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EUROPEAN HOSPITAL

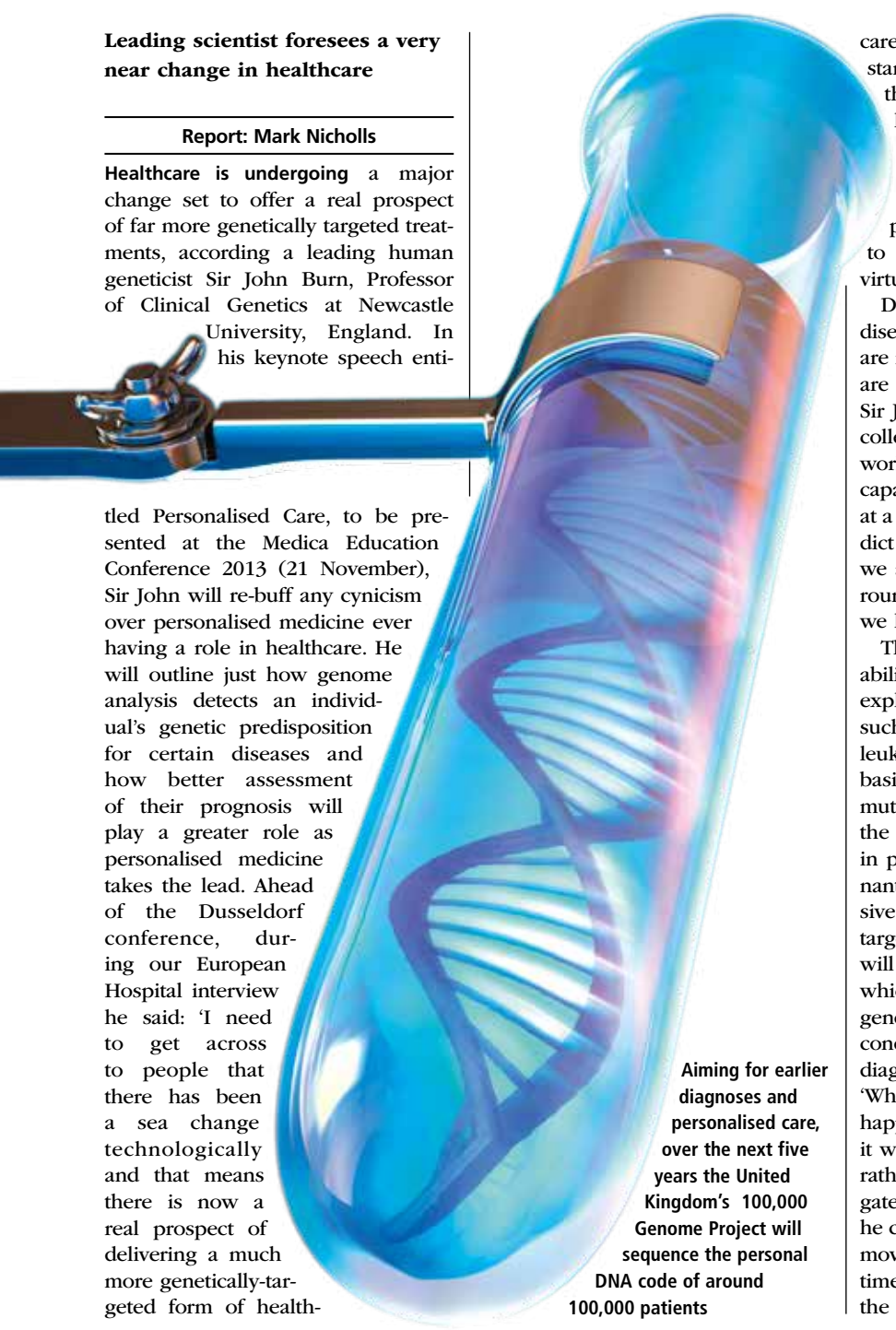
THE EUROPEAN FORUM FOR THOSE IN THE BUSINESS OF MAKING HEALTHCARE WORK

Genetically targeted medicine forges ahead

Leading scientist foresees a very near change in healthcare

Report: Mark Nicholls

Healthcare is undergoing a major change set to offer a real prospect of far more genetically targeted treatments, according a leading human geneticist Sir John Burn, Professor of Clinical Genetics at Newcastle University, England. In his keynote speech entitled Personalised Care, to be presented at the Medica Education Conference 2013 (21 November), Sir John will re-buff any cynicism over personalised medicine ever having a role in healthcare. He will outline just how genome analysis detects an individual's genetic predisposition for certain diseases and how better assessment of their prognosis will play a greater role as personalised medicine takes the lead. Ahead of the Dusseldorf conference, during our European Hospital interview he said: 'I need to get across to people that there has been a sea change technologically and that means there is now a real prospect of delivering a much more genetically-targeted form of healthcare.' There is now better understanding of the molecular level of the diseases, particularly cancer, he explained, pointing out that scientists and clinicians can now find the explanation for rare genetic syndromes and identify people's genetic predispositions to anyone of a myriad of disease virtually at will.



Aiming for earlier diagnoses and personalised care, over the next five years the United Kingdom's 100,000 Genome Project will sequence the personal DNA code of around 100,000 patients

Doctors have to recognise that diseases once considered common are now rare and that rare conditions are 'in relative terms more common', Sir John said. 'Rare diseases are now collectively a large chunk of our workload and now that we have the capacity to understand those diseases at a much more precise level and predict which ones will run in families, we are duty bound to get our heads round this in a way that collectively we have avoided before.'

This is being driven by the availability of targeted medication, he explained, and cited early examples such as treating chronic myeloid leukaemia by targeting the molecular basis of the tumour, and with B-raf mutation in melanoma, which opened the way for dramatic improvements in prognosis for patients with malignant melanoma. 'These very expensive but highly effective drugs are targeted to individual patients, which will change the whole ground on which we operate. Up to now most genetic testing has been done in rare conditions and at the end of a long diagnostic chain,' he pointed out. 'What is happening, and is going to happen even more extensively, is that it will become the first thing you do, rather than the last thing, to investigate the genetic make-up.' The shift, he continued, will also see geneticists move from looking at one gene at a time to capturing the fragments of all the genes they think are relevant to a specific disease and on to exome sequencing to capture fragments of all the genes in the coding sequences.

The ultimate step was to move to whole genome sequencing which has now fallen in price to a few thousand euros, Sir John said. Problems that he plans to identify during his address include incidental findings that suggest an individual is at risk of a genetic disorder and knowing how to tell them about it; and the need to acknowledge that subtle variations in gene expression – an area he believes is grossly under-estimated even by experts in the field – may be very important. 'Subtle variation in gene expression in many of the common diseases will not be about gross loss of gene function but will be about a particular set of genes being slightly dis-regulated and causing a discord, which is very difficult to demonstrate unless you have the most subtle understanding of gene expression,' Sir John emphasised. The professor also stated that interventions need not be expensive. For many years he has pioneered the use of Aspirin as a means of preventing cancer. 'We proved in people at the highest genetic risk that taking two aspirins a day for two years cuts their risk of cancer by 60%,' he pointed out.

His keynote speech will conclude with a focus on the UK's 100,000 Genome Project, which will sequence the personal DNA code of 100,000 patients over the next five years to help lead to better and earlier diagnoses and personalised care. He believes a major challenge is to encourage the European Union to embrace the initiative.

'Personalised medicine is so important that it won't be called personalised medicine,' he said. 'It will just be called medicine. It will be so integral to what we do.'

Sir John Burn, Professor of Clinical Genetics at Newcastle University, England, was knighted in 2010 for services to medicine and healthcare. An Honorary Consultant Clinical Geneticist at Newcastle Hospitals NHS Foundation Trust, he was Lead Clinician NHS North East until March 2013 and chairs the Genetics Speciality Group (NIHR). He is also a Director of the Collaborative Group on Genetics in Healthcare (NIHR and Department of Health), a member of the UK Human Genomics Strategy Group, Chair of the British Society for Human Genetics (2011-13), Medical Director QuantuMDx Ltd and a current member of the National Health Service (NHS) Genomics Strategy Board.

NB: Professor Sir John Burn's keynote lecture on Personalised Medicine will be delivered at the Medica Education Conference 2013, in Dusseldorf, on 21 November 2013, at 1 p.m. in CCD South, Room 3.

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relatively modern ☐ Yes ☐ No
state-of-the-art ☐ Yes ☐ No

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If so, what do you use of this kind?

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EH 5/13

EU doctors not 'trained for pain'

Despite one in five EU citizens suffering chronic pain, doctors across Europe are woefully under-educated about pain management, according to a major EU survey unveiled at The European Pain Federation (EFIC) Congress, held in Florence, Italy (October 10th).

The findings, from the APPEAL (Advancing the Provision of Pain Education And Learning) study – the first Europe-wide study on pain education, show an 'alarming' lack of dedicated teaching about pain in undergraduate medical schools in Europe, say researchers. Even medical schools with compulsory courses on pain allocate an average of only 12 hours within a six-year degree programme – just 0.2 percent of the medical student teaching time.

According to EFIC President Professor Hans G Kress, from Vienna, Austria), more than 80 million people in Europe suffer from chronic pain – meaning pain that occurs repeatedly over three months or longer. This pain, he said, is currently inadequately treated. 'More than half of chronic pain patients suffer for two years or more before they receive adequate treatment. Lack of knowledge about pain among physicians has long been recognised as a key barrier to effective pain treatment and management.'

Dr Emma Briggs, King's College London lecturer; Chair of the British Pain Society Pain Education Special Interest Group

Professor Hans G Kress, President of the European Pain Federation

The APPEAL study involved 242 undergraduate medical schools in 15 EU countries and found that 82 percent of these schools have no dedicated courses on pain that are compulsory for all students.

'With the exception of France and a handful of schools in other countries that have made headway in the provision of pain teaching, there is a striking lack of dedicated teaching on pain across Europe,' said Dr Emma Briggs, lecturer at King's College London, and Chair of the British Pain Society Pain Education Special Interest Group. 'This raises the question as to whether the provision of pain education in undergraduate medical studies is fit for purpose to address the current and growing unmet public health need.'

Based on the findings, the APPEAL researchers say that medical schools and relevant policymakers must ensure that medical undergraduate pain education is fit for purpose. They recommend the introduction of compulsory pain teaching for all EU undergraduate medical students and the establishment of a European framework for pain education, developed jointly by pain specialists and educators and drawing on the EFIC® Core Curriculum in Pain Management, to ensure consistency in pain teaching within the EU.

www.efic.org/index.asp?sub=40275570Ac7l08

Global financial crisis linked to higher death rate

Spanish, Greek, Italian and Irish suicide rates and antidepressant consumption increase

Report: Dr Eduardo de la Sota

The current financial crisis is having a major impact on European economies, especially that of Spain. Past evidence suggests that adverse macro-economic conditions exacerbate mental illness, but evidence from the current crisis is limited. However, in a recent study *(Lopez bernal et al, European Journal of Public Health, 2013)* to analyse the association between the financial crisis and suicide rates in Spain between 2005 and 2010, the researchers identified an 8.0% increase in the suicide rate since the financial crisis.

A control analysis showed no change in deaths from accidental falls associated with the crisis, which improves validity and liability of the research work. Males, and those of working age, may be at particular risk of suicide associated with the crisis and may benefit from targeted interventions.

Another article, published this year *(El Triangle, September 2013)* by J Palomés, pointed out that, according to data from the Spanish Psychiatric Association, there has been a 50% increase in suicide rates in Spain over the last three decades, jumping from 10 suicides per 100,000 population to 15/100,000.

It is true that data from the Spanish National Institute of Statistics only reports 3,180 suicides in Spain for the year 2011 (a 7/100,000 rate), but in all probability the numbers are under-represented.

The Catalonia Institute for Legal Medicine estimates increases of suicides rates, from 2009 to 2011 in Greece (37%), Ireland (16%) and Italy (58%).

Increase of antidepressants

According to Spanish Ministry of Health data, the use of antidepressants and benzodiazepines increased from 5.1% of the Spanish population in 2005, up to a 15% in 2012 – and even these data may not identify self- prescriptions, a reality we all know happens on a daily basis.

Recently, The Spanish Consumer Organisation estimated 29% of Spaniards have used antidepressants or anxiolytics sometime in the past in order to treat depressions and anxiety disorders. This evidence is stunning and, of course, reflects the high level of suffering for patients and families, as well as economic costs (including medications, use of medical services and labour losses), which even further deteriorates the health and welfare situations of Spaniards. If we add to this cocktail the fact that Spanish Healthcare Services are suffering shortages, the conclusion will can only be that global healthcare problems need global, complex and efficient solutions.

Politicians as well as healthcare professionals must act.

A growing number of National Health Service (NHS) Trusts are introducing new private treatment options to offset increased cost pressures

UK's hospitals find ways to boost income

Report: Mark Nicholls

This year a further one in six of England's hospitals started to offer patients the choice of 'self-funding' for treatments and services that are subject to restrictions or long NHS waiting times. These include IVF treatment, cataract surgery, varicose veins, carpal tunnel syndrome therapy and hernia repair. Often, these are offered at cheaper rates than in the private sector but are increasingly seen as a new revenue stream to boost hospital incomes at a time that the NHS is making stringent savings.

The data was obtained by the *British Medical Association's BMJ* journal from 134 acute hospital trusts in England. It found that 119 trusts (89%) now offer traditional private care or self-funded services, with 21 (16%) having added new self-funding or private treatment options for 2013-14. Also, among those surveyed there are also 17 hospitals (13%) that now allow patients to pay for one or more services at notional NHS rates, under the self-funding scheme. However, this shift has triggered a debate within the NHS.

Providers claim that self-funding schemes 'allowed patients to access restricted treatments at a cheaper rate than in the private sector, making care more accessible, and are fair because patients are treated exactly the same as NHS patients and any income is reinvested into the service.

Critics argue that the growth of self-funding clouds the waters between private care and the NHS by creating a two tier system and could also disadvantage NHS patients because, unlike more traditional private patients, self-funding patients are often treated in the same premises as NHS patients.

NHS Trusts that have introduced new options for patients in the past year include Warrington and Halton Hospitals (varicose vein surgery), Epsom and St Helier University Hospitals (liver scans and age-related macular degeneration) and Princess Alexandra Hospital in Essex (imaging services and chemotherapy), while Mid-Cheshire Hospitals NHS Foundation Trust also recently began to offer self-funded treatment cycles of IVF treatment for patients who used up their NHS funded cycles.

The Foundation Trust Network (FTN), which represents NHS foundation hospital trusts in England, said such self-funding schemes would not impact significantly on NHS care because most hospital trusts ran self-funded care alongside NHS care and had systems in place to ensure self-funded patients did not queue-jump if treated in the same facility.

Frances Blunden, the FTN's commercial and regulatory advisor, said: 'It is clear that the NHS is under pressure and commissioners are doing more to scrutinise referrals and are being much tighter about the treatments they fund. 'What self-funding means is that patients can get treatment that they will not otherwise receive unless they cover the cost.' She believes such schemes are not disadvantaging general NHS patients and there is a patient demand for the self-funding option. 'At a time of serious financial difficulties, this brings additional income, which helps to cover fixed costs' – and thus 'a benefit to the wider NHS organisation'. However, the King's Fund (healthcare think tank) said that regardless of price, care is still funded from patients' own pockets and driven by cost restrictions. King's Fund chief economist John Appleby believes it's 'a private scheme', essentially paying privately for NHS care. As self-pay schemes expand, he adds, they must be strictly governed and separated from NHS care to ensure those patients are not adversely affected.

David Hunter, Professor of health policy and management at Durham University, warns that self-funding schemes could herald 'a two-tier or multi-tier system that's complicated and inequitable,' and lead to commissioners and providers focusing energies on more lucrative procedures to raise additional funds.

The Foundation Trust Network (FTN) is the membership organisation for NHS public provider trusts and represents more than 200 large acute and specialist hospitals through to community, ambulance and mental health trusts. Previously a senior policy manager at the NHS Confederation, a membership body for organisations that commission and provide NHS services, **Frances Blunden**, the FTN's commercial and regulatory advisor, plays a leading role in the networks' efforts at a time when the NHS regulatory framework is undergoing constant change.

Swiss give thumbs up to Masimo's remote monitoring system

Raising small patients' safety yet reducing staff mileages

Switzerland – The safety of little children at the University Children's Hospital Basel (UKBB) has been assured since February by the installation of *Patient SafetyNet*, an advanced remote monitoring and clinician notification system manufactured by the California-based company Masimo.

Basel's multi-department paediatric facility – the first of its kind in Central Europe – has the system linked to every one of its 80 general ward beds for in-patient care. Result: Patient SafetyNet has not only augmented the children's safety but also saved nurses from lengthy, unnecessary footwork, thus contributing towards improved workflow.

Prior to this new installation, UKBB Nurse Manager Ruth Spalinger recalls: 'We had moved departments and there were stand-alone monitoring devices in the patient rooms. There were no alarms in the corridors or in the wards to alert nurses. Therefore, staff had to carry phones along, which proved to be very distracting, especially due to the high occurrence of false alarms. Nurses had to run back and forth continuously to check on alarms, putting extreme stress on staff and also hindering important bedside conversations with patients and their parents.'

Masimo's solution gives hospitals exactly what they have been asking for to improve patient safety – a clinically proven and cost-effective system that requires no additional nursing resources.

When an alarm went off, she added, a nurse arriving in the ward where it had been activated could not quickly identify which patient's bed was involved, and the measurements were not archived, she told *European Hospital*: 'This situation had to change – and we designed a strategy for improvement.'

The one and only manufacturer

An extensive evaluation process resulted in the hospital's standardisation to Masimo SET pulse oximetry. 'Masimo was the only manufacturer willing to provide equipment and services according to the tall requirements we had defined,' Ruth Spalinger points out. 'This included handling artefacts – meaning false alarms produced by patient movement. Masimo offered us a system that measures through the artefacts and results in dramatically fewer false alarms.'

Today, UKBB's new, non-invasive monitoring devices provide continuous measurements of patient functions, such as oxygen saturation and pulse rate, and, optionally, breathing rate – a value only measured by nurses in the intensive care unit and during anaesthesia.

Based on the data set produced by the device, a "Halo" index is generated – meaning an indicator developed by Masimo that facilitates the assessment of multiple physiological parameters to quantify changes in patient status. A readout ranging from 1 to 100, with a higher number indicating a higher risk, gives clinicians a quick assessment of each patient throughout the ward; patient movements do not impair results, thus clearly eliminating false alarms. All data are stored for 30 days, before they are overwritten. Important sequences can always be stored via PDF for means of patient documentation.

When values no longer match the individual HALO norm, an automatic alert is transmitted wirelessly direct to clinicians. Sensibly, those alarms are generated even before some alarm limits are reached, so that patients can be checked far sooner. The staff is also aided by readouts enabling them to judge the level of urgency in each situation.

A tangible change for the best

'Installation of the Masimo system has resulted in significant improvements regarding patient safety and it has greatly reduced the staff workload, allowing nurses to concentrate on their task of caring for patients instead of doing miles on foot,' the Nurse Manager confirms. 'We've observed that the system is particularly beneficial for our most vulnerable patients, who potentially suffer from respiratory depression.' The staff, she adds, is 'extremely satisfied with the system' including physicians who are distracted no longer by audio signals during their ward rounds.

'In many hospitals, decision makers think that implementing remote monitoring in general wards is highly complex, resource intensive and expensive,' says Paul Jansen, Masimo's Vice President of Marketing and Development. 'The unique implementation at UKBB has demonstrated the feasibility of Patient SafetyNet which, among other aspects, allows hospitals to utilise remote monitoring with an unchanged number of staff.' This hospital is leading the way, he adds, and many other care providers will soon follow suit.

Ruth Spalinger believes that 'remote monitoring based on systems such as Patient SafetyNet could help reduce the number of patients admitted to ICUs'. 'Across healthcare systems, large numbers of patients are sent to intensive care because they need to be monitored. In general wards, just like the situation was at UKBB, suitable monitoring is not available. This could be changed by the widespread implementation of the Masimo system, reducing risks for patients and also significantly cutting costs.'

Future integrations

Speaking of new developments: 'We can now connect Patient SafetyNet with hospital information systems (HIS),' he affirms. 'This allows us to feed patient demographics from the HIS into our system; and, with automatic communication of values to the HIS, manual charting by nurses might may become a thing of the past.'

Ruth Spalinger, Nurse Manager at Universitäts-Kinderspital beider Basel (UKBB): 'Installation of the Masimo system has resulted in significant improvements regarding patient safety and greatly reduced our staff workload.'

Typically, pumps that deliver medication are not connected to any alert communication system – 'now, these pumps can also be connected to Patient SafetyNet, with an icon on the application screen presenting alarms. There's increased interest for such a solution in the market,' Paul Jansen points out. Integration will be realised through Masimo's Root patient monitoring and connectivity platform.

In conclusion: As our meeting in Basel draws to a close, Paul Jansen declares: 'Far too many preventable deaths are still happening in hospitals today. Masimo's solution gives hospitals exactly what they have been asking for to improve patient safety – a clinically proven and cost-effective system that does not require additional nursing resources.'

The Masimo system allows nurses to concentrate on their task of caring for patients instead of doing miles on foot.

Masimo's Vice President of Marketing and Development Paul Jansen believes that decision makers in many hospitals think that remote monitoring implementation in general wards is highly complex, resource intensive, and expensive, but confirms that 'the unique implementation at UKBB has demonstrated the feasibility of Patient SafetyNet'.

PATIENT SAFETYNET

This solution combines Masimo SET pulse oximetry, which enables reliable patient monitoring in a general ward, with ventilation monitoring and wireless notification of clinicians.

Patient SafetyNet helps to ensure patient safety by non-invasively and continuously measuring and tracking underlying physiological conditions and changes that indicate a declining health status in real time.

When changes occur in the measured values, the system automatically sends wireless alerts directly to clinicians – prompting a potentially lifesaving response to reach the patient's bedside quickly. Patient SafetyNet has been clinically shown to reduce preventable and costly rescue situations, transfers to ICUs and deaths related to opioid-induced respiratory depression.

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7.5% reduced funding for medical analysis laboratories

Despite on-going negotiations with the Government, the Union for Medical Biologists has received a nasty surprise that threatens up to 8,000 jobs in the sector

Report: Jane McDougall

This summer the French Cour des Comptes (Court of Auditors) ruled that, in order to help balance the healthcare budget, currently standing at a €7.9 billion deficit, medical laboratory testing should be held accountable.

In its 164-page report the Court ruled that one of the main reasons behind the 'explosive increase' in laboratory medicine spending was linked to a redundancy in testing. The Court claims that, if just hospital testing was reduced by 10-15% then the Social Security (Assurance Maladie) would save between €200 to €300 million per annum. The Court also decided that, overall, too many medical tests are performed in France and claim much of this is due to duplication,

suggesting that once tests have been performed there is no need to repeat them. It also showed that the overall number of tests is increasing exponentially and, as an example, demonstrated that testing for vitamin D has seen a 60% increase in volume over the past 10 years.

To reduce spending on laboratory testing it suggests that laboratories cut their tariffs by 7.5%, a move that would cut lab business by €316 million, saving Social Security €220 million a year. Since 2006, the price of laboratory tests has been revised downwards regularly, much against the wishes of biologists, who would prefer stabilised pricing.

Biologists' unions fear that this drastic saving is irresponsible and would have further repercussions on laboratory medicine leading to 8,000 job losses in the sector and force smaller laboratories in rural areas to close, potentially reducing the areas' quality of care. Arguments on the economic value of medical laboratory testing will be discussed on the final day of the JIB meeting in Paris this November and also is the focus of our interview on pages 28-29 of this issue of European Hospital.

In conclusion, the magistrates recommend that there be increased control over spending in medical analysis despite the fact that, in the overall healthcare budget, lab tests account for less than 2% of the total costs and yet are involved in 60% of diagnoses.

Nutrition and Health

Sponsored by seca Precision for health

Pulling in crowds at ESPEN 2013

seca's Bioelectrical Impedance Analysis (BIA) Workshop

The fact that BIA is now very much accepted by nutritionists was underlined by the capacity filled seats and 50 people standing for the seca BIA Workshop 'Bioelectrical Impedance Analysis in Malnutrition and Obesity: Meet the Experts'. Held recently during the 35th ESPEN Congress on Clinical Nutrition & Metabolism 2013 (ESPEN) in Leipzig, nutritionists heard talks presented by leading experts and researchers who work with BIA for body composition analysis.

'Information gained from BIA in the diagnosis and treatment of nutrition-related diseases is now recognised around the world,' Martin Höfler, team leader of seca Product Management, explained, adding that analysis of body composition using BIA 'will also have an influence on diabetology and nephrology'.

Dr Anja Bosy-Westphal, Professor at the Institute for Nutrition at the University of Hohenheim, Germany, described the benefits of using BIA in the treatment of overweight patients. BIA raw data, such as the phase angle and Bioelectric Impedance Vector Analysis, help to provide an estimate of body composition in cases of obesity, she explained.

In her lecture Dr Kristina Norman, nutritionist in the Department of Gastroenterology, Infectiology and Rheumatology at the Charité medical university in Berlin, Germany, covered the applicability of BIA for malnourished patients. The BIVA in particular, she said, delivers valuable information to detect malnutrition caused by disease and helps to monitor patients' nutritional therapy.

None other than Dr Manfred J Müller, Professor and head of the Institute of Human Nutrition and Food Science, Christian-Albrechts-University in Kiel, Germany, and Dr Marinos Elia, Professor at the Institute of Human Nutrition and Faculty of Medicine,

University of Southampton, Southampton General Hospital, UK, co-chaired the workshop and led the lively follow-up discussion.

'The medical Body Composition AnalTer seca mBCA 515 features state-of-the-art analysis technology. The innovative device achieves unmatched medical precision, according to international studies* in which the technology was validated against medical gold standards,' the manufacturer reports. 'The seca mBCA is intuitively operated and specially designed for working conditions in medical practice. The integrated electrodes on the device's railing, for example, prevent measurement errors and ensure reproducible results.'

