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EUROPEAN HOSPITAL

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

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Tavi´s unsung Danish hero

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Pre-operative risk stratification

Acute hospital care in England could be on the verge of collapse

Around 65% of in-patients are over 65 years old

Report: Mark Nicholls

With growing bed shortages and increased demand on clinical services, the Royal College of Physicians (RCP) says that the country's National Health Service (NHS) is approaching the point where acute care cannot keep pace in its current form.

Figures contained in the college's hard-hitting report *'Hospitals on the edge?'* show there are a third fewer general and acute beds in the NHS today than there were 25 years ago, but there has been a 37% rise in admissions over the last decade.

According to RCP President Sir Richard Thompson, 'It is difficult to measure how close we are to collapse but a lot of hospitals are only just managing at the moment so any major unforeseen emergency could tip them over the edge and see them close to acute admissions.'

Treating patients with dignity

The fall in bed numbers is coupled with more older people being admitted to hospital. Some 65% of people admitted are aged over 65, with a significant number over 85. An increasing number are frail with hospital buildings, services and staff often not equipped to deal with people with multiple, complex needs including dementia, diabetes, stroke and urinary tract infections.

'It is a very complex mix of patients coming in,' Sir Richard explained. 'We do not have a good social care structure out in the community, nor good primary care, so these patients come into hospital because there is nowhere else for them to be looked after.

'We have noticed the situation getting worse, year on year. The number of A&E attendances and admissions to acute beds goes up each year, while there has been a continuing reduction of acute beds across the country.

That progressive reduction has been to save money with the hope that better community care will reduce admissions but at the moment it is not doing that.'

A survey of RCP members showed their biggest concern was a lack of continuity of care with hospitals particularly failing to look after patients properly at evenings and weekends. It is not uncommon for patients, particularly older patients, to be moved four or five times during a hospital stay because of a shortage of beds and often with incomplete notes and no formal handover.

'As a medical profession we have to look at how we are handling acute patients in the hospital - the fact so many are moved beds at night or having blood tests at night is appalling and that is the sort of thing we are going to have to resolve,' he added.

Additionally, the RCP report said that hospital staff often see the elderly as 'unwelcome' and think they 'shouldn't be there', even though they make up two thirds of patients. 'One doctor told me that his Trust does not function well at night or at the weekend and he is 'relieved' that nothing catastrophic has happened when he arrives at work on Monday morning,' Sir Richard said. 'This is no way to run a health service. Excellent care must be available to patients at all times of the day and night. We call on government, the medical profession and the wider NHS to work together to address these problems.'

To help tackle the looming crisis, the RCP is calling for: all health professionals to promote patient-centred care and to treat all patients with dignity at all times; the redesign of services to better meet patients'

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Does Germany top Europe in unnecessary diagnostics?

Statistics show significant increase in scans and left heart catheterisations

Report: Susanne Werner

When it comes to the number of individual medical examinations, Germany among Europe's frontrunners, according to statistics from the scientific institute of the AOK (WIdO). Heart catheterisations are carried out far more frequently there than in Austria or Switzerland.

Uwe Deh, Head of the Federal Association of the AOK, is indignant. He speculates that financial interests rather than medical reasons are behind this increase. However, representatives of medical societies argue otherwise. For instance, Professor Michael Forsting, President of the German Radiological Society (DRG) and Director of the Institute of Diagnostic and Interventional Radiology and Neuroradiology at Essen University Hospital, emphasises that these increases are founded in medical advances.

The data to which Uwe Deh refers come from the 'Quality Assurance with Routine Data' (QSR), a procedure developed by the WIdO with other partners, including hospitals. According to this data, hospital use of imaging diagnostics has increased by more than 50% between 2006 and 2010 and, since 1990, the number of left heart catheterisations in Germany more than tripled. In 2010 it was around 70% higher in this country than in Austria, and 98% higher than in Switzerland. 'The QSR procedure is recognised across Europe,' explained Christian Günster, WIdO Head of Research. Its particular feature is the assessment of

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Does Germany tops Europe in unnecessary diagnostics?

