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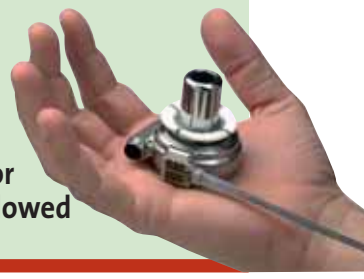

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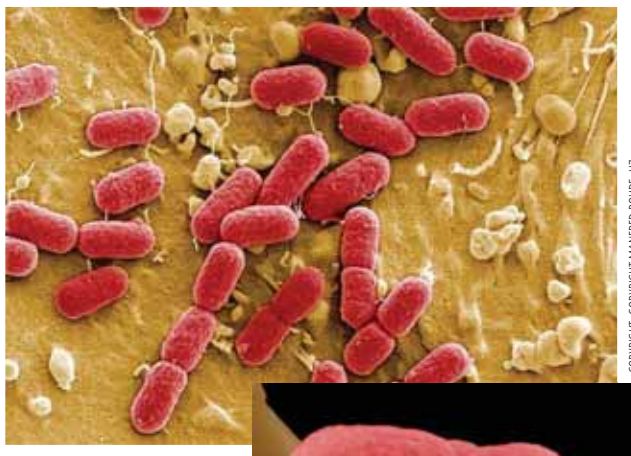
Well organised against EHEC

Endemics management in the hospital

In late May, a particularly aggressive and new strain of enterohaemorrhagic Escherichia coli (EHEC) posed an enormous challenge for northern German hospitals. In Hamburg, the focus of the epidemic, more than 1,000 people fell ill, about 180 of them seriously, after getting into contact with the bacterium. Many of the precise consequences of the pathologies were unknown. 150 patients who suffered complications were referred to the University Hospital Hamburg-Eppendorf (UKE). It was a challenge for both clinicians and management. Within hours several isolation units with highly specialized staff had to be set up, the number of dialysis systems had to be increased significantly and 400 units of plasma concentrate had to be available every day. Professor Jörg F. Debatin, Medical Director and CEO of UKE, told Meike Lerner (European Hospital) how the University Hospital Hamburg managed this gigantic task with the help of its well established interdisciplinary cooperation, fast and efficient structures and non-bureaucratic support from other institutions.



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Jörg F. Debatin

When faced with a sudden crisis such as the recent E. coli outbreak in Germany, Prof. Jörg F. Debatin explained that coordinated action and interdisciplinary cooperation are initially vital. 'We were lucky, so to speak, since these management approaches are well established at UKE, so we could respond immediately to the EHEC outbreak and set up a crisis management team,' he explained. 'This team consisted of about 20 people from different areas – obviously clinicians, mainly nephrologists and gastroenterologists, later on also neurologists, but also key staff from nursing care management, logistics and hygiene, microbiologists, the blood bank and medical technology. Moreover, the interdisciplinary intensive care team and the interdisciplinary emergency team played a crucial role in the process.'

Another important issue, he pointed out, is flexibility. 'Our new hospital, with its modular design, turned out to be a major advantage because it provided us with sufficient room to manoeuvre. But, above all, it was the flexibility of our staff that was really impressive – they were prepared to work across departments and even professional lines.

'Reorganising the tasks and schedules of 8,500 employees is quite a management task, but it can only be done successfully if everybody moves in the same direction and if everybody pulls his or her weight. It worked out great. As a matter of course the cardiologists, for example, helped out in the internal medicine department because the internists were more than busy with the acute care of the EHEC patients.

'Another advantage was the fact that all our ICU beds are centrally managed. This allowed us to set priorities quickly and to establish two HUS (haemolytic uremic syndrome) units with 12 beds each, without having to neglect the other 1,300 ICU patients.

'In addition, the electronic patient record proved invaluable. The fact that all patient data are available in digital format and accessible from anywhere in the hospital significantly facilitated both interdisciplinary cooperation and bed management. We always knew exactly the status of resources and patients, which helped us to identify and manage reserves. Even on the busiest wards, the situation was always under control. The electronic patient record was also an advantage in terms of real-time documentation.

'Administration of the antibody Eculizumab has to be documented tightly and exactly. During the peak of the crisis two nursing team members were relieved of their usual tasks and took care of all documentation requirements. It went smoothly – without the EPR I'm sure this would have been a major nightmare.

When did you realise that, despite those positive basic conditions, the hospital was reaching its limits?

'In the beginning we considered two factors to be crucial: paediatric dialysis and plasmapheresis for adult patients. While paediatric dialysis turned out to be fairly easy to handle, plasmapheresis was one of the biggest challenges throughout the crisis.

'Every day, 60 patients required a plasmapheresis, which meant that we had to immediately increase our capacities tenfold. We managed by recruiting UKE staff who were familiar with plasmapheresis no matter what their actual field of work was. We had cardio technicians, cardio surgeons, nurses from the anaesthesia department and people from the blood bank help out. We also received fast and non-bureaucratic support from external institutions, such as the Association for Home Dialysis, office-based physicians and other hospitals.

'In this critical initial phase, we transferred ten percent of the patients who suffered from less severe haemolytic uremic syndrome to hospitals in Hannover and Berlin. When we started to administer Eculizumab towards the end of the first week after the outbreak we were able to reduce the plasmapheresis procedures, which freed up some resources.

EHEC became a Germany-wide problem. How did coordination and communication work nationally?

'Kudos to the German medical community! Within twelve hours, the German Society for Nephrology managed to agree on a nationwide review protocol for Eculizumab. This means that the patients can be sure to be treated according to the same high standards, no matter which hospital they are in. Praise also for the cooperation of all hospitals and healthcare institutions. They all went out of their way to help – some even sent staff to support us, for example from the University Hospital Heidelberg, the Armed Forces Hospital and the Association for Home Dialysis. Not to forget the industry: companies responded immediately and made additional dialysis equipment available.

As a university hospital UKE is also involved in EHEC research. In this sudden crisis, what were its tasks and how did it coordinate that work with other university hospitals?

'From a scientific point of view it was important to design methods very quickly for the collection and reporting of data. We focused on issues surrounding data collection and archiving, and drafting questionnaires. This is crucial for the follow-up and is the domain of epidemiologists and statisticians in our Clinical Trial Centre.

'As far as coordination with other institutions is concerned the exchange of knowledge has top priority. All scientists at UKE who were involved in this crisis are eager to analyse the data quickly and comprehensively. We thus hope to be able to present initial scientific insights from UKE physicians on this endemic shortly.

Medical devices are not scrutinised enough

Investigators call for tighter regulatory controls

United Kingdom – A call has been made for tighter regulatory controls to ensure the safety regulation of medical devices, following joint investigations carried out by the British Medical Journal and the Channel 4 TV programme *Dispatches*, which were televised and published online at BMJ.com this May.

According to the investigators, thousands of people face painful and expensive surgery to remove failing medical devices such as metal hip replacements and cardiovascular implants.

They raise serious concerns about the regulation of medical devices and ask how well these high-risk devices are tested before they come onto the market.

The investigators explored a European approval process negotiated by private companies behind closed doors and revealed a worrying lack of public information about the number of devices being used and their potential risks.

They also discussed links between surgeons paid to design devices and the companies promoting them.

'The investigations findings are clear: The current system is not fit for purpose and we urgently need better regulation to protect patients,' the investigators state.

There are thousands of medical devices on the market and, worldwide, the industry is worth over £200 billion a year. Yet, the investigators report, the approval process is far less stringent than for drugs, particularly in Europe. 'What's more, it is the manufacturer's responsibility to monitor the performance of their devices once they are on the market. But rather than have large post-marketing studies, manufacturers may rely simply on doctors and patients to report problems. And,' they add, 'there is no publicly available central register of adverse effects to allow early detection of emerging problems."

The Dispatches programme revealed examples of failing devices that have remained on the market, despite companies being aware of problems. In the case of articular surface replacement (ASR) metal hip implants, the manufacturer, Depuy, waited until 2010 to take its hip fully off the market, despite repeated warnings from doctors as early as 2007, the investigators point out.

Other examples include the case of a patient who had a combined pacemaker/defibrillator fitted in his chest that misfired over thirty times in one day. The manufacturer recalled it after reports of five deaths and well over 600 reports of a broken component inside the device.

The programme also revealed another

continued on page 2

contents

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I can purchase from manufacturers directly ☐ Yes ☐ No

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relatively modern ☐ Yes ☐ No

state-of-the-art ☐ Yes ☐ No

Do you use/buy second-hand equipment? ☐ Yes ☐ No

If so, what do you use of this kind?

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Is your department involved with telemedicine in the community? ☐ Yes ☐ No

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Are you given ample opportunities to up-date knowledge? ☐ Yes ☐ No

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This information will be used only in an analysis for European Hospital,Theodor-Althoff-Str. 39, 45133 Essen, Germany, and for the mailing out of future issues and the EH electronic newsletter.

EH 3/11

LETTER TO THE EDITOR

Concerns: How Green Is Your Hospital?

With this article*, *European Hospital* has pinpointed an issue of growing concern for modern hospital management. Sustainability and ecological awareness are increasingly a key for economic efficiency as well as the positive public image of a hospital.

There is still a long way to go, and a lot could be done if European hospitals would adopt best-practice models for ecological sustainability.

An interesting example for potential improvements in sustainability and cost efficiency can be found in Austrian operating rooms. Whereas elsewhere in Europe the share of disposable textiles is approximately 80%, in Austria the situation is exactly the opposite: the share of disposable textiles is just 20%, whereas 80% of the textiles used by doctors and medical staff in the operating rooms are washed and re-used.

The positive effect on the environment is enormous because, first, this has absolutely no negative impact on hygiene due to the high standards in medical washing facilities and, second, the textiles are more comfortable to wear, as they are real rather than paper. This prevents thousands of tons of hospital rubbish that would otherwise have to be burnt and it noticeably reduces overall costs.

Surprisingly, most hospital managers have failed to even consider or assess the costs of this alternative, despite sufficient evidence that the hygienic standard of reusable textiles is at least equal to disposable OR-wear, costs are lower and a hospital's sustainability and ecological footprint are clearly improved.

I would be delighted to see this issue tackled in other countries, too, as it is a perfect example of the fact that financial efficiency and ecological improvement go hand in hand.

Thomas Brey

EH reader Thomas Brey works for Lustig + Brey in Vienna/ Austria, a PR & marketing agency that has represented the European Health Forum Gastein for past six years.

** European Hospital issue 2-2011*

Human error – or a fault in the system?

Medication safety from the anaesthetists' perspective

Medication errors sit among the top ten causes of harm to patients. They can, of course, occur in any department, but it's still a surprise that they happen as frequently in anaesthetics departments, considering anaesthetists' expertise is in handling tricky medication. However, apparently they are not the fault of the professional, but of the nature of the processes. 'Only one percent of human failures in a hospital emerge out of incompetence. 99% of the time, people are trying to do a good job,' explained **Professor Ravi P Mahajan**, Head of University Division of Anaesthesia and Intensive Care at Queen's Medical Centre, Nottingham, UK.


Ravi Mahajan

Speaking on the reasons behind medication mistakes and their prevention at the Euroanaesthesia Congress in Amsterdam in June, Prof. Mahajan said: 'In terms of progress, we first need to change our thinking about errors. We need to build up a safety culture in hospitals that is open, capable of learning and adjustable – and this would include everybody in the hospital team, from senior manager to clinician, to nurse. Secondly, we need to improve our managing systems, closing the loopholes which still allow for mistakes to propagate.'

In terms of human failure, he said in our EH interview that errors are less about doctors' medical knowledge and more about a lack of awareness among hospital staff in general. 'Only recently, I went to operating theatre and picked up an ampoule to find that the name of the drug was written in German. Probably, somebody went out to look for a cost-effective supplier without realising that inadequate labelling of drugs puts patients at risk. If I had been in a hurry in a life-threatening situation, I might have been tempted to make a guess and just deliver the drug to the patient. So, in this situation, I would be lost in a system that set me up to make a mistake. We have to think about how we can improve these systems so that humans are less likely to make errors.'

Failure spots lurk in various places – drugs storage, safety design, staffing in the operating theatre, etc. Many hopes are pinned on smart electronically solutions. Here, healthcare can learn a lot from other industries, where technologies are already in the line of duty when it comes to managing processes, Prof Mahajan continued: 'Every aubergine that you buy in a supermarket can be tracked down to the field it comes from. Why can't we do the same with our hospital drugs? Barcode systems are a good example how technology devices can be adapted.'

One of those tools was tested last year in a national study (*Staender SE, Mahajan RP; PMID:21330916*) by the Royal College of Anaesthetists and National Patient Safety Agency (NPSA). The system was firstly described in Auckland, New Zealand, and then adapted in seven UK hospitals (pilot sites for the study).

It works like a hotel electronic mini bar and includes many helpful features, such as storing potentially harmful drugs, such as adrenalin or potassium, separately from the routine drugs, and also an automated record system. So, every time an ampoule is taken from the fridge, a label is attached and scanned into the computer system, so that the individual medication is registered in the logistics centre. In addition, as a decision aid, the name of the drug, its prescription, possible interactions with other drugs, potential allergies and other important details are shown onscreen. Therefore, double-checking with a second physician is no longer necessary. This device showed considerable success in reducing error rates and workflow.

Such small reminders, Prof. Mahajan believes, provide accurate services in medication safety. 'They are like the seatbelt in a car that restrains us from making mistakes. Any hope that technology can give us in the prevention of medication error now and in the future, is a good thing.'

Medical devices are not scrutinised enough

continued from page 1

emerging problem with artificial hips, this time with large head metal on metal implants. Some surgeons are now raising concerns about these. Whilst one manufacturer has agreed to fund costs associated with the recall of its ASR hip, it is unclear who will pick up the bill for this new looming health crisis if all large diameter metal on metal hips require revision operations, the investigators point out.

When the BMJ/Dispatches team asked companies for data to support the safety and effectiveness of their devices, access was denied on the grounds that it was 'company confidential information'.

Even Freedom of Information requests made to the UK regulator, the MHRA, for data on adverse events for two different kinds of hip implants and one model of cochlear implant were refused as 'overriden by medical device legislation'.

The MHRA has concerns about the lack of transparency and variable standards in the current system, but they said, 'if we were to inhibit innovation by imposing a more burdensome regulatory regime we would have to have some extra evidence that the burden actually provided a greater degree of patient safety'.

'This story shows the power that companies have in deciding the fate of their devices, their hold over surgeons, the lack of regulatory power in Europe, and the lack of premarket clinical studies that may well have picked up some of these problems earlier,' said Dr Deborah Cohen, Investigations Editor at the BMJ. 'We have still not learned from past failures,' she added.

'Nearly 20 years ago, the BMJ highlighted the dangers of early failure of unproved implants, yet the NHS is currently picking up the bill for faulty devices,' Dr Cohen pointed out. 'Unlike kettles and toasters, which come with warranties, when devices do not last as long as they ought to companies are not necessarily held financially responsible.'

Dr Carl Heneghan, a GP and Clinical Reader at the University of Oxford added: 'Patients should have access to the evidence about the nature of their devices, the true benefits, the true harms. At the moment that's not happening and patients are acting as guinea pigs and that's not good enough.'

Professor Nick Freemantle at the University of Birmingham agreed 'Rather than devices being subject to an inferior regulatory model, we should extend and strengthen the approach taken for pharmaceuticals,' he said.

**Investigation contributors included Dr Carl Heneghan, Director of the Centre for Evidence-Based Medicine & Clinical Reader, University of Oxford; Nick Freemantle, Professor of Clinical Epidemiology and Biostatistics, University College London; Tony Nargol, Orthopaedic Surgeon, University Hospital of North Tees, Hartlepool; Alan Fraser, Reader in Cardiology, Wales Heart Research Institute, Cardiff University; David Langton, Surgical Registrar and Researcher, University Hospital of North Tees and Newcastle University; Peter Wilmshurst, Consultant Cardiologist, Royal Shrewsbury Hospital.*

Coronary heart disease

Germany is not following EU treatment guidelines, *Anja Behringer* reports

Bypass surgery figures declined again in 2010. Reason: Most coronary heart disease (CHD) patients are being treated by removal of the obstruction followed by stent implantation – a situation criticised by **Professor Jochen Cremer**, first Vice President of the DGTHG (German Society for Thoracic and Cardiovascular Surgery): 'The results of scientific studies confirm that this cannot be the right treatment for all patients. Particularly in cases of three vessel disease, the likelihood of dying within three years of being fitted with a stent is almost twice as high as after bypass surgery.' For this reason, the European associations of cardiologists and cardiac surgeons have developed very precise guidelines for the treatment of coronary disease. These provide clear directions on which cases should receive stent implantation and which should have bypass surgery.


Jochen Cremer

The guidelines also include the setting up of 'heart teams' comprised of cardiologists and heart surgeons, to ensure that each patient is given the best possible treatment based on a joint decision. A current survey carried out by the DGTHG of German cardiac surgery departments reveals that 80% of hospitals with cardiac surgery and cardiology departments hold so-called heart catheter conferences. However, in over 70% of hospitals both specialists do not jointly plan the best type of therapy for all patients but only for those who were scheduled for coronary bypass surgery. The cardiac teams envisaged by the European guidelines currently only exist in fewer than 14% of hospitals – and only 9% of hospitals now actually abide by the new European guidelines.

German heart surgeons carried out 122,000 procedures in 2010. Although this overall figure corresponds to the number of interventions carried out in the previous years, the average age of patients operated on increased significantly in 2010. More than half of all cardiac surgery patients last year were 70 years old and over; in 1994 only a quarter of all patients were in that age range.

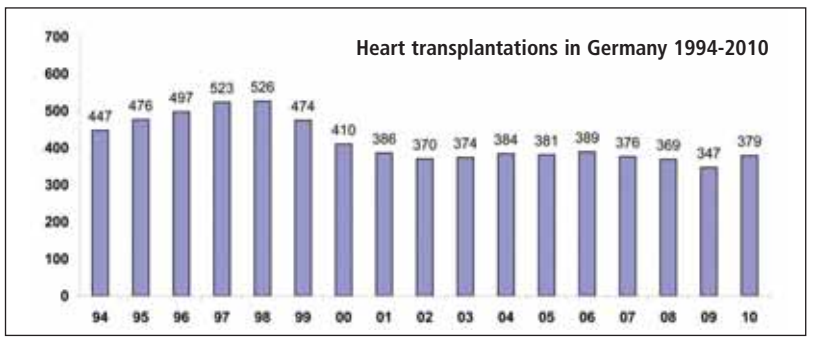
The number of cardiac valve surgery interventions increased significantly in 2010 to 25,000. Of these, 11,689 were conventional operations to replace aortic valves and there were 3,600 transcatheter aortic valve implants. Thus, fewer than 25% of aortic valve interventions were carried out with the transcatheter method. 'The clear advantage of this procedure is that it is a lot less stressful for the patient than surgery. However, not for no reason do the specialist heart surgeon and cardiologist associations only recommend this procedure for patients over the age of 75 who are also suffering from severe concomitant diseases,' said **Professor Friedrich Wilhelm Mohr**, president of the DGTHG.

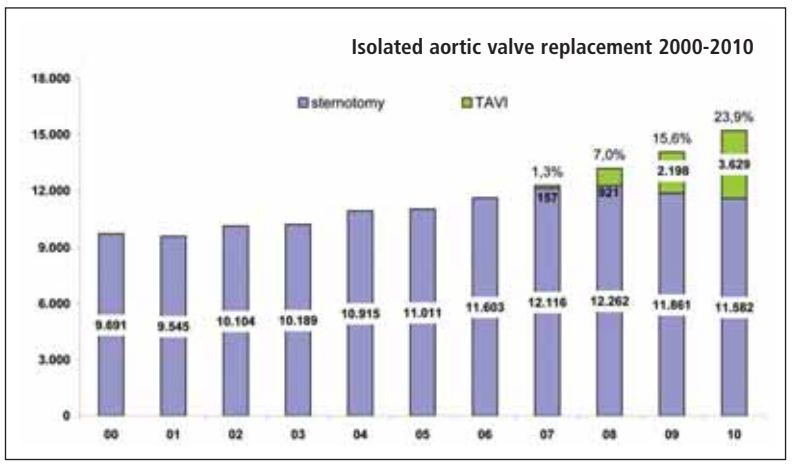
'The mortality rate for conventional aortic valve surgery, depending on age and the patient's general state of health, is between one and three percent. In the case of transcatheter implants, mortality rates of up to 7% have also been observed in younger, healthier patients,' he pointed out. Therefore, he insistently appealed to all cardiologists and cardiac surgeons only to carry out transcatheter aortic valve implants jointly, and after thorough consideration of the treatment options. Prof. Mohr also mentioned the German Aortic Valve Register, a national log of all aortic valve interventions, inclusive of follow-up observation of patients over five years. The log was set up jointly by cardiologists and cardiac surgeons to enable them to make scientifically based, valid statements on the benefit of the procedures.

With a total of 5,341, last year also saw an increase in mitral valve interventions compared to the previous year. 'In just under two thirds of interventions it is now possible to reconstruct a defective mitral valve. The likelihood of surviving this intervention is 98%,' the professor said. However, if the mitral valve is beyond repair, a prosthetic heart valve must be fitted. This intervention particularly affects older patients weakened by concomitant disease, which is why the procedure shows a higher mortality rate.

Slight heart transplants increase

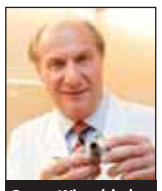
In Germany, the number of heart transplants (HT) in 2010 increased slightly, to 379, whilst 2009 saw the lowest number so far since German reunification: 347 transplants. 'However,' Prof. Mohr pointed out, 'this number is still unsatisfactory considering that the number of cardiac support systems increased from 479 in 2009 to 652 in 2010. As these cardiac support systems are not permanent, but interim solutions, the figures confirm that the need for donor hearts has increased further still.'





Celebrating a 25-year-old 'heart'

Ventricular assist devices are in a continuous evolution


Georg Wieselthaler

Initially meant to bridge the gap before a heart transplant is performed, today ventricular assist devices (VADs) are increasingly considered 'a lasting therapy option', according to Professor Heinrich Schima, Head of the Centre for Medical Physics and Biomedical Technology at the Medical University of Vienna.

Donor organs are scarce and the number of transplants is decreasing, despite the increasing number of patients with heart insufficiency. Additionally, patients are often so content with ventricular assist devices that they want to keep them.

'We now have patients who actually refuse transplant surgery,' said Professor Georg Wieselthaler of the Clinical Department for Heart Surgery at the Medical University of Vienna and Medical Director of the Vienna Artificial Heart Programme.

Vienna has a long tradition in cardiac surgery and ventricular assist devices and the Medical University is currently commemorating the 25th anniversary of its pioneering 'New Vienna Heart' procedure, first used in 1986. This artificial organ, a pulsating membrane and valves modelled on the heart, was implanted as a total cardiac replacement.


Researchers at the Medical University of Vienna are cooperating with medical technology companies to develop significantly smaller devices, as well as cannulae for cardiac blood collection without causing blood clot

In the meantime, the procedure has evolved: the diseased heart is left in the body as a 'safety backup' (Schima) while a support pump (in most cases) is inserted into the left ventricle to undertake that cardiac function. Rotary pumps with up to 30,000 rotations per minute are used, as well as centrifugal pumps that move the blood by centrifugal force, and axial pumps with a similar design to that of turbines.

'Due to liability considerations, we were no longer permitted to use devices designed in-house after the use of the first New Vienna Heart,' Prof. Wieselthaler pointed out. However, the Medical University of Vienna has remained an important partner in ventricular assist devices development.

The world's first patient to be fitted with a continuous-flow rotary blood pump was discharged from hospital in 1999. In 2006, the first rotary blood pump with hydromagnetic contact-free bearings was implanted in Vienna, and, since then, 300 have been implanted there – currently 35 patients are using the system. The two-year survival rate is 85%, which compares favourably with the best international results. 'Vienna,' said Prof. Wieselthaler proudly, 'is one of the three leading heart support centres worldwide.'

Currently the Vienna researchers are developing new components, evaluating new systems and optimising existing ventricular assist devices. A new cannula is currently also being developed for a new generation pump. This will collect blood from the heart without causing blood clots.


In 2006, the world's first rotary blood pump with hydromagnetic contact-free bearings was implanted in Vienna


PHOTOGRAPHS: © MEDUNI WIEN


The first New Vienna Heart was implanted as a total heart replacement

A study is investigating the systems' user friendliness and ease of use to ensure intuitive operation. Other developments include the examination of control algorithms for an adaption of the pump output to the respective physiological requirements, as well as the development of diagnostic parameters for the continuous recording of the remaining heart function.

Miniaturisation is the main theme for the next generation of VADs. 'These systems are likely to be just thumb-size and implantation will be carried out via a cut of only 10 cm between the ribs,' Prof. Schima predicted and, Prof. Wieselthaler added, these should be ready for clinical use within two to three years.

Cardiac research in Vienna meanwhile goes far beyond ventricular assist devices. Both professors and their team are part of the Ludwig-Boltzmann Cluster for Cardiovascular Research, which is comprised of four institutions. Current research projects deal with the connection between fatty tissue and cardiovascular disease, protection of the heart during cardiac surgery, the use of stem cells to treat cardiovascular disease and the development of new, small-calibre vascular prostheses.