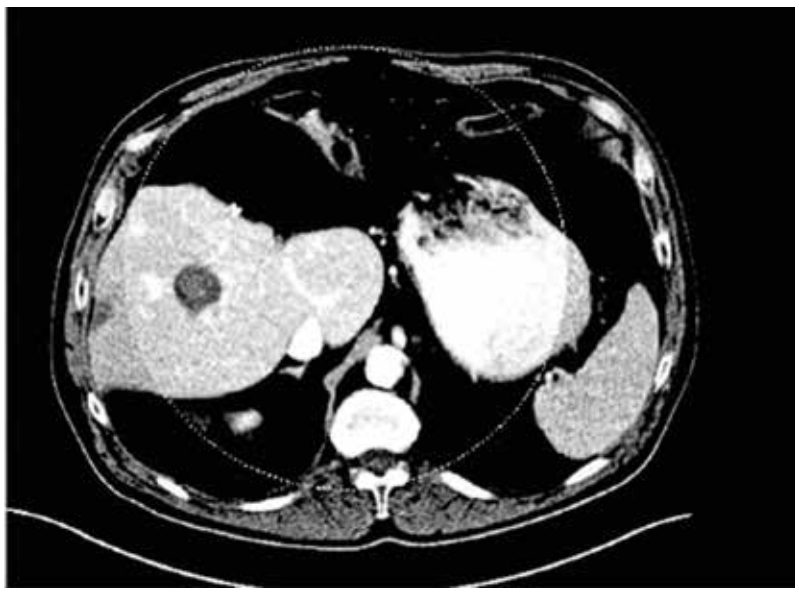
The device can also be integrated in the seca 360° wireless system and in computer networks in medical practices and hospitals.

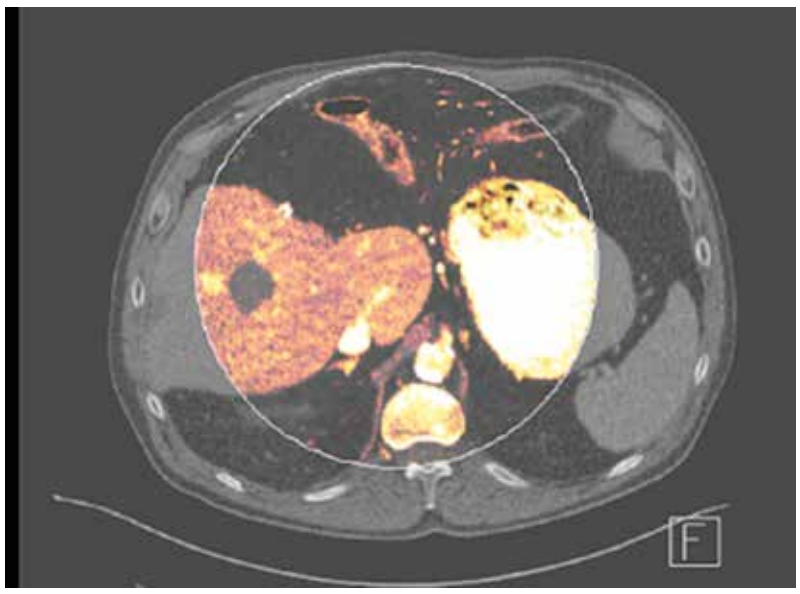
* Details: www.seca.com/studies

seca mBCA at mbca.seca.com

Precision technology raises the stakes in the hunt for tumours

Faster scanners, more parameters, better markers…





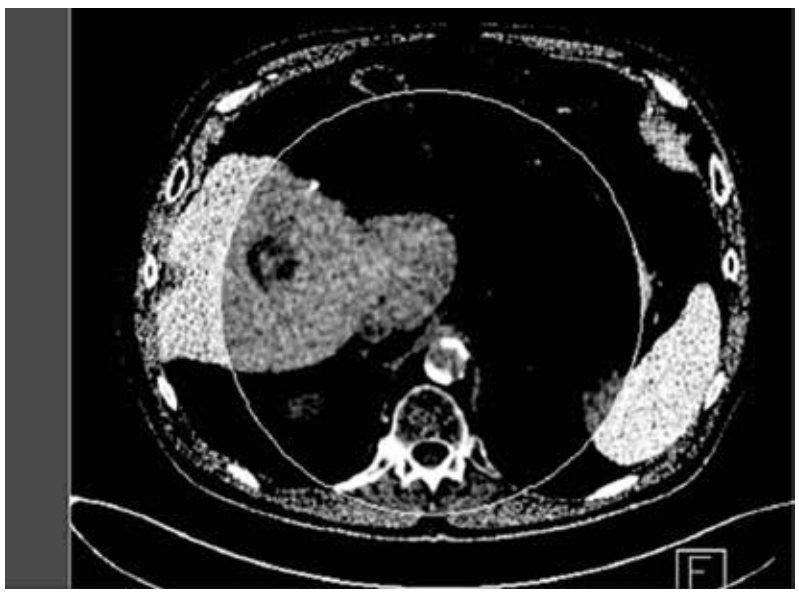
With MRI and CT scanners widely available in clinical routine, radiologists cull increasingly precise and relevant functional tumour information for diagnostics and monitoring purposes. Both modalities offer technological and methodological approaches, initiated by the discipline itself, that have become indispensable for certain frequent tumours. In primary diagnosis of prostate cancer for example multi-parametric MRI is a clinically established procedure today while dual-energy CT is about to become standard operating procedure for monitoring the response to gastrointestinal stromal tumour (GIST) or renal cell carcinoma therapy.

'Multi-parametric prostate MRI usually analyses four parameters: morphology using T2-weighted imaging and cellular density using diffusion-weighted imaging; MR spectroscopy provides information on the metabolism and contrast-enhanced imaging shows increased perfusion due to angiogenesis, that is new and immature tumour vessels,' explains Professor Stefan Schönberg, Director of the Institute of Clinical Radiology and Nuclear Medicine at the University Hospital Mannheim, Germany.

The European Society of Urogenital Radiology (ESUR) has published guidelines for multi-parametric prostate evaluation that include a classification system for structured reporting. Based on the individual scores of the four parameters, the final score allows the classification of the tumour according to its degree of malignancy.

Dynamic contrast-enhanced imaging involves the very fast acquisition of 3-D sequences with continuous contrast media injection and the analysis of three quantitative parameters: the wash-in rate indicates average blood flow, the mean transit time is usually shorter in tumour tissue and contrast differences between the intravascular space and interstitial tissue due to weak vessel walls. While the results of contrast-enhanced MRI cannot yet exclude tumour development, Prof. Schönberg says 'data from animal studies indicate that special volume CT scanners that offer extremely high spatial resolution can visualise angiogenesis at a very early stage. Moreover, there are targets that, in combination with substances visible in positron emission tomography, are directed towards avß3 integrines. These are structures that are typically associated with angiogenesis.'

Contrast-enhanced dual energy CT of a 70-year-old patient with GIST and liver metastasis: Stereotactic radiofrequency ablation, an interventional imaging procedure, was performed on the metastasis. In the four-month follow-up scan, standard CT images show enhanced lesion density that usually is associated with tumour progression (left).
The iodine related attenuation image created from the dual energy CT data volume shows the iodine in the tumour. Here, no increased iodine enhancement (right) is visible. The non-contrast image, created virtually from the same dual energy CT data volume, indicates that peri-interventional bleeding in the tumour caused the density visible in the standard CT image. Based on the additional functional and perfusion information provided by the iodine image of the tumour the patient was correctly classified as 'partial response' since the metastasis was entirely devascularised.



Anti-angiogenic substances inhibit tumour growth

Neovascularisation, which in a way is the basis for tumour formation and above all tumour growth, is stimulated by the release of vessel growth-promoting substances such as vascular endothelial growth factor (VEGF). Today, attempts are made to 'starve' the tumour with new biological substances, such as tyrosine-kinase inhibitors, on a molecular level.

When conventional tumour therapies fail or when highly vascularised tumours are present, anti-angiogenic substances are used either by themselves or in combination therapies – an important substance being Imatinib. 'These developments present us radiologists with new tasks. We have to monitor the efficacy of the substance over the course of the therapy with a functional diagnostic,' the professor explains, adding that in this respect MRI has a disadvantage: used with contrast media and with high temporal resolution it can visualise only very small volumes. CT on the other hand offers two different but very interesting approaches.

'Firstly, there is 4-D CT, dynamic volume CT with a moving table, which very much like 3-D MRI acquires sequence images with contrast media and can quantify the three perfusion parameters already mentioned,' he explains. 'Secondly, there is dual energy CT, which allows us to extract iodine information quantitatively as a marker for tumour perfusion – without increased radiation exposure. This approach has entered clinical routine for one tumour – GIST. We will elaborate on this approach in a multi-centre prospective study. Dual energy CT may indeed trigger a change of paradigm in general healthcare,' Prof. Schönberg concludes.

* Reprint from 'RöKo HEUTE 2013', the official publication of the German Radiology Congress

A medical graduate from Ruprecht-Karls-University, Heidelberg, **Professor Stefan Schönberg** then trained in radiology at the German Cancer Research Centre. In 2001 he joined the Institute of Clinical Radiology at Ludwig Maximilian University, Munich, initially as senior consultant and head of the MRI unit and later as managing senior consultant. Since 2007 he has directed the Institute of Clinical Radiology and Nuclear Medicine at the University Hospital, Mannheim.
His research focuses on vascular and abdominal imaging, functional MRI, high-field MRI and oncological imaging.

Vendors worked

Report: Cynthia E Keen

Nuclear medicine (NM) is the second largest source of medical radiation exposure after CT. However, patients who had a NM examination a decade ago most likely received a higher radiation dose than a patient in 2013. Over the past few years the efforts of vendors and providers began to make NM exams safer.

Initiatives by vendors and diagnostic imaging professionals to reduce radiation dose to patients undergoing a CT exam have been underway for many years. The global *Image Gently* campaign to reduce radiation dose exposure to children first started with CT. The campaign's website now includes nuclear medicine, as does the Image Wisely campaign targeted at adults.

However, nuclear medicine professionals still consider dose awareness in molecular imaging to be in its infancy, according to Dr Frederic Fahey, Director of Nuclear Medicine/PET Physics of Boston Children's Hospital and Dr Adam M Alessio, research associate professor of Radiology at the University of Washington in Seattle. They co-chair the SNMMI Dose Optimisation Working Group of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) – the largest international scientific organisation dedicated to molecular imaging and therapy, with over 18,000 global members. The organisation's five most important issues were listed in the society's outgoing presidential lecture delivered at its 2013 annual meeting in Vancouver. One of these 'Top 5' issues related to radiation exposure concerns. A second focused on the need to continue to develop, improve, and promote the use of evidenced-based and patient-centred guidelines as well as the appropriate use of nuclear medicine. The need to educate about dose optimisation has become so important to SNMMI that it established a dedicated section in its online resource centre *(www.snm.org)*.

Patient-specific dosimetry can reduce radiation dose because it is calculated specifically for the characteristics of a patient's body. For the first time in 30 years, a new generation of reference computational phantom model for standardised internal and external dose calculations have been defined. Introduced in 2012, these image-based models of variously sized adults, children, and pregnant women replace second-generation anatomic models.

The Radiation Dose Assessment ResourceTask Force's RADAR phantom series is being implemented in standardised software for internal dose calculations. This will be used to produce new standardised dose estimates for radiopharmaceuticals and other applications.

Associate professor Michael G Stabin PhD, of Vanderbilt University School of Medicine chairs the RADAR Task Force. In a keynote lecture at SNMMI's annual meeting, he emphasised that patient-centred dosimetry should be globally adopted, especially with the tools becoming available. All patients will benefit, especially obese patients.

Nuclear medicine

and providers have to make examinations safer

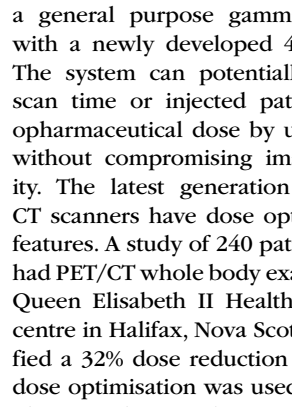
Today more than 300 million people are obese – and these need special protocols. Diagnostic quality exams can be difficult to obtain, hindered by soft-tissue attenuation and inadequate body coverage. New models of cadmium-zinc-telluride (CZT) systems for nuclear cardiology, such as the GE Healthcare Discovery NM 530c, have radiation dose reduction features and can significantly reduce scanning time by two to three times, reducing the risk of motion artefacts.

HybridSPECT/CT scanners, such as GE's Optima NM/ct 640, combines a general purpose gamma camera with a newly developed 4-slice CT. The system can potentially reduce scan time or injected patient radiopharmaceutical dose by up to 50% without compromising image quality. The latest generation of PET/CT scanners have dose optimisation features. A study of 240 patients who had PET/CT whole body exams at the Queen Elisabeth II Health Sciences centre in Halifax, Nova Scotia, identified a 32% dose reduction when CT dose optimisation was used. Medical physicist Elena Tonkopi wrote in the *American Journal of Roentgenology* article (August 2013) that the dose reduction was achieved with a faster X-ray tube rotation time, increased X-ray beam coverage, and higher noise index value.

The improvements in noise reduction software algorithms make it possible to obtain images of comparable quality using a low radiation dose as those images acquired with 'standard protocol' doses. Some software, such as that offered by UltraSPECT with wide beam reconstruction (WBR) image reconstruction technology for cardiac and bone applications, can be used with currently installed camera systems. A study of 462 patients presented by physicians from New York City's St. Luke's Roosevelt Hospital, at September's annual meeting American Society of Nuclear Cardiology (ASNC's), found that 77% of the SPECT/PET myocardial perfusion imaging used with a half-dose protocol were below a radiation dose of 9 mSv, exceeding ASNC's new 2014 low dose guidelines. At the SNMMI meeting, Siemens introduced a new scanner, the Biograph mCT Flow. Dr James Williams, CEO of Siemens Healthcare's molecular imaging business unit, stated that this is the first PET/CT system to offer continuous motion PET/CT scanning. Its anatomy-based FlowMotion technology moves the patient through the systems gantry while continuously acquiring PET data. When combined with its ultra HD•PET, a routine scan can be performed in five minutes. CT radiation dose can be reduced as much as 32%.

Philips' Astonish TF PET system has a new detector design and architecture, and incorporates time-of-flight functionality and patient motion management with respiratory and cardiac gaited imaging. The Ingenuity TF PET/CT allows low X-ray dose techniques without distortion and incorporates iPatient dose management tools.

New systems; new software for protocol planning and reconstruction; new patient-centric dosimetry models – a global NM radiation dose reduction may be only just beginning, but it's heading in the right direction to make these exams safer for patients.



Dr Frederic H Fahey has been director of nuclear medicine/PET physics at Boston Children's Hospital since 2003. He is also an associate professor of radiology at Harvard Medical School, and was President of the Society of Nuclear Medicine and Molecular Imaging in 2012-2013. He is actively involved in the paediatric *Image Gently* and adult *Image Wisely* campaigns to reduce radiation dose exposure to patients receiving nuclear medicine examinations. His research interests include PET and SPECT instrumentation, image processing, reconstruction of tomographic data and radiation dosimetry, particularly as they pertain to paediatric nuclear medicine.

Enhancing the patient experience

Report: Michael Reiter

When it comes to hospital choice, patients no longer rely on their doctor's advice alone. Improved health literacy and a growing awareness of potential risks (e.g. hospital acquired infections, medical errors) are encouraging patients to choose carefully by considering the quality of care delivered, patient satisfaction scores, patient safety and comfort in general.

Meeting patient expectations

The view that the overall patient experience is strongly linked to the level of satisfaction means patient expectations are rising rapidly. Add to this the growing influence of social media and other online tools used to influence a patient's choice of hospital, and it's clear that healthcare providers are exposed to greater levels of scrutiny and under pressure to deliver a better performance.

Although most healthcare providers do not shy away from their responsibility to improve the patient experience, they are facing enormous challenges due to severe cost cuts and a growing shortage of skilled medical professionals. These challenges are the driving force behind efforts to improve the efficiency and delivery of care – and, hence, the patient experience.

Interactive patient care

To fully address these key priorities in healthcare, Barco, a leader in healthcare IT systems, has developed the industry's only completely integrated offering for interactive patient care, raising clinical productivity and patient comfort to the next level. The solution, called CareConnex, is powered by Hospedia, the world's largest operator of point-of-care bedside software.

CareConnex is a patient entertainment and communication system delivered over a range of touchscreen all-in-one smart terminals. Critically, it includes an advanced software interface and all associated accessories and systems required for installation in the patient room. CareConnex also serves as an interface for clinicians to access electronic medical records, hospital information systems and other healthcare applications at the point of care. Focusing on the intersection of patient-centered care and clinical efficiency, CareConnex enables healthcare providers to position themselves for success.

Barco's CareConnex solution offers a choice of touchscreen smart terminals to install in patient rooms, from which patients and clinicians can access a host of applications.

Personalised patient experience

In a highly competitive healthcare market, patient-focused services are becoming increasingly important, and healthcare providers are willing to invest in solutions that put patient comfort first. After all, patient satisfaction is a valuable indicator of the quality of care delivered.

Barco's patient entertainment system offers these services at the touch of a button. TV, radio, Internet, games, and other media applications are accessible directly at the bedside. The system also serves as a dedicated patient portal, featuring self-service options – including room and bed control, electronic meal ordering, and satisfaction surveys – and digital educational resources to improve clinical outcomes.

As a proof point of what Barco is able to provide, the CareConnex Smart Terminals form the front end of a pioneering networked bed concept installed at the Alexianer Krefeld Hospital in Germany. In addition to full patient entertainment and communication services, patients can control their beds and access hospital management functions through the terminals. Using existing IT systems and infrastructure within a hospital, CareConnex can be deployed to improve everyday clinical routines too. In most hospitals today, a host of IT solutions such as HIS, EMR and PACS are already in place, but their benefits are often not fully realized. Often inaccessible at the point of care, these systems do not allow sharing of patient data at the bedside which can result in duplicated efforts and inefficiency.

CareConnex addresses this by providing a user-friendly IT platform directly at the bedside, from which staff can access a range of clinical applications, including HIS, EMR, PACS, blood results, e-pharmacy and patient admission systems – without facing the security and maintenance issues that are typical of mobile devices. This way, substantial measurable improvements in clinical efficiency can be achieved.

'Offering multimedia entertainment, CareConnex enhances our patients' quality of life during their stay with us. They can improve their comfort too, by adjusting their own beds using a single touch screen interface.'

Michael Wilke, Managing Director, Alexianer Krefeld Hospital

Tapping into new revenue streams

CareConnex creates new opportunities to improve hospital profitability as well as efficiency. The solution allows providers to offer and promote paid services that are personalized to the patient, such as video-on-demand, TV bundles and gaming to help generate additional revenue.

Capitalizing on the opportunity for patient interaction, the system offers dynamic advertising options – respecting the sensitivity of the hospital environment – to recommend particular brands and to communicate the hospital's values and qualifications, gaining patient trust and adding to the overall care experience. In a time when healthcare reform discussions are the order of the day, interactive solutions – such as Barco's CareConnex – hold the key to the transformation of the delivery of care.

Medical images improve treatme

Hans Vandewyngaerde has a sweeping vision for visualising healthcare: images from anywhere made available anytime to anyone involved in a patient's care.

Report: John Brosky

What sets Agfa Healthcare apart is that the firm not only has the tools and experience to get the job done, but also is now helping to realise this vision at major regional and hospital centres.

As President for Europe, the Middle East and Africa (EMEA) for Agfa HealthCare, Hans Vandewyngaerde intends to leave no image behind in the quest to bring digital medical images to the electronic medical record (EMR).

With hospitals still trying to figure out text-only EMRs, why should they also think about imaging?

'Today there are more and more digital imaging devices being used in the hospital setting,' he explains. 'These include endoscopy, pathology, even digital photos used for wound care. They significantly add to a trend for medical imaging outside of the traditional sources, such as the radiology or cardiology departments, to be used by clinicians outside of the image acquisition departments.'

Who would utilise this visual information?

'Everybody! The concept behind image-enabling the EMR is to give everyone a view. Clinicians, nurses, the patient's physician and even the patient, all sharing the same clinical information, the same clinical images.'

So, what's holding up this progress?

'There are boundaries from a functional perspective of how images are acquired. Imaging sources are fragmented; they can now come from everywhere in the hospital or in a service region, even from other hospitals. And imaging data is stored in silos linked to the different departments of care. There are boundaries between these departments inside a hospital, such as radiology, cardiology, endoscopy and so forth. And there are boundaries outside a hospital with other hospitals.

'This challenge has been recognised and there is a desire to move beyond radiology as the only source for clinical imaging,' he says. 'We have the example in France, where there is a funding by the national government to stimulate image sharing among hospitals within a region. We also see this in the United Kingdom, where there are Trusts forming consortia to stimulate greater image sharing. In the Nordic countries or the Netherlands there is now a great focus on integrating the clinical departments to collect clinical imaging. In all fairness, the main driver is also cost reduction next to improved patient care and we believe it is indeed possible and the right moment because technology is not the blocking factor any more.

Considering the cost of creating a text-driven EMR, how can a hospital justify adding images to those records?

'The efficiency gains. Today every department acquiring images in a hospital has a separate system for managing and archiving those images, some of which the hospital is not even aware. Moreover, these images are rarely available outside of the department. Add all this up and compare it with a centralised management/access and the gain is there, as well as a return on the investment,' he explains.

'Meanwhile, back in the various departments there is also a cost for someone to manage and maintain those separate image management systems. By centralising these tasks, there is a gain for staffing in a department. Hospitals who are deploying

Agfa HealthCare's ICIS brings images without boundaries to EMR

within clinical reports ent decisions and patient care

A member of Agfa HealthCare Executive Committee, **Hans Vandewyngaerde** is driving change across the company's EMEA sales and services organisation, building on his success as General Manager of several European countries and Agfa Healthcare IT organisations worldwide. He also serves as a member of the board for the trade organisation COCIR, member of the HIMSS Europe Governing Council, and was a founder and board member of Integrating the Healthcare Enterprise - Netherlands.

the system can see this and are convinced. Interestingly, hospitals that have not yet implemented any kind of EMR are already considering Agfa HealthCare's ICIS (Imaging Clinical Information System) because they believe they'll see a return on the investment just to manage all the imaging records already out there.'

Imaging: the missing piece in medical records

'There are clear cases showing the efficiency of treatment and diagnostic quality increases when clinical images are added to a patient record. This quality of care is what's missing in the EMR. I cannot speak about clinical effectiveness, because physicians will need to examine this aspect and publish studies, but we know from hospitals where images have been integrated with the EMR that there are significant advantages from a financial and workflow optimisation perspectives, and certainly from a patient perspective.'

At radiology exhibitions like RSNA in Chicago or ECR in Vienna, many companies say they can add images to records.

'It's true; many companies talk about this, but are they talking about image-enabling the EMR or just image management? Is it just viewing images? Or are we talking about the capture of images already out there? Are they talking about the distribution of the images? Archiving images? Are they addressing the workflow behind the images?

'Image-enabling the EMR is not just about viewing or archiving or distribution alone, it is about all of these combined within one comprehensive workflow. Here Agfa HealthCare is clearly well positioned with ICIS because we address all of these components. We also bring an experience of 13 years, with projects we have successfully completed, with programmes we are helping to develop, and in facing challenges that truly are unique and require the different components we have brought together with ICIS.'

Given Europe's fragmented landscape, could a single package meet their diverse needs?

'It would be a mistake to think of ICIS as a package, a one-size-fits-all product. In Europe, or anywhere else, there is no such thing as a universal EMR, or even the same approach for EMRs. There are different levels of development, different speeds of implementation, different financing methods, network performance issues, legacy systems or specific requirements for managing change.

'The ICIS approach,' Hans Vandewyngaerde adds, 'offers solutions that are modular, meaning we have created bricks for building a solid foundation by standardising common components that can be connected as required. They are generic enough to serve the entire hospital while still allowing specific requirements for each of the departments. ICIS also brings a workflow engine that adapts to the different needs of hospital departments.

'But, before you start building you need to decide what bricks best fit your design. Integrating ICIS is not about selling the bricks but assessing where the organisation is ready for change, the readiness of diverse departments, whether current systems and the digital devices are ready to share images.

'This programme approach and methodology makes Agfa HealthCare stand out as unique when combined with ICIS.'

A plea for stronger strategic cooperation between individual diagnostic

Now is the time to poo

Cooperation between the individual diagnostic fields of radiology, pathology and laboratory medicine has increased in daily clinical routine over the last few years.

To a large extent, the three disciplines are faced with the same requirements and problems. They are interdisciplinary specialties that must satisfy the requirements of their clinical colleagues through the provision of diagnostic procedures, and they are present at almost all tumour conferences.

Digitisation facilitates an exchange of data to obtain second opinions as well as teleradiology and telepathology. *European Hospital* asked Dr Gabriel Krestin, Professor of Radiology and Chairman of the Department of Radiology at Erasmus Medical Centre in Rotterdam and Past-President of the European Society of Radiology (ESR), whether now is also time for the individual European specialist medical societies to close ranks.

Prof. Krestin believes there has been stronger strategic cooperation between individual diagnostic disciplines for some years, beginning in the USA. This cooperation has a substantial as well as political level: 'Driven by technological developments, diagnostics has become increasingly complex, which leads to a situation where the requesting medical disciplines can no longer keep up with developments and lose their overview. Therefore, it would certainly benefit all sides if the diagnostic disciplines act together and pool their knowledge.' he explains.

'This movement towards integrated diagnostics was already discused two years ago at the International Society for Strategic Studies in Radiology (ISSSR) symposium – incidentally with strong support from the industry itself.

'In the USA, such diagnostic units are already a reality, and at Rotterdam's Erasmus Medical Centre all diagnostic disciplines are combined in a joint cluster for "Diagnostics and Advice".'

One factor that favours this development is the shift in imaging from an interpretative modality towards quantitative science. 'We measure a growing number of details in images and can even show diseases in concrete numbers; we talk of imaging biomarkers, a term that goes to show that we are becoming increasingly similar to laboratory chemists.'


© Brüderkrankenhaus St. Josef Paderborn

The conclusion of this integration of diagnostic disciplines could have a single endpoint, a front office for all diagnostic questions arising among clinicians. The objective is a simplification of the process and a gain of time and resources: the clinician does not have to proceed step by step and work from discipline to discipline but receives a single answer and recommendation from the combined diagnostic profession for his patient.

In Rotterdam the emphasis is on the advisory function for clinical colleagues, for primary diagnostics as well as recommendations or therapy monitoring. 'The organisational structures are there already, but the support from the IT department, which has to process large volumes of data in an efficient manner, is as yet lacking.'

