams at East Midlands Congenital Heart Centre specialise in performing very complicated and unusual procedures with ECMO support; both for people with malformed hearts and also for babies with major heart rhythm problems.

We are increasingly using ECMO to allow us to do procedures that otherwise we could not safely do – and that other units would not do,’ Dr Bu’Lock pointed out with a justifiable note of pride. ‘In this case, the patient made a complete recovery – he woke up and said my heart feels different – he’s gone back.
study in the US involving 144,757 patients in 1,091 hospitals, which suggested that almost half the stenting carried out was unnecessary. Another study, which found that 80% of patients undergoing a procedure for stable angina believed that angioplasty would prevent myocardial infarction, showed that, given various scenarios, 43% of cardiologists would go ahead with stenting even when they thought it would not be of benefit.

Dr Malthota suggests that making clear these facts should become a mandatory part of the consenting procedure process. ‘We need to address how we can reduce the potential over-use of stenting. One way I’d like to see that happen is to see it included on the consent form as a caveat to the risks and benefits we outline to patients. We need to be saying to patients that, while this may have symptomatic benefits, stenting will not reduce their risk of a heart attack or death and it does not prolong your life. It’s imperative to provide patients with all the information before subjecting them to a procedure that still carries a 1% risk of heart attack, stroke or death,’ he added.

He did point out that the procedure could help those suffering from angina, reducing the amount of chest pain, but said too often patients were given an impression it would achieve far more. ‘Of course elective stenting has an important role in the treatment of patients with limiting angina to improve the quality of life when medical therapy is inadequate but few patients are explicitly told that stent won’t prevent a heart attack or prolong life,’ he believes. Research has also indicated that up to half of stenting procedures carried out in the USA were either ‘inappropriate’ or of ‘uncertain appropriateness, he points out. ‘The elephant in the room is that randomised studies have not demonstrated outcomes benefit for stenting stable coronary artery disease in addition to optimal medical therapy despite its widespread use.’ His comments have received high-level support from Professor Huon Gray, NHS England’s heart disease ‘tsar’, and Professor Terence Stephenson, chairman of the Academy of Medical Royal Colleges, and have also triggered debate on their patients about this.’ Professor Stephenson: ‘This is an example of a legitimate debate of appropriate or inappropriate use of clinical procedures or interventions.’

Mobile C-arms in hybrid operating theatres

Valuable for transcatheter valve and aortic interventions and more

Hybrid operating theatres that combine conventional surgical tools with image-guided diagnostic tools, allow cardiologists and cardiac surgeons to perform minimally invasive surgery (MIS). In such surroundings, mobile C-arms offer a flexible, space and cost saving alternative to fixed installations in such surroundings.

In a study of mobile C-arm use, Dr Nikolaos Bonaros MD, at the University Hospital of Cardiac Surgery, Innsbruck Medical University, found that periprocedural new generation mobile C-arm imaging is very useful for transcatheter valve and aortic interventions as well as coronary artery graft evaluation and allows bail-out procedures without time delay (A Bridging Solution for Hybrid Operating Suites: Periprocedural New Generation C-arm Imaging During Cardiac Interventional Procedures, Journal of the American College of Cardiology, 2012).

High quality MIS imaging

Dr Bonaros uses the Ziehm Vision RFD for cardiac surgery and valve implantation. He experienced the first C-arm motorised in four axes storing up to three positions. This allows the operator to select/restore a position again at any time to access the desired viewing angles and anatomic visualisations without having to constantly reposition the system around the operating table. ‘Ziehm Vision RFD Hybrid Edition is the only mobile C-arm to offer an active liquid cooling system in the standard version,’ the system’s manufacturer reports. ‘Advanced Active Cooling ensures reliable imaging without interruption even during lengthy procedures. With its rotating anode and 25 kW power, the mobile C-arm is one of the most powerful C-arms in the market and delivers crystal-clear images even of moving objects such as a beating heart.’

Mobile X-ray imaging is used for various interventions such as heart valve implantation, vascular procedures for extremities (left image) or triple A procedures (right image)
Vector flow mapping via echocardiography

Rapidly advancing cardiac imaging capabilities aid precise planning and intervention guidance

There are aspects of the heart’s physiology that we know about, but now we can see them, and this is absolutely different,’ said Patrizio Lancellotti, President of the European Association of Cardiovascular Imaging (EACVI). ‘The working group is moving beyond a focus on transcatheter aortic valve replacement (TAVR) to cover a range of new procedures and new devices that have emerged since the recommendations were published in 2011.

This year, at the ESC congress in Barcelona, he will present his review of new imaging tools during the Spotlight Symposium on 1 September 2014, which aims to be devoted to ‘Innovation in Interventional Imaging.’

‘There are two innovations 1 will present that will have a high impact for interventional cardiologists, and specifically for TAVR,’ explained Lancellotti. ‘The first, a new 3D echocardiography system, will show how interventions can be better planned and that the imaging information can go further to help guide the selection of the prosthesis.

Then, once we move to the cath lab, I will show how interventions can be guided in real-time guidance with synchronised image fusion of fluoroscopy and 3D echo.’

The cardiology centre at the Ramón y Cajal University Hospital in Madrid, headed by the professor, is the European reference centre for both systems.

Developed by Siemens, cutting edge planning tool for TAVR procedures generates offline 3D images of a patient’s native valve with an automatic generation of morphological data that are very relevant for an interventional cardiologist, such as the area of the valve, the area of the annulus, or the distance to the coronary arteries, he pointed out.

The immediate application of this tool is a major advance to address the critical issue of valve implantation of the prosthesis. ‘Innovation in Interventional Imaging’ also inspires new possibilities, he confirmed.

Looking further in the future, with all of this actual anatomical information and quantification, why not take it to a next step where we will be able to truly simulate the implantation of a specific valve in order to see what actually will happen, to see the positioning and the different aspects of the intervention in advance.’

Such modelling would become a predictive model for patient compliances, identifying what is unique for each patient, and matching these conditions against a library of specific valve types and sizes. ‘This is where we hope to go with this technology and I have already spoken with the engineers who see no reason it can’t be done,’ the professor revealed.

‘We are focusing on his presentation of innovation in interventional imaging in the EchoNavigator development.’

‘The real-time fusion of 3D cardiac ultrasound with fluoroscopy is something that cardiologists have never seen before,’ he said.

EchoNavigator use during left atrial appendage closure: fluoroscopy and 3D live-echocardiography fusion.