Report: Michael Krassnitzer

Sharper scrutiny on valve repair

More compelling evidence for TAVI is required, even as cardiologists advance to the next generation of devices. *John Brosky* reports from Paris

One year ago interventional cardiologists raised champagne glasses to celebrate the first publication of clinical evidence showing that transcatheter valve implants (TAVI) is safe and effective.

In May at EuroPCR 2011, cardiologists raised magnifying glasses to look closer at further clinical results.

The clinical consensus remains unshaken. Data across diverse patient registries presented at Europe's largest congress for interventional cardiologists consistently shows that TAVI is an effective alternative for patients suffering degenerative aortic stenosis who are considered a high risk for conventional open surgery for valve replacement.

A deeper dive into the data opened debate and discussion touching concerns for lowering the incidence of stroke among TAVI patients, defining better criteria for patient selection and developing new devices to fix shortcomings in the first-generation of valves.

'We know the procedure is feasible, predictable and quite safe,' said **Jean Fajadet MD**, from the Clinique Pasteur (Toulouse, France), who is the newly elected president of the European Association for Percutaneous Intervention that organises EuroPCR. 'Where there are problems is when the patient selection is wrong and the issue is screening,' he said during a plenary session. 'Do we need to perform TAVI on patients with a high rate of comorbidity when we know that the survival will be low?'

Behind the clinical code words the message is one that was repeated throughout EuroPCR, which is a need to expand TAVI beyond its original indication as a last hope for frail and inoperable patients.

As TAVI enters a new stage in its development the commercial pressure for moving to a larger population of patients and the demand by the patients themselves, who want to avoid the risks of open surgery, are compelling.

Until now, TAVI has been uniquely European. The technique was invented here, the technology perfected at European centres, and the procedure won the first regulatory approvals and reimbursement in Europe.

Since TAVI was approved for European use at the end of 2007, over 40,000 valves have been implanted using this minimally invasive technique, the majority of those cases in France, Germany and Italy. More than half of those procedures were performed in the past 18 months, a rapid uptake that may be running faster than clinical evidence can be collected to support the widening use of what remains a controversial intervention.

Attention is shifting this year to the USA, where the manufacturers of the two systems approved for use in Europe, Edwards LifeSciences and CoreValve/Medtronic, are seeking Food & Drug Administration (FDA) approval.

This new level of regulatory scrutiny combined with the growing experience at European heart centres is ratcheting up the pressure for manufacturers to produce more compelling and conclusive clinical evidence.

At EuroPCR 2011, the data presented by both companies covered results for 4,456 patients with most of the procedures dating back before 2009, before utilisation doubled.

Medtronic consolidated data previously presented from seven European registries in order to create a single meta-analysis of 2,156 patients.

The patient selection criteria across the different studies are highly variable with self-reported clinical outcomes, a lack of standardised definitions and under-reported events. 'The data cannot give a clear answer to the scope of the issues raised, but this meta analysis is absolutely fundamental for furthering the science and is important for planning future studies,' declared **Carlos Ruiz MD**, from Lenox Hill Hospital (New York) who presented the results at EuroPCR 2011. 'I would not make any black-and-white conclusions from this data, but it is very informative and in a way it is beautiful for showing what is really going on,' he said, adding: 'This is absolutely fundamental for furthering the science.'


Jean Fajadet


Carlos Ruiz

One-month survival rates were consistent across five CoreValve registries at 93.8%, while all-cause mortality at one year using the transfemoral route was 17.1%. The average age of patients was 81.6 years.

This finding is consistent with the data from the monitored results of the Edwards SOURCE registry that also covers European centres and was updated at EuroPCR 2011 with an additional 1,269 patients bringing the total registry enrolment to 2,300.

Survival for Edward's Sapien valve patients who underwent a transfemoral procedure was 93.7%, while all-cause mortality at one year was 19.9%, reported **Olaf Wendler MD**, from King's College Hospital (London). The average age of Sapien valve patients was 81 years.

One result of the wide variation in the reporting from the European TAVI experience is a consensus document from the Valve Academic Research Consortium (VARC) that sets terminology for adverse events and recommendations for clinical endpoints for future studies.

Diabesity surgery

Advanced techniques, promising results: Bariatric surgery is established, metabolic surgery is on the horizon – and interventional procedures are also an option.

Holger Zorn reports

Overweight and obesity are defined by the World Health Organisation as abnormal or excessive fat accumulation that may impair health.

BMI [kg/m²]	Classification
<18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
≥40.0	class III obesity

For a better definition of higher grades, surgeons often use two different scales whose exact values are still under discussion:

Obesity	BMI	BMI
severe	≥35	≥40
morbid	≥40	≥45
super	≥45	≥50

According to the 2007 published Interdisciplinary European Guidelines on Surgery of Severe Obesity, bariatric surgery may be indicated for patients within 18-60 years and with BMI ≥40 or with BMI 35-40 with co-morbidity in which surgically induced weight loss is expected to improve the disorder. To be considered for surgery, patients must have failed to lose weight or to maintain long-term weight loss, despite appropriate non-surgical medical care. Further, patients must have shown their compliance with medical appointments.

Metabolic surgery is bariatric surgery in patients with lower grades of obesity or normal weight to treat type II diabetes mellitus.

Morbid obesity is a chronic, lifelong, multifactorial, constitutional disease with negative medical, psychological, physical, social and economic side-effects. Obesity-related secondary diseases are Type 2 diabetes mellitus (T2DM), cardiovascular diseases such as hypertension or sleep apnoea.

With more than 300 million cases estimated worldwide, the World Health Organisation regards obesity as an epidemic in developed and developing countries. Extreme forms are barely controlled by diet, behaviour therapy or medication. No matter which conservative therapy is chosen, there is a recurrence rate of up to 90%.

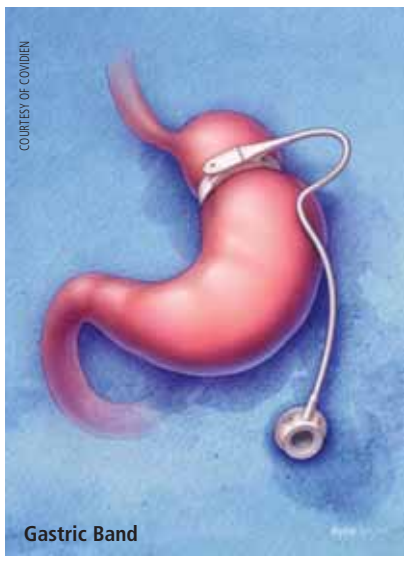
In 1991, the American National Institute of Health stated: 'Gastric restrictive or bypass procedures could be considered for well-informed and motivated patients with acceptable operative risks' [*NIH Consens Statement 1991 Mar 25-27;9(1):1-20*]. Naturally, such a statement attracted the attention of the industry: With over 11 million morbidly obese and over 90,000 weight loss surgeries performed annually in Europe, the market potential is very high.

Meanwhile many clinics began surgical programmes – and there is evidence to do that: The 2007 published Swedish Obese Subjects (SOS) study, a prospective, controlled cohort study with 4,047 patients in 25 surgical departments and 480 primary healthcare centres, includes 2,010 patients who underwent a bariatric surgical procedure and 2,037 patients who were treated conventionally. While the average weight change in the control group was only ± 2%, the patients in the three surgical subgroups – gastric bypass, vertical banded gastroplasty (VBG) and gastric band – had an average weight loss of 32%, 25% and 10% after two years and of 25%, 16% and 14% after 10 years [*N. Engl J Med 357:741-52*].

It should be noted that the VBG or Mason procedure, developed in 1980, is now obsolete while the newer sleeve gastrectomy was not included in that study. Current surgical interventions are, in order of invasiveness, Gastric Balloon, Gastric Band, Gastric Bypass, Biliopancreatic Diversion and Sleeve Gastrectomy.

This is made of soft silicone, deflated inserted into the stomach via the mouth and filled with liquid, thus lowering the stomach volume, reducing the amount of food the stomach can hold and causing the patient to feel fuller faster. As the balloon can be left in place for up to six months, this is a temporary procedure and often used as a first step for conditioning the patient for further interventions, e.g. aiming to reduce 10% of weight within six month.

This is useful not only in the bariatric surgery but also for weight loss before a knee or hip replacement. Once removed, the stomach returns to normal. The balloon is also suitable for those patients who won't tolerate an invasive procedure or who are inoperable because of cardiac insufficiency or chronic obstructive pulmonary disease.



Gastric Band

The band is placed laparascopically around the upper section of the stomach. This limits food intake and stimulates the sense of feeling full, resulting in a marked weight loss for the patient.

Johannes Heimbucher, chief surgeon at Maria Hospital Kassel: 'The gastric band is associated with the lowest short-term risks as well as the fewest side effects long-term.'

The operation gives an expected weight loss of 40% to 50% loss of surplus weight and an improvement in obesity-related secondary disease. Further, it is a reversible technique: if the patient wants, the band may explanted during a minor keyhole surgical intervention. This makes the procedure suitable for a stage concept: if necessary, a more invasive operation can be performed later.

Adjustable bands require that the patient regularly visits an outpatient clinic. If the patient fails to attend the outpatient controls, the practical consequence is that no weight is lost.

Developed in 1966 at the University of Iowa, by Edward Mason MD, in this procedure first,

Gastric Bypass

a large part of the stomach is cut so that the oesophagus ends in a small mini-stomach and the original stomach volume is reduced. The (large) rest, where the hunger stimulation hormone ghrelin is produced, remains 'set down' in the body, and is bypassed without normal function.

The small intestine is then cut at one point and directly connected to the truncated small stomach. The digestive juices will also be diverted and meet the digested food far into the small intestine.

The procedure thus leads the food past most of the stomach and a part of the duodenum, thus considerably reducing fat digestion, food absorption and appetite.

As a result, the patient can then only eat small meals , since the small, new stomach can only hold 20 to 30 ml. Simultaneously the operation presumably reduces the absorption of nutrients.

A gastric bypass leads to a weight loss of approximately 60% to 70% of the overweight and cures or improves secondary diseases. Markus Buechler, head of General, Visceral and Transplant Surgery at Heidelberg University Hospital and President of the German Society for General and Visceral Surgery, actually prefers this procedure. 'The gastric bypass is technically challenging, but can be performed very safe in experienced hands. The success of this operation is impressive,' he explains.

continued on page 6

Medtronic is conducting two large-scale studies using the VARC standards, one that is aimed at winning FDA approval, and the second, called SURTAVI, that aims to directly challenge the sick-and-frail threshold for patients by comparing results for moderate risk patients.

Meanwhile as the FDA considers approval of first-generation devices, European cardiologists are pressing forward with a next-generation of valves and delivery systems to refine the procedure further.

In his presentation, Dr Fajadet described the key elements for future devices, saying they will be better adapted to the anatomy of the aorta to reduce problems with leakage (*European Hospital*, 04/19/2011), they will have a lower profile for less intrusive delivery and 'certainly the next generation valve will be based on the principle of being repositionable and retrievable, which is not the case today'.

At EuroPCR 2011, **Joerg Kempfert MD**, of the University of Leipzig Heart Centre, reported six-month results for the first 40 patients to receive the Symetis Acurate transapical aortic valve. Enrolment for Symetis CE mark trial is now completed, he said.

In June, sector analyst Wells Fargo Securities reported St Jude Medical implanted for the first time a retrievable and repositionable TAVI device in Canada. The company expects to launch its transcatheter valve in Europe by 2013.

JenaValve (Munich) is now completing a CE-mark pivotal study for a new transapical valve and said it expects to enter the European market in 2011. JenaValve's second-generation TAVI systems are designed to enable re-positioning and retrievability.

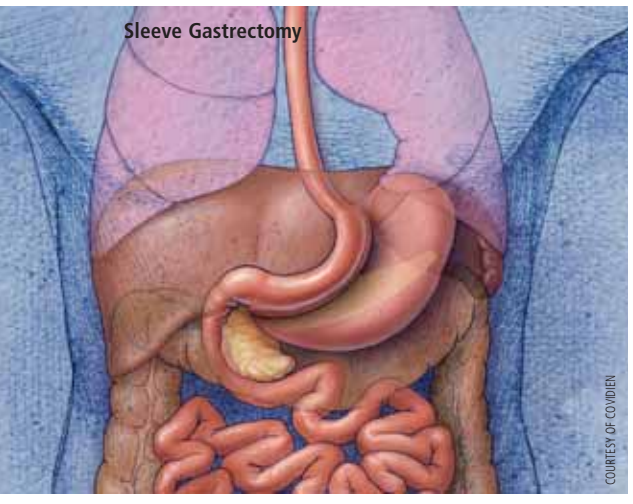
The most critical quality of these valves – their long-term durability – will remain unknown for quite some time. Providing an extra eight years of life for a patient that is 81 years old is unquestionably a tremendous benefit. Yet, as cardiologists push to perform TAVI on younger patients, the unknown durability of the devices becomes a more critical factor in a patient decision.

The biliopancreatic diversion (BPD)

Developed in 1976 by Nicola Scopinaro in Genoa, this is similar to the gastric bypass procedure but surgically very demanding. The stomach is reduced to a residual volume of 200-250 ml, the small intestine is bypassed and an approximately 50 cm long common digestive tract (common channel) is formed in which food, bile and pancreatic juice are mixed. This leads to a highly effective malabsorption of fat, a rapid and long-lasting excess weight loss of 65-75% with proven results for 25 years – and in 20% of cases to gall stones.

The BPD with duodenal switch is an enhanced procedure, introduced into clinical practice for weight loss surgery in 1988 by Douglas Hess, from Bowling Green, Ohio, using the duodenal switch developed by Tom DeMeester from Los Angeles to treat bile reflux.

Here, the pylorus is preserved, the duodenal stump is closed, the postpyloric duodenum is connected to the ileum, and the built common channel 100 cm long. Thus, the BPD-associated gastric dumping syndrome may avoided – the rapid gastric emptying that happens when the duodenum expands too quickly due to the presence of sweets or hyperosmolar food from the stomach and leads to nausea, vomiting, sweating, cramping, dizziness or fatigue.


Sleeve Gastrectomy

COURTESY OF COVIDIEN

Sleeve gastrectomy for obesity surgery is derived from the very similar Magenstrasse-Mill procedure developed in the 1970 by David Johnston from Leeds and was performed as part of the open duodenal switch procedure 1988 by Doug Hess from Bowling Green, Ohio, and laparascopically as single-stage procedure 1997 by Michel Gagner from Mount Sinai School of Medicine, New York.

Here the biggest part of the stomach is removed. What remains is a two to three inches slim, banana-shaped stomach tube with a volume of 150–200 ml. The stomach is filled faster, the patient feels satiated after small quantities of food. In addition, appetite is reduced because of a drastic decrease of ghrelin from pre-operative 109.6±32.6 fmol/ml down to 35.8±12.3 fmol/ml the first postoperative day (p=0.005), an effect that remains at least six month [*Obes Surg (2005) 15:1024-9*].

Actually, sleeve gastrectomy is the most increasing bariatric procedure in Germany with about 2,400 procedures in 2010 versus 1,440 in 2009 – a plus of 67%. One reason: sleeve gastrectomy is technically less complex than gastric bypass while the possible excess weight loss is similar to that procedure.

The advantages: There is no anastomosis or new connections made between the stomach and small intestine in this procedure, no rerouting of the intestine, no malabsorption and no dumping syndrome.

Post-surgical lifelong care

A common feature of all surgical procedures is that the patient must take life-long additional vitamins, micronutrients and protein because the organism is put in a deficiency state. For example, iron deficiency may cause anaemia.

Hence, patients must continue to change their lifestyle and food patterns, and life-long aftercare is necessary to maintain the weight loss. Moreover, massive weight loss of ≥15 BMI units results in surplus skin in those regions of the body where the volume of weight loss was greatest. These are typically the stomach, chest, thighs and upper arms, but may also include the face, neck, back and buttocks.

Additionally, there may be residual fat deposits and male mammary gland development that do not go away in association with weight loss. Mostly, plastic surgery is required following weight loss surgery. Indications range from physical difficulties (e.g., skin problems as a consequence of poor skin anchoring) through psychosocial indications (problems in sex life, sport and leisure activities, as well as problems finding clothes that fit over the surplus skin folds) to purely cosmetic indications. Patients often describe themselves as less attractive than before their large loss of weight.

Diabetes surgery on the horizon

Obesity is directly correlated with Type 2 Diabetes mellitus. However, the treatment of Type 2 diabetes mellitus (T2DM) is still a domain of internal medicine.

The therapy consisted of changes in diet, intake of blood sugar-lowering drugs and the injection of insulin. For some time, the above described surgical procedures, bypass and sleeve, have shown that an operation may be an option: The aforementioned SOS study showed that, two years after the bariatric procedure, almost three-quarters of affected patients no longer have diabetes.

In 2009, Henry Buchwald from the University of Minnesota – often called the 'father of metabolic surgery' – and his co-workers got the same result in a systematic review and large meta-analysis: The dataset includes 621 studies with 888 treatment arms and 135,246 patients; 103 treatment arms with 3,188 patients reported on resolution of the clinical and laboratory manifestations of Type 2 diabetes.

Nineteen studies with 43 treatment arms and 11,175 patients reported both weight loss and diabetes resolution separately for the 4,070 T2DM patients in these studies. At baseline, the mean age was 40.2 years; body mass index was 47.9 kg/m2; 80% were female, and 10.5% had previous bariatric procedures.

Meta-analysis of weight loss overall was 38.5 kg or 55.9% excess body weight loss. Overall, 78.1% of diabetic patients had complete resolution, and T2DM was improved or resolved in 86.6% of patients. Weight loss and diabetes resolution were greatest for patients undergoing biliopancreatic diversion/duodenal switch, followed by gastric bypass, and least for banding procedures. Insulin levels declined significantly postoperatively, as did glycohaemoglobin HbA1c and fasting glucose values.

Weight and diabetes parameters showed little difference at less than two years and at two years or more [*Am J Med 122(3):248-256.e5]*. As in the SOS study, the sleeve gastrectomy was not included in this work.

But in 2008, Vidal and co-workers demonstrated in a randomised controlled study of 91 patients that with sleeve gastrectomy, at least short term, the same anti-diabetic effect can be achieved as with the gastric bypass procedure: At 12 months after surgery, subjects undergoing SG and GBP had lost a similar amount of excessive weight (SG 63.00±2.89% vs. GBP: 66.06±2.34%; p=0.413).

On that evaluation, T2DM had resolved, respectively, in 33 out of 39 (84.6%) and 44 out of 52 (84.6%) subjects after SG and GBP (p=0.618). A shorter DM duration (p<0.05), a DM treatment not including pharmacological agents (p<0.05), and a better glycaemic control (p<0.05), were significantly associated with T2DM resolution in both surgical groups [Source: Obes Surg 18(9):1077-82].

Often the diabetes immediately disappeared after surgery, even though the patients have not yet lost much weight. Rubino and Marescaux from the IRCAD institute in Strasbourg reproduced this observation in an animal study in 29 normal-weight rats with diabetes. After gastric bypass, the diabetes mellitus has been improved, although the animals gained weight after the surgical procedure [*Ann Surg (2004) 239:1-11*].

Meanwhile, at individual centres, diabetics without severe obesity have been surgically treated and the results are promising. Lee and co-workers from Min-Sheng General Hospital, Taiwan, compared the anti-diabetic effect of a gastric bypass in 201 patients with BMI less than 35 and 619 patients with BMI more than 35 one year after the operation. The treatment goal of T2DM, defined by HbA1C<7.0%, LDL<150 mg/dl and triglyceride<150 mg/dl, was met in 76.5% of BMI < 35 and 92.4% of BMI > 35 patients (p=0.059) [*J Gastrointest Surg (2008) 12(5):945-52*].

The same author now reports a series of 24 male and 38 female consecutive patients (age 43.1 ± 10.8 years) with T2DM and a BMI of 23-35 who underwent gastric bypass. The mean HbA1c decreased from 9.7 ± 1.9% to 5.8 ± 0.5% in one year and 5.9 ± 0.5% in two years. Complete remission of T2DM was achieved in 57% in one year and 55% in 2 years after surgery [*Obes Surg (2011) Apr 17, Epub ahead of print*].

De Paula and colleagues from Goiania, Brazil, achieved in 20 diabetic patients with a BMI of 21-34, i.e. with normal weight or class I obesity, two years after surgical intervention even in 90% of cases a good control of T2DM. Bariatric surgery becomes metabolic surgery [*Surg Obes Relat Dis (2010) 6(3):296-304*].

As a potential mechanism they assume that laparoscopic sleeve gastrectomy induced changes on T2DM by mechanisms in part distinct from weight loss, principally involving restoration of insulin sensitivity and improvement of ß-cell function [*J Gastrointest Surg (2011) May 10, Epub ahead of print*].

All these results lead to a reasonable assumption that bariatric surgery evolves to metabolic surgery. Professor Markus Buechler: 'Thus, the diabetes is no longer the domain of internal medicine but requires multidisciplinary management. This is especially relevant in light of the frequency of the disease and the associated comorbidities and costs.'

According to the German health report *Diabetes 2008* about one in three Germans suffers Diabetes mellitus in the course of his or her lifetime. Presently, around eight million people are diabetic and two million need daily insulin injections.

After the United Kingdom, Germany is the European country with the most diabetics. According to the 2005 published *Cost of Diabetes mellitus study*, the average annual direct cost per treated diabetic were at €5,262 in 2001, compared with €2,755 for treated the non-diabetic.

In the case of diabetes-related complications, e.g. stroke, kidney failure or severe arteriosclerosis, these costs rise quickly to 20,000 € and more. There are also the additional indirect costs of disability and early retirement in the average amount of €5,019 for diabetics, compared with €3,691 for non-diabetics. Extrapolated to eight million people with diabetes, the annual costs in Germany are €20 billion.

Therefore, surgery as a therapy option is particularly interesting. A single operation may be cheaper than life-long insulin therapy.

Hence, the first International Diabetes Surgery Summit (DSS), held at the Catholic University of Rome in 2009, called careful interdisciplinary scientific work on this topic: The cut-off of current guidelines – only patients with severe obesity and an obesity-related condition or morbid obesity are considered candidates for bariatric surgery – was rather arbitrary than supported by scientific evidence.

Gastric electro stimulation to treat obesity and Type 2 diabetes

The gastric stimulator is an almost 20-year-old idea that now becomes a promising interventional approach for the treatment of obesity as well as Type 2 Diabetes mellitus. Actually, there are two CE certified devices in the market: The abiliti system from IntraPace Inc, Mountain View, CA, to treat severe and morbid obesity, and the Diamond system from MetaCure Inc., Kfar Saba, Israel, to treat T2DM with moderate obesity.

The Diamond system

Formerly marketed as Tantalus system, this is a gastric stimulator for inducing comprehensive glycaemic and metabolic control in T2DM. DIAMOND stands for **D**iabetes **I**mprovement **a**nd **M**etabolic **N**ormalisation **D**evice.

The OPERON D 760 high-tech OR-Table

An all-rounder with many applications

NEW


Split leg plates provide surgeons with optimal access during laparoscopic surgery

Height can be adjusted from 635 mm to 1075 mm

Given the increase in overweight or obese populations (estimated at around 50% in Europe alone), hospital equipment that supports patients must be tried, tested and proved to be robust indeed.

Like many hospital equipment manufacturers, the Tuttlingen-based firm Berchtold is well aware of this growing concern, already providing components and accessories for obesity surgery.

Now the firm has launched a new *Operon D 760* surgical table for operating theatre or out-patient use. Versatile, with premium construction and high capacity, this new product can support extremely obese patients – weighing up to 450 kg.

The surgeon can not only adjust the new table height by 440 mm for ergonomic working, but patients can also be positioned flexibly on a surface of four modules and it also comes with an extensive range of accessories and various mutually compatible leg plates.

The basic version includes a head rest, and back and seat plates. The leg plate drive is available either in one piece as a standard or short version, or as split leg plates, ideal for laparoscopic abdominal surgery.

The Operon D 760 is suitable for all surgical aspects, as well as for out-patient treatment. With a minimum height of 635 millimetres, a Trendelenburg position of 30 degrees and a tilt of up to 20 degrees, all major positions are easily achieved. Also, its wide height adjustment range up to 1075 mm meets needs when procedures require surgeons to stand or sit. An infinitely adjustable kidney elevator goes up to 75 millimetres in height.

The robust construction of the table, along with four hydraulic cylinders ensures secure positioning and optimal patient safety. This is also due to the 534 mm wide bearing surface.

In addition, special padding protects the patient from pressure sores. Berchtold says it achieves this pressure ulcer prophylaxis by a pad of high-quality viscoelastic and thermoactive foam that adjusts to the body. 'The table is equipped with an X-ray cassette tunnel along its entire length, even over the column. This is fully integrated under the tabletop so that, for conventional X-rays, there's no need for additional X-ray attachments. The carbon fibre imaging extension plate permits 1,117 mm metal-free imaging and unrestricted imaging above 1626 mm.'

The Operon is also adjusted by remote control. 'All functions are clearly

laid out with keys on the user-friendly hand pendant. Comfort functions for all important patient positions are already programmed in,' Berchtold points out. 'This makes the table intuitive and fast to use.'

Easy-moving rollers and the InstaDrive electro-hydraulic traction drive facilitate patient transport, the firm adds. 'This makes it easy to move and manoeuvre the table. Slow deceleration provides a high level of patient safety. The table has a serial interface that can be used for rapid and accurate status analysis, fault diagnosis or individual adaptation of parameters such as adjustment speeds.'

The operator can adjust the Operon D 760 manually by foot pump and an additional hand pendant attached directly to the table column.