Prof. Krestin also deems stronger cooperation sensible on a political level. Under his ESR presidency, bilateral talks with a large number of European specialist societies have indeed begun, and stronger cooperation on a political level was not only called for but also implemented.

One of the first success stories of this cooperation between many individual specialist societies was the *Alliance for MRI* on the EMF guidelines. 'But there are, of course, more levels of cooperation,' he pointed

Too many tumour b

Meeting virtually, defining expertise and measuring effectiveness become key to dealing with a proliferation of cancer working groups in the Netherlands

Multidisciplinary tumour boards (MDTs) are widespread in the Netherlands, and 'they tend to be proliferating lately,' according to Professor Folkert van Kemenade, Chair of the Pathology department at the VU University Medical Centre in Amsterdam.

There are a couple of national consultant boards focused on specific cancers (e.g. bone cancers) that convene every month, as well as regional mono-disciplinary groups focusing on one tumour type, but also regional multidisciplinary consulting boards covering several tumours types. Where mono-disciplinary groups do not typically follow individual patients but focus more on diagnostic dilemmas, at local level are multiple forms a patient-centred tumour board might take, such as combinations of several disciplines coming together for MDT meetings, weekly or less frequently or, alternatively, tumour workgroups focusing on improving diagnosis (slide board for regional pathologists), treatment & follow-up (radiotherapists, oncologists) for the proverbial 20% of cases that require more than the straightforward mode of the MDT.

No certification is needed to sit on a tumour board. Local boards are not legal entities with separate requirements for a certain level of expertise, notes Prof. van Kemenade. On these boards, clinicians are either certified or accredited for their work in the hospital department or esteemed as knowledgeable.

Regional comprehensive cancer centres, of which there are nine to ten in the Netherlands, are the driving force behind many tumour boards. Members of national tumour boards are typically selected for their expertise and scientific reputation, and while these boards are legal entities, no accreditation or certification is required.

Similarly, the insurance companies that are the co-drivers for tumour boards also look to the clinic or institution to evaluate quality of oncological treatment, setting volume norms that require a certain number of treatments at a hospital each year before reimbursement is provided for treatment.

Yet, defining the level of expertise necessary to participate on a tumour board 'is quite a hot debate currently in the Netherlands,' the professor points out. 'How do you objectively assess expertise? What is required for that? If you've been looking at tumours for 20 years, you certainly are experienced and this would put as much weight in the balance as your scientific output on a particular tumour. Assessing experience is harder, though one can look to the number of consultative cases where a pathologist is called for expert opinion, or perhaps certification for regular attendance at accredited courses.

'In my specialty of pathology there are some examples of tumour boards outside the university hospital. That usually provokes tension because the university hospitals claim a prerogative for doing this, which makes some sense because their expertise is usually connected with some scientific clout, accompanied by a number of publications, and the number of students trained. These are things you can hardly do properly outside a university medical centre.'

'Yet, there are exemptions on this rule of thumb and there are certainly experts with scientific weight in general hospitals, outside academic hospitals. There is no rule against creating a tumour board in a general hospital, but you have to be aware that to do this is you are going against the grain, and you will have to prove that you deserve this recognition.'

The proliferation of MDTs increasingly puts pressure on staff, he acknowledged. *(See European Hospital, N° 4, 2013)*

'Participating in regional tumour board activities (in contrast to MDT's) is not as difficult because they meet less often and work at a higher level, as they are not implicated in direct patient care,' he added. 'However, working with the local boards or working groups dedicated to a specific tumour type does create problems for staff. It becomes difficult to attend all the meetings. In a pathology lab such as ours, which serve three hospitals, each of which has multiple MDTs, it becomes tough to participate on three teams with a staff of five pathologists.'

Virtual meetings solve the problem

'Whole slide imaging, which is digitising pathology, makes it easier for pathologists belonging to the multidisciplinary groups to attend meetings via the computer at their work desks. They can present slides and deliver an opinion with a digitised support system. There is also video conferencing, where you actually sit inside the multidisciplinary team. It may not be optimal, but it works. It saves the displacement of going from A to B,' Prof. van Kemenade explained. 'You can participate in the whole discussion, intervene and respond to questions directly. We do this every couple of weeks with centres located some kilometres from here, and I can see them and participate in the discussion and debates.'

A working group within a hospital intuitively believes it improves patient care, he added, although proving effectiveness scientifically becomes problematic. 'As pathologists, for example, we have a job to do. If on one hand we are trying to define what is expertise, I believe we are morally obliged on the

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out. 'In July, representatives of ten European specialist societies came together, including radiologists, pathologists, radiotherapists, anaesthetists and surgeons, to discuss the formation of a joint organisation, enabling them to talk to the European Union and the industry with one voice,' he explained. Two political organisational models are conceivable – either an entirely new alliance will form or the Alliance for Biomedical Research, which was set up two years ago and comprised of 21 specialist societies, initially formed to have an impact on EU science policies – will extend its focus to political matters.

In any case, the need for action for this political representation of interests is extensive, ranging from European legislation on the subject of clinical trials, for instance, to professional qualifications, data privacy and code of conduct for a clear regulation of relationships with the industry. Individual diagnostic disciplines are also due to find common ground on questions of education and training. Although joint training events now exist for assistants, in the future, individual diagnostic disciplines could still learn more from one another and move away from approaching problems based only on their own specialist perspective. 'Pathological and radiological interrelations have existed for a long time; as radiologists we always look for correlations with pathology in our images. However,' Prof. Krestin concludes, 'whether or not all three diagnostic disciplines will be combined into one joint diagnostic profession remains to be seen.'

Professor Gabriel Krestin, Head of Radiology in one of Europe's biggest hospitals, the Erasmus Medical Centre in the Netherlands, is also Past President of the European Society of Radiology (ESR) and founder of the European Institute for Biomedical Imaging Research (EIBIR).

He graduated at the Medical Faculty at the University of Cologne, Germany, where he completed his radiology residency and doctoral thesis and then appointed head of the MRI Centre at University Hospital in Zurich, Switzerland.

From October 1995 to May '97 he was acting chairman of the Department of Diagnostic Radiology in Zurich before moving to his present position in the Netherlands. He has also served as a permanent visiting Professor at Stanford University USA, since 1998.

other hand to demonstrate what are the effects of the existing tumour boards on the diagnosis of patients, and whether the MDT did, indeed, make a change.'

Professor van Kemenade suggests testing the use of a methodology based on the Goldman criteria for autopsy discrepancies in post-mortem investigations in pathology, in order to class the level of discrepancies with clinical diagnoses. Then, the frequency and severity of diagnostic discrepancies generated by a tumour board could be measured objectively.

Expert in orthopaedics, endocrinology and cytopathology, **Folkert van Kemenade** gained a PhD in immunology at Sanguin Amsterdam and a specialty in Leiden Medical University Hospital. He became a consultant pathologist in 1998 and mid-west regional coordinating pathologist in 2000. For a decade he also chaired a regional contact group to improve the quality of cancer pathology, and he was secretary of the Netherlands Society of Pathology for five years. Connected to the VU research group, focused on HPV screening effectiveness, triage and treatment tests (e.g. trials Vusascreen, Pobascam), from 2005 the group began self-sampling for non-attendees of the screening programme.
In 2012, with PALGA and Prof Gerrit Meijer, he obtained a BBRMI grant (RP7) to set up a Dutch National Tissue Portal to research blocks in all Dutch pathology archives.
In 2013 he became Chair of the pathology department at Erasmus Medical Centre.

Mandatory tumour boards

France: Cancer Plan III aims to correct disparities in quality and unequal access to care

Report: John Brosky

The government of France takes cancer very seriously. With 150,000 deaths each year, this is the leading cause of mortality in the country. The national health system pays for 100% of the care. Patients also have an enforceable right to the review of their diagnosis by a multidisciplinary team (MDT) as well as for the management of their treatment. Hospitals and clinics must meet national standards for care and prove they actually provide coordinated care by an MDT. More than half of the 2,000 cancer centres treating patients 10 years ago have been closed for not meeting these standards.

Trouble with numbers

Cancer care is well structured, at least in theory, by successive five-year plans that also cover initiatives for cancer prevention and screening. In September, the third Cancer Plan was submitted to the Health Ministry by Professor Jean-Paul Vernant, who had been personally asked by the President of the Republic to review progress of the first two plans and make his recommendations. Cancer Plan III will come into effect at the beginning of 2014, though it will likely be under-funded.

The universal requirement for MDTs, he wrote, 'is a heavy action requiring significant medical resources that are often difficult to meet, and a systematic deployment for every patient is likely to pose problems, taking into account the increasing incidence of cancer and the expected decrease in the number of oncologists.'

The good news, Prof. Vernant reports, is that a review of 794 authorised cancer centres in 2011 showed a clear progression, with 70% of MDTs composed of at least three different specialists, compared to 38% the previous year.

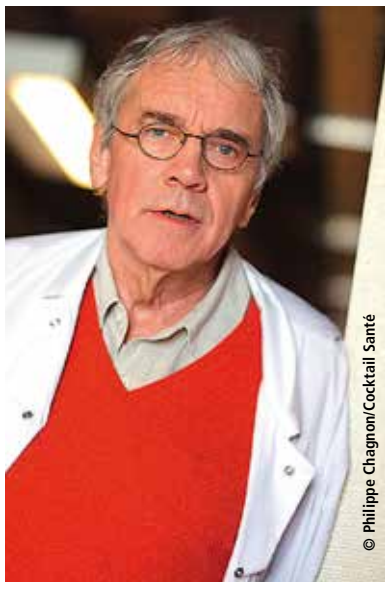
Unequal access

Disparities remain, he noted, pointing out that there has never been an evaluation of the impact of this key component of the plan. Areas of concern include the unequal access across the regions for patients to MDT-supervised care, communication to the treating physician of the decisions proposed by the MDT, the time and resources dedicated to MDTs, and the lack of regional consulting boards with expertise that can be called upon for urgent decisions, for rare cancers and for unusual clinical issues.

There is also a need to set standards with a procedural manual for tumour boards spelling out roles, responsibilities, documentation requirements and especially communications with the patient's physician.

Ignoring, for the moment, the lack of funding and resources, Prof. Vernant fulfils his commission by recommending three levels of MDTs in France: the first-line, or local, tumour board; a series of expert panels on the regional and the national level that can be called upon by the first-line team and, a MDT of last resort to manage patients where therapy has failed, either to supervise an alternative treatment or palliative care.

Prof. Vernant is especially critical of the failure to establish the networks for sharing files among MDT members. Considered key to the organisation of MDTs in the first Caner Plan in 2003, cancer files were to be linked with the national patient medical record, according to the second Cancer Plan in 2009.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Jean-Paul Vernant, Professor of haematology at l'Hôpital de la Pitié-Salpêtrière in Paris

A sophisticated, dedicated network

How many files-sharing networks were established in the first place is unknown, he notes, adding that MDT members do not use the few that exist to exchange information. Theoretically there could be 25 such networks, he wrote, each developed locally, and none able to communicate with another network. The initiative to link cancer files with a patient's record remains stuck in a half-dozen regional pilot projects.

Again in fulfilment of his commission, Professor Vernant spells out recommendations to rapidly deploy a national network to kick-start file sharing, to disconnect the cancer files from the national patient record, and to progressively build a more sophisticated, dedicated network that can include the referring physicians as well as general practitioners.

New UK diag imaging guic

Quicker diagnoses through faster communication, open-image report sharing across healthcare networks and better access to archived images

Report: Mark Nicholls

United Kingdom – The Royal College of General Practitioners, Royal College of Radiologists and the Society and College of Radiographers have worked together on recommendations that outline improvements for patients by ensuring that timely and appropriate medical imaging services are provided to them and their referring doctors. The resulting publication – *Quality Imaging Services for Primary care: A Good Practice Guide* – sets out necessary changes to make a 'tremendous difference' to the care of patients needing an National Health Service (NHS) scans.

The document aims to reinforce the links between local NHS clinical imaging departments and the new GP-led Clinical Commissioning Groups (CCGs), which, following the restructure of health services in Britain in April 2013, took control of NHS budgets and are responsible for commissioning services within the NHS.

The three colleges recommend boosting communication through the open sharing of images and reports across local and regional healthcare networks, as well as making previous imaging history reports available to all providers to ensure patients receive the fastest possible diagnosis.

The guidance also states that, following their GPs' referrals patients needing urgent NHS scans should be seen within a week and routine screenings should be performed within two weeks. Patients in rural areas would also have improved access under the recommendations.

The clinical relationship and dialogue between primary care and radiology clinicians also need improvement, the three organisations stressed, adding that if their

Through his early interest in MRI and musculoskeletal imaging, **Dr Peter Cavanagh,** Dean of the Faculty of Clinical Radiology and Vice President of The Royal College of Radiologists and a consultant radiologist in Taunton, developed the Somerset MRI Course, the UK's largest MRI course for 20 years.
He has lectured internationally on MRI and was Deputy Chair of England's National Imaging Board (2006-10). Other roles include hospital medical director and acting hospital CEO.

On its firs

The prototype of the open X-ray system OR

In the summer of 2011 European Hospital first presented ORBIT, a joint project by the Fraunhofer Institute for Production Systems and Design Technology (IPK), Charité Universitätsmedisin Berlin and Ziehm Imaging, and funded by the German Ministry of Education and Research (BMBF).

Today, the project director Professor Erwin Keeve PhD-Eng is proud to announce that the system has generated the first 3-D images: 'We are very happy with these initial results, which motivate us to enter the next funding phase and move ahead towards clinical use.'

The second prototype is most likely to be installed in the state-of-the-art robotics operating theatre that he is currently setting up at Charité. 'If everything runs according to schedule we will be able to demonstrate clinical usability of ORBIT by mid-2015,' he says. If this pans out,

gnostic delines

guide was used correctly it should significantly improve patient care, increase efficiency and shorten waiting times, as well as cut NHS costs.

Dr Peter Cavanagh, Vice-President of the Royal College of Radiologists: 'Diagnostic radiology is at the heart of most patient pathways and it is important that those commissioning and providing such services have a clear, shared understanding of what needs to be in place for patient safety and to ensure the effective use of healthcare resources.

'It is essential that such services are commissioned in a way that ensures that the patient and referring doctor have access not only to an image and a report but the medical expertise of a clinical radiologist as well as other members of the radiology team.

'The shared goal of providing the highest quality, seamless care to patients is what has driven the work of the colleges and is why this guide is an important step in this aim.'

RCGP Chair Dr Clare Gerada said: 'By working together and using this guidance, GPs, radiologists and radiographers can really make a difference to patients needing scans, be it urgent or routine. It will help Clinical Commissioning Groups to highlight where current services need to change and where they could become more localised.

Director of Professional Policy at the Society and College of Radiographers, Professor Audrey Paterson, said the guide would provide a real opportunity to embed best practice for GPs and their patients in clinical radiology departments across the country. 'Services may well find aspects of the guide challenging,' she pointed out, 'but their well-established principles of effective team working and skills mix will enable them to more than rise to them, developing strong and effective partnerships with GPs and the Clinical Commissioning Groups as they do so.'

Director of Professional Policy at the Society and College of Radiographers, and Gold Medal recipient, **Professor Audrey Paterson** was also a member of the society's UK Council for 12 years and a past president of the organisation. She has also been the United Kingdom council member for the International Society of Radiographers and Radiological Technologists for four years.
This June, when giving the Stanley Melville Memorial Lecture at the UKRC, she identified two major developments that could shape the future of radiography: molecular imaging and theranostics (the fusion of therapeutics and diagnostics).

Chair of RCGP Council **Dr Clare Gerada** has held leadership positions that include Director of Primary Care for the National Clinical Governance Team and Senior Medical Advisor to the Department of Health. Dr Gerada has published a number of academic papers, articles, books and chapters, and established RCGP's ground-breaking Substance Misuse Unit. Dr Gerada has also led on the strategic and logistical delivery of the RCGP Annual National Conference. A general practitioner (since 1992), she is a partner at the Hurley Clinic in South London.

t test path

BIT generates detailed 3-D images

The ORBIT – the final system will support virtually all applications in trauma and reconstructive surgery

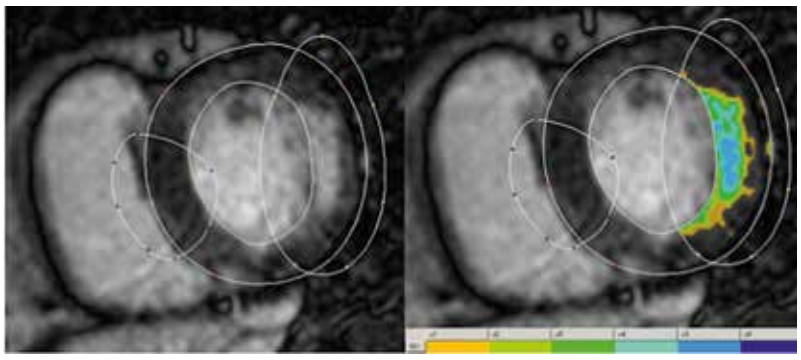
the system, which is designed for minimum impact on surgical procedures and routine use in operating theatres, could be launched in 2016 for use in shock rooms, for example.

The clinical significance of a device like this was recently highlighted by a study based on the German trauma registry, which indicated that an immediate whole-body CT might significantly reduce mortality among polytrauma patients.

'The advantages of ORBIT,' Professor Keeve points out, 'are the facts that, unlike a CT, it can be installed in the shock room itself and that it offers unrestricted access to the patient during image acquisition. Moreover, ORBIT is much simpler and faster to set-up for each individual exam.'

Infarction size and transmurality

A cardiac catheter is insufficient to evaluate the effects of a myocardial infarction. The size of the infarction and post-event cardiac muscle activity are crucial predictive parameters that determine therapy decisions



Quantitative, computer-guided assessment of infarction size with a threshold method: The infarction area (light myocardium area on the delayed enhancement MRI) is outlined (yellow dots). In a second step, the non-affected myocardium is marked (blue dots). The size of the infarction is calculated based on a threshold method and marked in colour. The infarction area shows signal intensity with a standard deviation of ≥2 above the non-affected myocardium (outlined in light green). The centre of the infarction is shown in blue.

The size of the infarction and infarction transmurality offer important prognostic information on the future course of the disease. Research indicates a direct correlation between the size of the infarction and the probability of later complications. 'After an infarction the patient's cardiac function can deteriorate – he develops cardiac insufficiency. Or, the patient may experience relevant arrhythmias, which increase the risk fatal ventricular fibrillation,' explains Professor Gunnar Lund, Senior Resident at the Clinic and Policlinic for Diagnostic and Interventional Radiology, University Hospital Hamburg-Eppendorf. Therefore, it is of paramount importance, he adds, to collect cardiac muscle data, which provide crucial information that determines therapy decisions.

Revascularisation of a coronary artery, as such, improves neither heart function nor prognosis. The decisive factor after a myocardial infarction is the remaining myocardial viability, which needs to be assessed as objectively as possible. The acquired data can be used to risk stratify the patient. 'Today, cardiovascular MR is the gold standard to determine size of the infarction and transmurality,' Prof. Lund points out. The size of the infarction, for example, indicates whether a patient will require intensified cardiac insufficiency therapy after the cardiac event.

Professor Gunnar Lund MD is a triple specialist – covering internal medicine, cardiology and radiology. He began medical studies at RWTH Aachen (1984), and in 1991 he joined the Department of Cardiology at University Hospital Hamburg-Eppendorf (UKE). Seven years later, Dr Lund was in the USA as a researcher in the radiology department, University of California, San Francisco, until 2000 when he continued MRI research in Hamburg. In 2004 he received his teaching qualification for internal medicine. In 2010, after two years as a general practitioner in Düsseldorf, he was appointed Professor at the University of Hamburg. He has been Senior Resident at the Clinic for Diagnostic and Interventional Radiology at UKE since 2012.

Transmurality determines actions

The second important question that needs answers: Is sufficient vital myocardium left for the patient to benefit from the improved cardiac perfusion that was achieved either surgically or interventionally? Transmurality is the parameter that provides the answer, as Prof. Lund explains: 'An infarction always moves from the subendocardium to the epicardium, i.e. from inside to the outside. If only the internal layers are affected, and thus the infarction, transmurality is at only 10 to 25 percent, so the chances for recovery are very high. The higher the transmurality, the slimmer the chances of recovery, particularly if the infarction affected more than 50 percent of the cardiac wall.' Based on these data the cardiologists decide whether a patient requires revascularisation – dilation – or a bypass.

Cardiovascular resonance imaging (CMR) or scintigraphy can acquire these viability data. While research indicates that both methods are equally reliable, Professor Lund prefers CMR because, in his experience, this modality allows better evaluation of the transmural extent of the infarction: 'Scintigraphy is not quite as useful here because it has a lower resolution than CMR.'

A further disadvantage of scintigraphy, he points out, is radiation exposure since this technology requires a radiopharmaceutical to be injected. Nevertheless, at least in Germany, scintigraphy is still the most frequently used modality because of, he suspects, the unfortunate fact that the country's statutory health insurers do not cover CMR costs.

Angiography cannot reliably assess infarction size

While percutaneous transluminal coronary interventions in patients suffering an acute myocardial infarction have significantly improved outcomes, these interventions hardly yield much information on cardiac viability. 'The size of the infarction itself cannot be assessed reliably in angiography,' he explains. 'There might be rather clear findings, such as a large aneurysm, which indicate a major infarction; nevertheless misinterpretations are possible since the angiography does not allow a differentiated and precise diagnosis of the size of the infarction and current viability.' Consequently an angiography with unambiguous findings such as several coronary occlusions or stenoses is usually followed up by CMR or scintigraphy to definitely assess viability.

Fusing images from different sources

Okan Ekinci, Global Director of Cardiology at Siemens Healthcare, is convinced that, ultimately, ultrasound will remain the 'entry level' imaging procedure for patients. *European Hospital* met up with him at this year's ESC congress to hear his thoughts on the potential of ultrasound – and particularly its fusion with other imaging modalities.

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'Ultrasound will not become obsolete – to the contrary,' confirmed Okan Ekinci, Siemens Healthcare's Global Director of Cardiology. 'Because the modality is continuously developing, and more ultrasound scanning is actually done from inside the body, the significance of this modality is increasing.'

He also believes that three important points will also make ultrasound indispensable in the future – the costs, which are lower than those for any other imaging modality; real-time images, which facilitate conclusions in real time, and finally the ability to fuse ultrasound images with other imaging modalities. Helped by adapted software algorithms for image reconstruction and processing, data from almost all imaging modalities can be fused

with one another. This makes fusion a technological reality utilised by various types of users to a different extent. 'The hype around visual fusion seen a few years ago has calmed down somewhat. Now it's all about proving the clinical added value.

'One exciting trend,' he added, 'is the generation of new information through the fusion of image data from different modalities and through modelling.' One graphic example of this is the fusion of ultrasound scans that visualise the movement patterns of the heart in high temporal resolution with the anatomical precision of CT scans. During the fusion process the images are increasingly not only being visually fused, but complex three-dimensional flow patterns can be shown, which are not measured but calculated.

'The basis is complex cardiac computer modelling, in this case fed from high resolution CT information – such as the ventricular cavity shape, wall thickness - and functional information such as heart muscle movement and valve function, from the ultrasound scan.' Similar to a car no longer needs to be tested in a wind tunnel because the aerodynamics can be calculated via a computer based on established principles, he explained, heart modelling enables information to be gained about the entire flow pattern in a patient's heart. 'The virtual heart model will not only enhance diagnostic opportunities but also revolutionise the optimisation of treatment planning.'

Designed with continuously increasing attention to detail, he pointed out that models of the heart could make it possible to predict the effect of interventions on heart function and morphology with sufficient accuracy. A surgeon or cardiologist could, for instance, use the model to simulate how the heart will 'react' to the implantation of different heart valve models and sizes, possibly reducing the occurrence of paravalvular leaks or other complications. This enhanced choice of valves would constitute personalised medicine in the best sense of the term.

Dr Ekinci sees great potential for the 'virtual heart model' as well as Cardiac Resynchronisation Therapy (CRT). Patients with heart failure (HF) are often given a pacemaker to help synchronise the pumping function of right and left ventricles. Even when implanted according to guidelines, up to half of those patients do not respond to treatment. 'Many factors can impact on therapy response,' he stressed. 'One is that many patients have CRT devices implanted in parts of the heart muscle affected by scar tissue, where no electric impulse can be transmitted. However, it also depends on the size and transmural extent of the scar where the best place for implantation would be. A personalised heart model, taking into account the complex, electrophysiological effects of a scar, could predict the success of CRT even before an intervention and therefore improve patient selection.'

This would not only lower treatment costs but also the rate of complications for implanted pacemakers. Dr Ekinci believes the fact that each imaging modality can test its strengths with the modelling approach is also an advantage: 'Modelling and simulation of the integrated view of data from different sources means a new era for imaging, and we are very motivated to generate new and novel information from the data measured. In the future, imaging will not only be restricted to the visualisation of the "best possible" images, but will revolve around extracting as much information as possible from data integration – for the advantage of patient and examiner.' Not least, these procedures should also help to drastically cut exam times and time to diagnosis.

A further, still relatively new procedure to deliver real-time images from inside the heart in 3-D is the ultrasound catheter AcuNav V. With a diameter of only a few millimetres, the system is inserted through vessels in the groin to reach and be positioned in the atria or ventricles. For many cardiac procedures this would provide an unlimited view of the exact location where an intervention is being performed. 'Particularly with electrophysiological procedures or TAVI, cardiologists ideally would like to know in real-time where they are and what they are doing,' Okan Ekinci explained.

The advantages of the new catheter system compared to conventional procedures such as the TEE transducer are obvious: With the AcuNav V the patient does not need a general anaesthetic and the procedure is only semi-invasive because the catheter can be inserted via venous access. 'Previously, there was a lack of spatial orientation with catheter transducers. The AcuNav V now facilitates a 3-D view of the implantation area during the TAVI procedure. The orthogonal view of a newly implanted valve allows the search for paravalvular leaks.'

AcuNav V also has practical, procedural advantages: Many interventionists do not like the look of the voluminous TEE transducer on fluoroscopic images – therefore, a transducer of only a few millimetres in size, which can be manoeuvred quickly, is an advantage.'