-EchoNavigator, Philips Healthcare, The Netherlands has been introduced that allows synchronisation and fusion of echocardiography and fluoroscopy images in real-time, as an aid during structural heart disease interventions. In the image on the left we can see the 3D transoesophageal echocardiography image of the LAA closure device during introduction into the LAA. The image on the right shows fusion between the 3D echocardiography and fluoroscopy images with the same orientation, during LAA closure device implant. It allows visualisation in one same screen, fused and in real-time of both imaging techniques, as well as what will help during procedure guidance and device deployment. (Prof. Zamorano, Dr A Gonzalez-Gómez. University Hospital Ramón y Cajal, Madrid, Spain.)

The VFM consortium is currently developing by Vector Flow Mapping, or VFM. Developed by Hitachi-Aloka Medical, VFM is an innovative application of the well-established cardiovascular imaging technologies for colour Doppler velocity data and speckle tracking combined with novel software that generates velocity fields on a 2D image.

‘Simply put, this advanced technical prowess means a cardiologist can now assess cardiovascular blood flow distribution in real-time at a patient’s bedside using the non-invasive and familiar examination of echocardiography.’

‘Flow motion has been described in the past mainly using MRI; Lancellotti pointed out. ‘Cardiologists know that we can see beautiful images from MRI, that we can even see the heart in three dimensions, but the issue is the availability and the high technical requirements for MRI. It is very imaging tool that these images so, to this point, cardiac imaging for flow motion has been done primarily to research, not for routine clinical use.’

‘In contrast, he said, ‘echo is very simple, readily available and with the VFM software, once we are able to define patterns, cardiologists can easily use it.’

Here lies the challenge on the frontier of a new science. Understanding the new VFM images and the significance of dozens of parameters of heart performance the software is capable of generating is where Lancellotti said help is needed.

‘VFM allows us to associate a visual aspect to a condition we suspect, which is amazing,’ he said. ‘We now see so many new things regarding flow; but what’s behind flow direction, vectors, vortices, energy loss, or shear stress? This is very complex and we do not yet really understand the expanding vocabulary. We don’t know exactly which of these different measurements can be used to improve our decision-making and the clinical outcome for the patient.’

A core group of European and Japanese cardiologists have formed a VFM task force with the goal of creating a homogenous nomenclature that links specific measures to visual patterns in order to identify a specific disease state. Once we have a pattern for a disease we’d be able to define different degrees and extents of the disease process, which would allow us to stage the disease,’ he said. ‘Once we can stage a disease, we could follow the progression or regression changes in the heart. This will allow us to better follow-up the patient.’

The VFM consortium is currently discussing the design of a large-scale study that would begin with the assessment of normal heart pre-
In 99.9% of cardiac interventions, the interventionist is guided by conventional angiogram that requires interpretation of where the wire and prosthesis are located by watching a flat grey-scale image that never actually shows the interventionist the heart.

By placing on the same interventional monitor a synchronised image of the heart, the use of 3D echo guidance becomes more intuitive. With EchoNavigator we can now superimpose over the angiogram the anatomical structure at the same moment as the angiogram shows the wire for positioning the valve prosthesis. There is no longer any question of interpreting the image,' Prof. Zamorano confirmed, because we are seeing the anatomy exactly the way it is.'

Professor Jose Luis Zamorano Gomez is Head of Cardiology at the University Hospital Ramón y Cajal in Madrid. A Fellow of the European Society of Cardiology (ESC), he currently chairs the ESC Guidelines Committee and he is a past-President of the European Association of Echocardiography of the ESC. He is also on the editorial board of many leading journals, including the European Heart Journal and JACC Cardiovascular Imaging.

Patrizio Lancellotti MD PhD FECS FACC, is a Board Member of the European Association of Echocardiography, of the European Society of Cardiology and an active contributor to several professional journals, including as an editorial advisor for the European Heart Journal and the European Heart Journal – Cardiovascular Imaging. Cardiologists interested in participating in a large-scale study for Vector Flow Mapping are invited to contact a member of the consortium or Prof. Lancellotti at the University of Liège, Belgium, where he is a Professor of Cardiology.
Evidence is scant on the cooling of comatose patients who have suffered cardiac arrest, stroke or traumatic brain injuries; nevertheless, new methods for cooling patients are continuously being developed.

Therapeutic hypothermia is also being used in the cardiac catheter laboratory to prevent reperfusion injury during recanalisation of coronary vessels, EH correspondent Matthias Simon reports, although noting that its use has not been documented sufficiently for this purpose. Currently available availing methods are used either invasively (venous cooling catheters, cold infusions) or superficially (cooling pads, ice packs), or by utilising natural body orifices, such as the administration of perfluorocarbon into the nasal cavity.

There are many different views on the point at which cooling should be initiated: during re-animation, during transport to the hospital, or even only once the patient has arrived at a hospital. There are also different recommendations as to the correct target temperature. A study published in 2002 by the European Hypothermia After Cardiac Arrest Study Group showed an improved six-month survival rate (59% v. 45%) and improved neurological outcome (55% v. 59%) in 275 patients who had suffered out-of-hospital cardiac arrest (OHCA) and vertebral fibrillation when they were treated with therapeutic hypothermia (target temperature range between 32°C-34°C) compared to those given normothermic treatment [N Engl J Med 2002; 346:349-56].

However, Australian medics found a significantly improved neurological result (49% hypothermic v. 26% normothermic) in 77 patients after OHCA with vertebral fibrillation if they were treated with therapeutic hypothermia to 35°C. However, there was no significant advantage to the survival rate with 49% v. 52%. After adjustment for baseline differences in age and time from collapse to return of spontaneous circulation, the odds ratio for a good neurological outcome was 3.52 (95% CI: 0.9-12.4). This was also significantly better than those in the control group [N Engl J Med 2006; 354:1500-09].

In 2005 these results led to the development of a guideline recommending the treatment of patients with therapeutic hypothermia (32°C v. 34°C) over a period of 24 hours after OHCA with shock-able rhythm. However, the initial high hopes for the treatment were replaced by disillusion in 2013, when Nielsen et al published the results of the Targeted Temperature Management (TTM) Trial, a prospective randomised multi-centre study on post-cardiac arrest patients with shock-able rhythms. 950 patients in 36 European and Australian hospitals were randomly cooled to either 33°C (Hypothermia group) or 36°C (TMM group).

The respective temperature was maintained for 28 hours; if patients developed a temperature above 37°C, after rewarming, fever-reducing medication was administered for 72 hours. There was neither an improved neurological outcome nor a significant difference in survival [N Engl J Med 2013; 369:2197-2208].