Existing accessories from the company's Operon OR-Table range is compatible with the standard rails of the table and can be fully integrated.

Bariatric surgery

A last resort – or the only way to go?

More than half of the European population is overweight, or worst, obese. When diet and lifestyle changes do not result in permanent weight reduction in obese patients, bariatric surgery is now considered a final option. But, that's far too late, says Professor Rudolf A Weiner, head of the surgical department at Sachsenhausen Hospital in Frankfurt/Main, Germany, and President of the German Society for Surgery for Obesity. Although surgery is mostly the ultimate step after a long chain of therapy measures, he believes it to be the only treatment that actually delivers long-term success – and effectively reduces treatment and post-treatment costs

'Obesity is a chronic disease which today – just like diabetes mellitus – is not curable,' points out Professor Weiner, President of this year's World Congress of the International Federation for Surgery of Obesity and Metabolic Disorders (31 August - 3 September, Hamburg, Germany). 'We can try to manage overweight and moderate obesity with conservation therapies. However, as far as extreme obesity is concerned, bariatric surgery is the only method that shows long-term success. Conservation therapies can only support successful surgery, never replace it.'

What he deplores is that, in Germany, this proven fact is widely ignored, and thus many patients undergo surgery too late. When bariatric surgery is performed, patients are older and, on average, their body-mass index (BMI) is seven points above that of patients in other European countries. At that stage many patients already suffer severe medical conditions: only 15% of German patients undergoing weight-loss surgery have not yet developed severe co-morbid conditions, compared to 40% internationally. At the same time, the guidelines are unambiguous: with a BMI <35 kg/m² accompanied by severe co-morbid conditions and a BMI <40 kg/m² without co-morbid conditions only surgical intervention has proved really effective.

The International Diabetes Federation new research indicates that, in certain cases, bariatric surgery can also be considered for patients with a BMI of 30 to 35 kg/m² with Type 2 diabetes that is difficult to manage and who did not respond to conservation measures. However, this innovative approach is highly controversial. Its critics oppose the manipulation of healthy organs.

Nevertheless, diabetologists increasingly support bariatric surgery. 'Today, surgical procedures are extremely safe; in a high-volume surgical centre morbidity rates are between 0.1 to 0.1% – much lower than for gall bladder or hip surgery. Meanwhile morbidity among patients who do not undergo surgery increases by 100%,' as shown in a 2005 Canadian study by Raj S Padwal.

Bariatric surgery in children and adolescents is also hotly debated. Professor

Rudolf A Weiner

Weiner, who has performed bariatric surgery in 84 patients under 18 years in the past decade, strongly advocates surgery at an early stage. For young patients, however, he recommends reversible procedures such as gastric bands, which do not change a patient's anatomy.

The decision for a certain therapy is based on the patient's individual risk profile, which considers factors such as current body weight, weight history or co-morbid conditions. Moreover country-specific differences can play a role in the selection of the appropriate therapy as Professor Weiner points out: 'This has socio-economic reasons. In Germany, you can observe a trend away from gastric banding towards bypasses, while in the USA gastric banding is gaining ground due to the fact that it has passed official approval procedures. In addition in Germany, the number of tube gastrectomies has reached its apex. In this intervention, the fundus of the stomach, where the appetite-stimulating hormone ghrelin is produced, is partially removed. After this intervention the patient feels less hungry and can intake only a certain amount of food. In other countries the so-called gastroplication is increasingly performed, which means the size of the stomach is reduced by suturing or removing a stomach fold.'

As a rather young medical discipline, bariatric surgery will no doubt offer interesting surprises and developments in procedures and applications.

IFSO 2011 this summer offers a forum for experts to discuss the future of surgical weight loss interventions.

Report: Karoline Laarmann

The system consists of an implantable stimulator, a set of electrodes and an external charger. Under general anaesthesia, the electrodes are implanted laparascopically in the stomach muscle.

The system includes a unique and robust eating detection mechanism that, without being inserted into the stomach, senses when the patient eats and induces the non-excitatory stimulation of the stomach causing the stomach to contract stronger. As opposed to gastric pacers the Diamond system only enhances the natural physiological response to a meal at the correct physiological context.

Since 2007, the system is CE approved for treating T2DM. Wolfgang Karl, Managing Director for Germany, about the clinical results: 'Implanted in over 230 Type 2 diabetics who have exhausted pharmacological options, 90% of the patients benefit by HbA1c or weight reduction, 43% experience a reduction of 1% or over in HbA1c, and 40% reach HbA1c levels of below 7.0%. This is accompanied by a significant reduction in blood pressure, blood lipid profile, and some reduction in weight and waist circumference – with minimal compliance from patients and without the need for an accompanying exercise and diet regime.'

The abiliti gastric stimulator

CE approved for obesity treatment since 2011, this consists of a pacemaker-like implant that is placed on the outside of a patient's stomach using standard laparoscopic instruments.

The device detects food via sensors placed in the top of the stomach wall and exercise using an integrated accelerator. When the system detects an eating or drinking event, it delivers a series of low-energy electrical impulses to the stomach to create a feeling of fullness, thereby encouraging reduced food intake.

Chuck Brynelsen, CEO of IntraPace, explains: 'Unlike restrictive procedures, the abiliti system does not impose limits on the type of food a person can consume. Nor does it cause nausea or vomiting should a patient eat too much.'

Information from the food detection sensor provides a detailed picture of food and drink consumption, while the activity sensor tracks exercise and can determine calories burned through various activities.

Using a simple wireless connection, the doctor and patient can view this critical consumption and exercise data, which help support behaviours that lead to sustained weight loss. Further, through an online resource, patients are connected to a valuable support network – a community of individuals helping one another to reach their weight loss goals. Patients in the first clinical study who completed at least 12 months of therapy lost an average of 21% of their excess weight. Based upon an analysis of these data, IntraPace has developed a screening methodology to assist physicians in identifying patients most likely to benefit from the abiliti therapy. Again Brynelsen: 'When applied to subjects from our first clinical trial, those subjects that would have passed the screening lost an average of 38% of their excess weight, or 18 kg. This tool was employed in the company's second trial, results that will be presented in August at the IFSO congress suggest it has benefit.'

Thomas Horbach MD, from Municipal Hospital Schwabach, Germany, is among the world's first to have large experience with both surgical and interventional procedures and explains the rebirth of gastric electrical stimulation: 'Former products, e.g. the IGS from Transneuronix Inc., were of limited efficacy due to their continuous stimulation. In contrast, the Diamond system stimulates only when a stomach strain stimulus is detected. Thus, a habituation or fatigue effect is avoided.'

This March, Horbach implanted the first CE certified abiliti device after being the principal investigator of the clinical studies leading to a CE certification. His opinion: 'Not only food and liquid intake is detected by the stomach sensor but also physical activity with the inbuilt accelerometer. This is the first time that I have the chance to guide a patient, to control his compliance. And that's even possible using inbuilt telemetry.'

Thus, new promising tools are available to broaden the surgeon's arsenal. 'Each technique has its indication, whether surgically or interventional,' Horbach says, and cites examples: 'The pilot of an airline, the self-employed roofer, the taxi driver, daily repeated injections of insulin would mean for all three the end of their professional life. And an irreversible surgical procedure like gastric bypass or sleeve gastrectomy is not for everyone.'

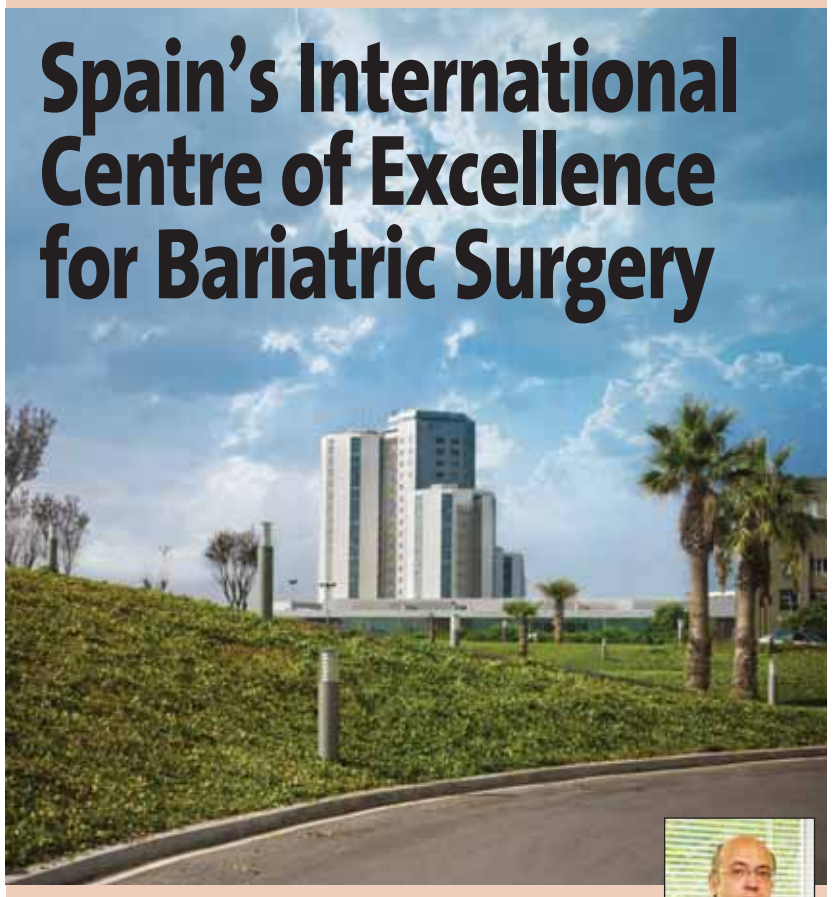
A comprehensible statement: The latest, as yet unpublished data from the German bariatric surgery registry suggest that staple line insufficiency is up to 7%. By contrast, electrical stimulation is less invasive, less aggressive – and potentially as effective as surgery without making any changes to the anatomy of the digestive system. However, the long-term result still remains unclear.

No more unclear are the results and value of surgical procedures. Regarding the excessive weight loss, biliopancreatic division seems more effective than sleeve gastrectomy, sleeve more than or similar to gastric bypass, and bypass more than gastric band.

As there is no ideal procedure, new surgical techniques are developed. Recently, Pujol Gebelli from the University Hospital of Bellvitge, Barcelona, presented the laparoscopic gastric plication, a reversible technique derived from sleeve gastrectomy. Because morbid obesity is strongly associated to Type 2 diabetes, about 90% of diabetics may benefit from a surgical procedure, even in cases of moderate obesity. Further, fully T2DM remission seems possible. To describe these facts, the term 'diabesity' has been coined.

BARIATRIC SURGERY

Spain's International Centre of Excellence for Bariatric Surgery



The Academe Hospital of Bellvitge, which is part of the Catalan Health Institute, has been designated an *International Centre of Excellence for Bariatric Surgery* (ICE) by the Surgical Review Corporation (SRC), a US-b ased non-profit-making organisation that aims to 'advance the safety, efficacy and efficiency of bariatric and metabolic surgical care'

Jordi Pujol Gebellí

The ICE designation is awarded not only to an institution but also individual surgeons – in the case of HUB, Dr Jordi Pujol Gebellí, Co-Director of the Bariatric and Metabolic Surgery Specialty and Director of International Training Courses for Bariatric and Metabolic Surgery at HUB. He performed the first laparoscopic surgical procedures at the hospital, has received numerous awards for his research in that field, and is a member of the Spanish Society for Bariatric Surgery. 'Receiving ICE designation reflects the willingness of our staff to be measured against the highest standards of performance,' he said.

HUB is located in the Hospitalet de Llobregat area of Barcelona, HUB serves a population of approximately two million people. It is consistently ranked among the top 20 hospitals in Spain and certified as a third-level centre, allowing the hospital to treat the most complex health check cases. HUB is a member of the Biomedical Research Institute of Bellvitge (IDIBELL) and certified by the Carlos III Research Institute of the Agency of Science and Innovation for the highest level of research.

'We are always updating our results for comparison to international levels,' said Dr Pujol, adding: 'We are also assessing diabetes surgery in patients with BMI of 30-35, robotic bariatric surgery as well as the evaluation of the gastric plication technique.'

The patients who benefit most from bariatric surgery, he said, are those with a BMI of 40 and BMI of 35 with severe comorbidities, and diabetic patients with BMI of 30-35, cases with sleep apnoea that use CPAP masks, morbidly obese patients with severe arthropathy or high blood pressure.

Due to what he calls the 'actual epidemic – globesity' he sees a future in which we need to treat the greatest possible number of patients – in controlled, accredited institutions. What would such institutions need to set up?

'Bariatric surgery is a subspecialty of gastrointestinal surgery with an important global projection due to its exponential increase,' he pointed out, adding: 'There's a general need for training in gastrointestinal surgery and advanced digestive laparoscopy. The global training will be five years of general and another 4-5 years between advanced laparoscopy and bariatric. You need extensive knowledge in terms of possible complications. Hospitals, practices, all structures and related services, psychiatry, pneumology, endocrinology, the dietician must all be adapted to these patients.

'As one of the pioneering bariatric centres in Europe, HUB and Dr Pujol have truly demonstrated a singular staunchness to bariatric surgery,' said Dr Raul Rosenthal, Chairman of the IBSRC and a bariatric general practitioner at the Cleveland Clinic in Weston, Florida. 'Patients from around the country and province can now choose to have their course of action performed by a centre that has met the global standard of excellence in bariatric surgical care.'

Report: Eduardo de la Sota

Cardiac conundrum

Diabetic patients continue to elude engineers of drug-eluting stents. New designs have brought only modest progress in improving outcomes for a complex and growing population of patients, *John Brosky* reports

France – Re-opening clogged arteries with metal stents has proved a life-saver for a majority of patients with coronary disease. Yet the high rates of complications and mortality for patients with diabetes following a percutaneous coronary intervention (PCI) continue to baffle cardiologists.

The stakes are high in the quest to find the right treatment strategy.

Car diovascular disease is the leading cause of death among diabetics and the prevalence of diabetes is significant, estimated to be 2.8% of the population in 2000 and projected to to increase to 4.4% by 2030.

Cardiologists find these patients tend to have more advanced coronary artery conditions, frequently presenting with two and three-vessel disease, suggesting that PCI as the right strategy for treatment.

Yet studies consistently find that both non-insulin dependent and insulin-dependent diabetics have a poorer clinical outcome after PCI compared to non-diabetic patients. The authors of the benchmark Swedish Coronary Angiography and Angioplasty Registry describe the prognosis as 'dismal'.

There is a greater tendency for restenosis, or reclosing of the artery, for diabetics after PCI. They have a higher risk of stent thrombosis and a greater need for returning to the operating table for another PCI revascularisation. Most significantly, diabetic patients have a higher incidence of death in the years following PCI.

A special session at EuroPCR 2011, Europe's largest congress for interventional cardiology, took up these clinical concerns during a review of clinical trials entitled *Which Drug Eluting Stent for Diabetics*?

The confidence of cardiologists in drug-eluting stents (DES) was shaken in 2008 by the landmark SYNTAX trial (SYNergy Between Percutaneous Coronary Intervention With TAXus and Cardiac Surgery) that included 452 diabetic patients among the 1,800 patients randomised between a minimally invasive stenting procedure and traditional coronary bypass surgery.

An editorial published in 2010 in the *Journal of the American College of Cardiology*, said the SYNTAX diabetes analysis did not tell clinicians to stop doing PCI in diabetic patients, but that it should only be done in patients in whom 'there is no reasonable surgical option'.

JACC cautioned: 'It is possible that a death penalty is not seen at one year but will appear at longer follow-up periods.'

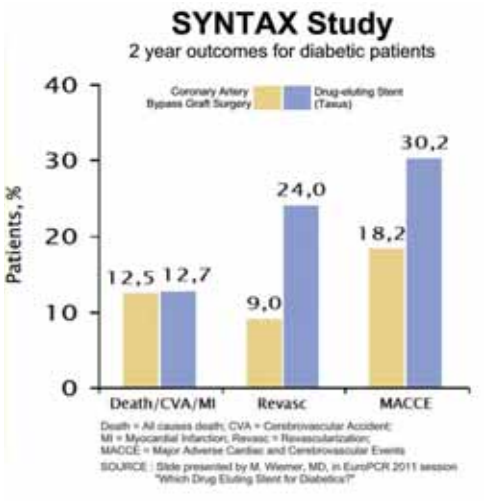
Responding to these concerns, a second generation of DES was designed and the results from trials of these new stents were the focus of the EuroPCR 2011 session.

Multiple presentations were made for two DES that have emerged as favourites among the second-generation, the Xience V from Abbott Vascular and the Resolute from Medtronic. Both feature a polymer to bind a drug to the metal stent that is meant to prevent restenosis, but which cardiologists now suspect may be a cause of irritation that stimulates the reclosing of the artery.

Two relative newcomers presented during the session represented a third generation design using a biodegradable polymer, the Norobi from Terumo and the Titan from Hexacath.

Stent performance was discussed primarily in terms of what the board of EuroPCR called device-oriented criteria.

The good news is that modest progress has been made using these criteria for in-stent thrombosis or target vessel revascularisation, according to the take-home messages delivered by session co-chair, Upendra Kaul MD, Director of Cardiology at Fortis Escorts Heart Institute in New Delhi, India.



The use of second generation DES in diabetic patients yields consistently acceptable one- and two-year results with major adverse cardiac events in single digits, he said, despite the more challenging and complex cases diabetics present compared to non-diabetic patients.

But for patient-oriented criteria, which includes mortality after the procedure, the rate of death following PCI continues to be significantly higher for diabetic patients, especially those who are insulin-dependent.

A shared image among the presentations from manufacturers was the widening gap after four months between mortality for

The Norfolk Diabetes Prevention Study

Could advice from Type 2 diabetics prevent others from developing the disease?

UK – Family doctors (GPs) in Norfolk are inviting patients aged over 40, with a Body Mass Index above 30 and a family history of diabetes, to take part in the Norfolk Diabetes Prevention Study (NDPS). Funded by the National Institute for Health Research, the innovative £2.2million project will run for five years at the Norfolk and Norwich University Hospital (NNUH) and will involve 10,000 people at high risk of Type 2 diabetes.

The study researchers at the NNUH and University of East Anglia (UEA) are aiming to discover whether preventative changes to lifestyle can help reduce the risk of developing Type 2 diabetes.

Whilst they expect that most of the participants in the NDPS study will have normal blood glucose levels, 11% will be in the 'pre-diabetes' phase with a higher than normal Impaired Fasting Glucose level and at increased risk of developing the condition.

Those in the pre-diabetes phase will not only receive professional healthcare support but also advice on ways to improve their diet and lifestyle, to be given by 50 Type 2 diabetics to be recruited as Diabetes Prevention Mentors (DPMs).

The volunteers will be randomly allocated to an intervention group with DPM input, an intervention group without DPMs, and a control group where the aim will be for people to achieve 7% weight loss through a better diet and exercise. They will also receive education from sports physiotherapists and nutritionists.

The participants will have blood samples taken at the start of the study and then at 6, 12, 24 and 40 months.

Senior research associate Nikki Murray from NNUH said: 'There'll never be enough trained NHS staff to help all the people in Norfolk who have diabetes or are at risk of it. Using members of the public

Germany to limit test strips prescriptions

Experts attack a Federal decision that will affect vital self-monitoring

Since the German Federal Ministry of Health did not oppose the Federal Joint Committee (G-BA) decision to eliminate reimbursement for urine and blood sugar test strips for Type 2 diabetics not dependent on insulin from the services provided by statutory medical insurers, from this October test strips will only be prescribed in exceptional cases.

'We are disappointed by stance the Federal Ministry of Health has taken under the leadership of Mr Daniel Bahr,' declared Professor Thomas Danne, president of the German Diabetes Association (DDG) and chairman of the board at diabetesDE. 'Along with other associations, diabetesDE and the German Diabetes Federation have campaigned vehemently against this ruling coming into force.'

The impression is that the decision was taken without an awareness of its effects on patients' everyday lives, with an anticipated deterioration in care, he said, adding that this has met with complete incomprehension by diabetesDE, as well as the diabetics, researchers and diabetologists it represents, and by the German Diabetes Federation, the largest patient organisation. Around two thirds of diabetics in the country are affected by the decision, i.e. 4.7 million people, mostly of retirement age.

Patients with Type 2 diabetes are being made to believe that regular blood sugar testing is 'not necessary' for disease management. However, that is a 'fatal signal', explained Michaela Berger, board member at diabetesDE and the German Association for Diabetes Education and Counselling Professions (VDBD): 'In future, blood sugar will only be tested in exceptional cases – but blood sugar level monitoring is much more than a means of crisis intervention. Regular control enhances patients' personal responsibility for their illness and their body – and it is the best way of damage regulation in a case of impending or already occurring hypoglycaemia. When the new ruling comes into force patients will be systematically disempowered rather than empowered.'

Dieter Möhler, national chairman of the German Diabetes Federation, added: 'We have not asked for everything for everyone, but we are adamant that there must be no treatment restrictions for doctors when it comes to providing individual treatment of patients. This is the only way that patients can be assured of treatment that corresponds with their special life and work situation.'

Living with Type 2 diabetes without test strips is like driving without a driving licence, he pointed out. Patients now have no feedback whatsoever as to how their lifestyle affects their blood sugar levels and therefore the development of secondary diseases in the long term.

diabetic patients compared with non-diabetics.

While the two types of patients do equally well at first, there is a sudden slide in the incidence of death after that point, for reasons that are still not understood.

Sigmund Silber MD, from the Heart Catheterisation Centre in Munich, Germany, highlighted this frustrating phenomenon presenting a pooled analysis of clinical data on 867 diabetic patients who received a Resolute DES.

The analysis suggested an intriguing homogeneous treatment effect across diabetic and non-diabetic patients with consistently low rates of adverse events in this patient population at one year of follow-up.

'Not surprisingly, a notable exception to this effect was seen in the insulin-dependent diabetic patient, which serves to underscore the challenges that persist in determining the ideal interventional treatment for these patients,' he said.

to help us is a novel aspect. We're hoping the mentors will build a strong rapport with the participants, because they know what it's like having to make lifestyle changes. It's a fantastic way for them to relate to each other in a way which some healthcare professionals won't be able to do.'

Study chief investigator Professor Mike Sampson said: 'We think this is an exciting study that holds a lot of promise for one of the big public health challenges of our time. The cost of diabetes care to the NHS is rising rapidly and if we can demonstrate that an interventional programme can help people from developing the condition, the savings in terms of the human costs and the financial cost to the NHS will be substantial.

'We think that mass screening and intervention programmes to prevent diabetes could well benefit from having people with Type 2 Diabetes provide some of the training and support, and that it will be more efficient to deliver this in group training, so people can support each other.'

Diabetes is one of the biggest public health challenges facing the country. In England it is estimated 2.4 million people have the condition. About 80% of those with diabetes in England have Type 2 Diabetes.

Report: Mark Nicholls

Two sides of the coin

Interactions between non-alcoholic fatty liver disease and diabetes


Jörg Bojunga

Too much unhealthy food, too little exercise – the risk factors for the development of non-alcoholic fatty liver disease and Type 2 diabetes are not only similar but also form a life-threatening alliance. **Dr Jörg Bojunga**, Head of Endocrinology and Diabetology at the Johann Wolfgang-Goethe-University, Frankfurt am Main, Germany, presented new scientific findings on the causes and effects of both diseases at this year's annual German Congress on Internal Medicine.

'For a long time, fatty liver disease was considered a kind of "trivial offence" without any impact on health. However, we now know that in 30% of cases fatty liver disease can lead to severe secondary diseases, such as fatty liver inflammation, cirrhosis of the liver, liver failure or liver cancer, and therefore shortened life expectancy,' Dr Bojunga explained, during an interview with *Karoline Laarmann*. Around 60% of diabetics develop fatty liver in the course of their disease, with fatty liver being defined by visceral fat levels over 5%. Insulin resistance means that fat is stored in the liver and also that the liver itself produces additional fat.

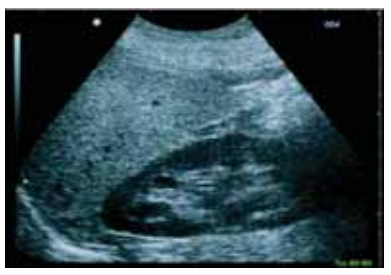
However, despite long-held views, there is also a reverse development of the disease, he added. 'At least in some patients fatty liver develops first and then, through the release of inflammatory mediators such as the protein Fetuin-A, also leads to the insulin sensitivity being lowered. We may have found an indicator here, which might enable us to predict the risk of diabetes and its complications.'

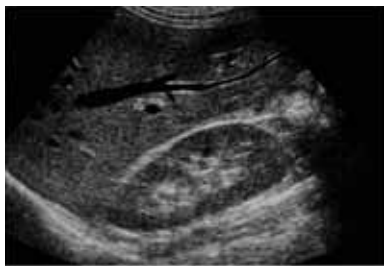
As fatty liver in itself does not generate any symptoms it is mostly diagnosed by chance during an abdominal ultrasound (enlarged liver) or a blood test (elevated liver count). Should the diagnosis be confirmed, long-term treatment should commence. This should include at least 20 minutes of daily exercise and a weight loss of about 7-10%.

Diabetes and fatty liver are mostly manifestations of the same problem, i.e. metabolic syndrome, which is why, in very obese patients, even slight weight loss has clear, positive effects on the fat distribution in the liver.