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a patient's health status over a long period and the data also includes the time after hospitalisation. 'In view of the increasingly shorter hospital stays we feel that the follow-up observation is an absolutely necessary step,' he said. This is also almost unique in Europe. 'In Germany, the legislator has created the opportunity to include this observation in the legally binding quality assurance process,' he pointed out. 'The Health and Social Fund in Lower Austria is currently preparing a very similar QSR project which includes follow-up observations.'

Studies do not attest to better medicine

How can the statistics increase be explained? Uwe Deh suspects it is due to the excess capacities in German hospitals. As hospitals are only working to 80% of their capacity, they try to increase revenue by scheduling more examinations than medically necessary. He is particularly annoyed about the 'medical products whose medical benefit is often dubious'. As an example, he quotes stents that are implanted into cerebral arteries to lower the risk of stroke. 'A 2011 study has shown that these do not actually lower the risk of strokes but, to the contrary, have almost doubled it within a year. In Germany alone, more than 3,500 patients have been treated with this uncontrolled procedure since its introduction. The study was stopped in the US after the treatment of only 451 patients because of this damage, he warns.

'Many German hospitals,' he concludes, 'can no longer guarantee patients that they are being operated on purely for medical reasons.' After all, the statistics also show that the large number of examinations doesn't necessarily lead to better patient care in Germany. 'Germany is one of the countries at the very top when it comes to mortality rates from heart attacks,' he adds.

Uwe Deh became a member of the board at the Federal Association of the AOK in October 2011. He is responsible for the business units Care/Contracts, Finances, and the AOK Scientific Institute (WIdO), Medicine, and Electronic Data Processing Control. He studied Business Administration with a focus on Health Economics at the universities of Göttingen and Magdeburg and began his career at the (VdAK/AEV) in Mecklenburg-Vorpommern. In 1999 he joined the AOK Sachsen-Anhalt, heading the Hospital Division and building up the Health and Medicine branch, comprised of all the Contracts and Services business. He was a board representative for AOK Sachsen-Anhalt from 2005, and was appointed its Chairman in 2008.

Modern treatments require more imaging

Prof. Forsting does not accept these accusations. He is convinced that the cause of the increase is modern treatment concepts. 'Cancer patients are treated in a much more individualised way than 10 or 20 years ago. Doctors need to carry out CT scans after only a few weeks to observe vascular growth,' he explains. Moreover, imaging procedures now deliver good and meaningful images, which no doctor can do without, the DRG President adds. 'MRI delivers particularly good images of joints. Whilst arthroscopies used to be the standard treatment MRI is now the procedure of choice. This spares patients invasive examinations.'

Professor Eckhart Fleck, Director of the Clinic for Internal Medicine at the German Heart Centre Berlin, and press officer of the German Cardiac Society (DGK), agrees. 'There are plausible reasons for the growth and these are founded in medical treatment,' and he points to the guidelines on emergency treatment for heart attacks. The large number of left heart catheter measuring stations is necessary to treat patients comprehensively and quickly – 'The patient should be in a location where they can be treated no later than one hour after the first symptoms.'

Paris: 6-7 December 2012

The 13th University Hospital Centres Conference

CHUs must become new to cope with the 'new' patient

Report: Annick Chapoy

Since University Hospitals in France were created in 1958, their three-fold focus has been on services for health, education and biomedical research and their effect has been to create such a fine medical service that its high quality is respected worldwide. December's 13th national University Hospital Centres (CHUs) Conference will draw their CEOs and Deans to Bordeaux to discuss 'new' patients and 'new' CHU. Why 'new' patient? They are better-informed and more demanding and also older thanks to better healthcare. Why a new CHU? Because those facts must be understood, along with emerging pathologies and therapies, to adjust CHU offerings while also adapting to economic or territorial constraints. Thus the leaders will explore new perspectives from research and training and the CHU network is prioritising quality care reference within inter-hospital cooperation.

Alain Hériaud graduated from the Ecole Nationale de Santé Publique (ENSP) in 1974 and was then in the management teams of various hospitals (Chartres, Agen, Marmande) before going to Bordeaux in 1986. He was elected President and CEO of the University Hospital Centres Conference in 2010. Since 1997, he has been CEO of the Bordeaux CHU.