New goal: Cath Lab

In 2007 Dr Derek Yellen of the Hatter Cardiovascular Institute in London, UK, wrote that the potentially fatal reperfusion injury, which can occur with any percutaneous coronary intervention, can be avoided through therapeutic hypothermia. ‘Therapeutic cool down before, during and shortly after the intervention [New Eng J Med 2007; 357:1121-13].’ Based on the results of the study involving 220 patients, with a subgroup who had suffered anterior myocardial infarction and had been treated with induced hypothermia below 35°C showing a lower mortality than those in the normothermic control group [Presented at Transcatheter Cardiovascular Therapies 2004, Washington, DC].

Dr Mathias Götber of the Skane University Hospital in Lund, Sweden, showed a significant reduction of the size of infarction in a pilot study of 18 patients when the target temperature was below 35°C (with an initial 4°C cold infusion with endovascular cooling catheter) [Circ Cardiovasc Interv. 2010; 3:400-7].

Dr David Erlinge, from Lund, recently published different results. 120 patients were examined in nine centres in Sweden, Denmark, Austria and Slovenia, with 61 patients in the hypothermia group and 59 in the control group. Therapeutic hypothermia did not result in a significant reduction in the infarction size, or in a subgroup-analysis either. The only benefit was seen in patients with anterior myocardial infarction who were re-perfused very early and showed a significant risk reduction [Am Coll Cardiol 2014; 63:1857-63].

Therapeutic cooling of patients in the cardiac shock is also being discussed: in animal experiments, Göttingen and Freiburg researchers showed an increase in cardiac contractive capacity in an increase in stroke volume under hypothermia [Basic Res Cardiol 2001; 96:198-205 and Circ 2004; 110:A1639].

However, the central questions remained unanswered: How quickly should the temperature be lowered? When should cooling commence? What is the right temperature to cool to? For how long should the target temperature be maintained? How should the degree of rewarming be carried out?

One needs to literally keep one's cool not to lose track here!
One year ago the enthusiasm for treating resistant hypertension with renal denervation was festive. ‘That party is over,’ laughed Mamo hy, president of Cardiologists, the Black Cardiology Centre in Malta. "The parade of trial results for the newly formed Resistant Hypertension program to continue to support our global HTN (hypertension) clinical program to develop our RDN in uncontrolled HTN."

"We are continuing our analyses of Symplicity-HTN 3 and are committed to better understanding the confounding factors observed in this trial. We believe there are many factors that may have contributed to the observed efficacy results in Symplicity-HTN 3, including key variables that have arisen such as population differences and medical and procedural variability in Symplicity-HTN 3 versus other Symplicity studies,” she stated.

St. Jude Medical is just as heavily invested in renal denervation as its rival Medtronic, and through the vice president for corporate relations, Rachel Ellington, said that it is also committed to this space.

"True innovation takes time and persistence to develop,” she said. "The good news is that industry, academia and demographics are keenly interested in talking about how to develop evidence that is supportive of the technology is not suitably paralleled and into the diseased native valve and into the diseased native valve squashing it to the metallic wall and taking over its function."

"Despite these advances, working in such a small island has its obvious limitations. ‘The Health Department does not have the financial resource to invest in the very latest cardiac imaging technology and even if it did, it would not be such a cost-effective exercise considering the size of the population and the small parallel diagnostic turnover,' Dr Schmieder explains. The particularly minuscule population size not only limits the financial resource but also puts a boundary on the level of expertise."

"Buying the latest in cardiac imaging technology is fruitless if there is no resource and expertise to complement it,' Dr Schemmbi asserts. "Unfortunately locally we have the knock of investing in ‘half-baked packages' where the investment in the technology is not suitably paralleled by the availability of trained personnel both to use the said technology and interpret the results, he regretfully adds. Obviously, this not only reduces drastically the potential of the imaging technique but also stretches the limit in an already stressed resource."

Dr Schemmbi believes that another hurdle stemming from Malta's size, and thus limited resources, is the paucity of research centres. 'Research drives people and spurs innovation,' he asserts. ‘Unfortunately, we do not invest enough in basic science research as much as we do in epidemiological research and this hinders greatly our academic growth.' He adds that their tight resource should not inhibit or limit us in any way but we should understand that collaborations with larger, more advanced European, or indeed transatlantic, centres would go a long way in supporting us to make the best out of the wealth of ever-growing medical and surgical specialities.

Dr Kevin Schemmbi, resident cardiologist at the Hospital Mater Dei in Malta

Malta needs to nurture collaborations

Imaging has progressed at vertiginous paces since X-rays were invented, not only as a diagnostic tool but as a valuable counter in the realm of interventional procedures. Sandipan Chatterjee, professor of Cardiology at the University of Erlangen in Germany, told European Hospital that renal denervation means two things. First we need to move forward with more robust study designs. It does not need to have sham-control, but it does need to be randomized with a real control group. ‘As for the technology, we have heard of new technologies for a while now, for example such as ultrasound, or 360-degree radiofrequency. What will become clear in the coming months is making the procedure less operator-dependent with reproducible effects. We are not there yet."

One year ago the enthusiasm for treating resistant hypertension with renal denervation was festive. ‘That party is over,’ laughed Mamo hy, president of Cardiologists, the Black Cardiology Centre in Malta. "The parade of trial results for the newly formed Resistant Hypertension program to continue to support our global HTN (hypertension) clinical program to develop our RDN in uncontrolled HTN."

"We are continuing our analyses of Symplicity-HTN 3 and are committed to better understanding the confounding factors observed in this trial. We believe there are many factors that may have contributed to the observed efficacy results in Symplicity-HTN 3, including key variables that have arisen such as population differences and medical and procedural variability in Symplicity-HTN 3 versus other Symplicity studies,” she stated.

St. Jude Medical is just as heavily invested in renal denervation as its rival Medtronic, and through the vice president for corporate relations, Rachel Ellington, said that it is also committed to this space.

"True innovation takes time and persistence to develop,” she said. "The good news is that industry, academia and demographics are keenly interested in talking about how to develop evidence that is supportive of the technology is not suitably paralleled and into the diseased native valve and into the diseased native valve squashing it to the metallic wall and taking over its function."

"Despite these advances, working in such a small island has its obvious limitations. ‘The Health Department does not have the financial resource to invest in the very latest cardiac imaging technology and even if it did, it would not be such a cost-effective exercise considering the size of the population and the small parallel diagnostic turnover,' Dr Schemmbi explains. The particularly minuscule population size not only limits the financial resource but also puts a boundary on the level of expertise."