To what extent cost savings can be achieved with the procedure remains to be proved. 'On one hand the AcuNav V catheters are disposable,' he said. 'However, on the other, the fact that the procedure can be carried out under sedation rather than a general anaesthetic means there may be no need for the presence of an anaesthetist during an interventional procedure.'

Okan Ekinci

A new day for troponin in

An innovative, complex clinical study sets reliable levels for myocardial infarction risk

Beckman Coulter's new *Access AccuTnI+3* troponin I assay has received FDA clearance for its *UniCel DxI* series of immunoassay systems at the same time as having a new CE Mark approved on the UniCel DxI and Access 2 immunoassay instruments. This follows FDA clearance (June) for use of the assay on the company's Access 2 immunoassay instruments.

The new troponin assay is now cleared for use with all of the company's immunoassay systems, as well as the UniCel DxC integrated chemistry and immunoassay series.

'First, it's important to stress that this is the same powerful assay and reagent kit that has already provided clinicians with a decade of clinical performance, delivering the clinical sensitivity they require,' explained Dr Bernard Cook, Senior Scientific Affairs Manager, during an interview with *Daniela Zimmerman*, who asked:

Why all the excitement surrounding an established assay?

'It's the quality and credibility of the study that is inciting interest in clinical circles', Dr Cook explained. 'Beckman Coulter has taken the indicated standards used by Europe's leading cardiac experts and used them to clinically validate the AccuTnI assay for use in contemporary practice. Clinicians will see the same numbers and good clinical performance from our assay – but now we can provide them with new evidence of its diagnostic robustness.'

This is presented as a 'New Day in Evolving Clinical Practice'. What is different?

'The role of a troponin assay is to provide an early as possible diagnosis of patients with acute myocardial infarction (AMI). Experience gained over the last decade by clinical investigators has led them to change the way they use the assay to assess the risk of a cardiac event. They came to realise that a lower level of cut-off value was a far better indicator for AMI. As soon as this was understood, the cut offs for troponin levels went quickly, very aggressively, down to a 99th percentile upper reference limit (URL). Today, that is the standard incorporated in all clinical practice guidelines and reflects the way the test is actually being used in the clinic. Yet the actual troponin tests continued to be labelled for use according to standards from a decade ago. In Europe especially, the difference was always understood and adjusted for in clinical practice.

Coming from an academic and commercial background, for the past 13 years **Dr Bernard Cook** has worked at a senior scientific level at Beckman Coulter, specifically on the expansion of its global immunoassay business. He has co-authored several scientific papers and is actively involved in the diagnostics industry, which includes being the former chairman of the industry division of the American Association for Clinical Chemistry.

As you know, the FDA recommended that manufacturers introducing new troponin assays should now validate them according to contemporary practice. This requirement therefore became a very large part of a new clinical trial conducted by Beckman Coulter. First, we did a feasibility study that asked: What should be the most sensitive and specific cut off? We looked at different cut-off measures in our clinical study and confirmed that the receiver operating characteristic (ROC) curve closely followed the 99 percentile upper reference limit now being used by clinicians to diagnose AMI.

'The clinical study we instigated was a complex, prospective multicentre study across 14 US hospital sites, ranging from community hospitals and academic centres, to specialist centres of excellence. We deliberately wanted to demonstrate the effectiveness of the assay using the widest possible cross section of cardiac chest pain population. It became a large and significant study with over 1,900 patients recruited.

'We took serial samples from each subject at zero, 3, 6, and 9 hours. These serial samples were analyzed using two time frames: time from when the patient presented in the Emergency Department complaining of chest pain, and at the onset of symptoms, such as when they first felt chest discomfort. We chose to include sampling in this dual timeframe because there is still no agreement on the best time for determining the significance of changes in

The ESPOIR Study

Innovative data network facilitates research into transplanted heart valve tissue across Europe

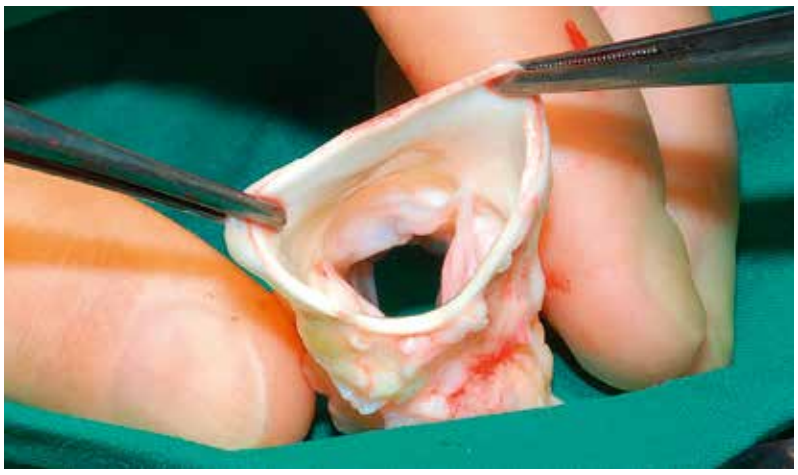
Professor Axel Haverich and team at the Clinic for Cardiothoracic, Transplant and Vascular Surgery in Hanover Medical School (MHH) have been carrying out research into decellularised heart valves for over 15 years. They trialled a procedure – initially in the laboratory and in animal experiments – which does not cause tissue rejection, is hoped to last a lifetime and, in the case of children, even to grow with the patient.

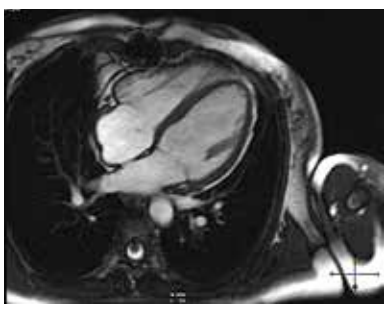
Since January 2012 this procedure has been tested at eight Paediatric Cardiology Centres based in Moldova, Italy, France, Belgium, The Netherlands and Great Britain in the context of the European Clinical Study of Regenerative Heart Valves (ESPOIR) under the leadership of the MHH.

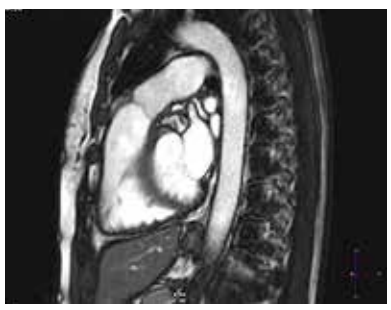
The European Union will support this regenerative medicine research project with €5.2 million until the end of 2016. At the heart of the study is the consolidation of research results from the individual cardiology centres into a joint database. Only through long-term follow-up of the patients examined along with a cross-centre evaluation will it be possible to confirm the success of the new procedure.

In May 2002, two children in Moldova where the first to he implanted with a decellularised heart valve. This not only launched the promising medical procedure but was also the beginning of a protracted, sometimes public debate. Finally, after 11 years, the Paul-Ehrlich-Institute recently authorised decellularised heart valves as pulmonary valve replacements, confirming the success of the treatment so far. 'We have now implanted one hundred decellularised heart valves and haven't had to remove a single one,' said Dr Samir Sarikouch, private docent, clinical trial leader and senior physician at the Clinic for Cardiothoracic, Transplant and Vascular Surgery Clinic in Hanover.

The new procedure uses donated human heart valves, which are supplied by the European Homograft Bank (EHB) and the German Society for Tissue Transplantation gGmbH (DGFG). As a sufficient supply of tissue donations is what the procedure relies upon, the study also aims to improve cooperation between tissue banks across Europe. The donor's protein is completely removed from the valves in a special laboratory. 'In the case of the so-called homografts only the collagen of the supporting tissue remains as a matrix, which is transplanted and then populated with the recipient's cells. These cells then progressively regenerate the body's own tissue. Depending on the recipient's age this process can take months or even years, but it works,' Dr Sarikouch pointed out. Removing the protein from the transplanted tissue prevents the recipient's immune system from detecting it as foreign and so avoids the onset of a rejection process.







Dr Sarikouch and colleagues could demonstrate this only recently, in a study with children and adolescents. Whereas the implantation of conventional mechanical heart valves requires lifetime medication to thin the patient's blood, and biological (human or animal) heart valves need to be replaced after eight to ten years, the new procedure has none of those disadvantages. 'There are strong indications that these heart valves will be much more durable than previous valves that were not decellularised – and even indications that they can grow with the patient,' he said. 'To monitor this, the patients treated have to be closely observed for years and decades.' As children require smaller homografts than adults, cutting larger heart valves to size for smaller organisms has been trialled in animal experiments, with good results.

MRI has become established as the imaging procedure of choice because it is the only procedure that does not cause children any permanent damage through X-ray radiation during the annual examinations.

Over the years, these examinations generate vast amounts of image data, which not only need safe storage but also collation in Hanover for the European study. 'We're very pleased that T-Systems recognised this market potential, and is developing a system that consolidates this data flow – the pseudonymised MRI images as well as the study data. The trick is to design the system so flexibly that secure access to the data will still be possible in 25 years' time. Ensuring this is obviously easier for a market leader than for a smaller company, such as an IT spin-off from a university,' Dr Sarikouch explains. Not only the longevity of data access but also speed, flexibility and, in particular, security, are important points that T-Systems must address.

In the future, it will be possible to access the corresponding MRI data sets in parallel to an analysis of case report from data, without the need to download them individually from the PACS. 'The data is centrally stored and we can sort and process it as we see fit. We can view the filtered data sets immediately and completely and can commence our work. It may sound trivial, but previously there was no such procedure available,' he explains.

In parallel, Dr Sarikouch will also have the CDs sent to him from the

Top left: A donated human heart valve from which all of the donor's protein has been removed. Only the tisue remains, which, when transplanted, becomes populated with the recipient's own cells and grows along with the child.
Above right: Eight leading pediatric cardiology centres are involved in the ESPOIR consortium.

clinical practice

patient troponin levels, i.e. when to "start the clock" for the event. We also included something new to cardiac markers in this clinical study. We calculated the positive and negative predictive values. In other words, if the test is positive, based on the cut-off values now being used to identify AMI, what actually is the chance that the subject has AMI? If the test is negative, what would be the likelihood that the patient genuinely did not suffer from AMI?'

How confident can you be to report that a patient did not have AMI?

'It's the quality of the statistics. First you need to look at all the true positives. Then you look at all the patients who had AMI. From this you can calculate the sensitivity and specificity of the values. The most important one, I think, is the negative predictive value. If you have a patient still presenting negative after a period of three or six hours, then you can be 97% sure that patient did not have an AMI. 'There remains just that 3% or less chance that they actually did. In actual practice, the universal wisdom is to use more than one troponin and look for a rising and/or falling pattern.

'However, in our clinical study we reported single time points and were able to demonstrate reliability of performance. Our new troponin I assay is now directly aligned with the US FDA's 2010 guidance to manufacturers of troponin assays and confirms our commitment to modernise the performance evaluation of this critical test.'

What does this statistical analysis mean in the clinic?

'The value that results from our study is that a clinician can make a decision about whether a specific patient does, or does not, have AMI. If they do not, then the patient can safely be sent home from the Emergency Department (ED), saving the hospital both time and money. They can be confident making a decision while the patient is still in the ED before transferring to a hospital bed.'

How are those analysis results incorporated into the new assay?

'What we have now is a calibration for the assay that is specific for the Beckman Coulter UniCel DxI and Access 2 analysers, so that the assays are harmonised and provide equivalent results.

'There can be other variations in assay results, depending on the instrument being used, due to how samples move through the analysis process, or a change in room temperature. We recognised, for example, there could be a difference in how AccuTnI responds to changes in temperature, when one system is compared to another. The absolute amount might not change a clinical decision, but analytically it would still be a different number. Because the temperature change is a linear function,' he continued, 'we were able to develop a model that automatically calculated a correction to overcome this. This solution has been integrated in the system software so that if you have an assay at 18° C and an assay at 28° C, you will automatically get the same troponin result.'

participating centres during the test phase. As is so often the case, the devil is in the detail.

He assumes that any teething problems with the solution will be resolved within a year (i.e. by 2015) and that the system will meet all expectations during trials.

After gaining a medical degree in Essen and doctorate at RWTH Aachen University, **Dr Samir Sarikouch** specialised in paediatric surgery and cardiology, practising at the Heart Centre Duisburg and the Heart and Diabetes Centre in Bad Oeynhausen, among others. Since 2008 he has been a senior physician at the Department for Cardiothoracic, Transplant and Vascular Surgery as well as Head of Clinical Research & Biostatistics at Hannover Medical School. He is a specialist in paediatric surgery, general paediatrics, paediatric cardiology, and paediatric intensive care and in treating adults with congenital heart disease.

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TMLR and da Vinci's demise created caution over newcomers such as TAVI

The fall and rise of cardiac surgery innovations

Grandly announced, the da Vinci became the must-have of any self-respecting cardiac surgeon, only to sink into obscurity as quickly as it had risen to stardom. Once the wunderkind of robotic surgery, today this surgical system is merely collecting dust on many a hospital cupboard. A whole slew of methods and technologies were launched with varied fanfares over the past ten years. European Hospital asked Professor Johannes Maximilian Albes of the Heart Centre Brandenburg in Bernau, about the hypes and the has-beens of cardiac surgery – and, of course, about the workhorses that are here to stay.

Report: Bettina Döbereiner

'da Vinci,' Johannes Maximilian Albes reflects, 'was not sufficiently aligned with the "human being" bio-system with its complex individual make-up.' Adjusting the surgical system to the patient's body took too much time. 'You spent four hours harvesting the mammary artery via the posterior thoracic wall… Expensive and time-consuming.'

That's an alarming assessment of any medical device. The final blow struck when it became evident that the robotic surgery system did not improve patient outcome. Worse: several complications were made public and the technology virtually disappeared from the cardiac surgical scene.

Patients suffer

However, da Vinci is not the only case of hyped medical technology turning sour. Remember transmyocardial laser revascularisation (TMLR) in the mid-1990s? Another technology that disappeared, because it turned out that holes cut by the laser in the right ventricle, to transport oxygen-rich blood into the heart muscle, closed far too quickly and also because lacerating the ventricle with fine needles proved equally effective.

Does that mean new devices need to be tested more thoroughly before release for clinical use? The professor is sceptical: 'A difficult issue… When products are launched too early, patients will suffer; but when innovations take too long, patients will also suffer.' Transcatheter aortic valve implantation, short-form TAVI, shows that an over-cautious healthcare system might miss out on innovations. The US-American FDA approved TAVI for clinical use only in November 2011, conditioning the approval on the Edwards Sapien valve and the transfemoral, not transapical approach. In Germany both approaches are allowed.

Image courtesy of Herzzentrum Brandenburg, Edgar Zippel

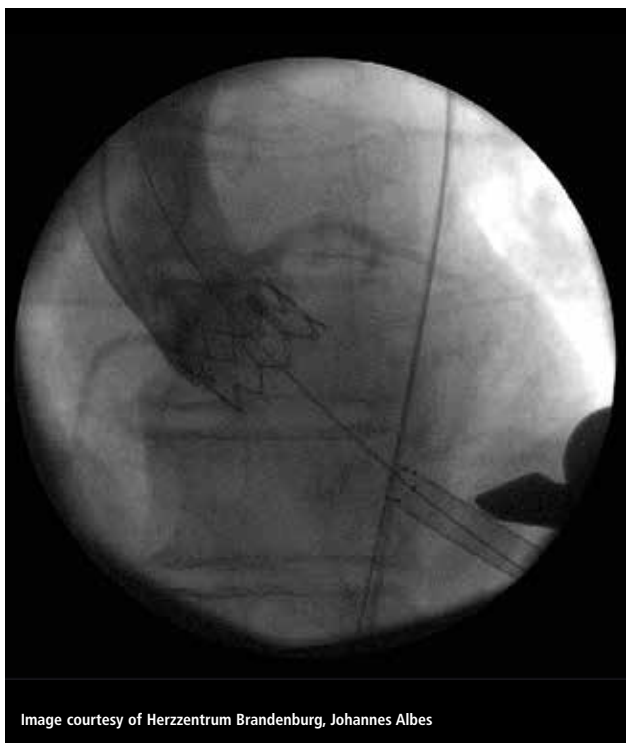


Image courtesy of Herzzentrum Brandenburg, Johannes Albes

Left: One of three cardiac cath lab workstations at the Heart Centre Brandenburg, a GE reference hospital that trains cardiologists from across Europe. In the control room, the second monitor screen from the left shows a catheter being inserted femorally. More than 4,300 interventions are performed in this cath lab annually. Since 2009, cardiologists and cardiac surgeons have completed 240 transapical and 492 transfemoral TAVIs.

Right: Intra-operative X-ray image directly after release of the TAVI (note the metal frame). Contrast agent in the main artery above valve enables correct positioning. Inserted transapically, the sleeve is at the bottom right. A guide wire passes through the sleeve, left ventricle and new valve to the main artery. As soon as the correct valve position is ascertained, sleeve and guide wire are removed. Note the transfemorally applied pigtail catheter in the main artery (somewhat blurred due to contrast agent). Used to apply contrast agent, this is removed after intervention.

The data of 78 German Heart Centres are collected in the TAVI registry and published annually by the German Society for Thoracic and Cardiovascular Surgery (DGTHG). Drawing on these data, Professor Albes highlights the TAVI success story in Germany: the number of these procedures rose from 78 in 2006 to 6479 in 2012. After only six years of clinical application TAVI accounts for 35% of all isolated aortic valve implantations per hospital. At the same time, the number of conventional valve surgeries remained stable: 11,603 in 2006 and 11,779 in 2012.

This development indicates that TAVI expands the range of available tools and opens up new patient cohorts. In Germany, this is the procedure of choice for over 80-year-olds where a conventional procedure is too risky. Age explains the rather high mortality rate among TAVI patients: 5.4% compared to 2.6% in conventional heart valve surgery. 'However, when you account for the higher risk profile of these patients, mortality is hardly higher,' Prof. Albes points out.

Questioning TAVI

He expects TAVI will soon be used in more than 50% of the aortic valve implants because more and more older patients will opt for the procedure. Nonetheless, conventional valve surgery is here to stay. In terms of quality, TAVI is still considered inferior to the conventional method due to paravalvular leaks associated with the implant: by pushing the calcifications to the side in the original valve, holes may be created that prevent proper sealing. Moreover, it remains to be seen whether the TAVI bioprosthesis, which has been in use for merely seven years, will match the conventional bioprosthesis in terms of durability (ten years) and performance.

The DGTHG statistics also show a significant increase in univentricular assist devices: 766 such implants in 2012 meant an increase of 21.5% over the previous. Due to the extremely limited availability of donor hearts and the increasing age of the patients, Prof. Albes expects ventricular assist devices to gain further ground rapidly.

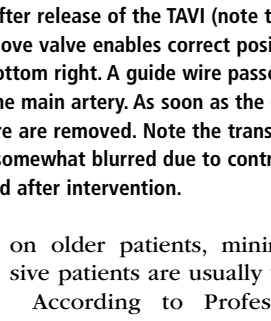
MIS for mitral valves

Minimally invasive mitral valve surgery has also become an established technique in Germany. Since 2007 the number of conventional procedures in isolated mitral valve surgery decreased by 24%, while the minimally invasive interventions increased by 65% in the same period. Today, minimally invasive isolated mitral valve surgery accounts for 44.7% of all such interventions. 'The figure will level out at around 50 percent,' he predicts, 'because not every patient is suited for this isolated procedure.' The patient cohort can also explain the difference in mortality –6% in conventional and 1.7% in minimally invasive procedures. Unlike TAVI, which focuses on older patients, minimally invasive patients are usually younger.

According to Professor Albes, off-pump coronary artery bypass (OPCAB), despite being controversial, has stood the test. The number of these procedures increased continuously since 2007 by about 1% per year, from 10% to roughly 15% in 2012. A mortality rate of 2% is recorded for off-pump and of 3.1% for on-pump procedures. Since patients who undergo surgery without a heart-lung machine are usually younger and in a better state of health, Professor Albes underlines that the difference in mortality does not provide conclusive evidence regarding the quality of the method as such.

DGTHG data are published annually in The Thoracic and Cardiovascular Surgeon, the official journal of the German Society for Thoracic and Cardiovascular Surgery.

For additional TAVI reporting see John Brosky's interview with John Webb on page 12 of European Hospital issue 4/2013.



Since 2003, **Professor Dr Johannes Maximilian Albes** has been Medical Director of the Department of Cardiac Surgery at Immanuel Klinikum Bernau

IN-TIME results show reduction in mortality of more than 50% in heart failure patients

ESC recommends implant-based remote monitoring


Biotronik Home Monitoring enables physicians to check up on patients remotely

The highly-anticipated and positive results from the IN-TIME study of home monitoring technology were recently presented in a hotline session at this year's European Society of Cardiology (ESC) congress by coordinating investigator Professor Gerhard Hindricks MD, from the Heart Centre, University of Leipzig, Germany. The ESC has recently issued a strong recommendation of remote monitoring technology, giving it a class lla indication with the highest level of evidence (A) in its guidelines, once again proving just how crucial this type of technology is in the early detection of clinically relevant events, Biotronik, the cardiovascular technology manufacturer reported.

Since its first implantable pacemaker was developed half a century ago, the Berlin-based company has presented ways to save lives as well as improve the ease and efficiency of routine tasks for doctors; e.g. their Biotronik Home Monitoring system, has contributed considerably – it automatically transmits data on a daily basis (e.g. of asymptomatic atrial fibrillation) and alerts the physician if a patient's clinical condition deteriorates rapidly, thus enabling him or her to adapt treatment.

Along with the new ESC rating, the positive outcome of the IN-TIME study demonstrated a significant reduction in all-cause mortality in heart failure (HF) patients, supported by implant-based Biotronik Home Monitoring compared to standard care. From an estimate based on the Kaplan-Meier curve, the mortality at one-year follow-up was 3.4% in the home monitoring group and 8.7% in patients with standard care.

'The occurrence of atrial or ventricular arrhythmias, or specific trends in certain clinical parameters, can often be the first sign of worsening heart failure that leads to hospitalisation or death,' Prof. Hindricks explained. 'Biotronik Home Monitoring allows physicians to identify crucial trends in cardiac device patients. They then have enough notice to intervene in time, thereby preventing serious or even fatal events and effectively supporting the management of heart failure patients.'

Christoph Böhmer, the company's International President, pointed out that numerous studies published over the past few years have confirmed the clinical and economic benefits of the system. 'The IN-TIME study reinforces these excellent clinical outcomes by demonstrating a reduction in mortality in HF patients for the first time. This latest inclusion in the ESC guidelines indicates that home monitoring will play an even more important role in the future. The ESC recommends device-based telemonitoring for the early detection of critical events in cardiac patients, and Biotronik Home Monitoring is particularly well suited to serving the HF patient population.'

/ Heart Centre Brandenburg near Berlin, Germany. After graduating from the Medical University in Hannover he joined the German air force as medical doctor. As resident and senior resident focusing on cardiac, thoracic and vascular as well as trauma surgery he worked at the Medical University of Hannover, at Landeskrankenanstalten Salzburg, Austria, and the University Hospital Tübingen, Germany. In 1999 Dr Albes was appointed Deputy Director of the Department of Cardiac, Thoracic and Vascular Surgery at Friedrich Schiller University in Jena, where he has also been adjunct professor since 2004.

PART 1: Announcing a targeted ultrasound contrast agent - a major breakthrough in molecular imaging

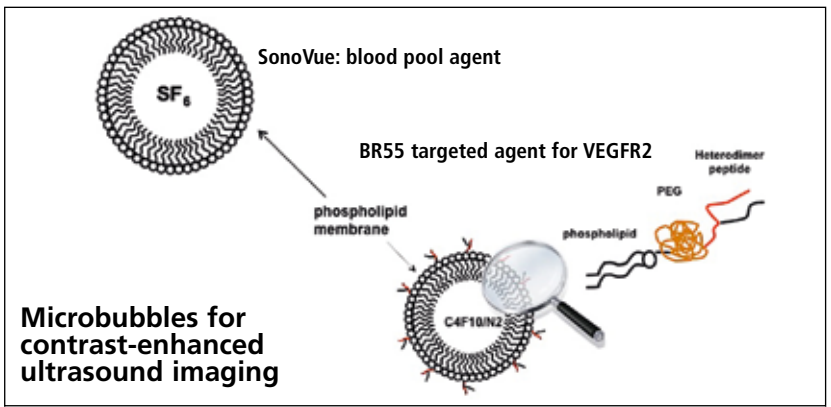
The complex science behind microbubbles

At Bracco Suisse SA in Geneva all efforts are dedicated to contrast media for ultrasound scans. During their visit to the firm's research centre and manufacturing site, Daniela Zimmermann and Ralf Mateblowski met with François Tranquart MD PhD, general manager of the Bracco Suisse research centre, to hear why SonoVue is now Europe's most popular ultrasound contrast agent, with research heading towards novel agents aimed at detecting and imaging specific molecules that are key targets in disease processes (molecular imaging).

Microbubbles are highly complex and effective. Basically, François Tranquart explains, the ultrasound contrast agent SonoVue is formulated with microscopic microbubbles, smaller than red blood cells, and a non-toxic gas – sulphur hexafluoride. SF6 has low water solubility to prevent diffusion into surrounding blood and it is fully exhaled via the lungs within minutes. Microbubbles can be injected repeatedly in patients for better characterisation or treatment guidance. The microbubble shell is highly flexible and made of phospholipids, like the membranes of natural cells.

Bubble size is vital, since they must quickly flow through capillaries. The type of gas is the most important component of the microbubble, he explains. 'There is a degree of diffusion between the microbubble core and surrounding environment – blood. A gas such as SF6 is not normally present in blood. It slowly diffuses from the inside towards the outside. With air, oxygen and nitrogen, however, there is a constant exchange of gas between bubbles and blood: the microbubbles would disappear right after injection. SF6 guarantees the microbubbles to last a few minutes, enough to make a diagnosis.

'Obviously, we also want to improve the shell properties to protect microbubbles and make them more resistant to pressure because, once injected, they circulate in the blood and are exposed to ventricle contraction. Even with excessive hydrostatic pressure, they must persist. In general each microbubble has its own properties. Some are soft and may present different behaviours when exposed to different acoustic pressures. Others are a bit more resilient and thus less sensitive to acoustic pressure such as ultrasound waves. We need to play with different properties depending on selected indications.