'CHUs carry the greatest missions of public service, healthcare excellence for all, teaching, research and innovation,' explained conference president Alain Hériaud. 'They represent the flagship of the French health system, account for its efficiency and contribute to the dynamism of the economy, while the "human factor" is at the core of our preoccupation, concerning patients as well as medical staff. It embodies, with universities and the scientific and technological public research institutions, the excellence of French medical research.'

Facing society's transformation and increasing competition, isn't the CHU in danger of 'losing its soul'? The primary principle of any hospital, local or university, is respect for the human being, one principle that unites the CHU community he stressed. 'This commitment means that we address a human being rather than a sick person, and we adapt to his needs, we take into account his personality, his culture, his beliefs. We serve meals according to his tastes and culinary habits. To this traditional humanism, the values specific to a public hospital are added – no selectivity, equal access to healthcare.'

A hospital does not ask for your credit card; you will be treated first, he stressed. Everyone knows that, whatever his background, religion, financial situation, he or she will receive hospital care. The 60-year-old CHUs have seen many changes since the change from being regional hospital centres, able to treat any pathology at any age of life. By law, the 32 CHUs had to be distributed across France, so that access to a university hospital could be available to all citizens. The marriage of university and hospital did not happen overnight, Prof. Hériaud said. Initially, research was not a priority; at best the hospital heads let it happen, at worse they preferred it to go somewhere else – to universities, at INSERM or CNRS.

Change came heterogeneously and with various intensities. Basically, under the department head's initiative, the Assistance Publique Hopitaux de Paris (AP-HP) was the first to enhance the hospital/university alliance. Others followed. It took about 30 years for the joint research university hospital to assert itself – really taking off in 2000, partly because hospital decision makers realised the importance of clinical research within the CHU missions,

Acute hospital care in England

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Having served as treasurer of the Royal College of Physicians (RCP) from 2003, **Sir Richard Thompson** became its President in 2010, a role in which he leads the organisation on behalf of its fellows and members.

Following his training in natural sciences and medicine at Oxford and St Thomas' Hospital Medical School, and junior posts in London, he joined Dr Roger Williams in the early days of the liver unit at King's College Hospital, and spent 18 months with Professor Alan Hofmann at the Mayo Clinic. He became a physician and gastroenterologist at St Thomas' Hospital in 1972, serving until his retirement in 2005.

For over 30 years he also led a clinical research laboratory, chiefly studying aspects of nutritional gastroenterology, and had also supervised 30 MD and PhD theses as well as publishing over 200 papers and, during 21 years of his career, Sir Richard also served as physician to Her Majesty Queen Elizabeth II.

needs with planning and implementation of new services clinically led; re-organisation of hospital care so that patients can access expert services seven days a week; and access to primary care to be improved so that patients can see their GP out of hours, relieving pressure on A&E services.

More money is no answer

The report said there should be a concentration of hospital services in fewer, larger sites that are able to provide excellent care round-the-clock and improvements in community services to avoid many patients ending up in hospital because of a lack of help close to home.

To examine better processes and standards for treating medical patients, the RCP has established the Future Hospital Commission (FHC), which will report in a few months' time. The RCP report, which plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence and represents over 27,500 fellows and members worldwide, coincides with a period that the NHS is under severe pressure to make financial savings amounting to billions of euros. However, Sir Richard said making more money available was not the only answer and he believes that junior hospital doctors' hours should be relaxed to help with more flexibility within rotas and with continuity of care, which is currently 'very poor'. He also wants to see a new cadre of generalists appointed in hospitals to provide the continuity of care, as well as more physician assistants.

Struggling with age and complexity

If action is not taken soon, he said, 'I think there will be a continued flight of doctors from this area of medicine because they are finding the strain very high and some are disillusioned. In addition, hospitals will be closing to acute admissions at times because they will not be able to cope. It is very serious.'