"Buying the latest in cardiac imaging technology is fruitless if there is no resource and expertise to complement it,' Dr Schemmbi asserts. "Unfortunately locally we have the knock of investing in ‘half-baked packages' where the investment in the technology is not suitably paralleled by the availability of trained personnel both to use the said technology and interpret the results, he regretfully adds. Obviously, this not only reduces drastically the potential of the imaging technique but also stretches the limit in an already stressed resource."

Dr Schemmbi believes that another hurdle stemming from Malta's size, and thus limited resources, is the paucity of research centres. ‘Research drives people and spurs innovation,' he asserts. ‘Unfortunately, we do not invest enough in basic science research as much as we do in epidemiological research and this hinders greatly our academic growth.' He adds that their tight resource should not inhibit or limit us in any way but we should understand that collaborations with larger, more advanced European, or indeed transatlantic, centres would go a long way in supporting us to make the best out of the wealth of ever-growing medical and surgical specialities.

For Malta, being part of the European Community should go hand in hand as in suffering, with bigger European centres lest limitations and nurture collaboration. ‘As for the technology, we have heard of new technologies for a while now, for example such as ultrasound, or 360-degree radiofrequency. What will become clear in the coming months is making the procedure less operator-dependent with reproducible effects. We are not there yet."

"As for the technology, we have heard of new technologies for a while now, for example such as ultrasound, or 360-degree radiofrequency. What will become clear in the coming months is making the procedure less operator-dependent with reproducible effects. We are not there yet."

One year ago the enthusiasm for treating resistant hypertension with renal denervation was festive. ‘That party is over,’ laughed Mamo hy, president of Cardiologists, the Black Cardiology Centre in Malta. "The parade of trial results for the newly formed Resistant Hypertension program to continue to support our global HTN (hypertension) clinical program to develop our RDN in uncontrolled HTN."

"We are continuing our analyses of Symplicity-HTN 3 and are committed to better understanding the confounding factors observed in this trial. We believe there are many factors that may have contributed to the observed efficacy results in Symplicity-HTN 3, including key variables that have arisen such as population differences and medical and procedural variability in Symplicity-HTN 3 versus other Symplicity studies,” she stated.

St. Jude Medical is just as heavily invested in renal denervation as its rival Medtronic, and through the vice president for corporate relations, Rachel Ellington, said that it is also committed to this space.

"True innovation takes time and persistence to develop,” she said. "The good news is that industry, academia and demographics are keenly interested in talking about how to develop evidence that is supportive of the technology is not suitably paralleled and into the diseased native valve and into the diseased native valve squashing it to the metallic wall and taking over its function."

"Despite these advances, working in such a small island has its obvious limitations. ‘The Health Department does not have the financial resource to invest in the very latest cardiac imaging technology and even if it did, it would not be such a cost-effective exercise considering the size of the population and the small parallel diagnostic turnover,' Dr Schemmbi explains. The particularly minuscule population size not only limits the financial resource but also puts a boundary on the level of expertise."

"Buying the latest in cardiac imaging technology is fruitless if there is no resource and expertise to complement it,' Dr Schemmbi asserts. "Unfortunately locally we have the knock of investing in ‘half-baked packages' where the investment in the technology is not suitably paralleled by the availability of trained personnel both to use the said technology and interpret the results, he regretfully adds. Obviously, this not only reduces drastically the potential of the imaging technique but also stretches the limit in an already stressed resource."

Dr Schemmbi believes that another hurdle stemming from Malta's size, and thus limited resources, is the paucity of research centres. ‘Research drives people and spurs innovation,' he asserts. ‘Unfortunately, we do not invest enough in basic science research as much as we do in epidemiological research and this hinders greatly our academic growth.' He adds that their tight resource should not inhibit or limit us in any way but we should understand that collaborations with larger, more advanced European, or indeed transatlantic, centres would go a long way in supporting us to make the best out of the wealth of ever-growing medical and surgical specialities.

For Malta, being part of the European Community should go hand in hand as in suffering, with bigger European centres lest limitations and nurture collaboration. ‘As for the technology, we have heard of new technologies for a while now, for example such as ultrasound, or 360-degree radiofrequency. What will become clear in the coming months is making the procedure less operator-dependent with reproducible effects. We are not there yet."

"As for the technology, we have heard of new technologies for a while now, for example such as ultrasound, or 360-degree radiofrequency. What will become clear in the coming months is making the procedure less operator-dependent with reproducible effects. We are not there yet."
Research: Seeking radiological routes to cure cardiac diseases

Stereotactic radiotherapy for hypertension and radiosurgery for AF

This is a dose distribution of a patient with 11 MRT fields and 1mm margins added to the target. (The team reports: Margins of up to 5mm were added to cover a range of potential treatment uncertainties. The dose limitations of nearly all organs at risk could be met, except for the heart dose, which was exceeded in all plans. An increase of the mean and maximum heart dose with growing margins was observed. (The relatively high cardiac dose, will require further investigations in terms of late effects.)

A group of very high risk patients with refractory hypertension for whom medication has not worked.

A huge body of evidence has demonstrated that kidney-brain connection to nerve communications plays a major role in controlling hypertension. The kidneys are responsible for creating and sustaining high blood pressure. Previous studies have shown that if the renal nerves are ablated – through surgical removal or damage to them – it is possible to significantly reduce high blood pressure,” he said in a media teleconference. ‘These invasive procedures, radiotherapy treatment held is non-invasive,’ he observed.

The research team used high-resolution CT images of six hypertensive pigs to develop treatment plans for each renal artery and nerve. A single 40 Gy fraction dose of radiation was delivered bilaterally by stereotactic radiotherapy to the renal nerves using a state-of-the-art linear accelerator. The animals were observed for six months. Clinical and behavioural exams were performed, blood pressure was measured, and a urinalysis and serum laboratory was performed. Plasma noradrenaline levels (ng/ml) were obtained at 30-day intervals.

‘We are very pleased that the animals showed a 6% reduction in noradrenaline and none of the animals showed any evidence of renal dysfunction,’ Maxim pointed out. ‘Pathology showed evidence of moderate nerve damage, but there was no histological or immunohistochemical evidence of damage to nearby organs such as the kidneys and spinal cord. The renal artery also was not damaged.‘ Because of these very successful findings, we believe the treatment will be safe and effective for people.’