Microbubbles for contrast-enhanced ultrasound imaging

'Ultrasound waves exert positive and negative pressures. We saw that soft shell bubbles respond sensitively to these acoustic waves when we matched the machine settings and microbubbles perfectly. Since this technology is complex we need to attune microbubble characteristics and the acoustic parameters of the equipment. If there's a good match between microbubble properties and the ultrasound equipment, we obtain a strong and easily visible signal from these microbubbles to acoustic waves, so we could detect minute amounts of them in vessels and parenchymal organs using very small contrast agent doses. We can observe the specific behaviour of microbubbles expanding and shrinking depending on the acoustic waves. Under positive acoustic pressure they shrink, but with negative pressure, microbubbles expand.

By playing with these two different responses we detected a specific ultrasound signal, representing the presence of microbubbles with- in the bloods without overlapping tissue signal.

'Ultrasound frequencies are relatively high and changes in acoustic pressures are very rapid. Under ultrasound all the microbubbles are oscillating around their stable state. This oscillation is the signal we detect. Its strength is proportional to the amount of microbubbles in the different areas. If we inject microbubbles they circulate and accumulate in some specific areas. By observing arrival, disappearance and persistence, we get important diagnostic information.

'We can diagnose a tumour or inflammation based on the behaviour of the agent within the specific area because we know that a cancer lesion will exhibit a specific behaviour compared to an inflammatory lesion or normal tissue. When you compare a lesion with normal parenchyma, or an inflammatory lesion with a cancer lesion you will observe differences regarding arrival time, enhancement, or washout.'

'In Europe, SonoVue is approved for use in echocardiography, Doppler sonography of large vessels and liver and breast lesions. Clinical trials demonstrated that ultrasound with this agent provides more diagnostic information than non-enhanced ultrasound in specific clinical settings.

Targeted microbubbles – the Ferrari in the Bracco garage

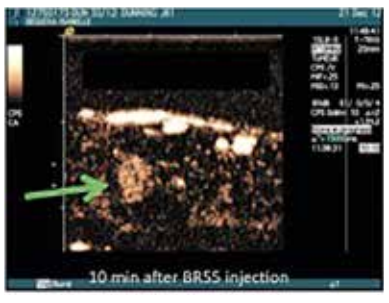
While SonoVue as a non-targeted agent reflecting blood flow and perfusion is state-of-the-art technology, the Bracco team is already highly engaged developing a new generation of microbubbles, 'targeted agents' as François Tranquart explains: a specific ligand placed on the shell so the microbubble can bind a specific receptor.

'When it comes to detection and characterisation of focal parenchymal lesions, with SonoVue we can tell where a lesions is, if such lesion is highly or poorly vascularised, and the type of enhancement (wash-in, peak, wash-out) can give us clues about its nature' he points out. 'With targeted microbubbles, on the other

Fundamental mode

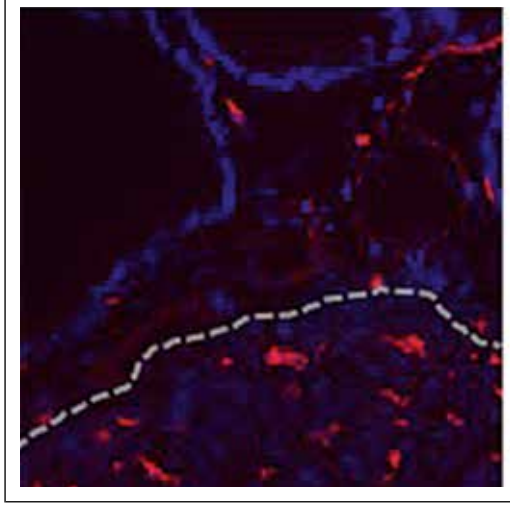
Peak enhancement

Late Phase Enhancement



Immunofluores

CD31



Dr François Tranquart

hand, we are moving into molecular imaging: the ligands bind specific receptors expressed by cells. Thus, we can image molecular patterns in some specific regions of the living body, comparable to immunohistochemistry used by the pathologist in biopsy specimens. The aim is to see exactly what is expressed and the level of expression in a living body. The presence of a specific receptor or specific protein could explain if and how disease processes are taking place. That means, firstly the information gathered with the targeted agent is much more specific. Secondly, in the future we may be able to monitor treatment efficacy in a different way, because some treatments could interact with this receptor changing its expression, which we could directly image.'

'We need to target receptors expressed within the vessels. Since the microbubbles remain strictly within the vessels we cannot target receptors expressed in tissues. This is a key point. As many diseases are associated with specific receptors, we have to select relevant receptors expressed on endothelial cells. This is the case for many receptors involved in the angiogenesis process where they are expressed at endothelial level and require a specific ligand (such as VEGF, HIF and many others) to induce angiogenesis. The aim of targeted bubbles is to use this process with a ligand which is close to the natural one.'

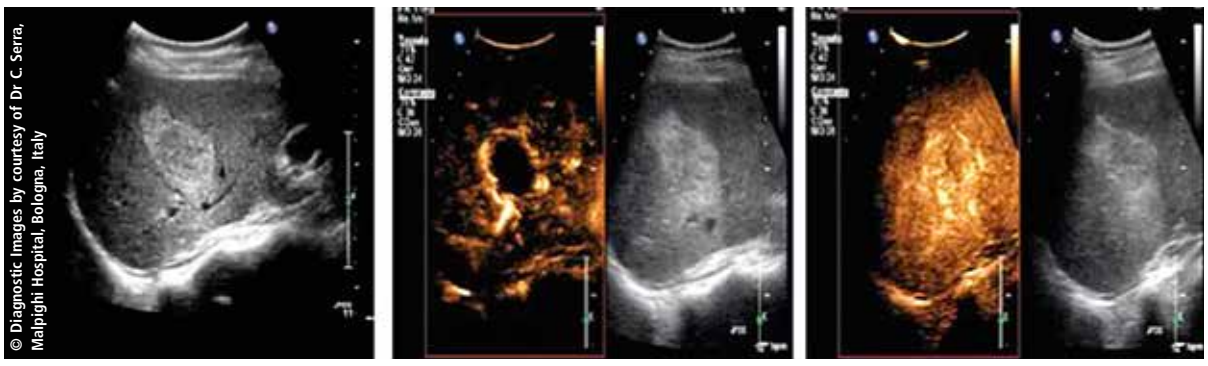
If these could detect angiogenesis, might suppression be a next step?

'Theoretically speaking, maybe; practically speaking, I don't think so. We have very few attached microbubbles but a huge number of receptors, which makes blocking the physiological process impossible. Besides, microbubbles disappear in minutes. However, demonstrating the presence of a specific receptor involved in the disease process might lead to treatment specifically directed towards such a target. If, for example, dealing with a local angiogenesis then having that ability would provide a clear indication that an anti-angiogenic treatment is effective in eliminating the blood supply to cancer cells. Such an approach, where medication is adjusted to the specific situation of the individual patient, is "precision medicine".'

What about a new generation?

'After identification and labelling of pathological tissue, a third generation could even guide drugs to a specific site.'

Part 2, EH-6-2013: Microbubbles made for drug delivery

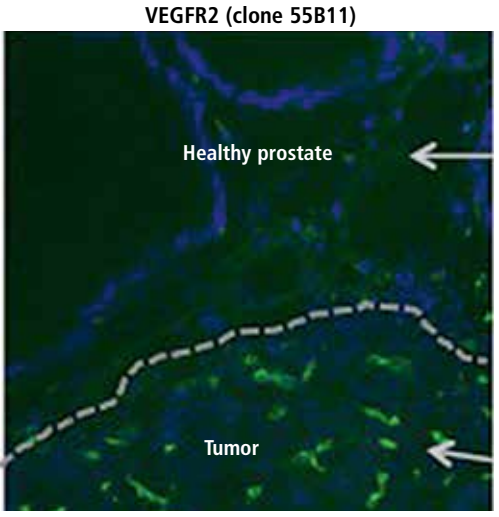


Typical hemangioma: Left: an hyperechoic lesion is clearly depicted in this liver with B-mode imaging. Middle: In the arterial phase after SonoVue injection, globular enhancement is visible at the margin of the lesion, slowly progressing centripetally towards the centre of the lesion. Right: In the portal-venous phase, the lesion shows progressive contrast fill-in, becoming completely enhanced in the late phase. This enhancement pattern is typical of most hemangiomas.

Preclinical ultrasound molecular imaging of Dunning prostate tumour with BR55 (ultrasound targeted agent for VEGFR2): Top panel: B-mode image of the rat prostate with the tumoural part in green and the healthy part in pink. Middle: 20 seconds after BR55 injection the enhancement was slightly higher on the tumour side. Bottom: 10 minutes after BR55 injection, there was an exclusive enhancement on the tumour side. Lower panel: Immunohistochemistry confirmed the over-expression of VEGFR2 in the tumour part while this was normal in the healthy part.

scence staining

VEGFR2 (clone 55B11)

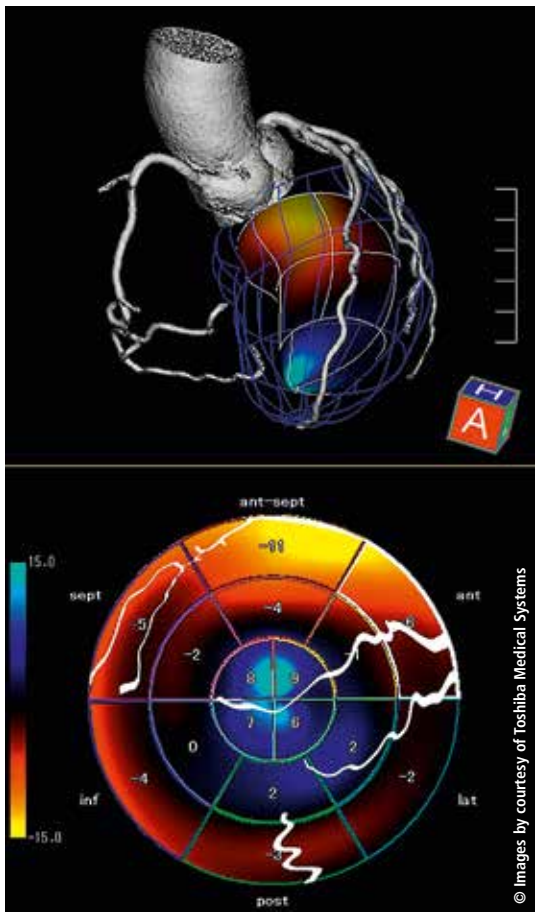


Smart Fusion of modalities enhances clinical output

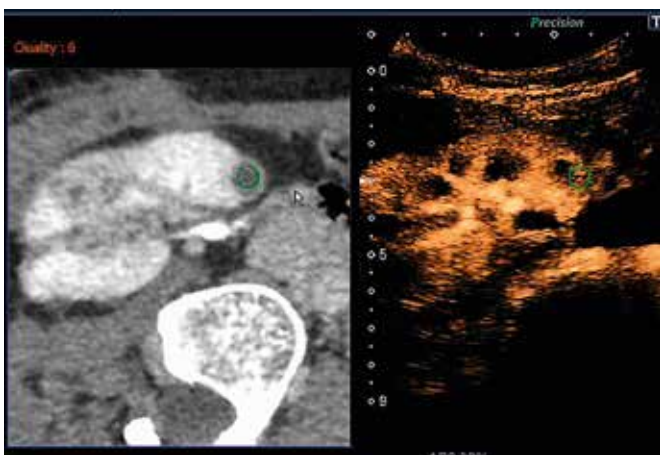
Adding high quality, dynamic ultrasound for hybrid imaging enables clinicians to improve detection of a range of lesions or to intervene better for improved clinical outcomes

'We can no longer be fascinated with pictures; what we need is proof of the clinical benefit from tools and techniques,' said Professor Jose Zamorano MD, Director of Cardiology at Ramón y Cajal University Hospital in Madrid. Currently, he is building a multi-centre study of cardiovascular imaging (CVI) to evaluate the severity of ischemia using a hybrid display combining CT Angiography and 3-D ultrasound called Smart Fusion from Toshiba.

Right: CVI fusion



Bottom: Fusion RCC w/ contrast



Meanwhile, at the University of Paris Necker Hospital, Jean-Michel Correas MD has also moved beyond fascination with the advanced capabilities of Smart Fusion by applying the technology to clinical practice. He has added advanced contrast-enhanced ultrasound images in real-time to both CT and MRI acquisitions better to target and treat even small isoechoic or non-visible lesions. 'There are clear benefits for lesion detection, Dr Correas said, adding, 'as well as for treatment planning with the possibility of finding new routes to the lesion, which is a key advance.'

At the University of Berlin's Charité Hospital, Thomas Fischer MD, Director of the Ultrasound Research Lab Radiology and Head of Ultrasound Diagnostics at the Institute of Radiology, finds the enhanced capabilities of hybrid imaging with Smart Fusion makes navigation more comfortable for positioning and performing ultrasound-guided biopsies of prostate tumours. 'Not all forms of prostate cancer are created equal,' he pointed out. 'Certain patients, those who have a non-aggressive form of prostate cancer, will not benefit in any significant way from the therapy. Thus we need to identify the tumours that will respond to the therapy.'

MRI remains the modality of choice for identifying the exact location of the dominant lesion in the prostate gland. For those patients who will benefit from treatment, the challenge become re-locating the tumour with an ultrasound system for guidance. 'Here the B-mode image, which is crucial for biopsy and treatment purposes, comes in,' he explained. 'Planes from both imaging modalities need to be fused as precisely as possible in order for the biopsy needle to hit the lesion. And this in turn means that I do need to see the needle.'

For this, the Smart Fusion platform offers superior image quality thanks to a special transducer developed by Toshiba. Fusing this high quality dynamic image with the static MRI acquisition of the organ is simplified with a sensor placed on the transducer handle. 'That's the trick behind Smart Fusion,' he explained. 'This sensor tells the system exactly where the transducer is positioned within the cavity. In other words, the hand movement can be quickly translated on the moving images.'

According to Dr Correas, the combination of dynamic tracking with the new transducer and the image quality effectively creates a new tool for interventional procedures. 'There is improved lesion detection and characterisation, which is the key step,' he said, adding, 'After all, if you cannot see the tumour, it will become very difficult to treat it.

'Without going into detail about the procedure itself, I can say it is rapid where volume data from CT or MRI were loaded to the Aplio 500 system to allow simultaneous dynamic display. We fix one transverse plane, locate one target point and can then fuse the images.'

The result is a clear benefit for better diagnosis, planning and treatment, '…and we can evaluate results almost immediately after ablation to be sure of correct coverage,' he said.

With a significant patient workload, the reduction in procedure time becomes an important advantage, as well as the benefit of reduced radiation exposure for patients and medical staff.

Applying this technological advance to an assessment of cardiovascular conditions is opening a new field of study for Professor Zamorano in Madrid: 'Smart Fusion in cardiovascular imaging has the potential to greatly aid in the assessment of coronary artery disease for ischemia and heart failure, an extraordinary advance through the integration of imaging information provided by the CT scan and echo.'

The resulting images display the coronary arteries and branches on a colour-coded myocardial volume, making it possible to correlate the degree of coronary stenosis with the information from myocardial strain in the surrounding myocardial territory. This holds the potential for a non-invasive assessment of myocardial mechanics and the relationship with coronary ischemia, he said. 'With CT images we get an excellent assessment of the morphology of the coronary arteries, but this is not enough for analysing coronary artery disease, which is caused by functional issues, such as ischemia,' the professor pointed out.

Where the CT may show a 70% stenosis in the left anterior descending (LAD) artery, he explained, 'this does not tell you a lot about the ischemia related to that stenosis. What we add with Smart Fusion is the data from stress echo, and now we clearly see if the area of ischemia is related to a specific coronary artery, as well as the severity of the stenosis at that level.

'We are at the very beginning of the process, and building evidence of the clinical benefit of the CVI technique is very important.' Prof. Zamorano added that he expects to join with other centres in Europe for a clinical study to validate initial findings. 'We are a university hospital, very proud of developing a new technique, but ultimately the tools and the technique must be oriented to a real clinical benefit,' he stressed. 'So many patients are affected by ischemia, and we are sharply focused on evidence of the clinical outcomes.'

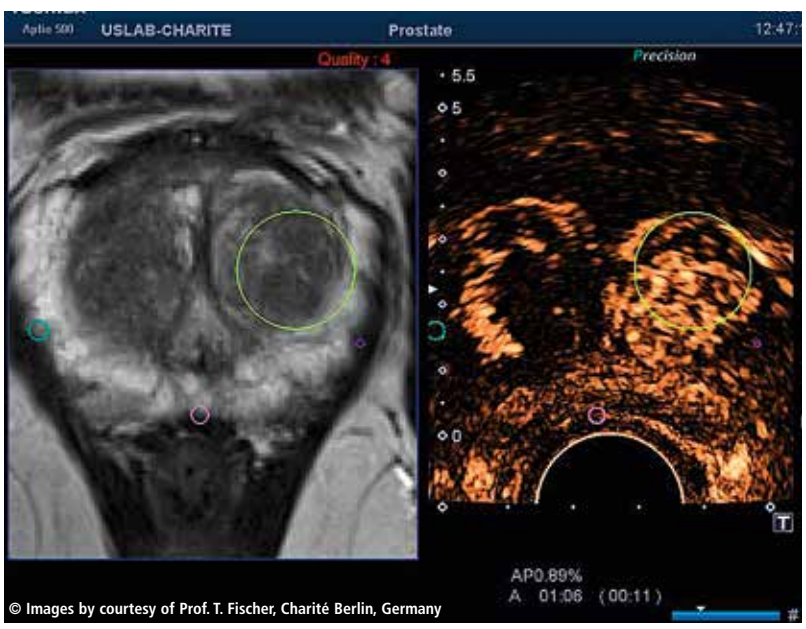


Image fusion of MRI and CEUS

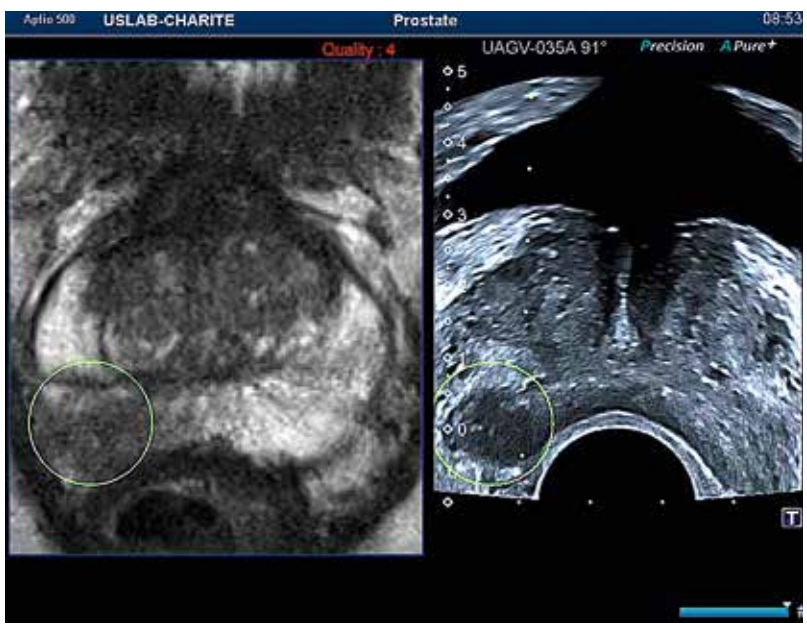


Image fusion, the green circle shows the tumour in both MRI (right) and US

Image fusion for p

Bringing in technologie

Prostate cancer is the most common cancerous disease in men. Since magnetic resonance imaging (MRI) arrived the diagnostic capabilities for early detection have improved considerably, along with more selective prostate cancer treatment. In particular, the capabilities for tissue differentiation and spatial resolution are much better with MRI compared to ultrasound imaging. However, despite these continuously developing imaging capabilities, the final differential diagnosis and clarification for an MRI result is still a biopsy. The most common type is the ultrasound-guided core biopsy, which systematically samples tissue in 12 locations where prostate cancer most commonly develops. So, why not combine the two technologies, MRI and ultrasound, to reduce the number of biopsies required and achieve higher accuracy with a new procedure?

The Urostation from KOELIS and Samsung Ultrasound

In partnership with the French company KOELIS, the Korean medical devices manufacturer Samsung has developed a urological workstation that combines the advantages of MRI imaging with the practical advantages of ultrasound-guided biopsy. In the Urostation, 3-D MRI images of the prostate are superimposed with live images from the Samsung ultrasound scanner taken with a transrectal 3-D ultrasound transducer.

At the Urology Clinic in University Hospital Dusseldorf, Professor Peter Albers and team are already using a combination of Samsung Ultrasound and Urostation. The clinic is a Prostate Cancer Treatment Centre certified by the German Cancer Society. More than 2,000 in-patients and 7,000 out-patients are examined and treated there every year.

rostate diagnostics

nnovative es together

Image fusion increases patient comfort additionally relieves the doctor in charge.
Ultrasound devices from Samsung and KOELIS´ Urostation form a strong combination and enable innovative image fusion for prostate diagnostics. The Urostation layers previously recorded 3-D MRI images of the prostate with live images from the Samsung ultrasound device. These are captured with the transrectal ultrasound probe.

Most biopsies are carried out with the Samsung-Urostation combination. 'With this procedure we can sample tissue very specifically in locations that look conspicuous on the MRI images,' Professor Albers explains. 'The MRI shows up small tissue changes in the prostate at an early stage, which we would not be able to see with ultrasound alone. To take very specific tissue samples, in some individual cases we carry out MRI-guided biopsies.'

However, tissue samples are not only taken from conspicuous locations but systematically from 12 typical locations, although the doctors aim at particularly conspicuous areas. 'The hypothesis that it suffices to only limit ourselves to particularly conspicuous MRI results has not been scientifically confirmed. Two large studies are currently being carried out to clarify this issue,' he adds. A welcome side effect: Whilst MRI-guided biopsies are not usually reimbursed by health insurers, this service can now be offered to patients in the university hospital as part of these studies.

More comfort for patients and improved hospital processes

Professor Albers sees the advantages of the new procedure for patients in the method itself. 'If a patient undergoes an MRI-guided biopsy he has to lie in the MRI scanner on his front for an hour with his arms over his head while we carry out a transrectal biopsy. With the capabilities of the new image fusion, we initially take the diagnostic MRI images and the patient can then lie on his back in the lithotomy position for the biopsy, with the whole procedure over in around ten minutes.' This not only makes things a lot more comfortable for the patient but also eases strain on doctors.

Hospital processes have also improved through the Ultrasound-Urostation combination. The Urology Clinic shares the MRI scanner with other clinics and the machine is only available for all examinations and biopsies one day a week. 'The capacity for MRI examinations represents a bottleneck, so we are happy to move the time-consuming biopsies from the MRI scanner to the Samsung Ultrasound-Urostation combination. This gives us more time for diagnostic MRI examinations,' the professor explains.

Further advantages of the Samsung Ultrasound-Urostation are that examinations and the localisations of biopsies are archived and each localisation can be assigned the corresponding histological result. Therefore, in the case of follow-on examinations, or control biopsies, the doctor can revert to the archived, previous results, inclusive of planning and treatment images as well as relevant diagnostic data.

Choosing the right partner

The combination of Samsung ultrasound scanners with the KOELIS Urostation has proved to be very successful. KOELIS chose Samsung as a partner due to the firm's high level of innovative technologies, specific design, user friendliness and high quality. The Samsung ultrasound systems SonoAce X8, Accuvix V10, SonoAce R7 and UGEO H60 are already compatible with the Urostation. Further systems, such as the Samsung Accuvix A30 and future models will also be compatible.

Peter Albers gained his medical degree at Mainz University (1988) and his urology residency at the Universities of Mainz and Bonn. In 1993-'94 he was research fellow at the Urology Department at Indiana University, USA. Earlier roles also include the chairmanship of the Urology Department at Klinikum Kassel (2003-2008), and Vice Chairman of the Urology Department at the University of Bonn (1998-2003). Since 2008, he has been Professor and Chairman of the Urology Department at the University of Düsseldorf.
Professor Albers´ main interests lie in uro-oncology.

Fusion technology is a major research focus

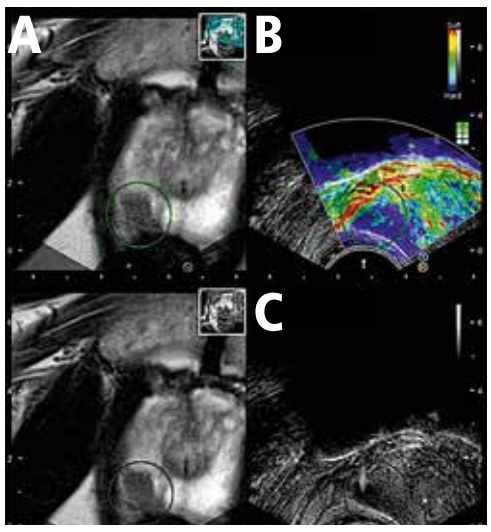
Advances in MRI/ ultrasound fusion biopsy

Widely considered a safe procedure for targeted tissue sampling, the fusion of MR and ultrasound images for prostate biopsy purposes is quickly gaining ground among radiologists. Currently, fusion technology is a major research focus at many radiology centres: MRI/ultrasound fusion biopsy is being implemented, new transducers are designed, the potential of elastography and other procedures are combined – and results are highly promising. This is good news for patients since in Germany alone every fourth male is affected by prostate cancer and more than 60,000 new cases are recorded annually.

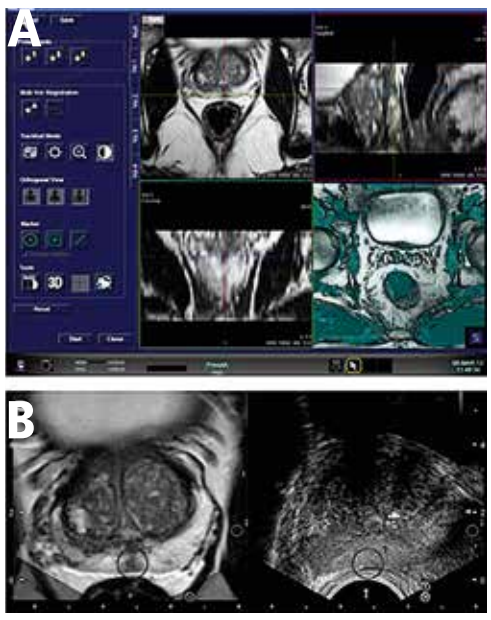
European Hospital asked one of the pioneers of fusion biopsy, Professor Thomas Fischer MD – Managing Senior Resident at the Radiology Department in Charité Campus Mitte and Head of the Interdisciplinary Ultrasound Centre at Charité, Berlin – about the challenges and prospect of the procedure and experiences in the use of a Hitachi ultrasound system for fusion biopsy.