However, Dr Bojunga said: 'Fast weight loss through crash dieting should definitely be avoided. In fact, this can actually make fatty liver disease even worse. Moreover, patients then mostly find it even more difficult to keep their weight down in the long run. Many patients have been living an unhealthy lifestyle for several decades. This makes it difficult to achieve changes with draconian recommendations. Nutrition counselling and care are therefore also extremely complex and one has to invest a lot to lead a relatively small proportion of patients to long-term success.'

In future, due to these difficult treatment conditions, experts will be reinforcing the importance of prevention. Children should be taught about the importance of healthy food even in nurseries and primary schools, a concept also supported by Dr Bojunga.


Ultrasound of a normal liver


Ultrasound of a fatty liver

It is not only the lack of basic knowledge, but also a lack of critical awareness when it comes to the advertising promises of the food industry: 'Many food labels such as "low in fat" or "diet" are misleading because the products may contain less fat, but actually large amounts of fructose, which can also lead to liver damage. Thanks to new EU legislation, however, it will become more difficult for the industry to cheat with labelling products as to their nutritional and health-related values.'

Furthermore, new findings have shown that in rare cases genetic change s may also be causes for fatty liver disease. This means that even slim individuals can be affected. Early diagnosis is also of great importance here to start the necessary treatment and avoid further complications – that is, if there is actually a risk, because, he said, 'Fatty liver disease is an increase of fat in the liver, which goes hand in hand with an inflammation and can lead to an increase of connective tissue, i.e. liver fibrosis.

'However, we are not yet medically able to determine exactly which patient with fatty liver inflammation is likely to develop progressive liver diseases. This is why the level of inflammation and increase of connective tissue play an important part in diagnosis as well as research.'

There is now less need for needle biopsies of the liver for this examination. Non-invasive tests, such as blood, and ultrasound-based procedures to measure the connective tissue ratio of the liver such as the FibroScan, are already delivering good, quick results on risk factors and the progression of liver disease.

SWEET news: A paediatric diabetes network

European centres of reference for paediatric diabetes demand improved cross-border cooperation


Thomas Danne

For three years the SWEET project, funded by the EU and the International Society for Paediatric and Adolescent Diabetes (ISPAD), has been preparing the establishment of centres of reference (CORs) for childhood diabetes. Now, the first 12 European CORs that are certified by SWEET have joined forces to promote improved cross-border cooperation in the treatment of young Type 1 and Type 2 diabetics. **Professor Thomas Danne**, director of SWEET, Secretary General of ISPAD and Senior Consultant at the 'auf der Bult' paediatric hospital in Hannover, Germany, explains why there is a need for cross-border centres and the major objectives of the European network

Prof. Danne: 'Currently, the quality of care of paediatric diabetics differs widely among the European centres. Not only between countries but also within facilities, metabolic objectives such as HbA1c, hypoglycaemia or the frequency of ketacedosis are achieved to varying degrees either due to socio-economic reasons or therapy strategies.

'We therefore want to promote the exchange of knowledge and best practices and to find out why some centres are more successful in reaching the metabolic objectives than others. Furthermore, we'd like to introduce standardised quality assurance measures to improve diagnosis and control Type 1 or Type 2 diabetes in children and adolescents.

'Another aspect we are concerned about is the fact that we are confronted with ever more complex and more expensive therapies, particularly with an increased orientation towards technology in the therapy. We want the CORs to help evaluate the usefulness of these therapies.'

Currently, are there country-specific differences?

'Italian centres are very successful whilst, in an international comparison, British centres do less well. This is not primarily a result of a country's economic situation but of the care concepts for paediatric diabetics.

'Insulin therapies for children differ significantly from those for adults because physical development and everyday life differ significantly. Nevertheless in many countries there are neither paediatric diabetologists, nor diabetes consultants or age-specific training programmes. In some countries on the other hand, such as France, well organised patient self-help groups take on many educational tasks.'

What is the accreditation procedure for a centre of reference like?

'Facilities that want to be accredited as centres of reference have to submit long-term data of at least 150 patients, or record the data in an electronic patient record – an EPR.

'The EPR system offers a function which anonymises data and loads them onto a server for statistical evaluation and comparison purposes. Additionally, the centres are audited for compliance with the relevant quality criteria. If a centre fulfils all these requirements accreditation is awarded for three years.

'During the accreditation period all data are reviewed and discussed twice a year by a quality panel. This is particularly interesting for the CORs because they can see where they stand compared to other centres.'

Which research objectives can the centres help to reach?

'Obviously registers, as provided by the centres, will facilitate research on rare forms of diabetes such as monogenic diabetes. However, more importantly we expect the reference centres to take on a leading role in the development of diabetes technology, with regard to telemedicine, for example, but also as far as insulin pumps and continuous glucose monitors are concerned.

'In the context of the project DREAM, we are already testing an artificial pancreas – a device that combines an insulin pump and a glucose monitoring sensor and which we hope will regulate the metabolism during the night.

'The study is being performed at three major paediatric diabetes centres in Tel Aviv, Ljubljana and here in Hannover and the initial results were very promising.

'For seven patients we recorded a decrease of average glucose levels from 182 to 126 mg/dl compared to conventional insulin pump therapies in twelve sessions. At the same time the periods of time when the targeted glucose level of 63 to 140 mg/dl was achieved, increased from 29% to 77%.

'We cannot yet use the artificial pancreas during the day because the algorithm that detects post-prandial glucose increases is too slow. But I am confident that we can solve this problem as soon as faster acting insulin is available.'

Further details: http://www.sweet-project.eu/

31st German Senology Congress

23-25 June 2011 • Dresden, Germany

More opportunities in breast diagnostics

Yes, it's in beautiful Dresden again and – as in 2006 when the city last hosted the Congress of the German Society for Senology – this year's Congress President is **Professor Rüdiger Schulz-Wendtland** (Department of Radiology, University of Erlangen). However, the repetition ends there; the congress topics will be anything but repeated. Rapidly developing technology and techniques attract ever new debates on their application and benefits. Key topics will include, for example, neo-adjuvant and adjuvant therapy, translational research and intra-operative radiotherapy (IORT), whilst other scientific sessions will focus on digital mammography, fusion technologies and molecular Imaging. Interview: *Meike Lerner*

During one of the sessions to be chaired by Professor Rüdiger Schulz-Wendtland the opportunities and limits of molecular imaging with hybrid systems will be examined.

At this stage, can certain methods be identified as taking the lead in this field?

There are, he pointed out, several approaches being explored in order to fuse or hybridise different imaging systems.

'The initial task consists of trying to differentiate between the concepts. In the case of hybridisation, two different systems are interfaced, such as with the PET-CT.

'In the case of fusion, the approach is to turn two different devices into one. A good example for the latter is the procedure where MRI images are sent to an ultrasound scanner so that the information from both modalities can be simultaneously used for the diagnosis. A further approach, which we are currently looking into at the University of Erlangen in cooperation with the Fraunhofer Institute and partners in industry, is to merge the images generated by mammography and ultrasound.

'The opportunities inherent in MRI scanning will be another key topic. This includes the examination of spectroscopic procedures that show the processes in the breast on a molecular-biological level, as well as discussion around the need for quality-assured standards for breast MRI, which, in Germany, are not yet available. One of the most exciting topics in the field of MRI is the significance of DCIS.

'Professor Christiane Kuhl has already published some findings on this topic and has shown that aggressive, high-grade DCIS enhances on MRI scans, although it was generally assumed that it only becomes visible on the MRI in the case of neoangiogenesis.

'We want to build on these results and to further quantify DCIS. We want to find out whether high-grade DCIS, which enhances on the MRI, has receptors that point towards the aggressive DCIS, later also turning into an aggressive tumour.

What is the role of tomography?

'Three-dimensional imaging of the breast obviously plays a very important part, for instance in the shape of tomosynthesis where, in addition to the two-dimensional image, images are taken in an angular range of +/- 15 or +/- 25 degrees.

'Companies such as GE, Siemens or Hologic are carrying out extensive work on these solutions. Fuji, which is continuing to produce 2-D images, is following a very different approach, with the 2-D images being shown on the monitor in 3-D through movement parallax. This currently still requires the use of special glasses; however, new monitors also achieve this effect without the glasses. These different options of 3-D imaging will be a topic at the congress and, very important to me personally, they are not just dreams of the future but very concrete options relevant for clinical use.'

Where does that leave ultrasound?

'This is another topic that will be given a lot of consideration at the congress, initially in relation to its use in mammography screening.

'There is currently a requirement to sound the mammary glands in addition to mammography for gland tissue of the density levels 3 and 4. This requirement is based on study results from screening scenarios where analogue mammography systems were being used. As we in Germany generally work digitally, the question as to the density of the mammary gland tissue needs less consideration. The more important, yet so far hypothetical question is: Can tomosynthesis, which may possibly become part of screening in the future, completely replace ultrasound in screening? This is obviously a very provocative assumption.'

Congress President Rüdiger Schulz-Wendtland

Especially as ultrasound is playing an increasingly important role in breast diagnostics due to new technological developments...

'Yes. For instance, elastography has definitely made progress here. However, the indications for elastography are currently not yet clearly defined enough. The procedure appears to play an important part in the differential diagnosis of benign and malignant tumours, and possibly in the field of follow-up of neoadjuvant chemotherapy, as elastography also takes into account morphology.

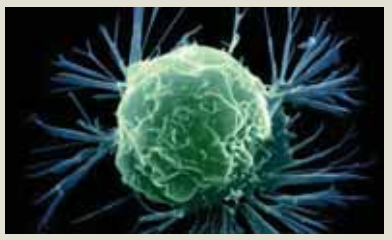
'In summary, the new procedures all offer great potential, but the respective, appropriate areas of application for each procedure will only become apparent over the next few years.'

NEW

A genomic test to predict chemotherapy outcomes

Although powerful, new, targeted treatments are regularly introduced to cancer clinics, choices for the first-line treatment of invasive breast cancer normally lie between preventive surgery and chemotherapy

Since the 1970s anthracyclines have remained the gold standard for efficacy in breast cancer, and chemotherapy regimens containing anthracycline consistently outperform those without it. However, not all tumours respond to this type of chemotherapy and several factors



are known to influence outcomes including: tumour grade, p53 status, Topo II alpha level, HER2 over-expression, ER status and expression of multiple drug resistance (MDR).

A recent study from the University of Texas MD Anderson Cancer Centre [*Hatzis C et al. A genomic predictor of response and survival following taxane-anthracycline chemotherapy for invasive breast cancer. JAMA. 2011 May 11;305(18):1873-81*], used genomic prediction combining multiple signatures to determine outcomes to standard chemotherapy.

This multicentre study enrolled 310 women, newly diagnosed with Stages II and III invasive breast cancer. All were Her2 negative and received a chemotherapy regimen of sequential taxane and anthracycline, followed by endocrine therapy if ER-positive.

Gene expression microarrays were then developed from the neo-adjuvant breast tumours to develop different predictive signatures for drug resistance and response. These signatures were then used to predict response to chemotherapy in another, 'independent' cohort of 198 breast cancer patients with similar diagnosis and treatment in a validation process.

The primary endpoint was distant relapse-free survival (DRFS) if predicted treatment sensitive and absolute risk reduction (ARR), difference in DRFS between two predicted groups. Median follow up was three years. The 28% patients in the independent validation cohort, who were predicted to be treatment sensitive, had a 56% probability of an excellent pathological response, their three-year DRFS was 92%, ARR was 18% and they had a five-fold reduction of risk of distant relapse.

When the data were analysed by ER status, treatment sensitivity was predicted in 30% of the ER-positive women and in 26% of those who were ER-negative. At three year follow-up, in the ER-positive group DRFS was 97% and significant ARR was 11%. In the ER-negative subgroup DRFS was 83% and ARR 26%, the positive predictive value was 83%.

Interestingly, other genomic predictors showed paradoxically worse survival for patients predicted to be responsive to chemotherapy.

To guide the selection of a standard adjuvant treatment regimen, any test based on predicted response to treatment should expect a high probability of survival for those patients predicted to be treatment sensitive (negative predictive value, no relapse if predicted to be treatment sensitive) and a clinically meaningful survival difference between those patients predicted to be treatment sensitive and those predicted to be insensitive (ARR) as well as bettering results based on odds using existing clinical-pathological information.

According to the authors, the performance of this new test met these criteria in the independent validation cohort. If corroborated in future studies a test like this could perhaps, within as few as five years be guiding treatment choices in an individualised way for all women newly diagnosed with breast cancer.

Those patients who find that standard treatments are not useful for them could then be encouraged to enter clinical trials of new, alternative treatments early in the treatment ladder, when they will be most effective in enabling cure.

Report: Jane MacDougall

Positron emission mammography is coming to Europe

Every medical congress is an opportunity for the manufacturers to showcase their products. This year's congress of the German Röntgen Society was no exception – and one innovation particularly caught the attention of our *European Hospital* team: positron emission mammography, PEM for short. At the Medicor booth we met with Stefanie Groes, Regional Director of the company, that will be selling the scanner in Germany, Austria and Switzerland, to hear about the technology of the new device and its applications

The PEM scanner is a mobile unit about the size of an ultrasound system. Two detectors acquire twelve slice images from which a high-value 3-D PET image is constructed. Just like a PET scan, the PEM image shows FDG accumulation. But, there the similarities end. PEM offers a much higher resolution than PET and the new technology's high sensitivity (>90%) and specificity (88% NPV and 92% accuracy) may turn out to be the key to detect lesions as small as 1 to 2 mm.

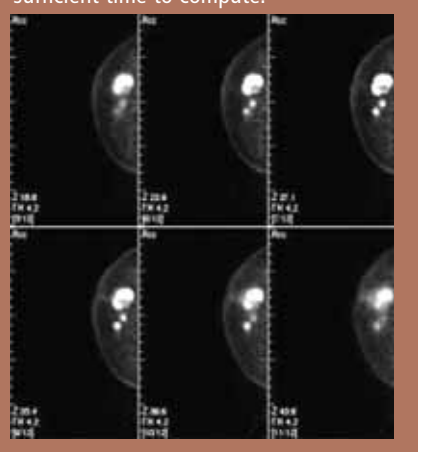
'PEM detects tumours long before ultrasound mammography and MRI even begin to get inkling that there might be something there. Malignant structures, no matter what size, literally gobble up glucose and store it. An MRI scanner can visualise tumours only when they have vascularised – that means, when they have developed a blood vessel system,' Stephanie Groes explained.

However, despite this impressive diagnostic performance, she added, PEM will most likely never be used for mammography screening.

In the US, where the PEM scanner is being manufactured by NaviScan, the new technology has proved particularly valuable in cancer follow-up. As soon as a tumour is detected it can be staged or removed directly by biopsy. 'Mammography and MRI often visualise lesions as a tissue mass. PEM images, however, allow the physician to distinguish individual tumours or multiple metastases,' Stefanie Gores pointed out, adding that the biopsy results can be assessed in one FDG cycle. PEM may also be used to monitor the body's response to chemotherapy.

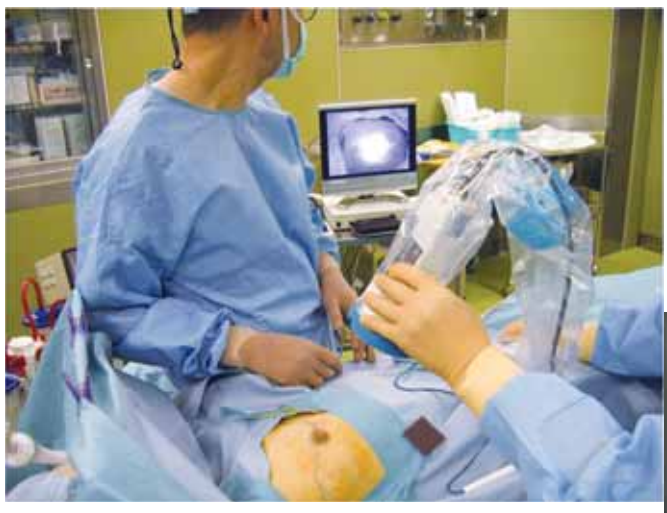
Before PEM can conquer German breast cancer centres a legal framework has to be established and necessary approvals obtained. Medicor is confident that it will receive the support of the authorities.

At this point it is clear that PEM – unlike other established breast cancer detection modalities – will not come under the auspices of radiologists because the technology, like whole-body PET, is subject to strict regulation on the use of the radioactive tracer FDG. Therefore, the first PEM scanners will be installed in PET centres. Radiology practices that have nuclear medicine facilities will follow later. 'This is necessary for practical purposes since FDG with a half-life of 110 minutes requires quick action,' the Medicor regional director explained. 'The later an image is acquired, the longer the scan times become to give the machine sufficient time to compute.'



Shining green - Seeing is

Breast cancer is the most common form of cancer in women. Evaluation of the axillary lymph nodes is essential to insure complete cancer removal. Fluorescence imaging instead of radioisotopes is an innovative method for sentinel lymph node detection, EH correspondent *Holger Zorn* reports



Fluorescence imaging with ICG and PDE. Above: The Photo Dynamic Eye is placed on the patient to detect the injected dye. Top right: Visual intra-operative image of a sentinel lymph node and a lymph vessel. Below right: The PDE screen shows the fluorescence image of that node and vessel

'Within the EU, every 2.5 minutes a woman is diagnosed with breast cancer,' said Stella Kyriakides, former President of Europa Donna, the European Breast Cancer Coalition, in 2004. 'Every 7.5 minutes a woman dies from the disease.' In 2008, an estimated 332,670 new cases of breast cancer occurred in the countries of the European Union [*Source: Eur J Cancer (2010) 46:765-81*].

To ensure complete removal of the cancer, and to find any metastasis, it is important to evaluate the axillary lymph nodes. In addition, their evaluation represents an important independent prognostic factor in patients with early breast cancer.

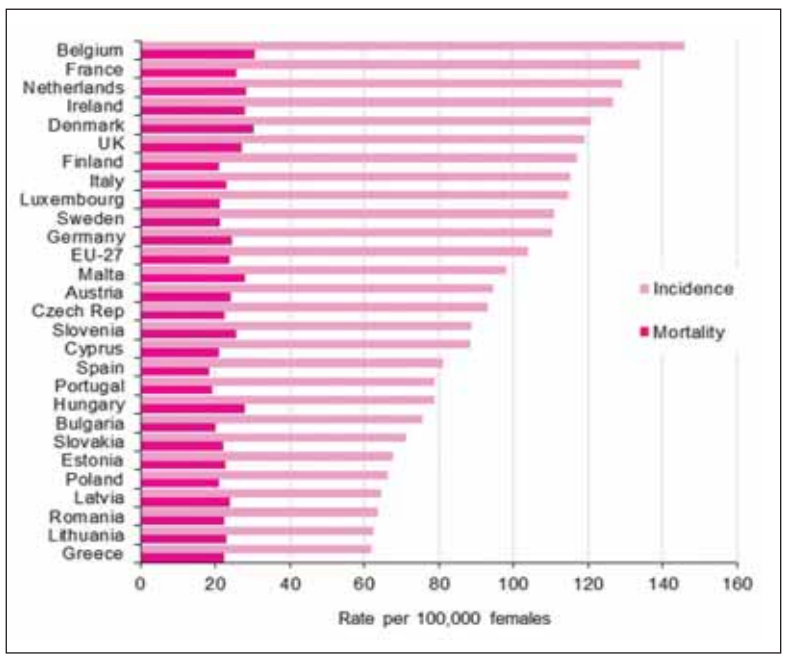
In 1993, David Krag from University of Vermont, Burlington, introduced sentinel lymph node (SLN) biopsy using a radioactive colloid. One year later, Armando Giuliano, from the John Wayne Cancer Institute in Santa Monica, California, followed by using a blue dye.

Actually, SLN biopsy is a standard method for evaluating axillary lymph node status in early breast cancer because of the high detection rate, low false-negative rate, and the avoidance of axillary lymph node dissection. Patients with a negative SLN have an improved disease-free and overall survival, resulting in an increased quality of life with reduced morbidity.

Radioisotopes are currently the standard tracers used to identify SLNs. However, their availability is limited at some institutions, the time interval from injection to operation varies, and a special gamma detector device is required for detection.

Fluorescence imaging using indocyanine green (ICG) and the photo dynamic eye (PDE) could represent a simple, effective and safe method for the detection of SLNs in patients with breast cancer. In 2005, Toshiyuki Kitai from Nara Social Security Hospital,

Below: Female breast cancer in EU-27 countries, age standardised incidence and mortality rates, 2008 estimates. Source: International Agency for Research on Cancer, Lyon, France



Hitachi Real-time Tissue Elastography (HI-RTE) with HI VISION Ascendus

HI VISION Ascendus

HI-RTE allows the assessment and real-time colour display of tissue elasticity. The current generation ultrasound modality has proven applications in breast, prostate, thyroid and pancreatic disease and where diagnostic biopsy is indicated, HI-RTE allows more accurate localization and targeting of lesions.

The flagship of Hitachi's ultrasound platforms, the HI VISION Ascendus benefits from expert modalities such as HI-RTE for imaging tissue elasticity, and dynamic Contrast Harmonic Imaging (dCHI) technology, that enhances visualisation of tissue microvasculature after the injection of an ultrasound contrast agent.

Moreover, the HI VISION Ascendus supports new leading edge technologies and is the world's first product able to display 4-D Real-time Tissue Elastography images so the precise tumour volume can be assessed. In addition, HI VISION Ascendus offers a unique combination of tools for interventional specialists: Hitachi Real-time Virtual Sonography (HI RVS) for displaying CT or MRI images in real-time alongside ultrasound slices; Real-time Bi-Plane imaging (RTBi); and support for dedicated biopsy, intra-operative and laparoscopic transducers.

High hopes for elastography

A leading UK radiologist has highlighted how elastography has an important part to play in the future of breast imaging

Dr Bill Svensson believes that elastography has the potential to improve diagnosis of breast cancer, reduce the number of false positives in the detection of the condition and also lead to fewer biopsies performed as accuracy of imaging improves further.

This June he highlighted the potential of elastography and the developments in the imaging modality at two sessions at the United Kingdom Radiology Congress (UKRC) held in Manchester, England.

Elastography measures stiffness or strain images of soft tissue to detect or classify tumours, with a cancerous growth between five and 28 times stiffer than the background of normal soft tissue. With compression, the tumour deforms less than surrounding tissue, indicating a cancerous growth may be present.

In recent years, elastography has proved an increasingly successful tool in detection of breast cancers, primarily because of the suitability of the breast to the modality.

However, Dr Svensson remains concerned that the variability from different manufacturers in the methods available for the technique and variations in readings and colour scales, which radiologists are having to be aware of and compensate for as they take advantage of the benefits that elastography offers as a non-invasive form of diagnosis.

Dr Svensson, Reader in Breast Imaging at Imperial College London and Consultant Radiologist and Nuclear Medicine Consultant at Charing Cross Hospital, said: 'If you add elastography into your routine work, the way in which the information is applied does not necessarily transfer directly from one manufacturer to the next.'

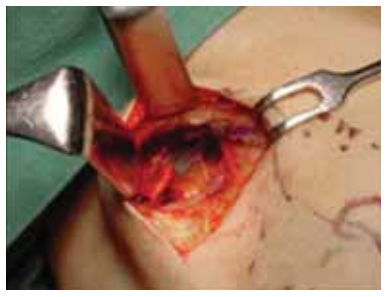
Siemens, for example, looks at the footprint from the stiffness strain image and the b-mode image, whereas Hitachi uses the Ueno (or variations of) pattern scoring method, said Dr Svensson. He believes it may be some years before uniformity between manufacturers is achieved. 'The basic idea of tissue stiffness imaging is sound. The problem is the way in which tissue deforms depends on the way in which you apply a force and there are a number of ways of applying a force to get that information. It makes elastography imaging quite complex but, if you understand the physics of the machine that you are using, then you will get better results.'

He said that, in breast imaging, elastography was allowing radiologists to detect stiffer and harder areas and is a more sensitive method of imaging. 'The ultrasound looks at those areas that deform more and those which deform less. Since we know that cancer is much stiffer than benign lesions in general and most lesions are stiffer than the fat within the breast, what elastography does is allow us to identify the stiffness.'

Advantages for the radiologist are that it provides more certainty in the image viewed and indicates what you should be getting from a biopsy result, he said, adding: 'There are potential advantages for the patient in that it will reduce the number of needle tests that we need to do, particularly when you are doing a screening examinations. If you pick up things that you are worried about, we can use elastography to downgrade the BIRADS score.

'Elastography may also inform the radiologist that the cancer is much more extensive than it looks on the b-mode, so that will raise the question as to whether a local excision needs to be increased or whether you need to be considering mastectomy. It will help determine the treatment.'

believing



IMAGES COURTESY OF PULSION MEDICAL AG

Nara, has reported this novel method for that indication [*Source: Breast Cancer (2005) 12:211-5*].

ICG, also known as Foxgreen, has been used for more than 50 years for fluorescence angiography purposes in numerous medical fields, e.g. ophthalmology, microsurgery or neurosurgery, and as Cardiogreen for cardiac surgery. It binds immediately with a very high affinity to plasma proteins and is exclusively removed by the liver. The absorption and emission spectrum of ICG is in the near infrared range. It can be detected and quantified by optical procedures.