MRI-guided radiotherapy for cardiac radiosurgery

Australian and German researchers have demonstrated that it is possible to image the beating heart accurately enough to guide radiation therapy treatment to AF arrhythmias. In AF, electrical signals that control the heartbeat become disorganised, making the heartbeat irregularly. The team’s previous research found that targeted cardiac radiotherapy radiation can allow the heart to return to a stable rhythm.

Professor Paul Keall PhD, director of the radiation oncology laboratory at the University of Sydney, observed that at the University of Sydney, and colleagues, believed that an integrated MRI and linear accelerator could solve this difficult real-time targeting and adaptation problem. He reported on a study involving four individuals who underwent real-time cardiac MRI under free breathing. The target motion on coronal and axial cine planes was analysed using a template-matching algorithm. The team quantified the target motion range on cardiac MRI and analysed the dosimetric benefits of margin reduction, assuming that real-time MRI tracking was applied. ‘Accurate image guidance for high-dose AF radiosurgery is essential since safety margins covering untargeted target motion will result in unacceptable treatment plans,’ he said.

Real-time MRI guidance and beam targeting are the enabling technologies that will make AF radiosurgery feasible. Our approach combines these to see the beating heart and treat the AF, by hitting the AF while avoiding critical structures near the heart, such as the oesophagus, blood vessels, and the spinal cord.’ The advantage of being able to use this innovative new treatment will be enormous. The standard treatment, catheter ablation is a five hour, long surgical procedure, requiring anaesthesia and involving fluoroscopy.

United States the cost is approximately $50,000. Up to 6% of patients experience side effects. By contrast, the researcher’s proposed procedure would take less than one hour to perform and cost substantially less.
Long-term managed lab automation

Dutch lab sets high workflow standards through a service partnership

The University Medical Center in Utrecht (UMCU), The Netherlands, is in the process of creating a multidisciplinary centre of excellence, and workflow has increased exponentially with the central laboratory operating 24/7, with 200 full-time equivalent staff. On average, it processes around 16,000 tests a day, 3.4 million a year, of which 1.5 million alone are for chemistry and immunosassay. One of the significant challenges to turn-round time has been the distance between wards in the different hospitals. Sample collection meant that they were coming into the lab in peaks, causing unpredictable bottlenecks.

To enhance the fast service, a dedicated tube post service from Dutch Telecom was installed to improve the peaks of sample arrival. Instead of large batches arriving together, samples arrive every five minutes with a maximum of 20 tubes per carrier. Beckman Coulter’s automation solution had the flexibility to incorporate this third party supplier’s system without under-mining promised TAT and throughput.

Jan den Hartog, Laboratory Manager for the Department of Clinical Chemistry and Hematology at the University Medical Center Utrecht, is an expert in lean six sigma thinking and led the project management team responsible for the design of the Fast Service and the total automation of the core lab.

Co-ordinated workflow

UMCU created one of Europe’s most innovative lab automation configurations when it became The Netherlands first academic hospital to install a Beckman Coulter total automation solution. The laboratory has worked with the company since 2010 to consistently expand and enhance its service.

Laboratories from around Europe, including the NHS, have been visiting UMCU to see first-hand how Beckman Coulter operates as a long-term managed service partner. Like NHS labs, Utrecht required a partner that could help move the lab’s workflow towards delivering workflow improvements and innovative systems, within ever tighter budget controls.

The modern UMCU was formed in 1999, when the existing medical faculty merged with the Academic Hospital and the Wilhelmina Children’s Hospital. Of its 1,000 beds, a fifth are exclusively for children. Areas of expertise in Utrecht include oncology, transplantation, diseases of the central nervous system, immunity and infectious diseases, vascular diseases, heart surgery as well as trauma.

Pre-automation Lean analysis also showed that performance was being affected by having too many suppliers offering different, incompatible analysers. This also reduced staff efficiency and created unnecessary training issues. The decision was taken to create the ‘Fast Service’ – integrating workflow for chemistry and immunoassay as well as the pre-analytical phase for haematology, coagulation, blood gases and HbAlc testing.

Once the samples arrived in the lab, turn-round time (TAT) had to be consistently within one hour for both routine and stat samples. Samples coming into the lab from wherever location still had to meet the same TAT commitment. In addition, the solution had to be effective, without requiring extra staff or facilities for STAT samples. The labour-intensive pre-analytic phase, with its high error rate, also had to be resolved.

As lab manager Jan den Hartog explained: ‘There were some critical moments which required Beckman both the UMCU as well as Dutch Telecom to ensure this new ‘tube post’ integrated successfully.

Streamlined workflow

Utrecht chose Beckman Coulter’s Power Processor, with dynamic inlet and automated sample handling to streamline workflow and increase capacity. A track with integrated centrifuges reduces manual steps, making a guaranteed TAT much more of a reality. We now have the capacity to deliver our promised ‘Fast Service’, but more importantly the variation in TAT has dropped significantly,’ explained Mr den Hartog. ‘There is less need for manual dilution, fewer analyser flags and we need less sample volume to achieve accurate and reliable results. This is especially important for our extensive pediatric service.’

The 3,000-capacity refrigerated storage unit offers fast and automated sample retrieval. Pre-analytical sample sorting is carried out by the high-speed AutoMate 2500, able to handle 1,200 samples per hour. From a single point of entry, the system manages all tubes, from sample receipt to archiving.

With a second sorter, the AutoMate 1250, the lab has additional aliquot capability for any special tests done elsewhere in the UMCU.

‘Dedicated tube post’ service from Dutch Telecom was installed to improve the peaks of sample arrival. Instead of large batches arriving together, samples arrive every five minutes with a maximum of 20 tubes per carrier. Beckman Coulter’s automation solution had the flexibility to incorporate this third party supplier’s system without undermining promised TAT and throughput.

‘Fast Service’ delivers greater efficiency

Demands on the lab have become increasingly diverse and complex. To resolve this, the ‘Fast Service’ was created – integrating workflow for chemistry and immunoassay as well as the pre-analytical phase for haematology, coagulation, blood gases and HbA1c testing.

The new Beckman Coulter systems worked, they devised a ‘dedicated tube post’ within a special 13 by 75 mm container that enables microtubes to be handled, throughout the whole process, as if they were standard tubes.

The Utrecht Medical Center is now in the third phase of its long-term plan to create a multidisciplinary centre of excellence and, from the start, looked for a diagnostic partner that shared its values to improve patient outcomes.

As that long-term partner, Beckman Coulter’s aim is to continue moving the lab forward to achieve its objectives.