Prof. Fischer: 'Hitachi Real-time Virtual Sonography – HI-RVS – has been around for more than ten years. Originally developed for radiology, in the meantime HI-RVS has conquered urology. What makes this system unique? Interestingly, the very fact that the system has been on the market for some years and uses a biplanar transducer, the EUP-CC531, which combines the advantages of conventional core biopsy with fusion ability, as well as elastography and contrast imaging. Due to its shape, this transducer is ideally suited for prostate examinations.

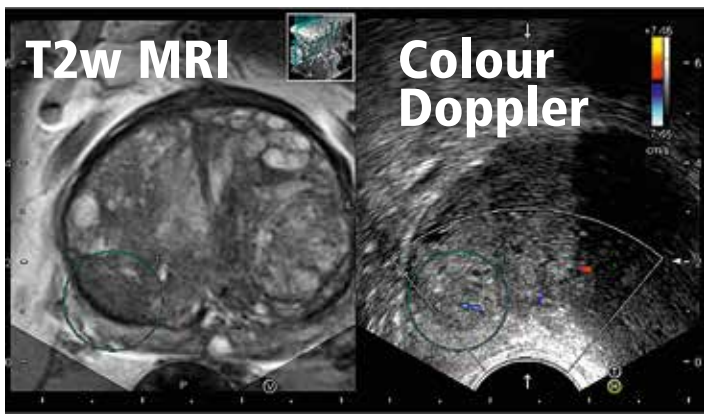
Professor Thomas Fischer has directed ultrasound diagnostics at the Radiology Institute at the Charité Clinic in Berlin, since 2007. Since 2009 he has also headed the ultrasound research laboratory at the Charité, which specialises in testing new ultrasound procedures and techniques in complementary studies.
Memberships include the European Society of Radiology (ESR), the German Radiology Society (DRG), the German Society for Ultrasound in Medicine (DEGUM) and honorary membership of the Polish Society of Ultrasound (PUS). In 2010 the professor received the Scientific Presentation Award for the best paper at the European Congress of Radiology. In 2011, he received the Herbert M Stauffer Prize for his scientific paper *Detection of Rheumatoid Arthritis Using Non-Specific Contrast Enhanced Fluorescence*, classed as the best basic science paper.

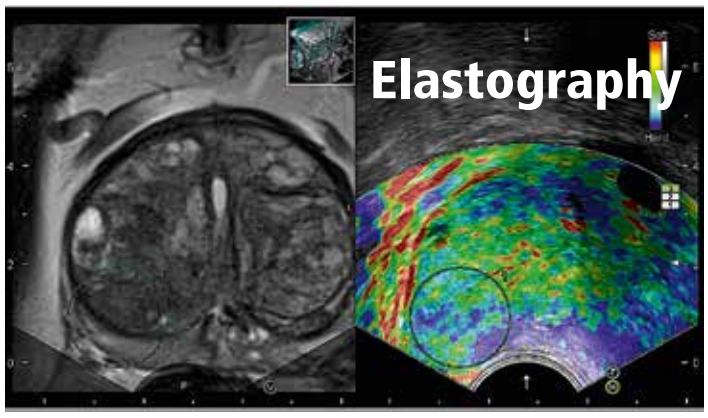


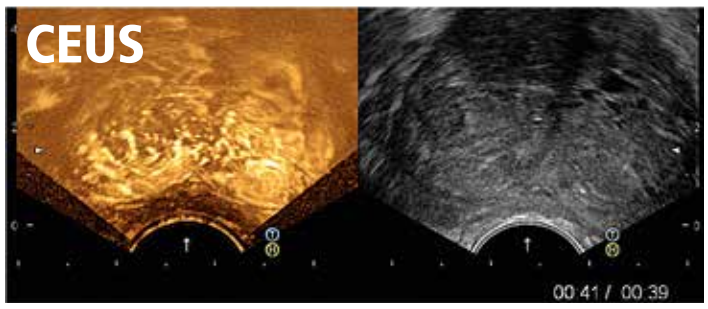
Hypointense prostate tumour in T2w (A) and comparable plane in ultrasound elastography with hard tissue area (B) and clear delineation of the prostate gland (red line) Core biopsy with needle visible in the circle (C) Confirmed prostate carcinoma



Left: The MRI dataset is uploaded to the US workstation (A), and the probe position is marked in the center at the transition of the seminal vesicles to the prostate (B).







Top: Examination of BPH with modern ultrasound technologies and MRI

tography and contrast imaging. Due to its shape, this transducer is ideally suited for prostate examinations.
'While it achieves the image quality of a state-of-the-art transducer, its anatomy fusion is faster and easier to understand, particularly for operators who are not so familiar with this procedure. The specific design of the probe, double curved array orthogonally positioned, allows an easier understanding of the prostate anatomy as seen on the MRI image, because it matches ultrasound planes easily with sagittal and axial views of the prostate MRI – a major advantage.'

Hitachi was the first to introduce elastography. Do you use this technology in prostate biopsies?
'Absolutely! Despite all efforts the images can never be compared one to one, one reason being that the pressure exerted by the transducer deforms the prostate. This deformation limits comparability. However, in order to hit the tumour I need to move in the correct plane. Since the lesion may be very small, around 5 mm, I use elastography to localise the aggressive stiff tumour tissue.
'With MRI we navigate to the tumour site plane, and then we use procedures such as elastography or contrast-enhanced ultrasound – CEUS – to fine-tune the lesion positioning. And here the biplanar transducer also plays an important role. During actual examinations I even turn off MRI for some time, to be able to see the second ultrasound plane, orthogonal to the one I was previously using, which gives me a better idea where exactly the tumour is located. If I can see the tumour in two image planes I can hit it precisely with the needle.'

Is fusion helpful for other organs?
'Fusion can be very helpful in liver studies although unfortunately, in this country, it is rarely used in this area because of diverging professional interests. On the international level, fusion is the domain of radiologists because you do have to be familiar with CT and MRI. For example, a patient presents with skin cancer. CT staging is performed to detect metastases. This is done on the basis of a particular protocol that encompasses one-time administration of a contrast agent. If a suspicious lesion in the liver is detected you cannot tell – due to the single-phase procedure – whether it's a cyst, a haemangioma or metastasis. This is where fusion comes in, especially in lesions difficult to see in Ultrasound.
'The radiologist takes the patient and CT data to the ultrasound lab, where he injects a contrast agent into the region of interest, fuses the CT and US image data and then can see whether it's a cyst, haemangioma or metastasis. Fusion of CT and US images, as described in our discussion, offers much more precise diagnostic possibilities. Moreover radiation dose can be saved and the results can be verified either right away with a biopsy or with a third modality, namely MRI.'
'Right now we are talking about detection only, meaning diagnostics. We'll begin with CT staging, an established standard procedure, to see if and where we are dealing with metastases. That is impossible with ultrasound. If a suspicious lesion is detected in the liver, or the spleen, which cannot be clarified with a single-phase CT study, then fusion comes in to help.
'In short: The other phases are added to the CT scan and by looking at the portal or any later phase we can tell – unambiguously – whether the suspicious lesion is a melanoma or a metastasis. With these data the case can be discussed by the Tumour Board and everyone present, no matter from which medical discipline, can understand the facts and findings. Why? We see the CT images plus the contrast-enhanced ultrasound image from the same plane.
'That's not all. What about treatment? I have to verify whether the patient responds to the therapy or not. That means looking at exactly the same spot in exactly the same planes, which is pretty difficult with ultrasound; but when I can call up the CT data with the reference lesion, I can compare the data, avoiding when possible a new CT examination of the patient (radiation dose saving).
'Identifying and differentiating lesion in CT staging – that's is the domain of this fusion technology.'

Ultrasound 60 ye

And getting better all the time, says Ivan Salgo MD MS, ***head of Cardiovascular Philips Healthcare, Andover, USA***

Through the miracle of modern-day ultrasound, we are able to see – in three dimensions and in real time – the functioning of arteries, veins and the many sophisticated structures of the heart. While most think of ultrasound technology as it relates to grinning parents getting a first glance of their baby in the womb, cardiovascular care is being revolutionised by advances in ultrasound technology.

This year, we celebrate 60 years of ultrasound in the medical field. Its use in the medical community began in 1953, when physician Inge Edler and engineer C Hellmuth Hertz produced the first echocardiogram of the heart in Sweden. Incredibly, they did this by using an industrial-sized ultrasonic tool from a neighbouring shipyard that was being used to detect cracks in the metal of ships.

In 1956, Japanese physicians used the Doppler Effect (the change in wave frequency relative to distance) to examine cardiac motion. Following the Japanese discovery, Doctors John Reid and John Wild in Minnesota developed the first ultrasonic scanner for clinical use.

Today's premium ultrasound systems meld live 3-D images with tools like 2-D Intracardiac Echo (ICE) capability that present very clear, rich images to aid clinicians in a host of intricate cardiovascular repairs that are increasingly done in a minimally invasive way. Procedures to treat conditions such as valve insufficiency or defects in the septal walls are made possible largely due to the ability of today's ultrasound technology to provide the road map.

Cardiology on the road

When Kathleen Retailleau MD leaves the Hôpital Civil de Charleroi she takes the cardiology practice along with her, John Brosky reports

Part of the University Hospital Centre at Charleroi, the cardiology service provides consultations for a cluster of other hospitals, polyclinics and private physicians, which means that Dr Kathleen Retailleau takes to the road several days of each week to see patients throughout the region. 'Back in the echo lab at the hospital we have all the equipment for examinations, but for visiting consultations I need to bring my own echo system,' she said, adding that at one moment she may be visiting a general practitioner's office and, later the same day, work at an out-patient clinic.

To assure a mobile capability for cardiology ultrasound her choice is the Mindray M7, a hand-carried diagnostic system.

'I tried four or five different systems before deciding that the Mindray M7 was the best suited for this assignment with the best image quality and colour mapping,' she explained. 'It's a really complete offering for cardiology practice with advanced functions such as tissue Doppler imaging and IMT [auto-measurement of carotid intimae-thickness], and very good probes for cardio-vascular exams.

'It was really complete and good for my practice whether for standard echography of the heart, trans-thoracic exams or carotid ultrasound,' to determine a risk for stroke from plaque build-up, she added.

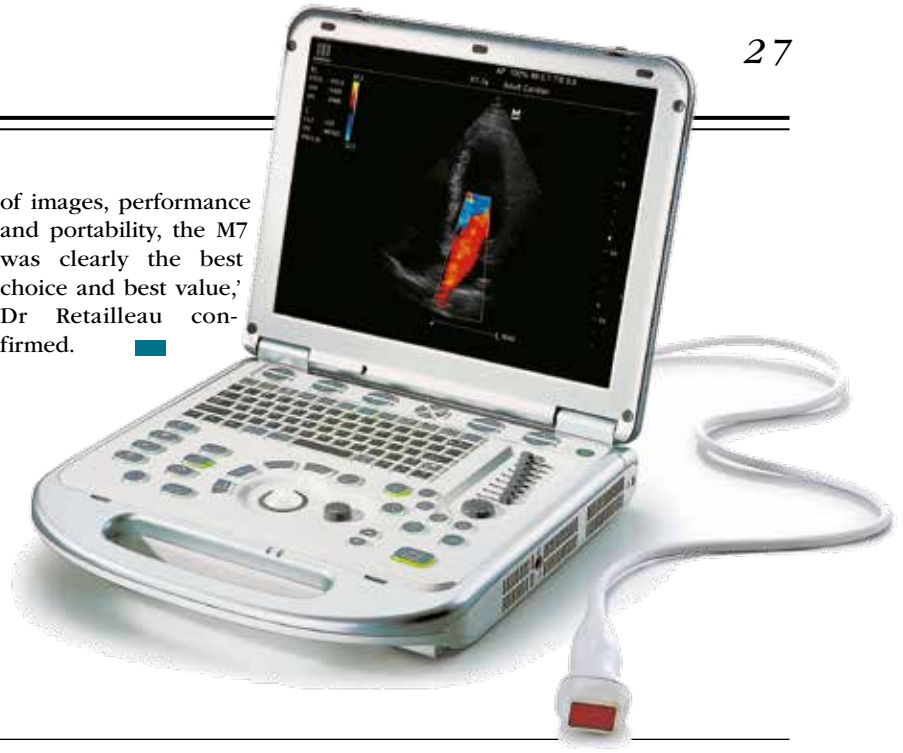
Designed for use at the point-of-care, the Mindray M7 portable ultrasound system delivers premium imaging performance across a broad range of specialties to assure an enhanced level of diagnostic confidence and efficiency.

For cardiologists, Mindray offers a suite of specialised functions, such as Free Xros imaging for anatomic M mode, as well as iClear for adaptive speckle suppression to improve contrast resolution and iTouch intelligent image optimisation.

Designed in a familiar laptop style, the M7 is built to travel with a robust magnesium construction reinforced with anti-shock and anti-splash features.

With a grab-and-go carry case, the machine can be powered either by high-capacity lithium-ion batteries or the nearest electrical outlet.

'When I compared the quality of images, performance and portability, the M7 was clearly the best choice and best value,' Dr Retailleau confirmed.



ears later

Investigations at

Ivan Salgo MD MS, head of Cardio-vascular Investigations at Philips Healthcare, Andover, USA

The next 60 years of ultrasound and other evolving imaging technologies are sure to bring us many more innovations aimed at improving healthcare in a variety of clinical settings around the world.

Droplet digital PCR allows detection of circulating cell-free nucleic acids

The liquid biopsy

Interview: Daniela Zimmermann

Donor transplant rejection and cancer relapse have two things in common: early recognition is vital and monitoring is hugely challenged. Much time and money invested in biomarker development for post-operative monitoring and early recognition of acute or chronic rejections has gained little success.

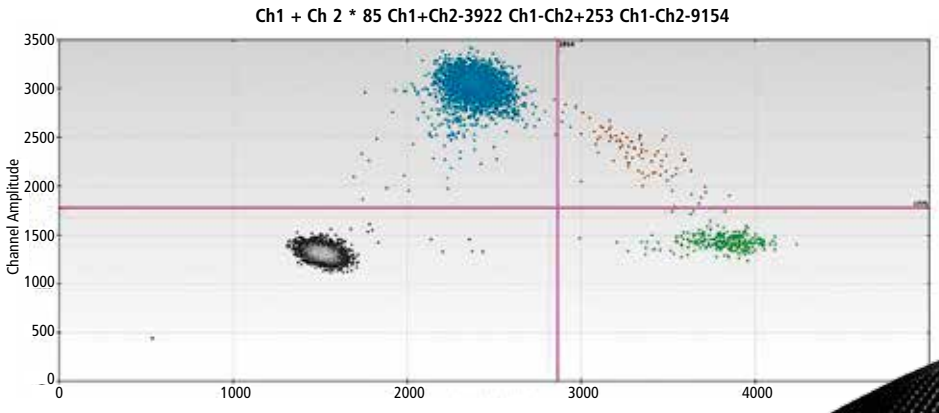
Now a likely breakthrough lies in a test developed by Chronix Biomedical scientists along with Professor Michael Oellerich at Göttingen University Medical Faculty. The Oellerich team's entirely new approach – using droplet digital PCR to measure cell-free DNA in transplant patients' blood allows early recognition of rejection. 'The great advantage of this new biomarker is that it yields direct information on the integrity of the organ,' Prof. Oellerich explains.

The team recently received the American National Academy of Clinical Biochemists (NACB) prize for the research results presentation.

Immense technical challenges

'The first challenge we faced was that circulating cell-free nucleic acids from the donor organ are diluted by the nucleic acids being released from all the other cells in the organ recipient's body, recalls Julia Beck PhD, Senior Scientist/Lab Supervisor at Chronix Biomedical. 'Therefore, we had to find some way of detecting a very weak signal from this organ against a very strong background signal from other DNA that stems from the recipient.'

The study leader indicated another obstacle: 'We wanted to be in a position to rapidly detect the circulating cell-free nucleic acids produced by the donor organ – if possible, within a day – to facilitate timely intervention by the surgeon undertaking the treatment.'



A blue fluorescence signal is generated by the template molecule from the organ, while a green fluorescence signal is produced by the molecules that stem from the cells of the recipient.

The QX200 Droplet Digital PCR System

Due to weak signal strength standard PCR could not be used: 'This method involves amplifying specific DNA sequences that contain a single nucleotide polymorphism - SNP. The organ and recipient must have different alleles at this location. The organ allele must then be detected against a huge background of alleles in the recipient,' Dr Beck explains. Droplet digital PCR provides a solution: 'This method no longer takes place in a single reaction vessel, but the sample is distributed across many tiny, individual reaction vessels in 20,000 "water-in-oil droplets", each composed of one nanolitre of liquid. In essence, each molecule thus has its "own" reaction vessel.'

Each of these one-nanolitre droplets contains a template molecule – i.e. in other words, a target molecule, which means the relevant signal is not drowned out by background signals. Additionally, the droplets can be counted individually: after using allele-specific hydrolysis probes, droplets containing a template molecule produce a fluorescence signal after PCR. Dr Beck: 'After marking the allele-specific probes with different fluorophores, a blue fluorescence signal is generated by the template molecule from the organ, while a green fluorescence signal is produced by the molecules that stem from the cells of the recipient.'

The donor organ releases DNA when cells die. 'For example, at a specific point in time, we measure ten percent of alleles that stem from the organ relative to ninety percent of alleles from the cells of the recipient in the patient's blood. This measurement shows us that a corresponding number of cells have died in the organ. If the signal increases from ten percent to thirty percent or more, then this is an indicator of the fact that too many cells are dying.' At this point, the recipient's immune system is attacking the organ, causing cell death.

Dr Schütz: 'This method's analytical simplicity is what makes it so attractive. We don't have to qualify anything, don't have to use circuitous routes for measurement through exclusion methods, rather more, we count, or the computer counts. In addition, it's easy to convince any surgeon, as they can understand the method immediately. A huge advantage.'

A precondition: assays must be developed

The team had to develop a set of different PCR assays as a basis for the early warning system, i.e., combinations of probes and primers, because at least five polymorphisms, each with different alleles, should be available for each combination of recipient and organ. To this end, a set made up of 41 such positions was developed, which are then tested in advance in each patient. Each assay must be designed to discriminate between the two SNPs and produce the signal reliably. In an initial study conducted in collaboration with Prof. Otto Kollmar, Director of Transplant Surgery in Göttingen, patients were investigated after a liver transplant. This study, which confirmed the validity of the approach, is part of a multi-centre study on biomarkers in transplant medicine, funded by the German Federal Ministry of Education and Research (BMBF).

Long-term organ survival

Based on changes in data collected during monitoring, the surgeon receives information on whether intervention is required and the immune system medicinally suppressed, or whether a biopsy must be taken for further tests. Prof. Oellerich: 'Half of donor kidneys, for example, are still being lost within ten years, and this against a background of a serious shortage of organs. A high percentage of patients exhibit levels of immunosuppression that are too low under standard therapy, resulting in chronic rejection in the long term; or, immunosuppression is too high, with resultant cardiovascular side effects, opportunistic infections, malignant diseases and kidney damage. For the first time, the circulating cell-free DNA gives us the opportunity to directly investigate donor organ integrity in a highly specific manner.' This method, he adds, can be combined with conventional drug monitoring and thus be used to achieve fine adjustments to immunosuppression for kidney and other organ transplants. Prof. Oellerich: 'The optimised treatment thus achieved for such patients could result in relevant improvements in long-term survival of the transplants.'

Detecting the genetic differences

Droplet digital PCR, Dr Schütz points out, 'also has applications in therapeutic follow-up after the resection of benign and malignant tumours and over the course of monitoring. To date, when a local relapse or metastases had developed in patients, this could only be detected using costly and complex techniques such as CT or MRI.' It is well-known that all malignant tumours differ genetically from the rest of the body. 'Therefore, our approach was to seek out these genetic differences, preferably in the primary tumour after it had been surgically removed, or when a biopsy was available. We then attempt to detect these differences in the blood, using the same approach as we described for transplants. We can assume that cancerous tissue is growing again as soon as we detect a genome sequence from the degenerated cancerous tissue.'

This application is far more complex, says Dr Urnovitz. No cancerous cell is the same. 'We must find a needle in the haystack.' Based on which changed genome sequences in tumours can be identified, his firm developed and patented the method in late 2012 .

Clinical acceptance

The Göttingen research team now aims for multi-centre studies to examine the new test's application to heart and kidney transplants in a larger patient cohort.

Communicating these new approaches to clinicians is now the most important task: 'We want to help patients at an early stage, avoid mid- and long-term damage and free the healthcare system from prohibitive costs. Our rapid, successful, low-cost method is well on the way to becoming the gold standard. To this end, we must communicate the method and, above all, the advantages to our colleagues.'

Links: www.chronixbiomedical.com
www.ndsprof.med.uni-goettingen.de

Key team members at Göttingen University Medical Faculty and Chronix Biomedical, from left: Howard Urnovitz, Julia Beck, Ekkehard Schütz and Michael Oellerich.

Approach and technique

Approach: Differentiation and quantification of circulating cell-free nucleic acids in the blood.
Technique: Droplet digital PCR, developed by QuantaLife, divides a sample into 20,000 nanodroplets and counts the nucleic acid targets. In 2011, QuantaLife was acquired by Bio-Rad Laboratories.

Renowned award for research team

During the annual AACC Conference, the American National Academy of Clinical Biochemists awarded Professor Michael Oellerich and team at the Medicine Faculty, Göttingen University, with a prize – a tribute to the test for recognising transplant rejections. At the event, the German team had presented initial study results in a poster presentation.

The economics of laboratory medicine

Report: Jane MacDougall

Over the past decade, laboratory medicine developed rapid, accurate tests that help in diagnoses, prognoses, treatments – and the overall theragnostics; but is it economical? This November, at the Journées Internationales de Biologie (JIB) meeting in Paris, that question will shape the medical economics session *Medical biology: a key factor in the healthcare effectiveness*, organised by the *in vitro* diagnostics industry union SIDIV.

When our *European Hospital* team asked session moderator Francis Megerlin and colleague Professor François Lhoste about medical biology's importance in France, they explained that this field is undergoing change. The medical element of biology has been the subject of two reforms, one in 2010 another in 2013, both covering not only the new role of the biologists and mandatory accreditation of laboratories performing medical analyses, but also a technical, capitalistic and geographic reorganisation of the sector. The French model is still very different from, for example, the German model, which is very concentrated with high productivity reducing analysis costs and with strong repercussion on the final price.

'In France the structure is still based on an older model, with high prices and an organisation of many small labs dispersed over the territory. Therefore, there are significant pockets of productivity and cost-effectiveness.

'The reform, however, equates to a deep change in the business model. The traditional monopolistic stakeholders are reticent, for the most part, mainly due to the possible impact on their career path and the current value of their business. Hence, France is adapting its ecosystem very gradually, although this may accelerate due to huge financial constraints on the way, as in many other European countries.'

Is our growing dependence on testing worrying? Could tests delay or complicate treatment?

'Technological progress enables growing quantitative and qualitative advantages with new applications (diagnoses, monitoring and observed efficacy). It also allows huge price reductions thanks to a productivity that, up to now, was not widely known despite its great interest for payers. Nevertheless, the amount of information now reliably produced must be interpreted, either by a person or computerised, due to the complexity of the data mass accumulated.

'In this context, the "medicalisation of biology" directs the change in the biologist's work; they must help in the choice of relevant analysis and interpretation of results, in a workable timeframe according to both clinical necessity and the patient's interest. The biologist who manages these data acquires a major role in the quality of the proceedings.

'Under these conditions, biology validates its decisive contribution to the cost-effectiveness of healthcare systems at local and national scale. Also, rapid tests that guide diagnosis, monitoring and follow-up of patients, are in full development. These potentially open the way to considerably faster and better care for patients; sometimes self-administered at a distance, with less risk and lower cost (tests by doctors, pharmacists, nurses, patient at home connected via smart devices, etc.). Other countries have already developed and adapted the routine use of microchips, which is rapidly taking off in Asia.'

Calculating the economic value of a biological test is also a topic to be covered during the JIB presentation. Talk about the economic value of a

Continued on page 30

Francis Megerlin PhD (International and Comparative Law), HDR (Pharmaceutical Sciences) is MCU at Paris-Descartes University, ESSEC Business School and Sciences Pro Paris, France. He is a Senior Fellow at the Berkeley Center for Health technology, UC Berkeley, California, and a member of the GRADES, University of Paris Sud.

François Lhoste MD is professor in clinical pharmacology and pharmaco-economics at Paris-Descartes University. He is also founder and co-chair of the Executive Master Strategy and Management of Health Industries at the ESSEC Business School, and past-president of the French Society for Health Economics. Researchers in biotechnology, drugs, medical devices, insurance and payment methods in both ambulatory care management and the hospital sectors, their French School is centred on the systemic assessment of innovative technologies, new performance-based pricing methods and more global market access in a constrained environment. They declare no conflicts or competing interests related to this interview.

French bio-terrorism network of labs

***European Hospital* correspondent Jane MacDougall asks Patrice Binder, retired 3-star Military General and President of the Scientific Board of Biotox-Piratox, about the country's national defence and safety measures**

Born in the USA out of the anthrax scare that followed the 9/11 attacks, the formation of a network of laboratories kept on 24/7 alert against potential bio-terrorism was introduced in France at the end of 2001. Initially interested only in the search for Bacillus anthracis, (the causative agent of anthrax) the structure was enlarged in 2004 with the mission to carry out the analysis of all chemical and biological agents that could present a terrorist threat. Under the jurisdiction of the Interior Minister for National Defence and Safety a network of laboratories known as Biotox-Piratox has evolved, within the context of the national security plan 'Vigipirate'.

Since 2011, the network has extended its missions to include the discovery of all substances of suspect nature in the environment, in drinking water, and/or the food chain, that could have been placed by a deliberate malevolent act, or by negligence. The aim of the network is to act efficiently and promptly in collaboration with the health services, police and army to eliminate the threat and protect the general public.