PDE is simple to use infrared camera system designed specially to observe ICG. Because of the physical properties of ICG, images can be obtained in tissue depth up to 1.5 cm. The images can not only be used to visualise SLNs, but are also useful for perfusion detection in plastic, abdominal, and vascular surgery, as well as for lymph oedema diagnosis and surgery.

For SLN detection the fluorescence method has four major advantages over the standard radioactive technique, says Anthony Harris PhD, Manager for Perfusion at Pulsion Medical AG: 'First, it works without radiation and its danger. Second, it can be applied directly in the operating room without preoperative scintigraphy. Third, it allows reliable identification and visual localisation of sentinel lymph nodes by ICG fluorescence. Fourth, lymphatic flow can be observed transcutaneously in real time, allowing pre- or intra-operative mapping.'

The technique is quite simple Prior to the surgery, ICG is injected intradermally around the nipple. Ten minutes later, the PDE is used to observe the fluorescence of the ICG, thus to follow the lymph flow and visualise the SLNs around the tumour. The visual image helps to plan the surgery better and to avoid damaging lymph vessels. Further, the nodes can also be removed using fluorescence.

Dr Tomoharu Sugie and co-workers from Department of Breast Surgery, Kyoto University Hospital, and two other institutes, have evaluated this novel method in 411 patients with early breast cancer and report a SLN identification rate of 99% (408/411) with a mean of 2.3 nodes identified per patient. Their conclusion: 'Thus, the ICG technique has a high SLN identification rate comparable with that of the radioisotope method' [*Source: Cancers (2010) 2: 713-20*].

Dr Nobumi Tagaya and colleagues from Dokkyo Medical University, Mibu, have used this technique in 50 patients with tumours < 2.0 cm not only for SLN identification but also for image overlay navigation surgery. They conclude: 'This combined navigation of fluorescence and 3-D imaging revealed more easy and effective to detect SLN intra-operatively than fluorescence imaging alone' [*Source: World J Surg (2011) 35:154-8*].

Diethelm Wallwiener, president of the German Society for Senology, is currently planning a study to compare the standard radioisotope method with the new fluorescence method. 'Should the two methods prove comparable', he states, 'then the fluorescence method could become the new standard'.

When the medical approval for the ICG dye will be extended to the indication SLN, the fluorescence method could lead to significant cost savings for hospitals and to improved safety not only for the patients but also the physicians.

Dr Svensson also reflected on nine years of clinical experience with breast elastography and the major developments over that period. 'We have seen an increase in the quality of the imaging and the ease of acquiring the elastographic data so it has become somewhat easier to interpret and understand.'

From basic strain imaging, elastography has evolved to utilise ShearWave and ARFI (acoustic radiation force impulse) imaging - a form of high energy ultrasound - to provide a more accurate way of estimating the stiffness of the tissue being examined.

Dr Svensson believes that breast elastography has tremendous potential and that in future it may be a combination of approaches that will provide better data rather than one single approach. 'The breast has been a good place to start in terms of elastography, because it is easy to get at from an ultrasound viewpoint,' he said, adding: 'Breast ultrasound is also bedevilled by a very high false positive rate but elastography has the potential to reduce that.'

Dr Svensson also outlined new ways of using ultrasound in the breast during UKRC, including whole breast ultrasound, using automated breast volume ultrasound (ABVS) for dense breasts and women who carry the BRCA gene associated with a high incidence of breast cancer.

Report: Mark Nicholls

Single shot spectral mammography

A colourful innovation in mammography

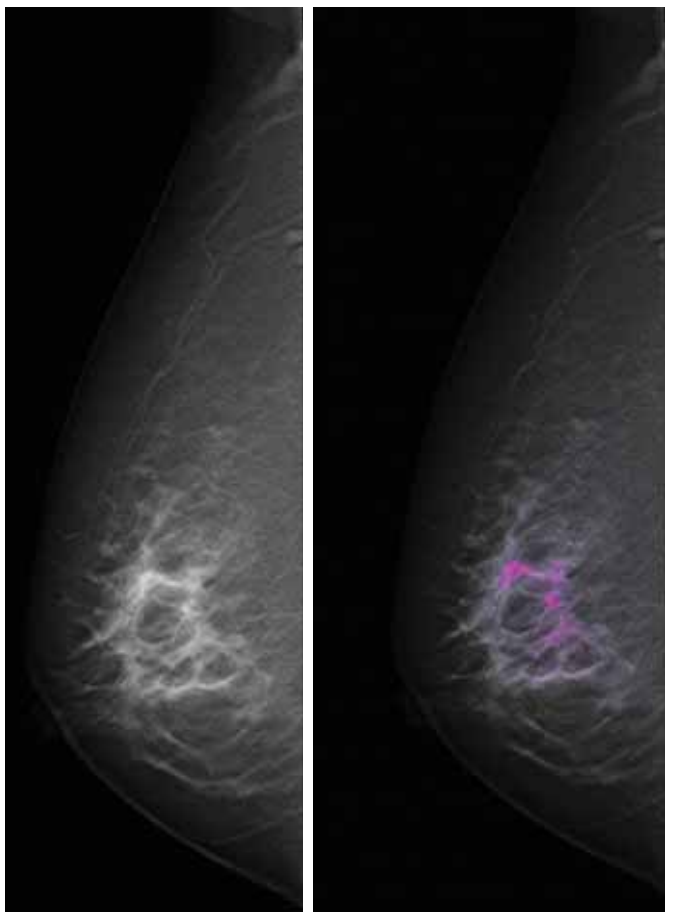
No imaging modality is infallible – not even mammography, the golden standard for early detection of breast cancer. Particularly in women with dense breast tissue, the diagnostic quality of conventional mammography frequently suffers in terms of sensitivity and specificity. However, the evolution of digital systems has produced technologies that optimise sensitivity as well as specificity and make detection of pre-cancerous masses in breasts possible.

Spectral Imaging is one of the most exciting and promising innovations in mammography. This new procedure offers possibilities in visualisation and analysis of suspicious findings that let you see the mammogram in a completely new light.

There's more to see …

While tomosynthesis gave three-dimensional insight into breast tissue, Spectral Mammography now adds information about the very nature of what we see in the image. The technology is based on the fact that X-rays consist of an energy spectrum – just like visual light gives a spectrum of colours. The way this spectrum is absorbed by the tissue allows for further analysis of the tissue characteristics.

With the unique photon counting detector of Sectra MicroDose Mammography, Spectral Mammography offers a further advantage since the mammography and the spectral image can be acquired in a single shot. Just like a regular mammogram, the examination is performed in one exposure, without compromising image quality or increasing patient dose. The Single Shot technology not only considerably shortens examination time and minimises risk of motion artifacts, but also significantly reduces radiation exposure compared to other digital mammography systems that rely on multiple exposures at different energies to acquire dual-energy images.



Iodine has been injected to enhance visualisation of the tumour. The picture on the left shows what the image would look like with ordinary mammography. In the image on the right the contrast agent has been visualised in colour thanks to the new Spectral technique, which can differentiate the iodine from other breast tissue

Some of the potential applications of Single Shot Spectral Mammography are currently being tested across Europe.

Within screening, lesion characterisation is being examined. Using Single Shot Spectral Mammography to characterise lesions brings the possibility of identifying benign cysts already in the screening thanks to additional information available in each image. This could significantly reduce unnecessary recalls for ultrasound and biopsies and lower healthcare costs.

In this image the added information available through the Spectral technique has been used to help the radiologist determine if the suspicious find is a benign cyst or not. The Spectral-detector can determine whether the mass in the mammogram consists of water or solid matter, in other cases the woman would have to be recalled for an ultra-sound to determine

There is also research ongoing within Spectral Mammography for clinical use. Contrast-enhanced Spectral Mammography is currently undergoing an evaluation at Charité, Berlin.

Clinical studies open new perspectives

Since 2010, Dr Felix Diekmann, consultant at the Institute for Radiology, Charité, Berlin, has been working with a Sectra MicroDose Mammography system with integrated Spectral Imaging technology. He is the first radiologist to test contrast-enhanced Spectral Mammography in the context of the EU-funded research project HIGHREX.

In late 2010, Professor Walter Heindel, head of the Mammography Reference Centre at Münster University Hospital, Germany, and a medical partner of Sectra, joined the study.

The Charité team in Berlin can already present exciting preliminary results of the HIGHREX study. 50 participants, for whom established procedures – clinical examination, mammo-graphy, ultrasound, MRI – had provided suspicious findings, were examined with Single Shot Spectral Mammography. 'We can already tell that the technology works well and, at least for this first participant group, offered significantly more information than conventional mammography', Dr Diekmann reports.

The study primarily compares contrast-enhanced Spectral Mammography data sets to mammography plus ultrasound. However, a further objective is the assessment of Spectral Mammography versus MRI.

There are plenty of encouraging indications that contrast-enhanced Spectral Mammography is equal, if not superior, to MRI. 'Spectral Imaging is not only faster and easier to perform than MRI, it also shows certain pathological changes, such as lobular intraepithelial neoplasia that MRI does not detect', Dr. Diekmann explains. 'Moreover, Spectral Imaging offers much higher spatial resolution, which allows enhanced evaluation of lesion morphology. Thus spectral technology might well be a cost-efficient alternative to MRI for questions such as scar or relapse or cancer of unknown primary'.

Spectral Mammography without contrast media

At this point in his clinical research, Dr Diekmann can well imagine integrating Spectral Imaging into standard mammography: 'Preliminary tests with Single Shot Spectral Mammography without contrast indicate that water imaging, similar to T2 weighting in MRI, might be possible. If these results can be confirmed, Single Shot Spectral Mammography might be suited for screening purposes, which could significantly reduce the recall rate in mammography screening. Many lesions could, without recall for ultrasound, be identified as cysts'.

Whether Single Shot Spectral Mammography will have a place in screening mammography, and in clinical work as well, remains to be seen. In the course of ongoing research projects – depending on preliminary study results – approximately 100 additional women will be examined by the end of 2011. However, Dr Diekmann is already confident that Single Shot Spectral Mammography can use established diagnostic criteria from MRI and that this innovative technology has the potential to overcome some of the current limitations of mammography screening.

Could high coffee intake cut breast cancer risk?

Oestrogen receptor (ER)-negative breast cancer remains hard to treat despite major advances in surgery and adjuvant therapies. The latest results from a Swedish study [*Pub: Breast Cancer Res. 2011 May 14;13(3):R49*] suggest that a high daily intake of coffee – more than five cups – is associated with a statistically significant decrease in ER-negative breast cancer among postmenopausal women (the median age at diagnosis of breast cancer is 61 years old).

Researchers from the Karolinska Institute in Sweden investigated the association between coffee consumption and postmenopausal breast cancer in a large population-based study of women aged 50-74, using a stratified case-control analysis treating ER status as a dependent variable, with coffee consumption included as a covariate. All 2,818 cases and 3,111 controls were Swedish born and resident at the time of the survey.

When adjusted for age only a 20% decrease in the risk for breast cancer was seen, but when the hormone receptor status of the tumours were considered the results became significant with a 57% (P= 0.0003) risk reduction for ER-negative disease and 33% (P= 0.034) for ER- and PR-negative disease. In an attempt to validate their results, Dr Jingmei Li used the same analysis procedure on results from the independent MARIE study, conducted in Germany. Although not reaching statistical significance, the strongest protective effect from heavy coffee consumption was similarly observed for the ER-negative subtype.

The Swedish group explain their findings by considering the complex composition of coffee itself.

Coffee contains trigonelline, a phyto-oestrogen that can activate ER through an oestrogen-independent mechanism. The compound is biologically active and capable of stimulating cell growth of ER-positive breast cancer cell lines at low concentrations. Coffee also has been shown to contribute to plasma levels of enterolactone, a phyto-oestrogen that has often been associated with a decreased risk of ER-negative breast cancer.

The presence of such compounds give a biological basis to support the finding that coffee consumption decreases breast cancer risk overall (both ER-negative and ER-positive), but the protection is less evident for the ER-positive subtype.

Coffee consumption has frequently been associated with the development of hormone-related cancers in women. One study found that women who consumed ≥4 cups of coffee daily had a lower risk of developing invasive epithelial ovarian cancer compared with non-coffee drinkers. Other studies have not demonstrated this association. Coffee consumption may also reduce the risk of developing endometrial cancer.

The data for the association between coffee consumption and breast cancer development is like that in ovarian cancer, variable. Several studies have found a reduced risk of breast cancer in women who were coffee drinkers while others have shown no correlation and some have even reported a (non-significant) increase. Inconsistencies in data related to the development of these hormone related cancers are likely to be due to several factors, including variations of coffee beans and preparation procedures. For example brewed coffee such as is popular in Sweden, contains complex mixtures of bioactive compounds that may have different effects based on the stage of carcinogenesis. Because of the widespread popularity of coffee, it is important to determine the effect of its bioactive components, other than caffeine, on our h*ealth.*

Report: Jane MacDougall

Dose discussion

How low can you go?

How low? During the GE Healthcare Lunch Symposium of GE Healthcare at this year's ECR in Vienna, Michael Maher, Professor of Radiology at the University College, Cork, provided an answer: 1.2 millisievert – at least for abdominal CT scans in patients with Crohn's disease

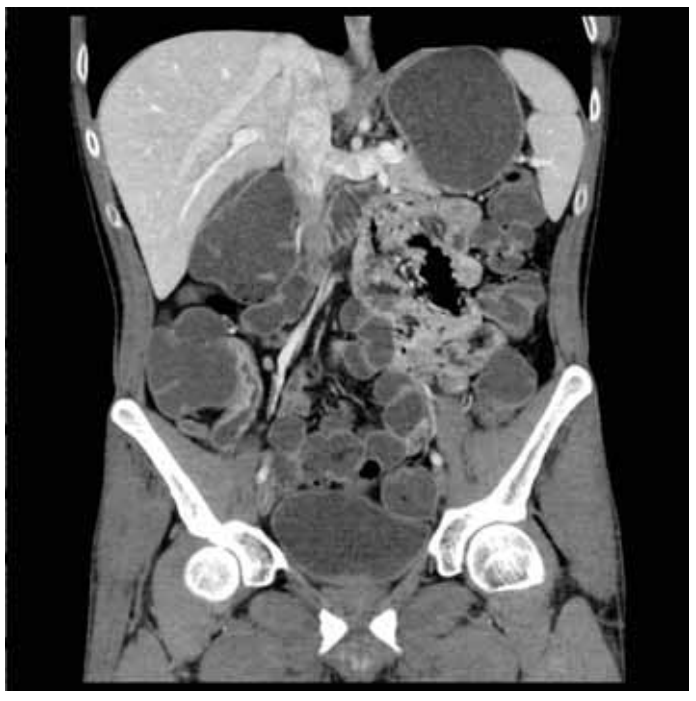
"Crohn's disease patients represent a group of patients that can need regular CT follow up exams and hence, lowering radiation dose associated with CT is vitally important in these patients. The question we studied at Cork University Hospital was how radiologists can use emerging CT technology to help these patients by significantly lowering the radiation dose per CT examination. Other centres (e.g. Massachusetts General Hospital, Boston, MA, USA) have recently reported significant reductions in radiation dose in Crohn's disease patients for CT scanning of abdomen and pelvis (CT ABD/PELVIS) using recently available Adaptive Statistical Iterative Reconstruction (ASiR). The MGH group reported a reduction in radiation exposure from an average dose of 7.7 millisieverts, to 5.6 millisieverts using ASiR.

Our ambition was to investigate the feasibility of reducing the radiation dose of CT ABD/PELVIS much more significantly, to the level approaching that of a plain radiograph of the abdomen, which is approximately 0.7 millisievert. Again, to attempt to achieve that ambitious aim, like the MGH group, we also used ASiR, which is iterative reconstruction software that reduces noise, which is inevitably found on ultra-low dose CT images. We found that ASiR successfully reduces the noise and therefore significantly improves the diagnostic acceptability of the ultra-low dose CT ABD/PELVIS images. With the iterative reconstruction technology we were able to reduce the dose to a mean of 1.2 millisieverts, which we consider to be much more acceptable level of exposure in this patient group.

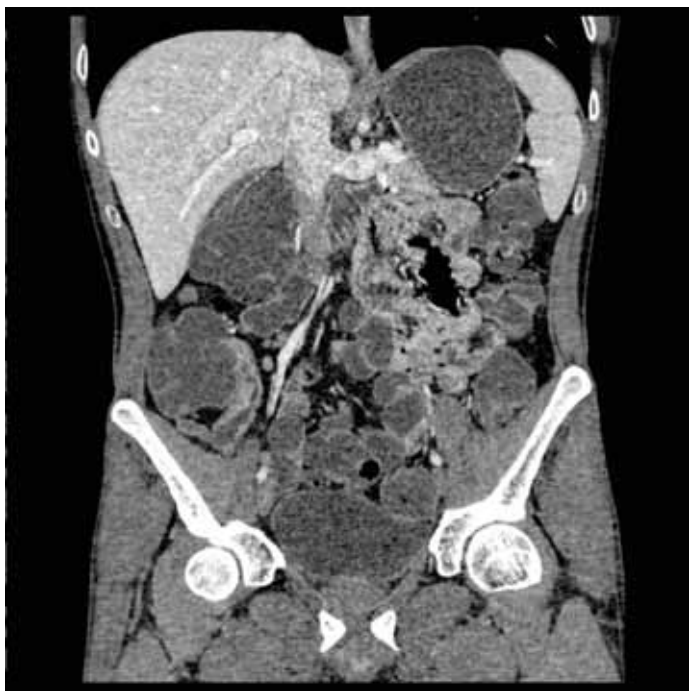
Our study includes approximately 50 patients and was prospective, and all patients recruited had two CT scans: one at a mean effective dose of 4.7 millisieverts and a second ultra-low dose CT ABD/PELVIS scan with a mean of 1.2 millisieverts. This study design facilitated a comparison of a low dose scan with an ultra-low dose scan for image quality, diagnostic acceptability and ability to detect pathological findings. We found that ASiR satisfactorily reduced image noise and produced diagnostic images of reasonable quality. All pathological findings seen on the low-dose images were also detected on the ultra-low dose images.

In our diagnostic imaging department, which serves a large tertiary referral centre, we use ASiR routinely for all CT scans, including CT scans of head, thorax, abdomen and pelvis and for peripheral and neuro CT angiography, and have been impressed by our ability to achieve radiation dose reductions while maintaining image quality."

Crohn's disease follow-up exam



FBP Reconstruction



ASiR Reconstruction
3.2 mSv* effective dose (DLP: 192 mGy.cm) 70 to 84 mAs, 120 kV
**Obtained by EUR-16262 EN, using an adult abdomen factor of 0.015*DLP and a pelvis factor of 0,019*DLP*

Adaptive Statistical Iterative Reconstruction (ASiR) by GE Healthcare

Typically, lowering dose has increased noise and image artifacts, creating an unfortunate trade-off between the high image quality and the low dose. To overcome this obstacle, GE has developed an industry breakthrough approach to image reconstruction — Adaptive Statistical Iterative Reconstruction (ASiR).

ASiR is designed to enhance image quality, increase low contrast detectability (LCD) and remove noise without degrading anatomical integrity. It overcomes the limitations of the conventional CT reconstruction approach known as filtered back projection and arrives at an optimised image using an advanced iterative computation, directly from raw data.

More than 900 GE sites are already using ASiR and more than 7,000,000 examinations have been performed using this technology.

Heading for PET/MRI

Preliminary research to integrate MRI technology with PET could lead to a brand new hybrid molecular imaging system, which would 'add the advantages of the extremely broad spectrum of diagnostic MRI procedures to the arsenal of available PET procedures,' explained the study's lead author Alexander Drzezga MD, of TU Muenchen, Munich, Germany. 'This could potentially result in the development of new imaging agents that bring together specific diagnostic strengths of PET and MRI. It offers exciting scientific options to image physiologic and pathophysiologic processes at the same time and to improve our understanding of both. This and further studies could potentially open a whole new hybrid imaging discipline within the field of nuclear medicine.'

** Scientific Paper 262, presented in June at SNM's 58th Annual Meeting (San Antonio, Texas). A. Drzezga, M. Souvatzoglou, A. Beer, S. Ziegler, S. Fürst, S. Nekolla, M. Schwaiger, TU Muenchen, Munich, Germany; 'Integrated simultaneous whole-body MR/PET: First comparison between MR/PET and PET/CT in patients'*

Innovations in non-invasive diagnostics

Although the 17 lectures delivered at this year's Medical Technology Congress in Berlin, Germany, focused on topics ranging from experimental and clinical research to routine daily diagnostic methods, the pervading interest was in the improvement, development and distribution of non-invasive imaging devices and corresponding software

In his welcoming address, **Professor Karl Max Einhäupl**, Chairperson of the Board of the Charité - University of Medicine Berlin, emphasised: 'Because of its lower risk of complications the means of non-invasive methods in diagnosing diseases become increasingly important.'


Max Einhäupl


Erwin Keeve


Johan Lock

One of these, the liver function test LiMAx, was presented by **Johan Lock** from the General-, Visceral and Transplantation surgery department at Charité Berlin. This test was invented by Charité **Professor Martin Stockmann** and developed in close cooperation with physicists at the Freie Universität Berlin.

The measuring method indicates the enzymatic activity and thereby liver function, and it is the first method to provide quantitative and immediate results at the bedside.

Aiming to replace the usual blood analysis, the entire procedure takes about 30 to 45 minutes (injection of 13C-methacetin, metabolised only in the liver, and flow-through-breath analysis).

Apart from the advantage of a real-time indication, measurement of enzymatic activity in the liver gives more precise information about liver function than the indicators of blood measurement so, for example, liver fibrosis and cirrhosis can be detected at a very early stage of disease.

The method also enables a valid calculation of the risk of postoperative liver failure in surgery by preoperative volume planning.

Finally, the test enables very close monitoring of liver regeneration.

In 2010, the device obtained CE Certification and is in use in all six university hospitals in Germany. According to **Johan Lock**, the costs for the measuring device - distributed by Humedics, a spin-off company from Charité and Freie Universität Berlin - actually amount to €50,000.

Another promising development was presented by **Professor Erwin Keeve**, from the Berlin Centre for Mechatronic Medical Technology, a joint Excellence Centre by Fraunhofer Gesellschaft and Charité. With Charité clinicians **Professor Norbert Haas**, director of the Centre for Musculoskeletal Surgery and **Professor Bodo Hofmeister**, director of the Cranio-maxillofacial Surgery department, and the company Ziehm Imaging Ltd, he and the team are developing an intra-operative X-ray imaging system that will provide a 3-D image recording method without surrounding the patient, allowing simultaneous intra-operative use of imaging.

Three dimensional imaging, while measuring less than 360 degree angle, is mathematically impossible, but the team calculated and defined the specific error function and thus could minimise and allocate the errors in imaging. 'Only the diagnose-ability has to be ensured, therefore image quality and pixel resolution can be ignored to a great extent,' Prof. Keeve explained.

In 2010, their *Orbit* project receive the innovation prize of the Federal Ministry of Education and Science, and Prof. Erwin Keeve is optimistic that he might present the first prototype in five years and finished product in seven or eight years.

Regarding the general development of new technologies, Prof. Einhäupl proclaimed in his keynote speech: 'We need a new culture of industrial cooperation that allows us to jointly develop new products – but also foresees a fair sharing of the intellectual property rights and the benefits.' The health industry takes another line in this regard, he pointed out, but he is convinced that the industry could and should be persuaded by fair sharing models, in a win-win situation for both partners in the future.

** The event was again initiated and organised by TSB medici, the medical technology division of the TSB Innovation Agency Berlin Ltd. in cooperation with the Charité Medical University and the city's chamber of commerce and industry.*

Report: Bettina Döbereiner

France ranks low in Europe for MRI equipment

On average, European countries possess 17 MRI machines per one million people. With only 9.4 MRI machines per million people, France ranks between Portugal and Turkey, putting it among the least well-equipped in Europe, according to the Société Française de Radiologie

It's not a flattering assessment and quite a paradox that in the MRI stakes its rank is so lowly, considering that France is the European country that spends the most on healthcare – second only to Germany.

France has four times less MRI machines than neighbouring Germany and two times less than Spain or Italy. In all, some 592 MRI scanners are operational (40 were installed only last year), which is simply insufficient according to radiology experts.

France stands far behind Japan, or the USA, for the best rate of equipment and falls far below its own national programme to combat cancer (Plan Cancer 2009-2013). For the optimum handling of the disease, this recommended the availability of 10 MRI scanners per one million people by 2011 and a maximum of 10 to 15 days wait for patients. In reality, the average wait still remained at 32.2 days in 2011, compared to 34.5 days in 2009, and up to 55 days – almost two months – in the most underprivileged areas (Pays de la Loire, Poitou-Charente or Alsace).

Considering the ageing population, which leads to new pathologies and new needs, it is considered that 63% of the French population is subjected to a waiting time exceeding 30 days, compared to 50% in 2006.

Since its creation in 1999, the ISA (Imagerie Santé Avenir), which gathers medical imaging information, has annually evaluated the delay before obtaining an MRI appointment. After having repeatedly pointed out the French backwardness in terms of equipment, in recent years ISA has been even more preoccupied by the increasing geographic inequalities. In some areas of the country patients might wait up to 75 days!

The low rate of MRI ownership is highly problematic. An MRI examination not performed immediately after the first symptoms of diseases that compress the spine means a patient's use of his legs might be totally impaired. Additionally, the chances of survival are greatly reduced if a patient has to wait for a few weeks of an MRI of the brain.