Jan den Hartog concluded: ‘This is a process of continuous improvement and, right from the start, the Beckman Coulter team were willing to adapt and be flexible, working with us to find the right long-term solutions.’

The NeXt generation of LED lamps

STARLED7 NX

www.european-hospital.com
The PointMan comes...

Founded in Germany 25 years ago, EKF Diagnostics’ PLC HQ is currently in Cardiff, Wales, where the firm is pursuing the development of a molecular assay for specific cancer types. Daniela Zimmermann met with the firm’s Product Manager for Molecular Biology Gary Dowthwaite to hear more about this important project.

‘PointMan is a molecular assay for mutations associated with specific cancer types: KRAS codons 12/13/61, which is associated with colorectal cancer; BRAF associated with melanoma, and EGFR mutations associated with lung cancer. That is the target market,’ explained Gary Dowthwaite of EKF Diagnostics, who went on to explain the complexities in the way the assay works.

‘There are two sets of primers and one, the wild type primer, incorporates a blocking entity. There are also two flanking primers. In a tumour biopsy there will be both wild type and mutations within that heterogeneous sample. When wild type DNA template is present, the wild type primers will anneal and extend on that wild type DNA. That reaction will also incorporate a blocking entity, which prevents daughter templates from acting as templates for further rounds of the amplification – so there is only linear amplification of wild type DNA.

‘In the variant, where a point mutation is present, leads to a three prime mismatch with the wild type primers. This mismatch allows variant or flanking primers, to anneal, extend and displace the wild type primers. ‘As there is no blocking entity, the reaction can proceed, yielding exponential amplification out of your variant. Therefore, what you are getting are lots and lots of the variant at the expense of a wild type. That makes the assay incredibly sensitive, and again that sensitivity is down to 0.001%. That is in orders of magnitude better than the current technology that’s out there.’

PointMan is a real-time PCR technology that EKF reports will provide reliable and extremely sensitive detection for cancer mutations.

When would this be used in a hospital? ‘At present this would be used as a diagnostic at the time of the initial diagnosis for the cancer. ‘That sensitivity is important; we hypothesise that you could use this as a blood assay to monitor patients who have cancer and are undergoing treatment. We have some proof of concept that you can use this assay to detect mutations in blood for cancer patients.’

‘The idea is, once a patient is on a particular medication regime, you can ask have they become sensitive to that? Has their mutation status changed to reflect that sensitivity or insensitivity to that particular medication?’

A big point: The medication is extremely expensive so it helps to know whether it works or not – quite soon.

‘Yes. For example, with the EGFR T790M in lung cancer, this mutation often isn’t present at diagnosis but it becomes apparent as the treatment progresses, so, the sooner you can spot the T790M, which is becoming exposed in the tumour, the sooner you can change course of the patient’s medication.

‘That is what we have been doing with Swansea University, at the Institute of Life Sciences. They took melanoma samples from the Wales Cancer Bank and they tested those samples for the BRAF gene. From the formalin fixed tissue sample they could confirm the BRAF status.

‘We also have blood from the same patient and can detect that same mutation in the blood. That’s a proof of concept, that you can use PointMan in a liquid biopsy; it has potential for a blood assay for cancers.

‘Swansea has also looked at endometrial cancer and, again, the same thing; they looked at the tissue biopsy and then the same patient’s blood, confirming the mutation status from the block to the block. To expand this clinical work with endometrial cancer it is really quite exciting about this.

‘When asked to see the device, he explained that there is no device. ‘It’s just tubes. Tubes with different coloured caps for different mutations encountered in different cancer types.’

‘This is a fluid. EKF supply the PointMan kits as consumables (primer sets, Taq, mastermix and controls), which can be run on industry standard qPCR instruments.’

* CE approval is expected this autumn or winter and EKF is discussing market entry with the FDA.

Peerin

In May, the World Health Organisation (WHO) warned that bacterial infections might lead to an increasing number of deaths because new resistance mechanisms threaten our ability to treat common infectious diseases. One factor accelerating the evolution of resistance is the incorrect or excessive use of antibiotics.

This June, the emergence of resistance, or rather its avoidance, was the focus of the 12th Congress on Infectious Diseases and Tropical Medicine (KIT). With around 1,000 participants, KIT is the largest event of its kind in the German-speaking countries, traditionally following an interdisciplinary approach, integrating areas such as microbiology, hygiene and internal medicine.

‘Resistant bacteria are an increasingly important issue not only in hospitals but also in out-patient facilities. Although we do make progress in terms of avoidance, the non-development of new anti-infection drugs, particularly antibiotics, is utterly incomprehensible in view of the rapid emergence of new resist-
Is chlorhexidine still the best decolonisation method?

Report: Brigitte Dinkloh

For many decades, decolonisation has been the selective, oral, or skin decontamination – it has been the accepted procedure to prevent infections caused by endogenous bacteria. At the 12th Congress on Infection Diseases and Tropical Medicine in Munich, Professor Petra Gastmeier, Director of the Institute for Hygiene and Environment and of the National Reference Centre for the Surveillance of Nosocomial Infections at Charité Berlin, presented new research on oral and skin decontamination with antibiotics.

The title of her talk indicates the surprising results of her study: 'Reduction of endogenous bacteria by an innovative approach to prevention?'

The problem is as old as artificial respiration. With intubated patients, bacteria possibly colonise the cuffs from where they migrate to the lower airways and cause pneumonia. 'Chlorhexidine is the best researched substance to prevent ventilator-associated pneumonia in intubated patients,' Professor Gastmeier explained at the symposium in Cologne.

In the study by Sonja Labbeau chlorhexidine received top marks: the scientist could show that the oral decontamination significantly reduces ventilator-associated pneumonia. However, Professor Winfried F Kern, a Boston-based Michael Klomps draws a more complex picture. He concluded that, as far as pneumonia risk is concerned, only cardiac surgery patients benefit from chlorhexidine. For other patient groups an increase in mortality has been recorded. 'With regard to oral decontamination the evidence of the benefits of chlorhexidine is not quite as obvious as with regard to selective intestinal decontamination.

One possible explanation of the higher mortality rate is the aspiration of chlorhexidine, which may cause changes to the lung. In view of the fact that, day by day, thousands of patients on ICU's receive oral care with chlorhexidine, further research is urgently needed,' the Charité professor emphasised, particularly since alternative substances, such as providone iodine have not yet proven to be particularly well suited.'

A further study published in the US shows chlorhexidine-impregnated washcloths in paediatrics to reduce sepsis by 36 percent.