President of the Network's Scientific Board and Security Defence Advisor for INSERM, Dr Patrice Binder will present the work of the network at the Journées Internationales de Biologie (JIB) in Paris at the beginning of November. Dr Binder spoke to European Hospital's correspondent to explain more about the role of Biotox-Piratox in France and his forthcoming talk at JIB.

Why was Biotox-Piratox chosen as a subject for JIB?

Dr Binder: In fact it was we who approached JIB. We felt that it was important to advertise the network's existence to the general public at large and in particular to other laboratory professionals because they are often in the frontline if there is a potentially dangerous situation. We want to inform them of the network's existence and also let them know where they can turn if confronted with an unexpected situation. The network is in fact four networks – one that can deal with packages, envelopes and other substances that could be dangerous; another that can ensure the analysis of drinking water on a round-the-clock basis; a third that can act to take environmental samples in a situation of actual, or suspected, chemical attack and, finally, the national network of reference laboratories that are not mobilised immediately but are there to confirm the identity of a suspected pathogen.

Does Biotox-Piratox recruit new laboratories to the network?

'Not at all; the network has been set up to work in a way that is optimal when confronted with a potential biological or chemical risk to public health. The network is organised over three levels. Level one is known as our 'sentinel laboratories'. These countrywide laboratories must be able to recognise a suspicious situation, package or sample, alert the authorities, and recognise which of the 100 or so, level 2 laboratories is best adapted to deal with the situation.

'Each geographical defence-zone in France has at least one reference laboratory for 'human health' and another reference laboratory for chemo-toxicological analysis of the environment. These include 10 water board and 10 military labs. All the level two laboratories were selected from the results of an inquiry carried out by the scientific board in 2005. In addition to their scientific excellence, their specialty, geographical localisation, equipment and ability to maintain a permanent 24-hour cover, were all taken into consideration.

'For the most part the human-health labs are connected to a public hospital in each zone. While the toxicology environmental labs belong to different bodies including amongst others the police, gendarmerie and the national agency for food safety. A full list of level two laboratories is available from the Biotox-Piratox council.

'The level three laboratories are not necessarily mobilised as soon as the level two labs, as they are the highly specialised members of the network. Their role is to confirm the nature of a suspected pathogen and therefore have to be able to carry out rapid identification techniques such as rt-PCR under security conditions of at least category three. They also must have trained personnel for dealing with the treatment and containment of a potential infection of the pathogen.

'Responsibility for communication with the public for allaying fears and ad hoc communication rests with the governmental services.

Has the network ever been tested?

'Looking at the archives, since its existence in 2003 the network has dealt with 1,300 alerts. In 2003, 207 separate incidences were recorded, but since 2010 this has reduced to a steady 150 a year. Due in part to better understanding of what we are looking at and the organisation of the network, the number of analyses for suspected agents for bio-terrorism has fallen from 77.8% to fewer than 2% in 2011.

Do similar networks exist in other countries?

'Many of our European neighbours have similar plans in place and we try to have joint seminars and training programmes with other countries to exchange information and improve techniques. One of the differences in the French system is that we have created a network within networks associating laboratories from different specialties and environments together, to form a multidisciplinary and multifunctional network that can, thanks to its integration and shared training, work optimally together in the face of underlying terrorist threat to maintain national security.

Medical laboratories produce a range of results

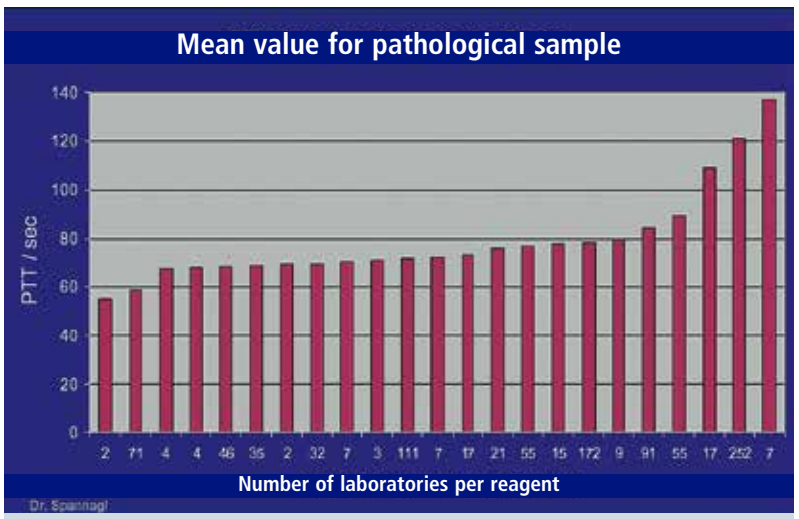
Understanding parameters

Report: Holger Zorn

Clinical chemistry influences almost all medical disciplines: most diagnoses are made or confirmed only after the laboratory has determined at least one or two parameters. Accurate results are a precondition for correct treatment. In this process, values from the laboratory can rarely be determined as absolutely as body temperature or blood pressure. However, even if the values are not identical, they must at least be comparable. This sounds simple, but is difficult to achieve.

Inter-laboratory comparisons, conducted at regular intervals, document the range of accurate results produced by medical laboratories. Based on a series of results, *European Hospital* demonstrates how certain laboratory parameters differ and what effect this can have.

Finally, Professor Gerd Schellenberg, from the Centre of Life Sciences at Anhalt University of Applied Sciences in Bernburg, explained by using the example of allergies to bees and wasps (cf. EUR. HOSP. 3/2013 p. 8). In this issue, Professor Michael Spannagl, Specialist in Haemostasiology at the Munich University Hospital and Chairman of INSTAND e. V., describes an example taken from coagulation diagnostics:



Activated partial thrombin time (aPTT) measures plasmatic coagulation and is the only rapidly available parameter for monitoring heparinisation. This is important, for example, during interventions requiring catheterisation, when using extracorporeal systems to stabilise the cardiovascular system or for supporting lung function. Heparin suppresses the natural blood coagulation functions and thus prevents the formation of clots and thromboses.

The test value for a normal, healthy adult is usually below 40 seconds, while it is generally 60-80 seconds under heparin. This figure shows how differently a quality control sample with a pathological value (1 unit of unfractionated heparin was added per millilitre of blood plasma) is assessed by different analytical systems: The values measured by the 1,035 participating laboratories ranged between < 60 and > 135 seconds.

We can only imagine what might happen if a patient undergoing heparin treatment was transferred from a 'low-value hospital' to a 'high-value hospital': without the knowledge of the variability in aPTT measurements, the heparin dose could potentially be reduced or treatment discontinued entirely and this could cause a thrombosis. Conversely, if the patient was transferred in the 'opposite direction' the heparin dose could be doubled and this could trigger severe bleeding.

The economics of laboratory medicine

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product or service generally aims to discuss price, they point out, quoting *Price is what you pay; value is what you get* (W. Buffet).

'Price must cover research and production costs (now essentially social), allow investment and generate revenue for the investor. Against this background the question of value is raised at different levels of use and/or purchasing – hospitals, healthcare organisations, biologists, other users (patients, or not), health insurers, pharmaceutical industry, etc.). When the bulk of healthcare is paid for by public or social funds, the value of a solution is sometimes viewed differently, depending on the social, organisational, economic, and of course, political background. All arguments (scientific or not) are good to determine value. However, ultimately this depends on a commercial contract i.e. social.'

Are newer, cost-effective and more accurate tests needed – albeit even if more expensive?

The end users test performance and know best. 'Their criteria are multiple and constantly changing; specificity, sensitivity, speed, ease-of-use, connectivity, cost, etc.). The best test is not necessarily the most expensive. A worthwhile innovation could be rewarded by market share, increase in volume of new activities, or a transformation in healthcare organisation. In all domains, technological progress leads to costs and prices reduction. Look at the smartphones! It is done to increase accessibility to powerful solutions. Almost everywhere the healthcare delivery chain is being reorganised under economic and demographic constraints. Technological progress and cost-effectiveness are a condition - and an opportunity - to maintain access to high quality care for all. That is also good for new businesses. The diagnostic industry has its future in front of it.

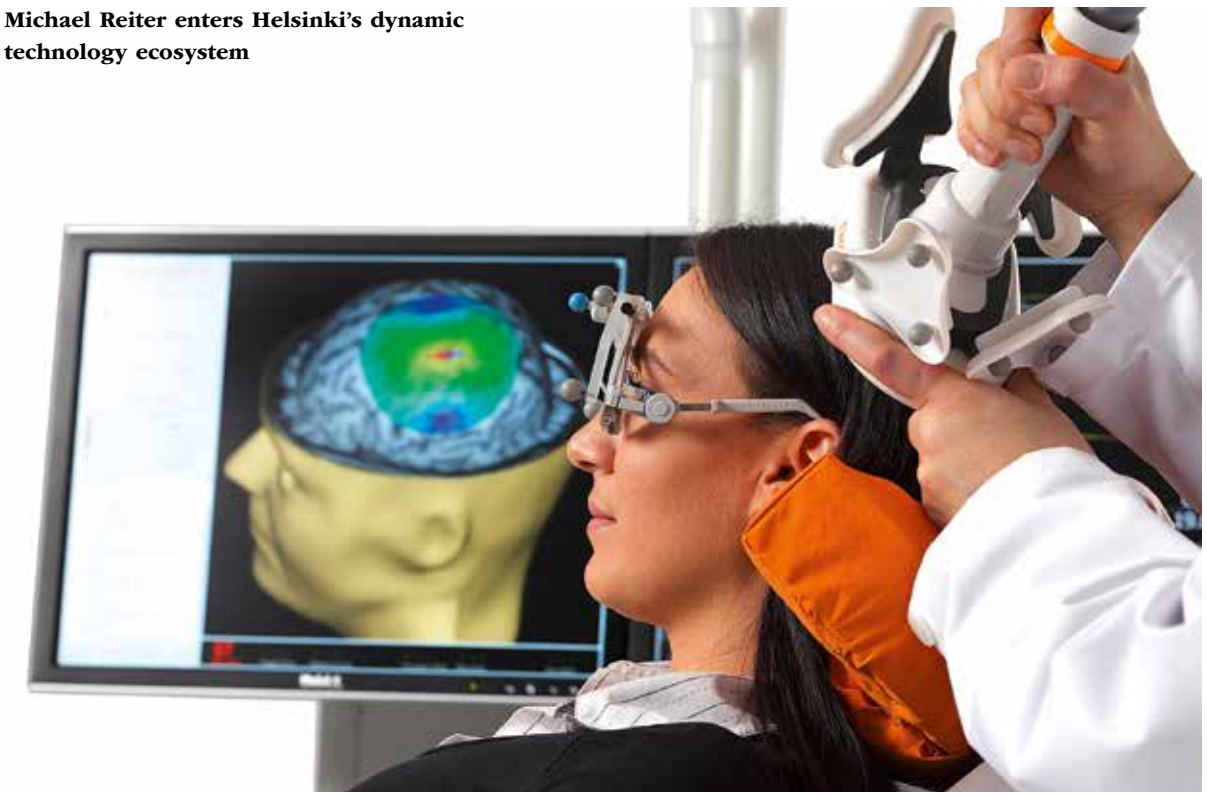
'However, the old fragmented and inflationist practices are not sustainable economically; sharing the progress is vital.'

What type of medical test would make the biggest difference?

'Tests have three main applications of interest to medicine; diagnosis, follow-up and observation of treatment/even cure. Some tests are individual markers of medico-economic efficacy in the case of expensive treatments e.g. oncology, immunology etc.). Therefore, they may become contracted Key Performance Indicators for highly specific medicines to obtain market access. In addition, there are in some countries, official lists of tests deemed "emergency", which can rapidly assess critical conditions. There are tests under development for hospital emergencies in neurology, cardiology etc. and also tests for use outside the hospital, as mentioned. These contribute to research of quality, safety, fluidity and cost-effectiveness of the healthcare journey. Their reach covers prevention just to the alteration of treatment dose by the patient himself, possibly connected with IT in the home and other new solutions. The field is enormous. JIB will be exciting!

Smart med-tech radiates from the New North

Michael Reiter enters Helsinki's dynamic technology ecosystem



Although traditionally exporting timber and machinery, today Finland has established itself as a producer of high-tech products. This includes innovative medical technology. In addition, in the post-Smartphone era following Nokia's sale of this business to Microsoft, med-tech may well emerge to fill the gaps – particularly in combining expertise from information and communication technology with know-how in biotechnology and medicine.

In recent years, the Greater Helsinki region has developed into a leading life science hub with hundreds of companies, numerous universities and various research institutes. Europe should look to this ecosystem – to be inspired, collaborate and purchase some of the advanced solutions originating from this area.

What are the drivers behind this impressive development? Finland is a great innovation environment, explained Minna Hendolin, who heads the Vitality segment of Tekes, the large funding organisation to focus on young and innovative pioneers. The excellent education system and significant overall investment in R&D foster progress; the country is a EU member and also provides easy access to the Russian market. 'Our investments have produced success stories mostly in ICT, but now healthcare is catching up,' added Minna Hendolin. Healthtech is non-monolothic. 'There is no Nokia in bio or pharma' In Nordic countries, as in many other regions, the way patients can access care needs to change – due to demographics, according to Micah Gland, CEO of Helsinki Business Hub: 'Demand is going up while budgets will go down. The system will have to be redesigned, driving the trend towards patient-owned care.'

From the same organisation, Indrek Vainu commented: 'Another change will concern big pharma – drugs are becoming too expensive to develop for the outcome they provide. Personalised medicine in the context of disease models is the way to go. And there will be a convergence of life sciences, ICT, nano technology and natural sciences. Neurogaming is a perfect illustration of this – supporting treatment, rehabilitation and learning.'

Against this backdrop, health technology will 'probably soon be the largest sector in Finland in the post-smartphone era,' said Veli Mäkelä, Chairman of the Finnish Medtech Manufacturers Organisation FIHTA and Chairman of the Board of Planmeca. Finland has enormous potential, which it has started to tap. However, the domestic market of 5.4 million inhabitants will not support this emerging industry, so exporting is the order of the day – just as it was hundreds of years ago. In 2012, med-tech exports reached €1.65 billion.

Impressive emerging products

Medtech Nordic Investing & Partnering is co-organised by Nordic industry associations in the field. The third edition, in Helsinki this summer, drew in 200 delegates and linked 30 funding applicants with investors and partners. Why does the sector need events like this? Health-tech is chronically underfunded, explained Terhi Kajaste from FIHTA. the R&D cycles are long, and budgets are needed particularly for sales and marketing because, in the rather small Nordic markets, emerging companies need to go global as soon as they get approval of a product.

The impressive range of start-ups presenting at the conference included, e.g., neonate clothing, bone density measuring, psoriasis therapeutics, data mining for genetic patterns, new developments in imaging, user-friendly and ecological casts, tongue control of devices for paralysed patients, and many more. This kaleidoscope demonstrates the extensive spectrum of existing and emerging health technology offerings from Nordic countries.

A purchasing event is to be held this autumn, and next year Medtech Nordic Investing & Partnering 2014 will take place in Oslo.

Established firms are here to stay – and grow

Numerous internationally established companies are active out of Finland. GE, for example, 'is here to stay and grow'. Having acquired the Finnish manufacturers Datex-Ohmeda and Instrumentarium, GE sees benefits in the skilled workforce, geographic location, in the EU and close to Russia, and the time zone.

The aesthetics and ergonomics of Nordic design are considered a particular asset, and the high output of patents from Helsinki operations indicates a high level of know-how. Thermo Fisher, a large international lab equipment and reagent manufacturer with several sites and R&D activities in the country, also appreciates the innovation climate, high level of education, and good relations with funding organisations.

Planmeca, a Finnish manufacturer, specialises in the design and manufacture of high-tech dental equipment, and is the world's largest privately owned company in this field. Planmed, part of Planmeca, produces the Verity Cone Beam Computed Tomography technology to provide high-resolution volumetric (3-D) images of extremities at a particularly low dose.

Research targets at the BioMag Laboratory include pre-surgical planning for epilepsy and tumours as well as biomarkers for neurodegenerative diseases.

Left: Nexstim's NBS is a new technique for accurately and reliably mapping the brain's vital functions.

Transition from physical to virtual

Merivaara is a perfect example of the transition the Finnish economy is experiencing: founded more than 110 years ago, the firm began to produce hospitals beds made from metal and wood. Manufacturing still takes place in the country, and exports take up 85% of revenue. A new product takes the company from the physical to the virtual, high-tech world, explained managing director Vesa Vihavainen: the interoperable OpenOR software platform enables integrated operating theatre management.

At the Helsinki hospital of the private Mehiläinen group, part of Ambea, orthopaedist Professor Jari Salo appreciates the high resolution of the Verity system in cartilage scanning for procedure planning in 3-D and also finds the OpenOR solution easy to use.

Routine and research in hospitals

The neonatal intensive care unit (ICU) at Helsinki University Central Hospital provides tertiary-level care to the region. In this country with a disparate population and large distances to travel for patients, the goal is to identify risk groups among pregnant women and to transport them to the small number of centres dedicated to neonatal care. Thanks to regional centres and good prenatal care, 'The percentage of pre-term births in Finland is merely 5-6%, and newborns below 1.5 kg make up only 0.8 percent,' according to Professor Sture Andersson, head of neonatal intensive care. 'The "per-kilo cost" of caring for these pre-term babies in ICUs may appear to be high, but if you take into account that these babies will be part of our future workforce, it makes economic sense to take good care of them – beyond the obvious ethical considerations.'

Subsequent to the research focus on lung and cardiac functions in neonates, today's research is very much centred on the brain, said adjunct professor Sampsa Vanhatalo, head of children's neurophysiology. 'A pre-term baby's brain is not a down-scaled version of a term baby's brain; a healthy brain emerges based on the wiring of various regions of the brain; lesions are detrimental to that fibre-based wiring.'

Whereas innovations in neuroimaging have not produced insights into functions of the organ, developments such as caps with numerous electrodes are yielding more detailed information about activities in the various cortical regions; also, stimulation of foot soles and other body areas have produced measurable signals in the in-lying regions.' The brain plays a pivotal role in the development of a newborn,' Prof. Vanhatalo pointed out. Whilst therapies for lesions may not be available yet, the research aims to identify risk patients among the neonates in order to invest even more time and effort in their care.

Magnetoencephalography (MEG)

The brain also plays a key role at the BioMag Laboratory. Owned by Helsinki University Hospital as well as the Helsinki and Aalto universities, this lab has opened the path to the clinical evaluation of biomagnetism. Its advanced equipment includes whole-head combined MEG and EEG and a navigated brain stimulation system.

The lab has research contracts with the instrumentation company Elekta and software manufacturer Nexstim; the main targets of in-house research are pre-surgical planning for epilepsy and tumours as well as biomarkers for neurodegenerative diseases. The only 3-T magnet in Finland reserved for research is located in the AMI Centre in Aalto University's Neuroimaging Lab. The 3-T MRI machine is rented out to user groups for functional testing of neuroscientific hypotheses. Brain research conducted there includes visual, audio, and social studies.

'The needs of young companies go well beyond funding,' Terhi Kajaste explained. To define their strategy, they require know-how from established companies, users in hospitals, and academia. 'In the European Union, regional ecosystems should expand beyond borders and collaborate to allow for international piloting and, in the end, international sales. We need to understand in Europe that we are in this together; let's do away with those R&D silos. This way, health-tech could gain significant economic momentum and help our health systems to survive.'

Premium neonatal care at the Helsinki University Central Hospital: Prof. Sture Andersson (right) and adjunct professor Sampsa Vanhatalo explain trends in routine and brain function research

Endovascular thrombolysis

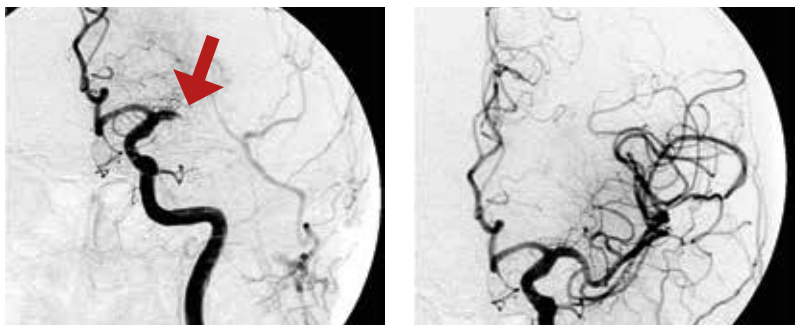
Who does what in mechanical unblocking of brain blood vessels?

Report: Michael Krassnitzer

Neurologists keenly debate the value of mechanical reopening of blocked blood vessels in the brain, as demonstrated during the 21st World Congress for Neurology (WCN) in Vienna this September. Theoretically, endovascular thrombolysis can only be considered for 20-30% of all incidents of stroke. In reality, only 0.2% of stroke patients in Europe are treated endovascularly, as a study presented at the WCN by the EFNS Stroke Scientist Panel showed.

Mechanical blood clot removal comes with several options, as Professor Heinrich P Mattle MD, head of the University Clinic for Neurology at Bern University Hospital (Switzerland) explains: 'The easiest and most successful method is thrombus aspiration with simultaneous proximal flow arrest. If this isn't possible there are various instruments available to grab the blood clot and remove it. The most success with recanalisation can be achieved with retractable stent retrievers.'

A good argument for endovascular thrombolysis: In the case of large blood clots or proximal arterial occlusions, for example carotid T occlusion, standard treatment, i.e. intravenous thrombolysis, only rarely dissolves the blood clot and reopens the blood vessel. 'In this situation there is a good chance of reopening the vessel with a stent retriever and to improve the patient's condition,' Prof. Mattle explains.



Occlusion of the main stem of the left middle cerebral artery, which was successfully endovascularly recanalysed. (Institute for Diagnostic and Interventional Neuroradiology at Bern University Hospital, Professor G Schroth)

Following the first promising experiences with this innovative procedure, expectations were very high. However, recently the euphoria was a little dampened when results of studies published so far have not yet allowed clear recommendations. Prof. Mattle summarised the available data as follows: In the case of proximal occlusion of the middle cerebral artery, three randomised studies with pro-urokinase and urokinase have shown that endovascular pharmacological therapy is superior to placebo treatment.

In a Swiss cohort comparison for media occlusions and a hyperdense artery sign on the CT scan, endovascular therapy (Bern cohort) was superior to intravenous treatment (Zurich cohort). The outcome of a randomised study (synthesis expansion) was neutral, and showed neither superiority of the intravenous nor the endovascular treatment. However, more than half of the patients in synthesis expansion had suffered mild strokes, so are not in the target group for endovascular treatment.

Two further studies, IMS III and MR RESCUE, compared intravenous thrombolysis and the combination of endovascular therapy after intravenous therapy. Again, no difference in outcome was seen between the two treatments. On the one hand treatment was carried out at a late stage and, on the other, almost no stent retrievers were used. Furthermore, the DEFUSE-2 Study showed that an intervention is only advantageous for those patients whose scans showed a mismatch - and therefore cerebral tissue that can be saved. 'Several further studies where stent retrievers are being used are currently on-going and in a few years' time will hopefully bring more clarity as to which patients will benefit from endovascular treatment and which method benefits them the most,' the Swiss neurologist points out.

In his lecture at the WCN, Prof. Mattle also answered the frequently asked question as to who is responsible for endovascular therapy: 'It is important for the interventionist to have good knowledge of, and skills in, endovascular therapy not for stroke treatment alone, and that they can coil aneurysms and treat AVMs. Whether the interventionist initially specialised in neurology or radiology is of secondary importance – and some specialist associations create unnecessary barriers here. The most important thing is for the doctor to have good interventional skills and be carrying out these interventions frequently.'

'At Bern University Hospital our well-rehearsed team, with neurologists and neuroradiologists as well as stroke nurses, MTRAs and anaesthetists, works really well,' the professor emphasises. The neurologist carries out the initial treatment and the follow-on treatment and the neuroradiologist carries out imaging and the actual intervention. The indication for the procedure is jointly decided. 'It is important that the treatment process, from emergency admission to imaging and intervention, as well as the follow-on treatment is organised and defined in a standardised manner.'

Professor Heinrich Mattle MD is Senior Consultant and Assistant Director of the University Clinic for Neurology at Bern University Hospital, Switzerland. He also heads the Neurological Polyclinic and is co-head of the Stroke Unit and Neurovascular Laboratory at the hospital. In 1992 he introduced endovascular stroke therapy to the clinic, and in following years developed the Stroke Unit at the University Hospital. Currently, his main scientific interests lie in pathophysiology, diagnostics, acute therapy and prevention of cerebrovascular diseases, general neurological problems and the treatment of multiple sclerosis.
His scientific publications include over 400 articles and contributions, more than 180 of which in renowned medical journals. Among his several awards for scientific work are the 1992 Robert Bing Prize and 2004 Theodor Nägeli Prize.

New quality standards are needed

Medical displays

Considering ambient lighting conditions, quality assurance of medical displays requires new standards. As a result of the development in medical imaging over the past 20 years, digital medical imaging has replaced the conventional film imaging in most hospitals.

However, softcopy reading is the upcoming standard for diagnostics in radiology and the greatest challenge to design is the parallel use of this and film-based diagnostics in the same room. This hybrid stage suffers from the large difference in the ambient conditions needed. The lighting needed for working with film and a medical display is different. Most reading stations cannot do this properly because the ambient conditions are still the same as for film reading in the past. Reading radiological images is an intense and repetitive process that needs suitable ambient conditions. Several studies confirmed the relation of true and false readings in relation to the best possible display, as well as ambient conditions. The reading room environment plays a significant role in diagnostic accuracy.

While a dark room might be very nice for image quality, this is hard to work in. With ambient light above 10 lux, the contrast of LCD displays starts to decrease more and more.

As the contrast ratio required for a proper reading is to be measured in the viewing distance by considering ambient conditions, the latest standards include a definition of the maximum ambient light. The new DIN 6868-157, in preparation at the moment, sets maximum ambient light levels in relation to the work carried out in the room. Inside a reading room used for diagnostic purposes, the maximum ambient light should be 50 EH-5-2013. The new test procedure for acceptance testing will include the ambient light measurement as well as the control of pixel defects on the screen. The measurement device to be used for the ambient light measurements needs to be a lux meter that is calibrated and can be recalibrated. The

spot meter used for the display measurements must comply with class B of DIN 5032-7. Because the luminance characteristics will be tested and calculated, the use of a software package for assistance in all test stages is recommended in the draft version of DIN 6868-157. Changes are also underway internally. The new IEC 62365-1 is published as a draft version. IEC publications have been issued as recommendations for international use and accepted accordingly by IEC National Committees. Prepared by subcommittee°62B, the IEC 625613-1 international standard includes medical diagnostic imaging and electrical equipment. To keep ambient conditions at a constant level, using an ambient light control system is always recommended. All these recommendations stem from evaluations to optimise the reading room environment. Combined with an ergonomic room design, this will create a low-stress and high-productivity environment for softcopy diagnosis.