A new report from the ASN (Authority for Nuclear Safety) has stressed the necessity to ensure an improvement in radiological performance. In France, irradiation in the medical environment has increased by 50% over the last five years, mainly due to the multiplication of scanners. France used to trail behind in this respect, but has somewhat caught up with its neighbours in terms of equipment. Now the country has 1,200, considered quite satisfactory.

Nonetheless, the low supply of MRI scanners is regrettable, according to the French radiologists, especially because the technology uses electromagnetic energy rather than X-rays and could be used instead in a lot of cases.

Radiologists, who share with the physicians the responsibility and decisions on the most appropriate therapeutic methods to be chosen, are sorry to report that, in 2011, the Guide du bon usage des examens d'imagerie, written in collaboration with the Haute Autorité de Santé (HAS) and the Autorité de Sureté Nucléaire (ASN), cannot be applied simply because of the insufficient number of MRI machines.

For the same pathology, a German patient has three times higher chance of an MRI examination than his French counterpart. According to specialists, some 350 more machines – each costing about €1 million – will be needed in the next four or five years.

Report: Annick Chapoy

The Gamma Knife goes to work in Paris

Bladeless and bloodless, the technique falls somewhere between radiotherapy and surgery

A major public hospital has become the first in Paris to be equipped with a Gamma Knife, the device that enables the surgeon to operate on the brain with no blade or blood involved.

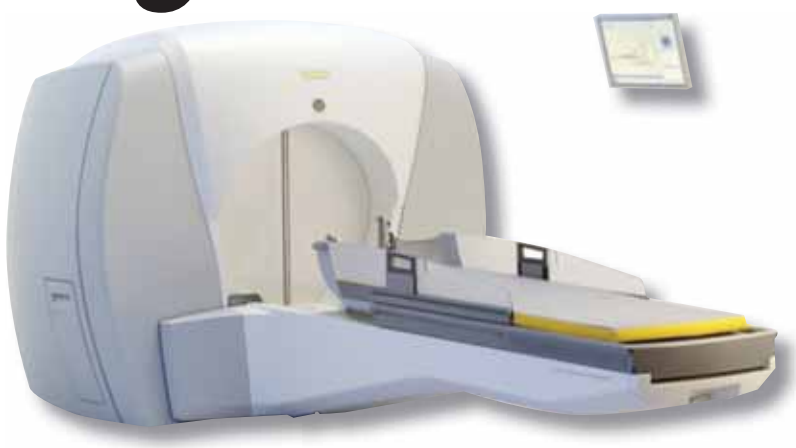
'Tumours are treated through a powerful gamma ray irradiation, a very efficient technique bringing no pain to the patient,' according to Charles Ambroise Valéry MD, neurosurgeon at the Pitié- Salpêtrière hospital and head of the gamma ray unit for the Région Ile de France (Paris and surrounding areas). 'We are talking about surgery, because a result similar to an actual surgical procedure is obtained by a one-session radiotherapy treatment,' he explains.

All the rays focus on a very specific area and the great advantage of the technique is that it only targets the diseased brain tissue, while leaving surrounding tissues intact.

Radiosurgery differs from conventional radiation therapy in several respects: with standard external beam radiation therapy techniques, tumours and much or all of the surrounding brain are treated to an equal amount of radiation. The radiation dose is given in small increments over several weeks to allow normal brain tissue to recover from its effect, while tumour tissue is less likely to recover.

Ultimately, the brain can absorb only a maximal dose of radiation, beyond which no further treatment is advisable. There is increasing evidence that over long periods of time, high doses of radiation are harmful to a normally functioning brain. However, Gamma Knife radiosurgery treats only the abnormal tissue, and that treatment occurs in a single session without significant radiation to adjacent brain areas.

In the more than 20 years since the introduction of the GK there has been no evidence that radiosurgery has led to the development of other malignant tumours. The Paris Gamma Knife is the third to be installed in France, following Lille and Marseille.



The equipment treats brain tumours by administering high-intensity radiation therapy in a manner that concentrates the radiation over a small volume

Invented in 1967 by neurosurgeon Lars Leskell, at the Karolinska Institute, Stockholm, it was developed by the Swedish public company Elekta AB.

Also known as stereotactic surgery, the technique enables surgeons to operate on brain lesions often considered inoperable, thus bringing hope to patients with brain tumours, vascular malformations or functional disorders. According to Philippe Cornu, head of neurosurgery at the Pitié Salpêtrière hospital, the Gamma Knife, acting like a sniper, can flush out an area of the brain difficult to target, in an extremely precise manner.

The equipment is huge – a two-meter high conical machine housing 192 radioactive cobalt rays (obtained from natural cobalt 59). These hit their target during a single three hour period. The multiplication of the rays, which divides the radioactive charge of the very penetrating gamma rays, enables minimal exposure to surrounding tissues.

'There's no more need for incision of the brain and trepanation, yet we get equal or even superior efficiency. We also avoid the danger of infections or excessive bleeding, which can happen with surgery,' Dr Valéry emphasises, although, he adds: 'In an emergency treatment, nothing can replace surgery.'

To avoid excessive toxicity only small tumours are treated with the Gamma Knife, and its effects can only be felt after a few weeks.

The cost of the Gamma Knife €4.7 million, is jointly supported by the AP-HP (public hospitals of Paris) and the private Rothschild Foundation. However, it brings considerable savings in terms of hospital staff and in-patient stays, according to Vincent-Nicolas Delpech, deputy director at Pitié-Salpêtrière.

Report: Annick Chapoy

Lars Leksell: *Father of Radiosurgery*

The concept of radiosurgery was developed in 1951 by neurosurgeon Lars Leksell, at Sweden's Karolinska Institute, with physicist and radiobiologist Borje Larsson.

Using the Uppsala University cyclotron, they began by using proton beams sent from different directions into one small brain area, gradually developing a technique that Dr Leskell named the 'ray knife'.

By 1968, the Gamma Knife had been developed and dedicated to radiosurgery.

In 1972, Dr Leksell and his son Laurent set up Elekta Instruments AB to manufacture the Leksell Gamma Knife and other sterotactic surgery and radiosurgery equipment based on its founder's inventions.

Today, the Gamma Knife is used effectively in many treatments.

Psycho-oncology in practice

Could a patient's state of mind affect cancer recovery?

The MediClin Kraichgau-Klinik in Bad Rappenau,Germany, specialises in cancer rehabilitation and chronic pain disorders.

Founded in 1962, the clinic has been part of MediClin AG, which has operated 34 clinics, seven nursing care facilities and ten medical care centres since 2008.

Therapeutic specialities at the 216-bed clinic in Bad Rappenau include subsequent nursing treatment and care for patients suffering tumours, the rehabilitation of chronic pain disorders and therapy for metabolic diseases.

Commenting on its awards – the *RAL Quality Mark* and the *EQR Certificate – Excellent Quality in Rehabilitation* – the clinic said: 'The objective of all treatment at the MediClin Kraichgau-Klinik is the improvement in the individual quality of a patient's life. A holistic therapeutic approach plays a fundamental role in achieving this aim.'

Having cancer is an extremely complex experience for those people concerned. Alongside the purely physiological aspects, those suffering from cancer find themselves in a highly threatening and an entirely different situation in life.

In the past, classical medicine has concentrated on the treatment of the carcinogenous changes. But what role does the patient's psyche play in treating the illness? Is there also a link to psychosocial factors in the treatment of cancer patients? Are there perhaps even some patients who have a better or worse chance of survival due to their basic mental conditioning? How closely are the psyche and social components linked to one another and to what extent do they have an influence on the recovery process? Psycho-oncology is a relatively new science that searches for answers to those questions.

Questions that are often difficult to answer because every oncological illness is different and the variables are highly diverse in nature. In addition, there is the fact that only those prospective studies that are difficult to conduct allow causal conclusions to be drawn. 'It's likely that there are many aspects where a generally accepted answer will probably never be found,' says Peter Trunzer MD, head physician at the MediClin Kraichgau-Klinik and specialist in the rehabilitation of oncological illnesses. 'The widely held belief among the general population that the psyche can trigger cancer does not appear to be confirmed by the current state of scientific knowledge. Nevertheless, we observe factors in day-to-day medical practice that positively influence the course of the illness. On the one hand, there are psychosocial variables and, on the other, the strategies employed by patients for coping with their illnesses.'

This has been confirmed by numerous studies carried out over the last few years. For the person concerned, a cancer diagnosis is associated with a death threat, an attack on their physical well-being, and a loss of autonomy, often with social isolation and the evaporation of a person's self esteem.

The first task for these people is to dig themselves out of this hole. 'If the patient receives an intensive level of emotional support from their partner or family, then this has been shown to have positive effects on the further course of the disease. The patient is ultimately less stressed,' Dr Trunzer points out.

Permanent stress has a negative effect on a person's attitude to life and on the body's own defences. It is particularly when faced with illness of this kind that the sufferer needs their physical and psychological strength in order to be able to cope with the effects of the cancer therapy – exhaustion, reduced retentiveness, sexual disorders, etc. 'All too often we must take on the role of the family. Changes in society have weakened family structures. And, particularly in large cities, we experience a high number of single-person households. In addition to psychotherapeutic approaches, we place a particular focus on precisely this aspect when training our personnel. The objective is to lovingly support and stabilise those patients in rehabilitation. However, this can only succeed if psychotherapists, clinic personnel and the clinic administration are all pulling together. We follow this approach because we experience the successes in day-to-day medical practice.'

Peter Trunzer

Newer studies have produced results supporting the practical experiences of engaged medicine. In the area of research there are also high hopes for the positive effects of tailor-made psychological and psychotherapeutic measures. Initial research findings on the psychological variables of the progression of illness in cancer patients substantiate Dr Trunzer's practical experience.

A further aspect is increasingly becoming the focus of current research studies: coping with the diagnosis. 'Our experience shows that patients who fight for their lives and deal head-on with their illness have a positive outlook on life. They perceive the strenuous treatments as a sensible means to an end. Cancer patients who give up the fight experience increased pain, become exhausted more quickly and their perceived quality of life is significantly lower,' observes Dr Trunzer, who had cancer himself 20 years ago.

In a 2003 study of melanoma patients it was possible to prove the positive influence of active-cognitive coping on the further development of the illness. Patients following passive coping strategies displayed a significantly lower chance of survival. 'We support our patients with a variety of measures for actively coping with illness. Alongside aspects for promoting a healthy lifestyle – nutrition, exercise and addictive behaviour – we also support our rehabilitation patients, in particular, on a psychological level in terms of coping with fear. The aim is to take up the fight, meaning to listen to the body, develop more awareness for a person's specific needs and to reduce stress levels.' Those cancer sufferers with a fundamentally positive outlook find this approach easier than pessimists.

The team at the MediClin Kraichgau-Klinik is convinced of the importance of psycho-oncological support. 'Our goal is to promote the recovery process of our patients at a fundamental level. Therefore, we use every opportunity to set the right course for a constant improvement of an individual's quality of life and their capabilities,' confirms Michael Schmid, Business Director of the MediClin Kraichgau-Klinik in Bad Rappenau. 'The basis for our success is the interdisciplinary approach, which sees all of our skilled personnel in the clinic applying their expertise for the good of the patient. Psycho-oncological treatment aims to draw upon the human care and attention that holds a position of great importance in our clinics. We support our patients on a daily basis in their fight against cancer – often with success.'

Source: MediClin Kraichgau-Klinik

IFCC-WORLDLAB BERLIN 2011

'Heal the world' sang the Berliner Rundfunk Children's Choir and Youth Orchestra, and thus aptly began the joint 21st International Congress of Clinical Chemistry and Laboratory Medicine and the 19th IFCC-EFCC European Congress of Clinical Chemistry and Laboratory Medicine, attracting 4,418 delegates, 2,833 visitors and 1,058 exhibiting staff to Berlin in May


Graham Beastall


Christoph Wagener


Detlev Ganten


Gregory H Reaman


Karl J Lackner


W Nicol Keith

With the motto *Fit for future – help heal the world,* the congress scientific programme covered the role of prevention, theragnostics, new technologies and biomarkers in this 'omics' era, as well as the relevance of automation and IT and education and training for future professionals in our difficult economic times.

Focusing on the *Evolution of Medicine to Evolutionary Medicine,* in his opening lecture **Professor Detlev Ganten** (Germany), President of the World Health Summit, took the audience on a journey through Evolutionary Darwinian Medicine, which understands the human body, its organs, cell function, biochemistry and genes to be a result of and living archive of evolution. By learning more of the details of those evolutionary mechanisms on a molecular and genomic basis, new vistas to a better understanding of the basis of health and diseases open up, the professor pointed out. In addition to asking proximate questions how a disease mechanism is best understood, science is now able to investigate the ultimate question: Why we become ill?

Prof. Ganten also elaborated on the burden of disease on civilization, leading to a gap between evolutionary body function and modern lifestyle in urban society.

The potential impact of individualised therapy approaches on paediatric cancer clinical research was aired during the session *Molecular Tumour Diagnostics*, chaired by IFCC president **Dr Graham Beastall** (Scotland) and **Professor Karl J Lackner**, President of the German Society of Clinical Chemistry and Laboratory Medicine. Giving the lecture, **Dr Gregory H Reaman**, Chair of the USA's Children's Oncology Group, pointed out that cells treated with GSK3B inhibitors showed repression of endogenous hTert expression, telomerase activity and decreased telomere lengths.

Given the role played by GSK3B in a variety of disease states, e.g. cancer, type 2 diabetes and of the nervous system, as well as its role in stem cell pluripotency, these data link telomerase into the emerging picture of pathways regulated by GSK3B with implications for regenerative medicine and cancer therapeutics.

Professor W Nicol Keith, from the Institute of Cancer Sciences, University of Glasgow, focused on cancer gene expression and a systems biology approach to biomarker and drug development. His research focuses on the development of novel therapies that target cellular senescence and telomerase. 'One of the fundamental changes required for tumourigenesis is escape from cellular senescence,' he emphasised. 'Strategies to induce senescence in cancer cells might provide future therapies complementary to existing interventions aimed at apoptosis.'

He believes that progress toward senescence targeted drug discovery could be accelerated by applying novel screening technologies and, particularly, cell-based screening approaches to identify and validate small molecule agonists/effectors or stabilisers of senescence. Recently, **Professor Christoph Wagener**, University Medical Centre Hamburg-Eppendorf, explained in his lecture *Post-translational modifications in tumour diagnosis* that, in the future, human glycoreceptors might be used as analytical tools to bind tumour-associated glycostructures. Since glycoreceptors are expressed in the cells of the tumour micro-environment, he concluded, the glycan structures of circulating cancer biomarkers recognized by the respective recombinant glycoreceptors might carry biological information and increase the specificity of tumour diagnosis.

** IFCC - Worldlab 2014 – Istanbul, Turkey. 22 - 27 June 2014*
Details: http://www.istanbul2014.org/

Unilabs diagnostic services

Established in 1987, Unilabs now has operations in 12 countries, employs more than 3,700 people, with 220 medical doctors, and presents the most comprehensive portfolio of diagnostic services, geographically covering a most extensive area of Europe

Unilabs integrates laboratory medicine, medical imaging, histopathology, assisted conception, and drug development services. 'The company is committed to providing efficient diagnostics with best in class procedures at the highest level of quality,' Unilabs explains.

Its clients include public and private healthcare providers (hospitals, clinics, general practitioners, occupational health units), county councils, the general public, insurance companies, the pharmaceutical industry and clinical research organizations.

European partnerships

As the leader in outsourcing in Europe, with more than 200 diagnostic contracts across the continent, Unilabs says that it has proved itself a reliable healthcare partner under different models in different countries. 'Among its public and private partners all over Europe we find city councils, physicians – to whom Unilabs offers electronic prescription in selected markets, public and private hospitals and clinics, as well as walk-in patients, for whom the company strives to offer a pleasant experience every time they walk through the doors of one of its hundreds of sample collection centres.'

Whenever joining with partners, the company says it has delivered measurable results and, to underline this, presented the following examples:

- 'In collaboration with the Oncology department in the County of Sörmland Sweden, Unilabs could shorten administration times for lung cancer patients by offering reliable result times, tailoring services to the needs of the healthcare organisation and patient, thus enabling physicians to be confident that the histopathology results are available when the patient is scheduled to visit the clinic.'
- 'At the Wirral Heart Support Centre in the UK, Unilabs succeeded in offering more effective patient-centred care following the installation of a point-of-care testing service. Clinical decisions about treatment and medication can

ROCHE on show and within reach

Roche Diagnostics showcased its full spectrum of cobas laboratory solutions at EuroMedLab this year. Visitors were given live demonstrations and shown videos of leading products for both small and large laboratories – including workflow automation, analytics and customised IT.

At desks with interactive screens they could virtually design their own laboratory, while large-sized digital posters gave a flip-through performance of the cobas catalogue to highlight the latest scientific testing efforts in oncology, cardiovascular, immuno diagnostics, and renal and bone health topics.

A virtual histology lab tour at the booth's tissue diagnostics section focused on patient-focused solutions, while the GS Junior System demonstrated its benefits as the next generation benchtop genome sequencer for applications in applied science.

Also, with the acquisition of PVT earlier this year, Roche Diagnostics presented its extended products and services portfolio with customised automation and workflow solutions for *in vitro* diagnostics.

Showcasing the Kolibri compact sorting system for small to medium laboratories, visitors were impressed by the integrated automation concept aligning with the cobas modular platform, the firm reports. 'Roche PVT enables clinical laboratories to reliably manage low to very high sample volumes and to arrange their lab space with unique flexibility,' explained Christoph Pedain, Head of Business Development and Project Management of Roche Professional Diagnostics.

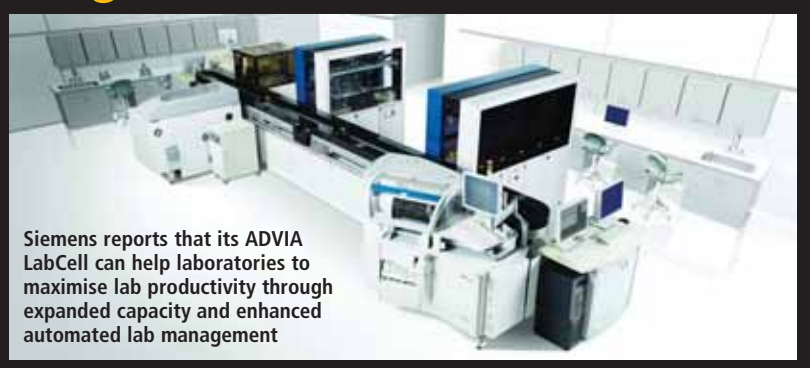
PVT and Roche have enjoyed a close partnership for over fifteen years, through which Roche has distributed PVT products, such as the RSA Pro and the RSD Pro system, in Europe, Asia and Latin America. 'Our trusted and long-term collaboration has been a key for growing success,' said Michael Ziegler, Managing Director of Roche PVT. 'At first-hand, we deliver the next generation of laboratory automation systems, now under Roche.'

Elecsys vitamin D total assay is launched

Utilising the Elecsys technology on cobas modular platforms, Roche Diagnostics presented the fully automated vitamin D total assay. This delivers '…robust clinical results from vitamin D deficiency detection to continuous patient therapy monitoring needs,' the firm explains.

Automation evolving from customers' own needs


Anne Palladino, Global Customer Care Manager, Siemens Healthcare Diagnostics


Siemens reports that its ADVIA LabCell can help laboratories to maximise lab productivity through expanded capacity and enhanced automated lab management

Adaptability and scalability were the buzz words at the Siemens Healthcare Diagnostics booth at this year's IFCC-Worldlab and EuroMedLab congress. With the ongoing generation of their high-performance automation systems as an example, the company offers a multi-discipline architecture that enables a lab team to build an automation solution following their individual demands

Represented by a distinctive track configuration positioned centrally in its exhibit, Siemens reinforced its new vision for '…total lab automation that promotes ever-more adaptable architecture, enabling lab teams to build an automation solution based on their specific testing requirements,' the company explains. 'Limitations in space are minimised because the customer can decide where to build their solution rather than being forced to fit the building to a predefined system.'

Along with its vision for how automation will evolve, the company also discussed its signature, high-performance ADVIA Automation Solutions and its compact StreamLAB Automation Solution, both of which deliver a wide range of throughput, extensive test menus, and multiple lab configuration set-ups.

'IFCC-WorldLab also served as an important stage for the latest in Siemens Diagnostic IT solutions, including ADVIA CentraLink, a data management system providing the customer with a central platform for consolidating lab data and automating workflow activities with the result of delivering faster and more secure data,' the company points out. 'It seamlessly integrates and consolidates patient and quality control data from multiple connected instruments. As a proven performer in high-volume, automated or non-automated hospital and commercial labs, ADVIA CentraLink streamlines processes and automates patient and quality control data management.'

Siemens also showcased the syngo Lab Process Manager. Now in development, this integrates process control with data management to deliver real-time information that can prompt proactive action.

The fully automated Vitamin D Total Assay

To meet increasing demands for vitamin D testing, Siemens is now offering a fully automated Vitamin D Total assay that is traceable to LC-MS/MS (liquid chromatography-mass spectrometry), considered a gold standard in testing.

Vitamin D deficiency has long been associated with rickets in children and osteomalacia in adults, and long-term insufficiency of calcium and vitamin D can lead to osteoporosis. More recently, studies are linking vitamin D deficiency to several other disease states, such as cancer, cardiovascular, diabetes and autoimmune diseases.

Siemens Vitamin D Total assay on ADVIA Centaur Systems measures a patient's total 25(OH) vitamin D level—~100% of D_2 and D_3, the two major forms of vitamin D. The most widely used indicator of vitamin D status is the measurement of the metabolite 25-hydroxyvitamin D in either serum or plasma. Because circulating 25(OH) vitamin D can arise from hydroxylation of either vitamin D_2 or D_3, measurement of total 25(OH) vitamin D (both D2 and D3) is essential for accurate assessment of vitamin D status.

Employees education with PEP

'The Personal Education Plan (PEP), a web-based teaching platform offered by Siemens as part of their Customer Care portfolio is a real premiere in the market,' the company points out. 'As the only fully customised, competency-based education software in the diagnostics industry built on knowledge, skills and job-specific laboratory responsibilities that can be accessed anywhere at anytime, PEP enables lab managers to individually assign and track their employees' personalised education paths depending on each employees' knowledge needs and specific responsibilities. And, by doing so, lab managers can better meet regulation requirements for individual competency benchmarks.'

The library itself contains all courses for all Siemens clinical laboratory products as well as information on disease states and general laboratory information. 'This promotes the possibility to perform personalised education for every level and type of work – even for hospital employees such as nurses using Point-of-Care instruments,' Siemens points out.

'The background is that clinical labs have become the gateway for new science of laboratory testing. They have become responsible to educate nurses or physicians with respect to what new assays mean and how they can be used in patient care.' explains Anne Palladino, Global Customer Care Manager, adding: 'Normally you have to invest plenty of time for training lessons without the possibility to check the individual level of knowledge. With PEP, the lab manager can decide by himself which lesson should be learned by whom and can control the results afterwards. And – the lessons can be performed anywhere and at anytime.'

now be made in a single visit, delivering lower costs per healthcare episode and leading to improved health outcomes.'

- 'Unilabs´ Mammography Department at St Göran´s Hospital in Sweden offers a holistic approach to breast patients. Every day, 300 women are received for a breast screening. All these patients will be closely followed from screening through the diagnostic procedures and clinical actions until, if necessary, the cancer finally is extirpated by surgeons.'

During its expert sessions, Derik Hermsen (Heinrich-Heine-University, Dusseldorf), Jos Wielders (Meander Medical Centre, Amersfoort, the Netherlands), Robert Hawkins (Laboratory Medicine Dept., Tan Tock Seng Hospital, Singapore) and Murat Oktem (Duzen Laboratories Group, Ankara, Turkey), presented visitors with their studies and shared their clinical experiences with the latest Elecsys vitamin D total assay.

'Big laboratories need reliable assays for vitamin D analysis in order to perform high amounts of vitamin D tests in a short time period,' said Kay Brunner, Lifecycle Leader for Cardio-Renal/ Critical Care & Women's Health, Roche Professional Diagnostics. 'The Elecsys vitamin D total assay enables better clinical decision making, providing high confidence for patient results for high convenience and efficiency in laboratory medicine.'

The cobas b 123 POC system

Marcel Gmuender, Head of EMEA/ LATAM Working Group Near Patient Testing, with Josef Hindinger, Project Leader cobas b 123, and Bernd Stoebel, Head of Project Management Hospital Point-of-Care, presented the cobas b 123 blood gas system during a trade press conference.

'The system is a fast, multi-parameter analyser, delivering many of the vital results that physicians need in order to make decisions in time critical situations,' Roche explained. 'It is primarily designed for use in intensive care units and in emergency departments and operating rooms.' The firm adds that the simplicity of the graphically guided user interface, coordinating all major workflows at a glance, impressed the journalists.

Ultra-high throughput and advanced testing methods

The new series AU5800

During the IFCC and EuroMedLab congress in Berlin Beckmann Coulter launched into Europe its AU 5800, which, the firm reports, improves processing time compared to current systems and therefore meets the demands of ever faster workflow in clinical laboratories. 'In figures, the system performs up to 2,000 photometric chemistry tests per hour for a single modus. With a four-unit configuration, labs can achieve up to 8,000 tests per hour and can gain even more efficiency by adding a dual ISE flow cell that increases maximum throughput of nearly 10,000 tests per hour.'