Susan Huang conducted the largest and best evidence-pragmatic cluster-randomised trial. More than 70,000 patients in 45 ICUs were decolonised for five days with chlorhexidine-impregnated clothes and mupirocin. Endpoints were the MRSA clinical isolate and bloodstream infections. The group undergoing universal decolonisation with chlorhexidine and mupirocin without prior screening showed the best results. Even if universal decolonisation will not reduce bloodstream infections, the reduction of MRSA and VRE-isolation days is a major success, Gastmeier underlined. However, she pointed out, 'the question of long-term efficacy when all ICU patients are universally decolonised remains to be answered.'

Conclusion

All four recent studies confirmed significant effects of decontamination on the bloodstream infection rate and on the reduction of resistant pathogens. Even if chlorhexidine works better with gram-positive bacteria than with gram-negative ones, gram-negative ICU patients should undergo skin decolonisation.

Care staff usually accept chlorhexidine bathing since it does not create additional burden. The side effects of the antiseptic are negligible, the Robert Koch Institute, however, reports that in Germany MRSA resistance to mupirocin has increased by seven percent over the past two years and even the number of chlorhexidine resistant organisms has been growing.

In Germany, polihexanide and ocre ditine are available as alternatives, albeit neither of these two substances has been thoroughly tested in clinical studies.

So far no resistances were reported for the cheaper of the two antiseptics, ocre ditine, and it seems to work better with gram-negative bacteria than chlorhexidine. In short, while the evidence on chlorhexidine to prevent ventilator-associated pneumonia is questionable, the evidence on decolonisation to reduce bloodstream infections and the transmission of multi-resistant pathogens is convincing.

'Most likely it is more effective to treat all patients at risk rather than only those with s. aureus and VRE.' Alternative substances have to be severely tested in clinical studies,' Prof. Gastmeier concluded, 'for us to be able to slow down the development of resistances.'

Excessive use of antibiotics

According to the guideline, the key component to improve the quality of hospital antibiotic prescribing is the so-called Antibiotic Stewardship Team (AStS team), an interdiscipli nary group headed by an infectiologist. 'Most clinicians cannot fully assess infections because the diseases are becoming ever more complex. If specialists such as infectologists are not integrated into the therapy, the therapy is usually not optimal.'

The AStS team is strategically oriented and looks beyond the individual patients. 'For the prevention and treatment of infections, we need a database with the necessary facts and data from infection registries, which record infections caused by resistant pathogens, can be analysed to assess the prescription quality. Based on the results, hospital-specific antibiotic-prescription guidelines can be initiated.'

'In such a scenario, hospital phar macists, specialist physicians in microbiology as well as hospital hygiene experts cooperate closely with the “antibiotics officer” of each department.'

'Such an investment in specialists will more than pay off,' Kern believes. 'It will most likely reduce costs for pharmaceuticals in an amount that’s comparable to the medical costs, not to mention the immense benefits in terms of patient safety and Environmental protection during and after the emergence of resistances. This,' he emphasises, 'is the only way to ensure successful therapies in the future. If we don’t get a grip on the resistance issue, we jeopardising medical progress.'

Back to Newsroom
Smart molecular diagnostic tools are on target

Pathogens and antibiotic resistant genes are identified in 4-5 hours

Personalised medicine is often equated with the development of drugs tailor-made to the needs of individual patients or cancers. However, while this type of personalised medicine is still in its infancy, targeted treatment is already a reality in infectious diseases - thanks to sophisticated molecular diagnostic tools. If applied, this novel approach greatly improves clinical outcome and saves lives, as well as decrease the risk of antibiotic resistance development.

In hospitals the standard of care in serious infectious diseases is empiric antibiotic therapy. However, with growing drug resistance among pathogens, and mixed infections, this approach might fail. Studies show that inadequate antibiotic therapy significantly increases the mean duration of hospital stay and mortality rate. Obviously insufficient treatment also supports the spread and development of antibiotic resistances.

The main reason for the empiric treatment approach is a lack of fast, reliable diagnostics to identify the pathogens and antibiotic resistances that they carry. The current diagnostic standard approach is microbiology culture, a slow process that can delay targeted therapy by days. Other methods, such as PCR assays, often require experienced personnel and special laboratory equipment and usually they are not available around the clock.

To address this urgent unmet medical need, German medical technology and molecular diagnostics firm Curetis AG has developed Unyvero, a novel diagnostic platform that can process native clinical samples to identify pathogens and antibiotic resistance genes automatically within four to five hours. Thereby, the system supports an informed therapy decision as early as possible, Curetis points out.

“Our CE-marked Unyvero System is designed to detect a broad panel of bacteria, fungi and antibiotic resistance markers from a single native sample in one run,” said Dr Anne Thews, Medical Director of Curetis. “It enables the DNA-based testing of all clinically relevant samples - body fluids such as sputum, aspirates, sonication fluids, swabs and tissues in a fully automated analysis process.”

The entire procedure takes a few, quick manual steps, followed by a few buttons clicked on a touchscreen. Thus the analysis can be performed in a few minutes, without the need of skilled staff or special infrastructure. The system processes the samples in a sealed, disposable cartridge providing all necessary reagents to complete the analysis.

By combining endpoint-PCR with microarrays, we achieve a much higher degree of multiplexing than any competing approach,” Oliver Schacht, CEO of Curetis added. “As an example, the i60 cartridge detects 114 pathogens relevant for eight different clinical indications. In terms of pricing, our disposable cartridges are very competitive compared to real-time PCR products.”

Devices and cartridges are marketed in Eastern Russia, Middle East and various other non-European countries. In the United States, Curetis is now launching the multi-centre clinical trial aimed at achieving FDA clearance.

Out-sourcing hospital services

Cleaning and quality shading in UK acute hospitals

Dr Shimaa Elkomy received her MSc and undergraduate degree in Economics from the School of Economics and Political Sciences at Cairo University. She joined Dr Elad’s PhD in ‘The impact of internationalisation on economic growth of developing countries’ at Lancaster University, and is currently a research fellow in the Department of Healthcare and Policy at Surrey Business School in Guildford, United Kingdom.