A DICOM calibrated display for diagnosis is also strongly recommended, so that weak points of our human eye can be compensated. An internal stabilisation of the calibrated values should reduce the number of scheduled constancy tests. The balancing of ambient conditions to avoid fatigue combined with the best picture performance on the diagnostic screen is the common target of all measures.

Source: Gossen Metrawatt

The full HD 3-Chip medical camera range

The Japanese firm Ikegami is introducing the MKC-310HD, a new 3x 2.1 mega pixel full HDTV 1/3-inch CMOS sensor camera based on FPGA signal processing technology. This provides: '1000 lines of high definition video images through 3G-SDI output interface, coupled with a High Sensitivity performance of F10/2000 lux providing the optimal video quality required for special applications,' the company reports.

'For a high-end medical video system the optimised signal processing circuitry achieves a high Signal-to-Noise Ratio of 54dB. Video signal processing is done in the same signal process ASIC as Ikegami's HDTV broadcast cameras to constantly achieve the same high level of quality and reliability, the firm adds.

As an optional function, the MKC-310HD camera will also stream video over IP (H.264 compression) and so can be used for any kind of telemedicine application or for simple recording to PC, Ikegami points out, adding that its remarkable picture quality comes at a very competitive price.

'Ikegami´s full HD 3-chip cameras allow a perfect view for diagnostic, cataract and retinal surgery as well as for very sensitive neurosurgery and spine operations. Many specialised surgery clinics, operating teams and leading operators recognise the high quality and benefits of Ikegami´s 3-chip full HD cameras and have installed them in their operating rooms.'

These surgeons include

Dr Luciano Mastronardi, head of Neurosurgery at the San Filippo Neri hospital in Rome, used for neurosurgery and skull base operations.

Prof. P Wiedemann MD, Director of the University Of Leipzig Department of Ophthalmology, used for diagnostic, cataract and eyelid operations as well as very sensitive retinal surgery.

Dr Tobias H Neuhann, Medical Director of the Ophthalmology Clinic at the Marienplatz in Munich, used for implantable contact lens (ICL), the retropupillary artificial lens and the (very deep lamellar) corneal transplant international recognition.

The Ikegami 3-chip full HD cameras are also easy to mount on all microscope systems (C-Mount) and therefore ideal for upgrading your SD microscope video system to Full HD resolution.

Details: www.ikegami.de
Contact: medical@ikegami.com

System analyses smoke to inform surgeons which tissue is cancerous

Scientists develop an intelligent knife

Scientists at Imperial College in London, United Kingdom, have developed an 'intelligent knife' that instantly informs surgeons whether the tissue they are operating on is cancerous.

Report: Mark Nicholls

The *iKnife* is based on electrosurgical knives that use an electrical current to rapidly heat tissue to cut through it. Smoke generated by vaporised tissue is normally sucked away by extraction systems, but iKnife inventor Dr Zoltan Takats realised the smoke was a rich source of biological information. As different types of cell produce thousands of metabolites in different concentrations, he connected an electrosurgical knife to a mass spectrometer and was able to profile the chemicals in a biological sample to reveal information about the state of a specific tissue sample.

In cancers involving solid tumours, surgeons normally take out the tumour with a margin of healthy tissue but acknowledge it is often impossible to tell by sight which tissue is cancerous. For example, one in five breast cancer patients who have surgery need a second operation to fully remove the cancer. With a high level of accuracy reported, the iKnife gives surgeons an immediate answer rather than having to wait up to 30 minutes for laboratory tests results – while the patient is still under general anaesthetic – to know whether tissue is cancerous or not.

'This is a unique tool because the tissue identification element is built into the cutting device, giving surgeons real-time information about exactly what type of tissue is being cut,' Dr Takats explained. 'The intelligent knife will give them an immediate answer, enabling them to continue the operation without interruption.'

Studies showed the iKnife was 100% accurate when diagnosing tissue samples from 91 patients and matching the post-operative diagnosis based on traditional methods.

Researchers have also used the iKnife to analyse tissue samples collected from 302 surgery patients, recording the characteristics of thousands of cancerous and non-cancerous tissues - including brain, lung, breast, stomach, colon and liver tumours - to create a reference library. The iKnife works by matching its readings during surgery to the reference library to determine what type of tissue is being cut, producing a result in less than three seconds.

Dr Takats, an analytical chemist at ICL, said: 'These results provide compelling evidence that the iKnife can be applied in a wide range of cancer surgery procedures. It provides a result almost instantly, allowing surgeons to carry out procedures with a level of accuracy not possible before. We believe it has the potential to reduce tumour recurrence rates and enable more patients to survive.'

He added that the benefits to patients include improved accuracy, meaning that resection is kept to a minimum, as well as reduced exposure to anaesthetic.

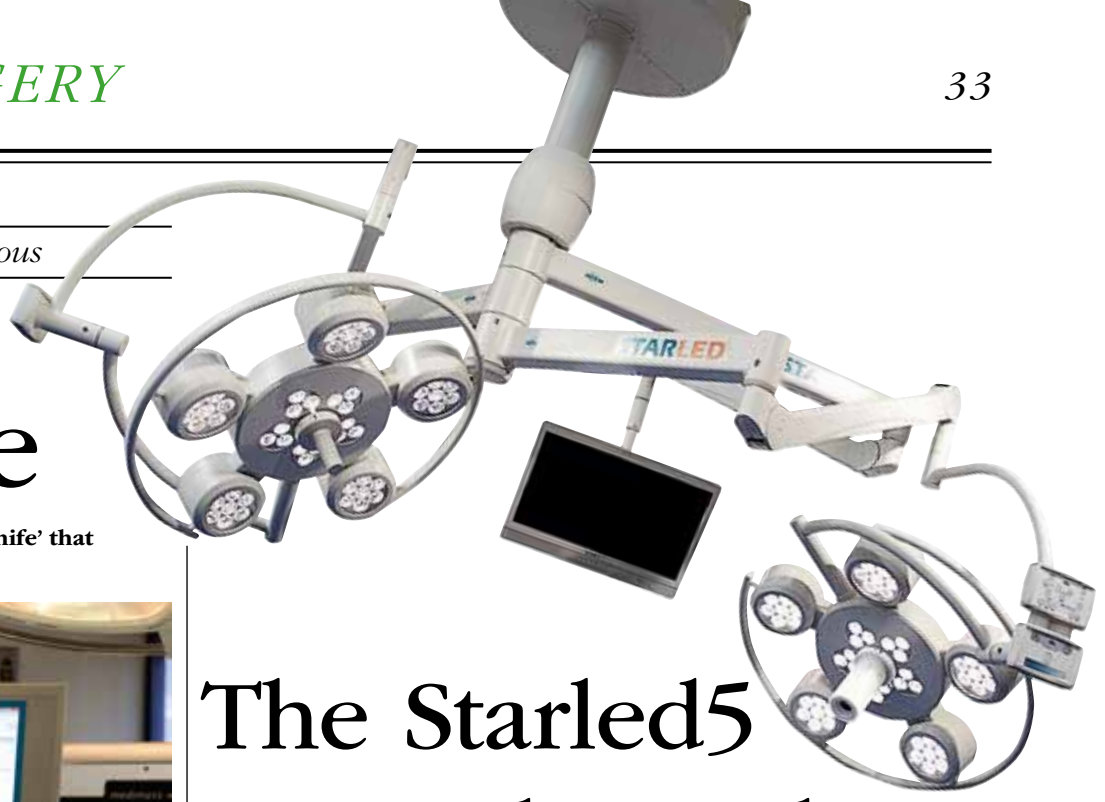
The iKnife is not commercially available at this stage. Whilst its accuracy has been proven in trials, Dr Takats said the next step is for a clinical trial to see whether giving surgeons access to the iKnife can improve patient outcomes.

Although the current study focused on cancer diagnosis, Dr Takats says the iKnife can identify other features, such as tissue with an inadequate blood supply or types of bacteria present in the tissue.

The National Institute for Health Research (NIHR) Imperial Biomedical Research Centre, the European Research Council and the Hungarian National Office for Research and Technology funded the study.

Lord Darzi, Professor of Surgery at ICL and the study's co-author, said: 'In cancer surgery, you want to take out as little healthy tissue as possible, but you have to ensure that you remove all the cancer. There is a real need for technology that can help the surgeon determine which tissue to cut out and which to leave in. This study shows that the iKnife has the potential to do this. The impact on cancer surgery could be enormous.'

A former post-doctoral research associate at Purdue University in Indiana, USA, as well as Director of the Cell Screen Research Centre and Head of Newborn Screening and Metabolic Diagnostic Laboratory at Semmelweis University, Budapest, **Dr Zoltan Takats** later became a Junior Research Group Leader at Justus Liebig University, Giessen, Germany. In 2012 he moved to the United Kingdom where he is a Reader at Imperial College, London. He has pioneered mass spectrometry research and is one of the founders of Ambient Mass Spectrometry, as well as primary inventor of six mass spectrometric ionisation techniques and the founder of several companies that pursue analytical and medical device development..



The Starled5 surgical LED lamp

Part of the Starled series incorporating LED (light emitting diodes) technology, produced by Italian firm ACEM Medical Company, the surgical lamp Starled5 is reported to produce light intensity of 160.000 lux, yet ensure low consumption.

'Starled5 grants optimal performances producing a light beam without infrared rays, with a CRI value of 95 and a colour temperature of 4900 °K reproducing the exact colour chromatic scale of the human body,' the manufacturer reports. 'Its ergonomic design takes into consideration the needs of operating rooms. It is comfortable and light to move thanks to its lateral handles assuring stability and constant illumination – even during its movement.'

Acem also points out that its smooth, resistant material makes cleaning quick and thorough, and also, 'The lamp shape assures visual comfort and is particularly suitable for laminar flows. Its structure has been studied to avoid obstructing airflows inside the operating room reducing considerably the turbulence areas.'

Functions are managed via the digital I–Sense control system. A simple touch adjusts light intensity, and can activate the ENDO (Light for Endoscopy) and DOF (Depth of Field) functions as well as the SYNC mode (optional), which enables the use of a control panel that is synchronised with the other lamps combined – all managed by just one operator.

'In order to achieve a correct illumination according to the different needs Starled5 can produce a Focused and Ambient light. Simply rotating the lamp's central handle controls the focusing system of the light field. Removable and sterilisable, the handle can also host (on demand) a fixed focus or zoom video camera.

Due to the particular light beams from the lamp's upper part, a diffuse lighting is produced that is particularly suitable for minimally invasive surgery and preparation/monitoring of a patient during the operation.

Acem S.p.A, based in Bologna, Italy, will be in Hall 10, at Stand D31 during Medica 2013 in Düsseldorf.

Information: www.acem.it
info@acem.it

Only reduced antibiotics use and better infection prevention and control can contain nosocomial infections

Two sides of the coin

A one-day course on Infection Prevention and Control (20 November. 9.30 a.m. - 6.00 p.m.) will focus on a vital issue at the Medica Education Conference 2013. In the run-up to the event, in discussion with *European Hospital*, Professor Franz-Josef Schmitz MD, the Course Chairman and Senior Consultant at the Institute for Laboratory Medicine, Microbiology, Infection Prevention and Control, Environmental Medicine and Transfusion Medicine at the Mühlenkreiskliniken in Minden, Germany, outlined the challenges and potential solutions.

Pointing out two problem areas in infection prevention and control, he said: 'More and more antibiotics are being administered in out- and in-patient treatment, which puts so-called selective pressure on the bacteria. This means that many pathogens are increasing resistance and a decreasing number can be successfully treated with antibiotics. We also see that these resistant pathogens can spread rapidly if infection prevention and control is inadequate.

'So, on the one side we have the spread of nosocomial pathogens when infection prevention and control is inadequate and, on the other, the increasing use of antibiotics, which leads to the pathogens becoming increasingly resistant against certain groups of antibiotics. The problematic pathogens are known – Methicillin-resistant Staphylococcus aureus (MRSA) Vancomycin-resistant Enterococci (VRE), multi-resistant gram-negative bacteria (MRGN) and the toxin-producing Clostridium difficile (CDI).

Improving control in hospitals

'In Germany, and some other countries, it took a long time to address the problems with the required intensity. The training of more infection and prevention control support staff and specialists in individual hospitals – which is currently being implemented in this country – is a sensible measure which, in the medium and long-term, will lead to increased awareness, and which could possibly prevent the expected, potential increase in nosocomial infections and pathogens. It remains to be seen whether in fact it will also achieve a decline in the number of these infections. At the very least it's an attempt to tackle the problem and there is a realistic chance that the situation can be improved.'

Although unlikely to solve the problem in the short term, the professor expects those measures to have a successful impact in five to ten years' time.

Tackling the cause of resistance – by law

'The Dutch pursue the principle that broad-spectrum antibiotics should only be used after a microbiological consultation. In Germany, doctors have the freedom to prescribe, but even here there are efforts in many hospitals to prescribe these 'reserve' antibiotics only after microbiological testing, and only after the respective approval from the local pharmacist.

'However, hospitals make up only a proportion of where antibiotics are being used, although their use, especially the peri-operative administration of antibiotics, should still be reduced. Antibiotics are used far more commonly in veterinary medicine, and in (human) out-patient care. Reductions in the use of antibiotics in animal husbandry as well as in out-patient care are desirable. In animal husbandry it should certainly be possible to make this a legal requirement, but in out-patient care colleagues would need convincing and respective training provided.

Franz-Josef Schmitz: Medics must be educated in prevention and control

'For infection prevention and control in hospital, financial aspects are decisive. The more staff is made available, the easier carrying out prophylactic measures will be.'

Of one thing Prof. Schmitz is certain – only if both nurses and doctors on wards are trained in infection prevention and control will awareness be raised and infections contained. 'More awareness of this topic amongst politicians is therefore extremely desirable,' he concludes.

Minute yet powerful pathogens, such as MRSA, VRE, MRGN and CDI, are omnipresent and can multiply and spread rapidly unless hospitals introduce and maintain a dedicated focus on hygiene standards.

Battling against antibiotic resistance

Better training could help

Report: Mark Nicholls

Internet-based training for clinicians could help lower antibiotic prescribing rates for acute respiratory tract infections by as much as 62%, according to British researchers. A study led by the University of Southampton comes at a time of growing concern at the high volume of prescribing antibiotics – particularly in primary care – believed to be a major driver of antibiotic resistance and may be having an impact on hospital care.

Paul Little, Professor of Primary Care Research at the University of Southampton, said the position is 'one of the great public health dangers of our time, and raises the real prospect of serious infections becoming untreatable.' He pointed out that, whilst training has been shown to have a positive effect on lowering prescription rates, he remains concerned that the way training has been delivered, and its reliance on highly-qualified staff in centres of excellence, severely limits the impact in everyday practice. 'Novel techniques are therefore needed to lead changes at a national and international level,' he added. 'Internet training has the advantage that it can be disseminated widely at a low cost and does not need much resource.'

Lower respiratory tract infections (LRTI) are one of the most common acute illnesses treated in primary care in developed countries. Although viruses are believed to cause most of these infections, there is still debate about whether or not antibiotics are beneficial for some patients in the treatment of LRTI, particularly in older patients. Meanwhile antibiotics are still being prescribed in high amounts, fuelling antibiotic resistance, say researchers. The Southampton-led team used the internet tool developed by Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe (GRACE) consortium for lower-respiratory-tract infections for the study.

Funded by the European Community's Sixth Framework Programme, 246 clinical practices from England, Wales, Belgium, Holland, Spain and Poland were recruited and randomised to one of four trial arms: usual care, internet-based training to use a C-reactive protein (CRP) test (an indicator test for pneumonia), internet-based training in enhanced communication skills, and combined training in both CRP and enhanced communication.

The study, supported by the National Institute for Health Research (NIHR) Clinical Research Network (CRN) in England, showed that clinicians trained in the use of the CRP test, or enhanced communications skills, significantly reduced their antibiotic prescribing rates for LRTI, compared to usual care (47% and 32% respectively). Clinicians trained in a combination of both reduced antibiotics prescribing by 62% while prescribing rates also fell for upper respiratory tract infections.

Professor Paul Little MD is Professor of Primary Care Research at the University of Southampton. A general practitioner (GP) for 20 years, he was the first GP to be awarded a Wellcome HSR training fellowship (for research on health promotion), and the first to receive an MRC Clinician Scientist Fellowship (for research on common self-limiting illness). His current research focuses on enabling behaviour change for health professionals and also to empower patients.

Professor Little: 'These interventions have shown that providing interactive training methods using the internet to modify antibiotic prescribing is remarkably effective. Moreover, internet-based training programmes are transferable between very different primary care settings.'

However, while there remain concerns about the impact of over-prescribing antibiotics in hospitals, it is unclear whether the findings of the study, and the training at primary care level, will benefit secondary care. 'Driving down resistance in primary care should results is less complicated management, and more prompt effective treatment in patients admitted in secondary care. The challenge will be trying to prove it.'

The European Centre for Disease Prevention and Control (ECDC) has worked across Europe to raise awareness of increasing infections due to antibiotic-resistant bacteria, which are rising globally due to over-use of antibiotics and inappropriate prescribing. It has urged doctors and nurses in hospitals and primary care to be more prudent in antibiotic prescribing and use.

In the UK guidance by the government's drugs regulator, the National Institute for Health and Clinical Excellence (NICE), on the prescribing of antibiotics for respiratory tract infections states that a no-antibiotic, or delayed antibiotic strategy should be used to treat people with infections.

Clostridium difficile infection

Experts must actively intervene over cleaning issues or there will be no improvement in infection and prevention control in hospitals

Report: Brigitte Dinkloh

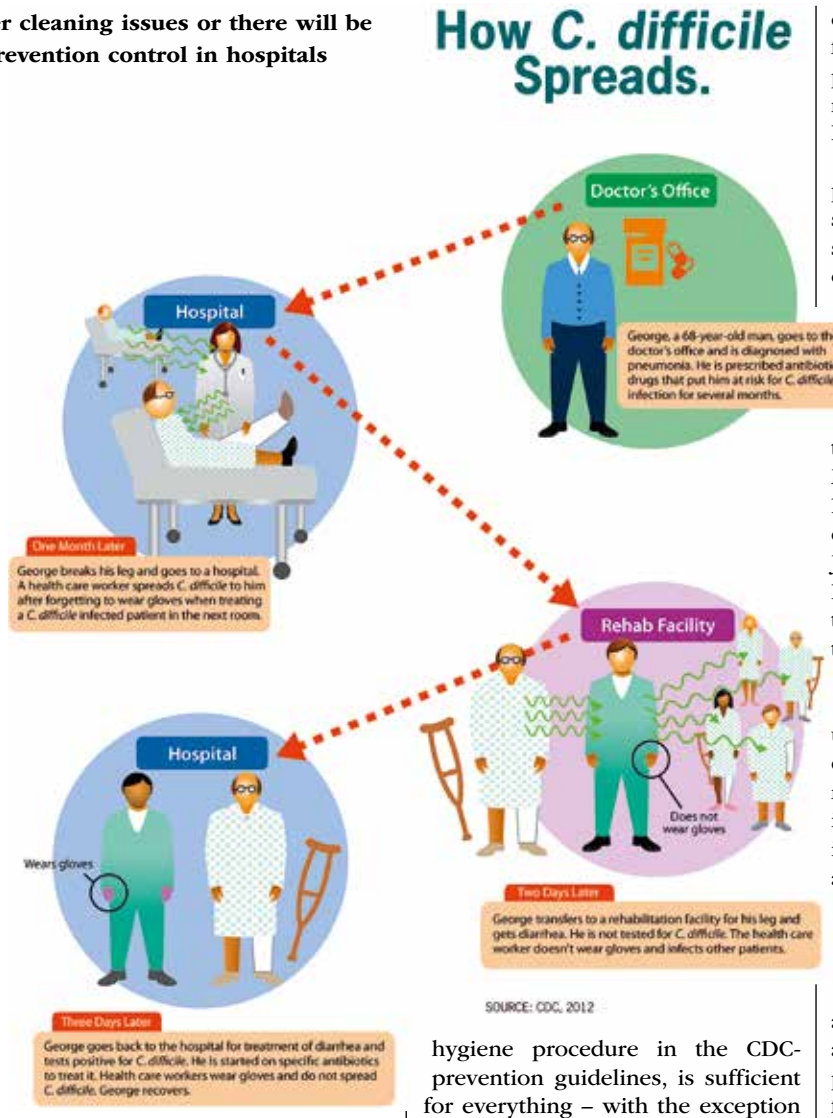
The realisation that the fight against C. difficile needs its own specific hygiene management dawned relatively recently. Up to the new millennium a common perception regarding European hospital infection prevention and control was that this bacterium was under control; it was considered a marginal phenomenon, which is why C. difficile was not the focus of problematic pathogen monitoring. A crass misjudgment, as the outbreaks in 2005 – 2007, with epidemic and hyper-virulent strains in almost all European hospitals, showed.

Ever since, C. difficile has been very much on the radar, but the fight against the bacterium requires a different type of management than that used against other pathogens.

In healthy people, C. difficile is a harmless intestinal bacterium. However, if competing types of normal enterobacteria are impaired by the administration of antibiotics Clostridium difficile can spread unhindered, producing toxins that can lead to life-threatening diarrhoeal diseases.

To survive in the air, C. difficile encapsulates in spores secreted via the gut and are not only resistant against many disinfection agents, particularly against alcohol-based hand disinfectants, but also against almost all antibiotics. They can survive in sinks, bedpans, on floors or in sanitary rooms on the wards and thus infect other patients.

'The phenomenon of the epidemic was associated with the introduction of new fluoroquinolones (quinolones of the 3rd and 4th generation), which initially were not thought to have a selection risk for the intestine, but against which the strains of Clostridia proved resistant,' explains Dr Markus Hell, Medical Director of the Division of Medical Microbiology at the Centre for Hospital Infection Prevention and Control in University Hospital, Paracelsus Private Medical University (PMU), Salzburg, Austria.



Subsequently, this led to a shift in awareness in infection prevention and control because these strains were very different from the pathogens known hitherto, also regarding their spore formation and infectiousness. Hygiene, particularly hand disinfection, was strongly scrutinised. Alcohol-based hand disinfectant, which, for the first time, was recommended as the preferred hand hygiene procedure in the CDC-prevention guidelines, is sufficient for everything – with the exception of bacterial spores. The only effective measure against C. difficile, a typical spore former, is mechanical removal, i.e. hand washing with water and soap.

'The procedure, as described in the guidelines, with the wearing of disposable gloves, alcohol-based hand disinfection to kill the vegetative pathogens and then hand-washing, has proved to be too time-consuming and extensive for patient management in hospital. Therefore, what I recommend is 'reverse surgical hand-washing': first you disinfect for the vegetative part of the pathogens, then you wash hands to mechanically remove the spores,' Dr Hell explains.

In the latest infection control and prevention examinations it has been shown that, apart from transmission via the hands, an important contributor to spores transmission is surfaces.

Surface disinfection v. specific disinfection

In a study first introduced at the European Congress of Clinical Microbiology and Infectious Diseases in Berlin last April, and due to be published soon in the Journal of Hospital Infection, Dr Hell showed that surface disinfection in defined areas is highly likely to prevent the infection of further patients. 'Systematic disinfection, which was introduced to reduce the use of aggressive chemicals, in fact does miss its target. By the time you realise that a patient has become infected and the laboratory result is available, several days will usually have passed and the spores will long since have spread and been transmitted to other patients.'

In an open intervention study at the PMU, hyperendemic zones, such as those found in gastroenterology and oncology and surfaces near patients, were preventively disinfected. Hospital-acquired C. difficile infection was clearly reduced, even when new patients were admitted to hospital with diarrhoea and C. difficile. The effect was particularly noticeable amongst older patients who are most prone to the disease.

'With our concept, we disinfect all patient contact surfaces around the bed, i.e. the bed base, door handles and sanitary fittings with so-called peroxides twice daily. The level of spores in the vicinity of patients was systematically reduced. Transmission does not occur from staff member to staff member but through the patients themselves releasing the spores into the environment and the nurses working with them then becoming reservoirs, and for the next person to absorb these spores,' Dr Hell concludes, referring to the study results. The rate of infection expected in over 70-year-old patients was reduced by more than 61.5% through the new surface disinfection concept. When a case of C. difficile occurs, disinfection is extended to include floors and all horizontal surfaces.

The study also evaluated disinfection agents. Unlike in the USA, where chlorine is used, Europe only allows so-called peroxides, organic compounds that release oxygen radicals with a sporicidal effect. Usually, the product is supplied as a powder and has to be manually prepared. As there is no guarantee as to the correct mixing ratio, the study also included a first ever evaluation of the only liquid peroxide available on the German market. This suspension has proved to be advantageous because inadequate disinfection due to incorrect preparation can be ruled out.

'With the enormous cost pressures the hospitals face, which often makes them save on cleaning concepts and staff, this is an important aspect,' Dr Hell explains. 'Disinfection is only effective if carried out correctly.' Therefore it is very important to employ long-term, qualified cleaning staff with whom communication is ensured. 'Ten, fifteen years ago we were just the experts on disinfection measures and we could rely on everything working correctly. However, this has changed. If we, the infection prevention and control specialists, do not actively intervene with cleaning issues there will be no improvement in infection and prevention control in hospitals!'

Dr Markus Hell has been head of Infection and Prevention Control at the University Hospital Salzburg since 2000. In 2012 he also became Medical Director of the Division of Microbiology. A specialist in infection and prevention control and microbiology, he studied and wrote his doctorate at the Medical Faculty of the University of Innsbruck and then worked at the Community Hospital Oberndorf, near Salzburg, and the city's Neurological University Clinic until 1995.
His particular interests are resistance epidemiology, management of nosocomial outbreaks, monitoring of problematic pathogens and management and prevention of nosocomial infections. C. difficile-associated infections (detection, epidemiology, prevention and treatment) have been his key interest and research focus for the past five years.

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