The system can be used as a stand-alone instrument or is designed for connectivity with the company's automation solution, further allowing for potential integration with clinical information systems and immunoassay testing platforms.

Increased clinical accuracy in PSA testing

Another highlight was the presentation of the *Prostate Health Index* (phi) featured in *European Hospital* 2/2011. This new test is reported to improve PSA measurement by combining three automated blood tests (p2PSA, total PSA and free PSA) in one index for improved specificity in estimating prostate cancer probability prior to biopsy.

When phi is installed, the analyser automatically calculates and reports the results, supporting a decision to recommend a prostate biopsy.

Presented during this year's European Congress of Urology, the first results of the clinical impact of the new tests indicate that phi significantly improves the accuracy of total and free PSA in predicting the presence of prostate cancer and in correlating cancer aggressiveness.

Lab medicine is on the move, but where exactly is it going?

Facing the fundamental changes that laboratory medicine is undergoing, in early June Roche Diagnostics Deutschland GmbH invited 50 high-profile speakers to a six-day symposium to discuss current research, economic and diagnostic issues in lab medicine with a professional audience

'*Quo vadis lab medicine?*' on which a panel discussion at the Roche Symposium 2011 was pinned, certainly presented a lively highlight that attracted representatives from private labs, hospitals, financial service providers and manufacturing. The event's patron, **Professor Rudolf Tauber**, director of the Central Institute for Laboratory Medicine and Pathobiochemistry at Charité Berlin and, this May, President of the IFCC WorldLab held in Berlin, opened the discussion by outlining the three major challenges laboratory medicine currently faces

Professor Rudolf Tauber opened up the question of where lab medicine is heading by first addressing socio-economic factors. Considering demographic developments and an increasingly well-informed public on medical options, a more proactive approach in preventive medicine and more personalised therapies are needed, he said.

His next point was that lab medicine must respond to healthcare developments such as the increase in conditions, for example diabetes mellitus or neurodegenerative diseases and the emergence of previously unknown conditions in the last few decades. 'Medical research contributes to our understanding and handling of causes of diseases and linkages between diseases on the level of molecules – even atoms. However, we must be able to translate these insights in quality-assured healthcare services.' While professional competence and knowledge in lab medicine are stunning, he added, 'we are well aware of the fact that much of our medical discipline is still uncharted territory.'

The third challenge are new technologies, he said, and is convinced that next generation sequencing, today an analytical method applied only in advanced research institutions, will soon become a daily diagnostic routine. Drivers of the technological development, the professor

At the symposium (from right), Jonas Schreyögg, Karl J Lackner, Harald Borrmann, Rudolf Tauber, Michael Müller, Klaus van Ackern and Helmut Wagner

predicted, will be miniaturisation and telemedicine.

Privatisation on the lab market

Professor Jonas Schreyögg, Director of the Department of Health Economies at Hamburg University, outlined the structural makeup of the German laboratory market.

Unlike other healthcare divisions, laboratory medicine is not a growth market in the conventional understanding of that term. While an estimated 65% of medical diagnostic services are currently provided by laboratory medicine, the number of labs in Germany continues to decrease. The business segment 'outpatient facilities' is particularly telling: a handful of lab networks account for a market share of 55%.

This concentration of revenue – and of market clout – is a result of the privatisation of labs, Prof. Schreyögg explained. Because materials and labour costs make up more than 50% of the overall costs in a laboratory, lab mergers offer very high potential for efficiency gains, for example due to discounted purchasing prices and the use of technology. Privatisation is a promising strategy above all in areas with a high degree of standardisation and specialisation.

In view of these trends, quality assurance efforts in laboratory medicine will have to be intensified. To ensure the provision of healthcare services for the entire society the lab ownership structure has to remain transparent, he advised.

At the same time privatisation is known to drive innovation and performance efficiency. Thus private actors tend to be the trail blazers who demonstrate how restructuring can be handled successfully. Prof. Schreyögg's take-home message: 'Privatisation increases efficiency in the healthcare market. However, public players have learnt from private players, which means that efficiency gains in the wake of privatisation will decrease in the future. Consequently the privatisation wave will also abate.'

Prediction and prevention

Early detection of risk factors is becoming increasingly important in preventive medicine. Thus state-of-the-art laboratory diagnostics is a crucial component of personalised medicine and in fact of the healthcare economy. It is the task of lab medicine to ensure efficient diagnostics as well as the rational application of therapies and to help avoid complications in in-patient and out-patient treatment. In short: lab medicine contributes to the reduction of disease and disease-related costs. Quick translation of new R&D knowledge into quality-assured routine procedures is thus of paramount importance.

During the audience discussion **Professor Klaus van Ackern**, managing director of the University Hospital Mannheim and dean of the Medical School Mannheim of Heidelberg University, demanded that clinical chemistry focus more strongly on genetic tasks to be able to ensure prevention and prediction. People with healthcare risks who are not acutely ill but suffer medical conditions, he said, must be recognised early and undergo preventive care.

However, **Harald Borrmann**, sales manager for lab diagnostic equipment at Roche, pointed out that academic medical institutions play a role here: 'Industry cannot fulfil this demand without help. We develop complete genome sequencing systems but we need the quality and knowledge in terms of the application and analysis of these systems. I wonder whether our training enables physicians to put the technical possibilities into practice.'

Dr Michael Müller of Medizinisches Labor Oldenburg added: 'Today we can describe the phenotype better than 20 years ago. I am convinced that we'll be able to develop tools that make therapies easier and more efficient, at least for the most important diagnoses with the most important healthcare economy implications.'

Professor Karl Lackner, President of the German Society for Clinical Chemistry and Laboratory medicine and director of the Institute for Clinical Chemistry and Laboratory Medicine at the University Hospital Mainz, agreed that laboratory medicine is on the right track with regard to prediction and prevention. Nevertheless, he said, institutions such as Professor von Ackern's teaching hospital have to bridge the gap between research, innovation and hospital care.

In conclusion, Professor Tauber emphasised that the translation of preclinical research into clinical development requires efficient recruitment and mentoring of junior professionals. 'We have to manage the transition to controlling modern diagnostic procedures. The technologies are available but we have to develop them further. However, in order to reach this goal we need qualified staff. Thus, clearly we must improve basic and continuous training and we make our discipline attractive for future generations. If we do not succeed in creating interest in lab medicine, we will not be able to turn scientific progress into daily healthcare.'

Report: Karoline Laarmann

Laboratory challenges in disasters and world tragedies

Last May, IFCC– WorldLab Berlin with its manifold scientific programme gave clinical lab physicians the opportunity to see over the rim of the tea cup of their working field. Within the congress theme 'Healing the world' came an exciting lecture on laboratory work in third world countries and disaster areas. Speaking of the challenges and issues affecting laboratory analyses in resource limited settings, Dr Cara Kosack, head of the Médecins Sans Frontières diagnostic network, emphasised: 'Laboratory resources are needed to address unanticipated disasters.'

When studying medicine in Hamburg, Germany, Dr Cara Kosack took one semester off to join Médecins Sans Frontières (MSF) on a six-month mission in Uganda, where she became involved in setting up a laboratory at a health centre and coordinating a field study to evaluate the efficacy of antimalarial drugs in children. Missions followed in Sierra Leone, Ethiopia, Pakistan and Zimbabwe, before she took up medical coordination at the MSF headquarters. From 2007 she has led the laboratory and diagnostic imaging working group in Amsterdam, the Netherlands, which also involves the coordination of lab activities in the organisation's five European headquarters.

MSF is now active in more than 65 countries. Along with medical help during chronic conflicts as well as the care given to neglected populations, emergency response is yet another activity – as occurred after Haiti's devastating earthquake that destroyed great tracts of the country and killed more than 200,000 people. Although lab procedures performed during disease outbreaks are quite different from the emergency needs in Haiti, emergency response management is similar.

MSF also deploys pre-packed laboratory modules that can be flown to disaster zones within hours. These contain, for example, blood transfusion kits that include blood group reagents, screening tests for infectious diseases in potential blood donors, centrifuges, a water bath for blood cross matching, and refrigerators. 'Blood donations can be problematic in disaster zones, not only due to limited access to equipment and a power supply, but also because of cultural differences', Dr Kosack explained. 'In African and Asian countries there are many cultural misconceptions about blood transfusion, so we often need to educate the population on the need and side effects of blood units first.'

The kinds of disasters vary as much as the contents of the pre-packed packages available for meningitis, malaria, cholera etc. Depending on need, a module or combination of modules can be selected.

Many tropical diseases faced by MSF aid workers show similar, nonspecific symptoms, such as fever, headache or general weakness in patients. Therefore, the list of differential diagnoses is long and a variety of blood tests is needed, commonly using microscopy and lateral-flow immune absorbent assays, also known as rapid diagnostic tests; depending on the disease, these are now very accurate. However, none is a 100% perfect. 'A lot of machines used in Western lab settings need constant electricity and are very sensitive to outside influences, such as heat or dust. So it's often impossible to sustain these systems in resource limited settings, not to forget the need for highly qualified staff,' Dr Kosack pointed out. 'That's why we try to achieve easy, affordable diagnostics that can be carried out not only by a trained lab technician but also by nurses.'

Lost time can costs lives, so the team often needs to start medication according to a presumptive diagnosis, initially based on the clinical picture and then on diagnostic test results retrospectively. This is particularly true for the early diagnosis of HIV in children under 18 months. For these babies, regular antibody testing cannot be carried out because they might still have antibodies from their mothers. In such cases, polymerase chain reaction (PCR) testing is needed, which involves samples being sent away to a reference lab for analysis. If the first result is positive, according to the WHO guidelines, the test is confirmed with a second sample, so the complete process takes weeks.

Dr Kosack with Giftie, a young Ugandan boy who had arrived malnourished, orphaned and with relatives all departed due to conflicts in his district. The child slept at the MSF feeding treatment centre while aid workers tried to find him a permanent home. He came regularly to the lab, where the malaria team gave him sweets and hugs. 'He was the sunshine of the hospital!' said Dr Kosack

Before a particular diagnostic test is routinely implemented into MSF laboratory work, it is very closely scrutinised. Dr Kosack and team meet regularly to discuss new diagnostic tools on the market, the performance of the regularly used tools and current and new policies in lab testing. 'We carry out literature reviews on diagnostic test accuracy evaluations from other researchers, or conduct our own in vitro studies by comparing the test of interest to a gold or reference standard,' Dr Kosack explained. 'Depending on our conclusions, we either decide for one diagnostic test method or a combination of several. For example, for HIV the use of two tests is recommended: a very sensitive test combined with a more specific test. Depending on country policy, we then carry out a third more complex test for confirmation.

'In Human African trypanosomiasis (sleeping sickness/ HAT) the diagnostic tree is even more complex and a number of tests is required to come to a diagnosis, proper staging and post-treatment monitoring of the disease. We use a screening test first and then move on to different methods for parasite detection and ultimately examination of cerebrospinal fluid for disease staging in order to decide on the right treatment strategy.'

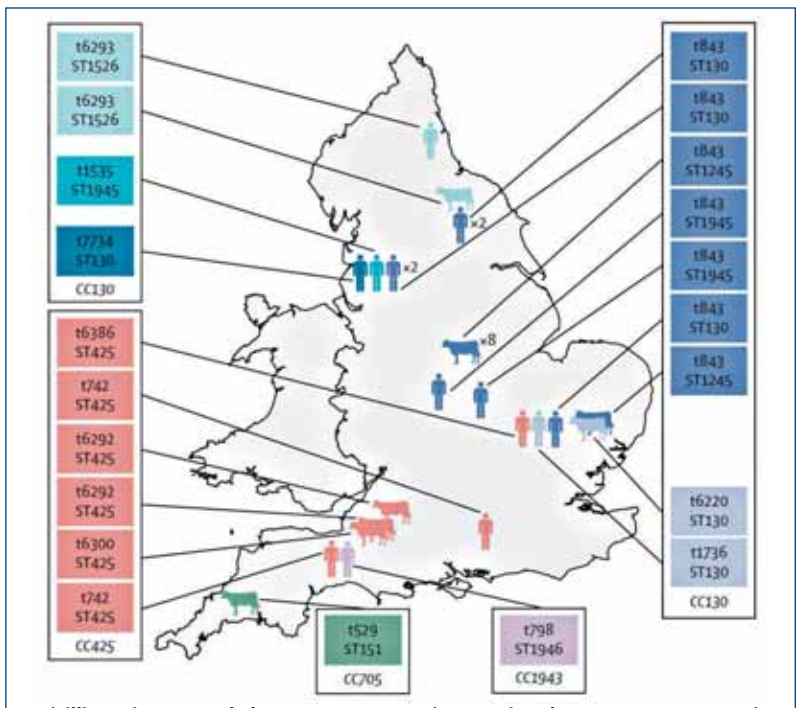
Cara Kosack, organising on day's malaria slides during her first MSF mission, in Bundibugyio Hospital, Uganda

On Dr Kosack's 'wish list' is greater effort from the biotech industry to develop simplified diagnostic tools, such as more sensitive and specific RDTs and simplified point-of-care clinical chemistry systems similar to the glucometers used daily by diabetics in the West. The need is big for quick, reliable tools from which millions of people could benefit every day.

Report: Karoline Laarmann

A new strain of MRSA discovered

Scientists have identified a new strain of methicillin-resistant *Staphylococcus aureus* (MRSA) which occurs both in human and dairy cow populations



Meticillin-resistant Staphylococcus aureus strains carrying the mecALGA251 gene in England. The colouring of the symbols and labels indicates common lineage, defined on the basis of spa typing, multi-locus sequence typing, or both. spa types and multi-locus sequence types are indicated in the labels.

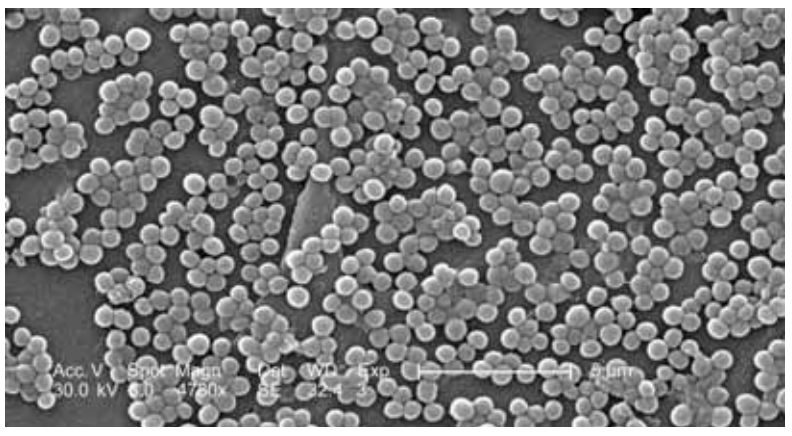
While researching bovine mastitis (an *S. aureus* infection that occurs in the cows' udders), researchers led by **Dr Mark Holmes** at the University of Cambridge, identified the new MRSA strain in milk from the dairy cows.

Despite the strain being able to grow in the presence of antibiotics, when the researchers tried to use the standard molecular tests available – a polymerase chain reaction technique (PCR) and slide agglutination testing which work by identifying the presence of the gene responsible for methicillin resistance (the mecA gene) – the tests came back negative for MRSA. The new strain's genetic makeup differs greatly from previous strains, according to the study findings published in June in *The Lancet Infectious Diseases journal*.

When **Dr Matt Holden** and a research team at the Wellcome Trust Sanger Institute sequenced the entire genome (decoding all of the genes in the bacteria's DNA) they realised that the new strain possessed unconventional DNA for MRSA. They found that the new strain does have a *mecA* gene but with only 60% similarity to the original mecA gene. Unfortunately, this results in molecular tests (which identify MRSA by the presence of the *mecA* gene) giving a false negative for this strain of MRSA.

Subsequent research revealed that the new strain was also present in humans. During the study, the new strain was found in samples from Scotland, England and Denmark (some from screening tests and others from people with MRSA disease). It has since been identified in Ireland and Germany. Additionally, by testing archived *S. aureus* samples, the researchers have also identified a recent upward trend in the prevalence of the antibiotic resistant bacteria.

Dr Mark Holmes said: 'The majority of MRSA testing in British hospitals is performed by seeing if the bacteria will grow in the presence of antibiotics, typically oxacillin and cefoxitin, rather than methicillin – which is now no longer manufactured. This type of testing detects both the new MRSA and conventional MRSA. However, it is important that any of the MRSA testing that is based on detection of the *mecA* gene – i.e. PCR based testing, or slide agglutination testing – be upgraded to ensure that the tests detect the new *mecA* gene found in the new MRSA. We have already been working with public health colleagues in the UK and Denmark to ensure that testing in these countries now detects the new MRSA.'



The new research also raises questions about whether cows could be a reservoir for the new strains of MRSA. 'Although there is circumstantial evidence that dairy cows are providing a reservoir of infection,' said Dr Holmes, 'it's still not known for certain if cows are infecting people, or people are infecting cows. This is one of the many things we will be looking into next. Although our research suggests that the new MRSA accounts for a small proportion of MRSA – probably less than 100 isolations per year in the UK, it does appear that the numbers are rising. The next step will be to explore how prevalent the new strain actually is and to track where it is coming from. If we are ever going to address the problem with MRSA, we need to determine its origins.'

Scientists at the Health Protection Agency (HPA) co-authored this paper, providing the analysis of the human samples of the new strain. **Dr Angela Kearns**, head of the HPA's Staphylococcus Reference Laboratory, said: 'There are numerous strains of MRSA circulating in the UK and the rest of Europe. Even though this new strain is not picked up by the current molecular tests, they do still remain effective for the detection of over 99% of MRSAs. This new strain can be picked up by another type of test, which has shown to be effective in trials in the UK and elsewhere in Europe.' This is, a very interesting find, she added: 'The HPA is currently involved in further research to screen a wider population of MRSA samples to ascertain how prevalent it is. It's important to remember MRSA is still treatable with a range of antibiotics and the risk of becoming infected with this new strain is very low.'

The first author of the paper, **Dr Laura García-Álvarez**, who discovered the new strain while a PhD student at the University of Cambridge's Veterinary School, said: 'To find the same new strain in both humans and cows is certainly worrying. However, pasteurisation of milk will prevent any risk of infection via the food chain. Workers on dairy farms may be at higher risk of carrying MRSA, but we do not yet know if this translates into a higher risk of infection. In the wider UK community, less than 1% of individuals carry MRSA – typically in their noses – without becoming ill.'

With funding from the Medical Research Council, the researchers will now undertake prevalence surveys in people and in dairy cattle in the UK to determine how much new MRSA is present in these populations. They will also be performing an epidemiological study on farms to identify any factors that may be associated with infection by the new MRSA, to look for further new MRSA strains, and to explore the potential risks of the new strain to farm workers.

Concerted efforts to combat prosthetic joint infections

Bacteria are highly flexible when it comes to choosing a vehicle to enter a human body. During orthopaedic surgery, they may well settle on a prosthetic joint and cause immediate or delayed infections. At the 12th EFORT (European Federation of National Associations of Orthopaedics and Traumatology) Congress this June, **Dr Andrej Trampuz**, senior physician and leader of the research team at the Division of Infectious Diseases, University Hospital (CHUV) and University of Lausanne, Switzerland, offered an update on the diagnosis and treatment of prosthetic joint infections

Joint prosthesis infections – they can happen anywhere, even in the squeaky cleanest of operating theatres and despite rigorous precautions such as perioperative antimicrobial prophylaxis.

Bacteria, airborne or through contact, reach the surface of the prosthesis where they form clusters and trigger the infection. Depending on the surgical technique and on tissue anatomy infection rates vary between 1% (knee) and 5% (ankle).

The wide range of pathogens encompasses highly virulent microorganisms such as *S. aureus* as well as less virulent microorganisms such as *S. epidermidis*. 'We distinguish between high-grade and low-grade infections,' Dr Trampuz explained. 'High-grade infections appear within three months. These acute infections require a quick response. If follow-up surgery is performed within three weeks of the first occurrence of symptoms and if the mobile parts of the implant can be replaced the prosthesis, as such, can be maintained. For the patient this means less tissue damage and less bone loss. This intervention obviously requires the infection to be diagnosed correctly.'

Olivier Borens (right) and Andrej Trampuz

Low-grade infections may even be more difficult to diagnose since the onset of symptoms can take three to 24 months. After such a long period the link between nonspecific symptoms and the surgical intervention in the past is not always immediately clear. 'It is important to inform the patients about possible infections while they are still in hospital so they can contact their orthopaedic surgeon right away when symptoms appear,' he emphasised. In the hospital, orthopaedic surgeons and infectiologists form an interdisciplinary team to treat patients with prosthetic joint infections. Dr Trampuz closely cooperates with his colleague, orthopaedic surgeon and traumatologist **Dr Olivier Borens**, who heads the Department for Septic Surgery at CHUV.

However, pain does not necessarily indicate an infection. If the implant is not placed correctly, biomechanics can cause the pain. Usually an x-ray examination and a joint aspiration are performed in order to determine whether septic loosening (infection) or aseptic loosening (mechanics) occurred. The aspired fluid is tested for bacteria. 'Since the prosthesis has to be replaced in any case the patient may opt for immediate surgery. During the procedure samples are taken from the tissue,' Dr Borens explains.

The surgeon makes two options: 'In most cases the prosthesis is replaced to preserve the function of the joint. However, this means, that the new part will also be infected. Consequently, a suitable antibiotic is needed that efficiently combats the bacteria. But the surgeon can also decide to replace the prosthesis after two, four or six weeks. In this case the microorganisms stay in the bone for some time. No matter which procedure is chosen, the type of bacteria has to be known to be able to launch the appropriate antimicrobial therapy.'

Today, the gold standard for the diagnosis of prosthetic joint infections is an ultrasound procedure called sonication, which increases sensitivity compared to joint aspiration from 60% to 90%. Since the microorganisms grow biofilms on the implants they are difficult to detect in the surrounding tissue. During sonication, rather than taking untargeted samples from the tissue around the prosthesis, the entire implant is immersed in an ultrasound bath: the biofilm is removed from the implant with the help of ultrasound.

The sonication fluid is then analysed in the lab. A resistance test is a quick method to determine the appropriate antibiotics therapy. 'If you do not have sonication equipment the removed implant can be sent to a lab where it is tested,' Dr Trampuz points out. 'In Switzerland alone we have more than twenty such centres. It is important that all orthopaedic and traumatology departments know these options so that we can increase the success rates of prosthetic joint infection therapies.'

Report: Karoline Laarmann

C. difficile increases death risk six-fold in IBD cases

Screen patients on admission!

The UK – Patients admitted to hospital with inflammatory bowel disease (IBD) face a six-fold greater risk of death if they become infected with *Clostridium difficile*, according to a new study carried out by researchers at Imperial College London and St George's Healthcare NHS Trust (pub: *Alimentary Pharmacology and Therapeutics*).

The researchers conclude that IBD patients should be screened on admission to protect them from serious illness.

IBD, consisting of Crohn's disease and ulcerative colitis, affects around 240,000 people in the UK. Symptoms include abdominal pain and diarrhoea. When sufferers experience a bout of severe symptoms, they often need hospitalisation.

Although *C. difficile* bacteria reside naturally in the gut in around two thirds of children and 3% of adults, causing no problems in healthy people, antibiotics can kill harmless bacteria in the gut, allowing *C. difficile* to flourish and produce toxins that cause diarrhoea and fever.

Measures to cut the spread of infection, such as improved hospital hygiene and changing antibiotic policies, have had some success, but high-risk patients are still not always adequately protected. Since IBD patients already suffer gut inflammation they are thought to be especially vulnerable to *C. difficile* infection, but the incidence of infection in these patients in the UK was unknown until now.

For their study the researchers examined NHS statistics on patient admissions between 2002 and 2008. After adjusting for differences between the groups, they found that IBD patients who contract *C. difficile* in hospital are six times more likely to die in hospital than patients who are admitted for IBD alone. In the patients followed in the study, the mortality rate for IBD patients with *C. difficile* at 30 days was 25%, compared with 3% for patients with IBD alone.

The results also showed that IBD patients with *C. difficile* stay in hospital longer – a median stay of 26 days compared with five days – and are almost twice as likely to need gastrointestinal surgery.

ROBERT KOCH-INSTITUT

***C. difficile* devastates IBD patients**

The study's senior author, Dr Richard Pollok, of St George's Healthcare NHS Trust, pointed out that although St. George's Hospital has seen a 70% reduction in nosocomial infections after implementing control measures such as careful hand washing and reduced use of broad spectrum antibiotics, 'We need to do more to protect vulnerable patients such as those with IBD'.

Dr Sonia Saxena, from the School of Public Health at Imperial College London, said: 'Hospitals must do everything they can to control infections such as *C. difficile*. We are asking for these high-risk patients to be screened for *C. difficile* proactively on admission to hospital so that if they are exposed, they can be diagnosed and treated more quickly.'

Childhood TB

Decreasing and rising in the EU and EEA

Although the overall rates of childhood tuberculosis (TB) are decreasing in the European Union (EU) and the European Economic Area (EEA), childhood TB is actually rising in certain countries. This March, during a two-day meeting* of at the 5th Scientific Symposium on Tuberculosis in Berlin, international experts discussed the burden, trends and impact of paediatric TB in Europe, Russia and other countries of the former Soviet Union.