The pros and cons of out-sourcing

The purpose of contracting out is mainly cost reduction, as supported by previous literature. There is widespread acceptance of increasing intensive activities that require less skill and that is auxiliary to the basic activity and specialisation as a whole, is suitable for out-sourcing. Since the 1980’s, privatisation and contracting out were conceived as the main tenets for structured reforms due to the benefits of specialisation and public institutions attempted to focus on providing core service to enhance the health-care delivery. Public services were fine-tuned and special laboratory equipment was increasingly provided public services based on the argument that this would increase efficiency through competition. Considerable literature finds greater cost efficiency under private provision of cleaning services in hospitals. At the University of Surrey, Research Fellow at the Department of Healthcare Management & Policy, Faculty of Business, Economics and Law, Dr Shimaa Elkomy and her colleagues carried out a study to assess the effect of out-sourcing cleaning services in the UK’s health-care sector. ‘Mainly, we were focusing on acute hospitals in 2011 and 2012 and the effects of out-sourcing cleaning services on microbiological and non-microbiological cleaning standards, as well as to examine whether the hospitals that are contracting out are cost-efficient and exhibit high-quality productivity compared to hospitals with in-house cleaning teams, Dr Elkomy points out.

The study was divided into a theoretical review of previous empirical papers and an empirical section. The study, involving 167 UK acute National Health Service (NHS) hospital trusts, had to eliminate 27 due to their mixed cleaning modes, so it worked with 140 acute hospitals. In 2011, 57% of acute NHS trusts were out-sourcing their cleaning services, while 60% depend on in-house teams. In 2012, the contracting out of services reached 40% while hospitals with in-house services decreased to 58%. Therefore, the majority of acute hospitals still have in-house cleaning services, although the number had slightly decreased from 60% in the observed period.

The importance of hospital cleanliness

In the UK alone, the number of deaths link MRSA and Clostridium difficile incidents – two of the most widely spread nosocomial infections affected by the level of cleanliness – increased by 43% between 2003-2006 for Clostridium difficile and 28% between 2006-2007 for MRSA, according to the Official National Statistics.

This legacy indicates the low quality of microbiological and non-microbiological cleaning, unskilled labour with less knowledge of optimum cleaning methods and the lack of the right equipment and materials. These factors are deemed to be the main reasons for the spread of hospital acquired infections.

The first CE-marked Unyvero Cartridge, Unyvero P50, focuses on pneumonia testing and simultaneously analyses 39 DNA targets. In winter 2014, a new and expanded version detecting additional anaerobes, such as metachloro-lactic-mase, will be launched. The second CE-marked application, the Unyvero i60 ITI cartridge for implant & tissue infections, is also commercially available in Europe. Cartridges for additional indications, such as gastrointestinal tract infections, sepsis and TB are in various stages of development.

“We consider ourselves pioneers of personalised medicine,” Schacht said. “However, we are not trying to identify sub-populations of patients for novel drug candidates.

“We are focusing on maintaining the efficacy of existing antibiotics by avoiding the administration of broad-spectrum antibiotics to pathogens already carry resistances.”
France reacts to antimicrobial resistance

Exploring the mechanisms to control nosocomial infections

France, like all European countries, is concerned about the increasing spread of multi-resistant bacteria but, as Professor Philippe Berthelot, infection control practitioner at the St Elism University Hospital, South-East France, says: ‘Although the over prescription of antibiotics in medicine has, without doubt, contributed to the problem we are facing today, there are misconceptions concerning involved. We include the widespread use of antibiotics in agriculture, poor hygiene and a lack of knowledge concerning infection and treatments given. They have all contributed to this rise and this complex picture needs careful consideration in order to control the emergence of resistance.’

France is a major consumer of antibiotics ranking 4th in the European hospital environment according to the latest data available, and 5th for community use. A recent press release from the French National Authority for Health (HAS) shows that, despite a programme initiated in 2011 to achieve a 25% reduction in antibiotic use by 2016, medical use is rising again in 2014, meaning France has an antibiotic consumption rate of 30% higher than the European average. However, its figures for antibiotic resistance ‘are good compared with those from most European countries’ Professor Berthelot points out.

So what measures have been put into place to combat the spread of drug-resistant bacteria in the hospital environment? All French hospitals have a medical community to deal with nosocomial infections and antibiotic use, respectively named Comité de Lutte contre les Infections Nosocomiales (CLIN) and Comité des Anti-infectieux. These now almost always include, as part of the team, an infection control practitioner. However, the background training profile of the infection control practitioner in France varies explains Professor Berthelot. ‘To become an infection control practitioner a doctor can come from a background in microbiology, infectious diseases, Public Health, pharmacy, or clinical care.’ This type of multiple training allows the infection control practitioner to work in more than one department, as Professor Berthelot does. He is part of the Hospital’s Infectious Disease Department and also part of the Microbiology Laboratory, which allows him a ‘transversal view of hospital infections’.

Hospitals develop protocols based on recommendations drawn up by one of the major national bodies in infection control, such as the French Society for Hospital Hygiene (SF2H), French Society of Infectious Diseases (SPILF), French Society of Microbiology (SFM) or those outlined by the HAS. However, individual hospitals are free to adapt the recommendations for best use in their particular establishment.

One way these recommendations have been proved effective in reducing infection is in the preventive use of antibiotics before surgery. Professor Berthelot explains that, ‘working in conjunction with the surgical team providing prophylactic antibiotics guided by the microbiology laboratory, and with reinforced hygiene measures, has seen a substantial decrease in nosocomial infections in surgical patients over the last few years.’

‘Additionally,’ he added, ‘measures that isolate patients who are already known, or recently identified as carriers of resistant organisms, although seemingly onerous and expensive have been shown to be highly effective in reducing the transmission of resistance.’

Some hospitals are also creating the role of ‘antibiotic therapy expert’, often a medical practitioner, who has a clear idea of the epidemiology of infections and the correct use of antibiotics.

In the absence of such experts in every hospital, there are guidelines for the prudent use of antibiotics that demand that the situation should be re-evaluated two to three days after the initial prescription, in order to confirm a response to the treatment and prevent the emergence of resistance.

‘A change in antibiotic is recommended if there is any sign of resistance to the first-line treatment, which should be as targeted as soon as possible. It is of course, Professor Berthelot emphasises, ‘extremely important that sufficient antibiotic is given for the correct length of time to achieve complete eradication of the infection.’ However, one thing we should remember he points out: ‘antibiotics have saved and continue to save millions of lives, with few new molecules on the horizon it is our duty to ensure they remain able to do so, we must use them wisely.’ (SMI)
IT’S MEDICA

Every November MEDICA is an outstanding event for experts from around the world. Some 4,600 exhibitors present a wide range of products at the World Forum for Medicine.

If you are looking for the latest professional know-how, new developments in medical technology or innovative applications, Düsseldorf is where you will find answers to your questions.

Take advantage of MEDICA and its special offers for your field of expertise, too.

Be part of the No. 1!