In Europe, the overall trend of TB in children significantly decreased – by 2.8% – in the last decade, according to Andreas Sandgren, TB expert at the European Centre for Disease Prevention and Control (ECDC) and co-author of the first comprehensive analysis of childhood TB epidemiology in the EU/EEA. However, in certain 'low-incidence' countries (less than 20 cases per 100,000 overall population) childhood TB is actually rising. 'Up to now, we could not unravel the reasons for this increase,' he said, assuming that childhood TB in low-incidence countries is particularly sensitive to unusual outbreaks, rather than representing an overall epidemic trend as appears to be the case in high-incidence-countries. 'The impact of foreign-born children could also affect this relationship,

Andreas Sandgren

particularly if many of the cases are infected before entering the country,' he explained, adding that physicians in low-incidence countries might no longer be sufficiently aware of the problem and therefore a TB diagnosis could be delayed, and thus the spread of infection interrupted too late.

Walter Haas, who is responsible for surveillance and prevention of respiratory diseases at German Robert Koch - Institute, affirmed that various factors probably contribute to this development: 'So far, no one knows the exact reason for the increase in these countries.' In Germany, childhood TB cases increased from 1.2 per 100,000 in 2008 to 1.3 in 2009, a rise so far continuing in 2010. At the same time, although the reduction is smaller than in previous years, adult TB numbers continue to decrease.

'We have to wait and see whether this increase in childhood TB is an early indicator of a general change of trend in Germany. Perhaps this observation only corresponds to a fluctuation due to small case numbers in children, we still don't know,' Walter Haas pointed out, at the same time, however, emphasising the importance of taking the sign seriously because paediatric TB indicates recent infections. Why? In children, after TB-infection the disease progresses faster and at a higher ratio than in adults. Whether or not the increase in paediatric TB cases is reflected by an increase in infections is not clear, because the number of TB infections identified by contact tracing is not reported.

In 2009, 48.4% of all diagnosed childhood TB cases were detected by active case finding. 'These cases represent a missed opportunity, because early recognition and treatment of latent infection can effectively prevent disease in children,' he added. Physicians' TB awareness should be heightened again and consequently preventive medication should be applied according to existing guidelines to face the increasing TB incidences adequately in children in Germany.

** Organised by the Koch-Metschnikow-Forum, a German-Russian research cooperation.*

Report: Bettina Döbereiner

At war with nosocomial infections

Software that looks hard to beat

The clinical informatics firm ICNet International Ltd, which develops case management and surveillance software, has produced a software package using the SSI (Surgical Site infection surveillance) Monitor to combine information about patient movements in a hospital with data held by the laboratory and theatre systems – and to alert staff if a patient is either infected or at risk of contracting a nosocomial infection (or HAI). 'ICNet is an innovative software package that allows real time collaboration of patient and laboratory data to enable proactive infection control case management and surveillance of HAI,' explained Tom Keith-Welsh, the firm's marketing manager. 'It also provides a powerful tool for the manipulation and analysis required for mandatory reporting of these infections.'

Through interfacing with third party databases such as the Laboratory system, Patient Administration/Hospital Information system, and surgical systems, ICNet has been designed to automate the collection of data as required by the Infection Control Team.

The University of Leicester Hospitals Trust is among several British healthcare organisations to have adopted the programme. There, senior nurse Susan Davey explained: 'ICNet supports the work of the Infection Prevention Team by retrieving data from multiple systems, which saves time, because we used to search for this information. We are able to respond more quickly as microbiology results come through automatically, so we no longer have to wait until we are notified by a microbiologist.'

The system posts an alert when there is more than one positive result in a single area, highlighting a potential outbreak at an early stage

The database also enables staff to create reports on any combination of factors they feel are relevant and then pass that on to clinical colleagues. 'Antibiotic resistance information is automatically recorded, providing an early warning to resistance patterns,' she added. 'We also use the system as part of our healthcare associated infection surveillance system, which will greatly improve our reporting facility.'

Installed in Leicester in March, evidence is already emerging that the system is valuable. 'It will,' said Liz Collins, the hospital's lead nurse for infection prevention, 'lead to earlier treatment and more effective infection prevention management for our patients and will enable my team to work more efficiently.'

Eventually, the ICNet system will also be used to control antibiotic use, helping the Leicester hospital to contend with antibiotic-resistant infections.

The Royal Chesterfield Hospital, with 19 wards and 569 general and acute beds, also installed the system. There, Diane Simpson, Senior Matron (Infection, Prevention & Control), said the system has saved 14.5 hours a week for each IP team member through significant reductions in the time taken to carry out common tasks such as data analysis, creation and collection of data and patient surveillance. Effectively, there was a 40% reduction in administrative time after the installation.

Report: Mark Nicholls

Battling the bugs

National strategies to raise hospital hygiene standards

In terms of health politics, no hospital-related subject is more explosive than hygiene. However, although this reaction is common across Europe, approaches towards tackling nosocomial infections varies among our EU countries. *Karoline Laarmann* reports from Germany and *Jane MacDougall* from France...

Germany – According to various estimates, every year between 400,000 and 600,000 patients in Germany fall ill with bacterial infections contracted in the hospital. The debate around nationwide standards for hospital hygiene began in 2010, after three infants died from infections caused by contaminated injections in the University Hospital in Mainz.

The Government recently passed a law on hospital hygiene to ensure better protection against infection through obligatory hygiene standards.

However, the fact is that there are already numerous valid guidelines on a Federal and national level – the problem has been the lack of implementation to minimise infection risk. This was mainly due to a lack of staff and necessary budgets, complained Rudolf Henke, Chairman of the German medical trade union Marburger Bund: 'No other industrial nation has a staff to patient ratio as low as Germany. This is why every hospital should have a hygiene commission and a hygiene commissioner.' Therefore, he considers a national law, with new hygiene rules, is unnecessary.

The German Society for Hospital Hygiene believes the problem lies not with the legal framework but with the economic constraints: 'Increasing cutbacks have resulted in 40,000 full-time nursing posts disappearing over the last ten years. Hygiene structures and procedures have been reduced or not been safely adhered to. Within the same period, an increasing number of patients have had to be looked after for ever shorter periods of time, with the corresponding respective risks for patients,' says Barbara Nussbaum, Head of the Department for Hygiene for out- and in-patients and geriatric care/rehabilitation. The competent implementation of hospital hygiene on site can only be carried out by appropriately trained hygiene officers, the health expert adds.

Therefore, a law on hospital hygiene only appears to be a potential way of tackling the problem of nosocomial infection. Experts believe a much more essential role is played by the number of staff responsible for hygiene in hospitals along with the staff to patient ratio, as determined in the Netherlands by Dutch law.

Germany's neighbour is often quoted as an example, particularly when it comes to fighting multi-resistant bugs. The MRSA rate there is <1%. 'The intensive fight against multi-resistant bugs in the Netherlands began in the 1990s. Patients were immediately transferred to single rooms, isolated and then the pathogens were tackled. This prevented a spread at an early stage,' explains Dr Jörg Hermann, Director of the Institute for Hospital Hygiene at Oldenburg Hospital, in an interview with the news programme tagesschau.de. Additionally, over the decades the Dutch have been much stricter about prescribing antibiotics.

Nonetheless, due to the extensive structural and cultural differences, it is not that simple to transfer the Dutch hygiene strategies to the German healthcare system. In the Netherlands specialist doctors do not have their own surgeries outside hospitals. If you need a specialist there, you need to go to the nearest hospital. Furthermore, the way people deal with expert opinions is very different: 'There is hardly any legislation on nosocomial infections in the Netherlands. Whilst the Germans back up their guidelines with legal texts, the Dutch completely rely on recommendations made by commissions of experts which are not queried by anyone but simply carried out.'

The prejudice against the Germans as a nation of bureaucratic sticklers over the letter of the law once again seems justified.

France – The Ministry of Health has had a national programme to prevent healthcare associated infections in place since 1995. The original aims were to reduce the number of nosocomial infections by one third and control the levels of multi-resistant bacteria by the year 2000.

The programme was founded on four major axes: to reinforce organisation, create recommendations, train professionals and put structured surveillance in place.

The emergence of patient support groups helped legislation that became applicable to all healthcare establishments at the end of the 1990's.

This legislation has been followed up and strengthened since the beginning of this century. Legal responsibility for nosocomial infections – defined as illness caused by a micro-organism after 48-72 hours of hospital admission, or 30 days following surgical intervention – is always with the hospital.

Every institution through its Clinical Committee against Nosocomial Infections (Clin) and operational hygiene team (EOH) had to develop an action plan with two major components: surveillance and alert.

The RAISIN Network (National programme for early warning, investigation and surveillance of healthcare-associated infections) was at the heart of this strategy throughout the 2000s. This has led to standardisation in reporting techniques and data coordination so that a true picture of the nationwide epidemiology was formed.

A potential weakness in the system is the composition of the EOHs, which varies from hospital to hospital. Depending on investment in the team, its effectiveness and commitment will vary. Teams may be composed of a doctor or pharmacist specialising in hygiene, a hygiene nurse and other personnel who may range from trained bio-hygiene technicians to secretaries depending on the size and activities of the establishment. To organise and finance these teams is expensive and has to be considered as a long-term investment for the hospital.

Recently, in accordance with the HPST law of July 2009, the hospital's medical committee (CME) took over Clin, and now responsibility for patient safety, which includes nosocomial infections, is in the hands of the hospital director and the president of the CME.

The CME will define the establishment's nosocomial infection programme as part of a wider remit of patient safety. Other new measures include, since November 2010 the obligation for every healthcare institution to report a serious incidence of infection and completion of an infection check-list, with the patient's contribution before any surgical intervention.

A publicly available annual audit is also obligatory. The ICALIN (l'indice composite des activités de lutte contre les infections nosocomiales) score is a composite measure of performance against nosocomial infections. The incidence of MRSA, number of surgical infections and annual consumption of alcoholic hand rubs and antibiotics contribute to the value. Overall performance of the establishment is ranked from A to E (taking into account size and number of beds) in each of three groups: organisation, means and action.

A new society SF2H created in May 2010, which regroups all health professionals involved in hospital hygiene will now take charge of the organisation of scientific meetings and the creation of new guidelines and recommendations, a thorough survey of the problems still facing hospitals and an action plan for training, information and education.

In association with the National Programme for 2009-2013, the battle to reduce the incidence of healthcare associated infections will continue in France.

Electronic reporting in France

The external reporting of nosocomial infection has been regimented in France since 2001, Jane MacDougall reports, adding: but this has always been achieved by means of a paper trail from the health establishment via its coordination centre for the control of nosocomial infections to the Regional Health Agency, this latter organisation then informs the French National Institute for Public Health, l'Institut de Veille Sanitaire (InVS).

In 2008, InVS launched an ambitious project to convert reporting of nosocomial infections to an electronic web-based system. This project, dubbed e-SIN for 'electronic-signalement des infections nosocomiales', aims to improve the management of report handling by all parties concerned and strengthen the commitment of health establishments to reporting incidences of nosocomial infection.

To electronically report an NI, one of the hospital staff, preferably a member of the operational hygiene team in that establishment, has to connect to a secure internet site. Once connected, they fill in their report and once it has been validated internally, publishing it makes it accessible to all the necessary bodies; the coordinating centre, Regional Health Authority and finally InVS.

The e-SIN system enables all documents relevant to the case to be uploaded e.g. antibiograms, investigational reports etc. creating a comprehensive electronic dossier of the infection. The idea is that this paperless format will allow greater exchange of information between the authorities and the reporting establishment, so that the latter will be able to see the evolution of the information they provide and more easily follow the progress of their reporting.

Depending on their role, each user will have access within the limits of their rights, to reporting histories and may anonymously interrogate the national data base, extract statistics or research previously reported similar experiences.

The roll-out of e-SIN will help to reduce delays in reporting times, allowing the intermediary centres to give answers and possible aid to the health establishment concerned. Importantly, the constitution, a single, shared national database, will make analysis by InVS (approximately 1,500 individual reports per year) easier to identify potential trends in terms of emerging or recurrent outbreaks. The use of e-SIN will therefore facilitate the work of each of the players in the NI reporting system and ultimately improve patient safety.

Since 2008, a group comprising members of all the parties concerned has been in discussion with InVS to establish which data are the most relevant and important to its needs, so that the new electronic system can be as comprehensive and useful as possible.

Once the format for reporting had been agreed, 2010 was dedicated to the first series of tests of the new system. This led to the initiation of a pilot phase, currently ongoing in several health establishments in eight different regions. This pilot phase will enable the system to be streamlined and modified to remove any potential bugs before the national launch of e-SIN, scheduled for this September.

The complete switch from paper to electronic reporting is, so far, on target for the 1st January 2012. When completed, e-SIN will connect more than 10,000 users from all echelons of the healthcare system and will be the first web-based collaborative tool for reporting hospital-based infections.

It is hoped that its success will be the precursor to the establishment of similar systems for the other medical situations that InVS monitors.

Copper: The relentless killer on our side

Professor Bill Keevil (right), Director of the Environmental Healthcare Unit at University of Southampton's School of Biological Sciences, was among the first microbiological researchers to experiment on copper's efficiency against pathogenic and non-pathogenic strains of *E. coli* bacteria and demonstrate the inherent anti-microbial property of the metal. *Karoline Laarmann* asked him to explain the advantages and history of copper in medical practice

Since 2009, the copper industry set up worldwide field trials in busy hospitals in the United Kingdom, Germany, Japan, the USA, Chile and South Africa, to transfer the research findings of Professor Bill Keevil and other experts into the real world of clinical practice.

Participating hospital wards were fitted with copper alloy surfaces and samples were taken daily from those surfaces and compared with control surfaces. The results showed that the copper surfaces led to a 90% reduction of microbial numbers.

However, does copper also reduce infection rates among patients? A current US study, introduced in the beginning of 2011, is trying to ascertain just that and the initial data reveals the effects of copper are very promising.

Notably, this mineral is not new in the sphere of health. 'Since ancient times, mankind has been aware of the beneficial properties of copper to reduce microbial infections – even though people did not understand the germ theory back then, they recognised the correlation between copper and disease protection,' explained Bill Keevil. '5,000 years ago, the Egyptians, for example, used copper to transport water and to heal wounds. Later on, in the 1850s, it was noticed that, during the Parisian Cholera outbreaks, the copper workers were not affected. But while in 20th Century copper alloys were used extensively for door handles, push plates, taps or work surfaces, the development of contemporary materials, such as stainless steel and plastics, began to eliminate copper from everyday life more and more.'

Explaining how he became involved in copper research, Prof. Keevil said: 'Back in the 1980s, we started to work on copper at the Public Health Laboratory Service's Centre at Porton Down and subsequently at Southampton University, first in water systems and later on in contact systems. The reason for that were the outbreaks of Legionella bacteria, which caused Legionnaires' disease in people. As a waterborne pathogen, Legionella is disseminated through drinking water and cooling systems. It showed that if people used copper pipes, the legionella numbers were much lower.

'Then, we started to examine *Escherichia coli* O157, often nicknamed the 'burger bug' and the 'pate bug', respectively, for the food industry and again it showed that the pathogens died very rapidly on copper surfaces. At the same time, we saw ourselves confronted with the drug-resistant 'super bugs' for the first time and wondered if copper surfaces would kill these, too.

'In the first experiments we applied wet inocula (microorganisms used in an inoculation) on surfaces. These showed that the pathogens all died within two hours of contact -- when 10 million cells were on the surface. If the number of cells was reduced to 1,000 cells – in ward environments there can be low concentrations of only 1,000 super bug cells on a surface like a door handle – they even died in 15 minutes.

'We then developed a dry inoculum test to mimic hand contact. We put a very low volume of organisms on the surface, the surface dries almost immediately and the equivalent of dry contacts showed that even 10 million cells died in under 10 minutes. When we reduced the concentration of cells, they died even faster. So, what we now know is copper alloy begins to kill pathogens as soon as they touch the surface. When the surface is wet it takes between 45 minutes and two hours to kill 10 million germs and if it is a dry surface, it takes 10 minutes or less.'

How does it work? 'Copper ions, Cu(I) and Cu(II), penetrate into the cell, where they inhibit its respiration. The copper ions also attack the DNA of the cell and destroy it, so gene transfer is no longer possible. In addition, they attack the cell membrane of Gram-negative bacteria such as E. coli, so that it becomes permeable and the membrane potential collapses. What we also found is that there is a chemical reaction called the Fenton reaction, whereby Cu(I) and Cu(II) recycling leads to the production of potent reactive oxygen species such as superoxide and hydroxyl radial: these work even faster than the copper ions themselves. When we think of shiga toxin producing E. coli (STEC), such as 0157 or the new 0104 strain involved in the German outbreak, they contain the very toxic stx genes that can be transferred as part of a lambda prophage virus which infects bacteria. We know that copper kills viruses and destroys DNA, including plasmids, so this should stop the transfer of DNA, which would include those toxic genes and also the transfer of antibody resistance from one species to another.'

So, could copper replace good hygiene practice? 'No, even though copper is a smart material that works 24/7, you still need a normal cleaning practice and good staff hygiene. It just gives you an extra level of protection. It is also budget-friendly; it costs similar prices to stainless steel. So if people build a new hospital, or plan to renovate their ward completely, they should definitely consider going for copper.'

Professor Keevil will present his findings at the forthcoming WHO International Conference on Prevention and Infection Control, in Geneva on 30 June.

Killing copper

In Europe, nosocomial infections cause about 25,000 deaths every year. Copper has strong antibiotic effects and may reduce hospital acquired infections, *Holger Zorn* reports

The European Centre for Disease Prevention and Control (ECDC) estimates that, in the EU, about 3,000,000 are infected annually with multidrug-resistant bacteria and about 25,000 patients die from this. Such infections also bring extra healthcare costs and annual productivity losses of at least €1.5 billion.

'The human body is settled by more bacteria than there are people on Earth,' points out Christine Geffers MD, of the German surveillance system for nosocomial infections, which collects data on the frequency of nosocomial infections and pathogens from about 800 of 2,100 hospitals and 586 intensive care units.

An extrapolation from these data yields an estimate of 57,900 ICU-acquired infections occurring in this country each year. Roughly 10,000 of patients die as a result. Dr Geffers lists three reasons: The patient's immunity that changes during a hospital stay; the pathogenicity of the agent, and its infectivity.

In 85% of all cases, it is the patient who brings in the pathogen; in 15% he becomes infected in hospital. Again 15% of the NCI occur in an ICU, although only 3.4% of patients are in ICUs.

Among the device-related sources, mechanical ventilation has the highest risk of infection, followed by urinary catheters and central venous catheters.

A recent study of 119,699 patients admitted for more than two days to 537 ICUs in ten countries, between 1st January 2005 and 31 December 2008, could prove that ICU patients with infections caused by multi-resistant bacteria have a significantly increased mortality. One of the findings – excess risk of death from pneumonia – was 1.7 (hazard ratio; 95% CI: 1.4-1.9) for drug-sensitive *Staphylococcus aureus*; and methicillin resistant S aureus (MRSA) results in an additional risk of death of 1.3 (1.0-1.6) [*Source: Lancet Infect Dis (2011) 11:30-38*].

There are well proven links. In 2009, Klaus Kaier and a co-worker at the University Medical Centre Freiburg, found that the incidence of MRSA is positively correlated with the use of broad spectrum antibiotics and negatively correlated with the use of alcohol-based hand rub solution [*Source: Infect Control Hosp Epidemiol (2009) 30:346-53*]. And the ECDC/EMEA joint technical report *The bacterial challenge: Time to react* shows that resistance to antibiotics reaches 25% or more in several EU Member States – especially in those countries where antibiotics are available without prescription, i.e. over the counter.

Thus, surgical washing remains the principal way to prevent bacteria spreading.

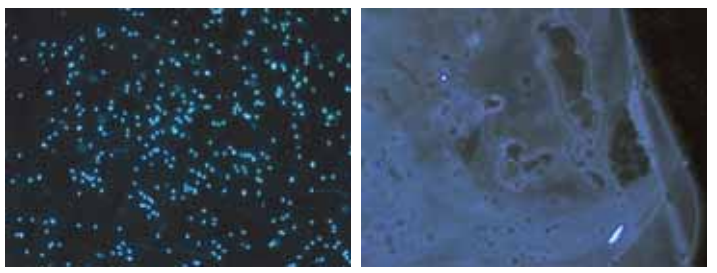
However, there is an additional promising mean: Copper and its antimicrobial properties.

Noyce and Keevil of the Environmental Healthcare Unit at University of Southampton (see article above) have studied the effectiveness of copper, brass and stainless steel to reduce the viability of three different air-dried deposits of MRSA strains. On pure copper surfaces, microbes were completely killed within 45, 60 and 90 min, respectively, at 22°C, and within six hours at 4°C.

In contrast, viable organisms for all three strains were detected on stainless steel after 72 hours at 22°C [*Source: J Hosp Infect (2006) 63:289-97*]. It seems that 'exposure to copper surfaces rapidly kills MRSA by compromising cellular respiration and damaging DNA, with little effect on cell membrane integrity' [*Source: J Appl Microbiol (2010) 109:2200-05*]. This and another result from the same authors showing that 'highly toxic E. coli survive for much shorter periods of time on copper and brass surfaces than on stainless steel', have prompted considerable interest from hospitals and manufacturers.

Sample being taken from a *cleanic* copper door handle made by the German firm Wilhelm May GmbH

COURTESY OF GERMAN COPPER INSTITUTE



COURTESY OF PROF. NIES, MARTIN LUTHER UNIVERSITY HALLE-WITTENBERG, AND THE GERMAN COPPER INSTITUTE

Six different copper alloys were examined over four days to determine their prevention of a marine bacterium colonisation under aerobic conditions, measured by microscopic counting after staining. Left: A stainless steel surface, used as the control, was colonised with increasing numbers of bacteria. Right: The $CuAl_{10}Ni_5Fe_4$ alloy shows almost no colonisation

Clinical expectations exceeded

At the Asklepios Clinic Hamburg-Wandsbek, two hospital wards were equipped for each 16 weeks in summer and winter with door handles and openers, as well as light switches, made of special copper alloys by Berker GmbH & Co KG.

The adjacent areas retained their standard handles and switches from aluminum, stainless steel or plastic. Independent scientists from the Martin Luther University Halle-Wittenberg, Germany, have taken regular samples and compared the number of bacteria on the different contact surfaces.

Professor Braun, head of the I. Medical Department at the hospital: 'The results obtained – a reduction of the bacteria by more than a third – gives hope. Contact surfaces, such as handles and switches, made from copper could thus be a useful addition to existing hygiene activities, such as hand hygiene.' Another positive aspect is the trend towards the decline of nosocomial transmission. 'This clinical effect has exceeded my expectations,' Prof. Braun commented.

Mikolay and Nies from the Institute for Microbiology at Martin Luther University Halle-Wittenberg have analysed the samples taken at Wandsbek. During both test periods of 16 weeks, the total number of colony-forming units (CFU) on metallic copper surfaces was 63% of that on control surfaces. The difference was highly significant in the CFU numbers on the doorknobs. In contrast, there was almost no difference in CFU numbers on the push plates, and the result concerning the light switches was between those on doorknobs and on push plates [*Source: Appl Microbiol Biotechnol (2010) 87:1875–1879*]. 'On copper surfaces copper ions are released in such a high concentration that the cells cannot fight them, even though they have detoxification systems for copper in their metabolism,' Nies explains.

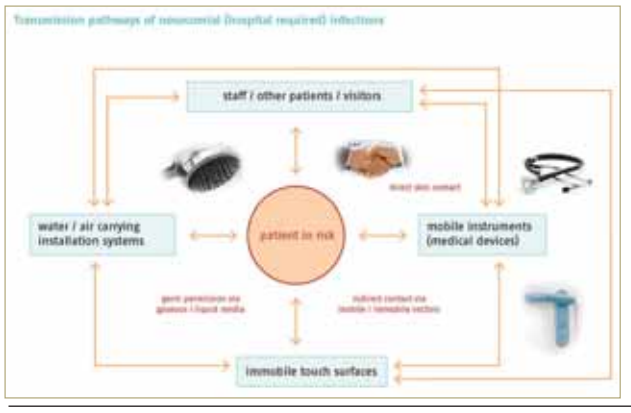
Based on those promising results, other hospitals have equipped selected departments, including ICUs, with copper items – amongst others, the Craigavon Area Hospital in Portadown, Northern Ireland, the Cancer Centre at the UMCG Hospital in Groningen, the Netherlands, and the Centre Inter Générationnel Multi Accueil (CIGMA) in Laval, France.

In addition, the first manufacturers of medical products have responded. A proposal from Heyer Medical AG in Bad Ems, Germany, titled *New applications for copper/copper alloy antimicrobial components in medical device*', has been selected by the International Copper Association (ICA) as one of six winning proposals – and the only that is not from an university – approved for funding from the more than 100 pre-proposals submitted to the ICA worldwide.

Heyer Medical's proposal was subjected to a rigorous screening by copper and technology experts, and it was selected based on a highly feasible research plan and its potential for positive impact on the global use of copper in the medical field. Klaus Schickhaus, president of the company, said, 'The replacing of certain components with copper provides further protection from infection-specific indicator organisms that continue to be a challenge in hospital and clinical environments.'

As mechanical ventilation is the highest device-related source of nosocomial infection, the 2009 launched inhalator Heyer maris III contains an aerosol tube made of a copper alloy. Also, the most touched surfaces, the handles, writing top and tray of the new anaesthesia system Heyer Ventor may also made with copper alloys – two products for two of the highest risk areas in a hospital.

The VentOR anaesthesia workstation from Heyer Medical AG is equipped with copper handles, tray and desk



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