Professor Tim Evans, one of the report's authors and also an intensive care consultant at the Royal Brompton Hospital in London, added: 'It's increasingly clear that our hospitals are struggling to cope with the challenge of an ageing population with multiple, complex diseases', and he warned that if steps were not taken to improve hospitals, there may be other scandals, such as that which occurred at Mid-Staffordshire NHS trust, where hundreds of patients died due to poor care between 2005 and 2009.

convinced that healthcare excellence comes from the search for new materials, molecules and approaches to both patient and disease.

André Hériaud believes that the pressure from growing consumerism, economic restraints and private clinic competition acts 'like an incentive that pushes us to improve'. He is well aware that we live within real life, facing a changing society, increasing precariousness, the arrival of marginal populations, often illegally, and the strain of the current economic crisis on patients and their families.'

The rise of consumerism can't be helped. The sick person is also a client in the noble sense of the term, someone who has rights and duties, someone who makes choices, someone who is entitled to proper information. The word hospital linked to enterprise does not shock him, when it refers to undertaking something to improve energy, efficiency, transparency and better communication.

He sees the image of the CHU as a paradox for economic decision-makers: the ones never needing a public hospital believe they are a monstrous waste of public money; the others, who use CHUs for self or family, particularly to tend severe pathologies, without exception recognise their high standards – in competence, technology and staff attention to the patient. In case of doubt about the relevancy of a medical procedure, he knows he is faced with a medical team of integrity, because no financial consideration governs medical decisions. If the doctor recommends surgery, he can do it without reflection.

The CHU model is admired beyond France. Their sheer size is considered impressive. In Paris, the AP-HP is the biggest hospital in Europe, and the Hospices Civils de Lyon is second in Europe.

Procurement – Procedures, financing and cultural philosophies can shape the difference

The needs of European hospitals are similar

Not only can advanced technologies significantly affect the health and well being of patients, but they can also improve patient safety, create more efficiency and contribute on many social levels. Good technology choices are therefore vital. How are such decisions made in our varied European hospitals? In the absence of comparative studies, our correspondents sought answers from leaders in the front line of health politics and procurement for hospitals.

Reports: Michael Reiter, Mark Nicholls, Eduardo de la Sota, Jane MacDougall

'Finding a common denominator for innovation strategies across European hospitals is difficult,' said Pascal Garel, CEO of HOPE. Healthcare systems are deeply rooted in individual national and even regional culture – also reflected in the diverse ways that hospitals identify their needs for new technologies. However, there are joint EU activities regarding health technology assessments (HTA), which HOPE supports and follows closely, and the organisation is keen to develop mini-HTAs at local and hospital levels further. 'This should help evaluate the additional value provided by new equipment regarding improved diagnostics, therapy and workflow.'

Mercedes Mengíbar, administrative council member and Managing Director of Xanit Hospital Internacional, a private care provider at the Costa del Sol: 'The new diagnostic, therapeutic and information/communication technologies (ICT) installed at hospitals in recent years help us to bring efficiency to processes that support care and the organisation. They require fewer human, financial, and infrastructural resources, and allow us to avoid duplication and unnecessary administrative tasks; they also facilitate collaboration, training and cross-sector delivery of care.' Thus Xanit's acquisitions include high-field MRI, multi-detector computed tomography (MDCT) with 64 detectors, a gamma camera for SPECT/CT, diagnostics for genetic counselling; a LINAC, brachytherapy, interventional haemodynamics and vascular radiology, laparoscopic surgery, immunofluorescence guided neurosurgery … and more devices for therapy. 'Our hospital also uses a comprehensive, powerful information system based on SAP, which fully integrates clinical information such as patient data, images, etc. plus business and logistics data, costs and financial information to enable efficient management of economics and strategic business planning.'

Pascal Garel – Educated in political science and European law, he has been CEO of HOPE, the European Hospital and Healthcare Federation, since 2005. With his main background is healthcare management, with decade spent in teaching hospital centres in Nantes and Rouen, his other previous posts include Director of the European and International Department of the French Hospital Federation and responsibilities for Central and Eastern Europe at the French Ministry of Health. He is an Associated Lecturer at the University Paris Dauphine and also teaches at the Alexandria University Senghor in Egypt.

At Xanit, the Directorate of the Procurement Commission oversees investments in clinical, financial, nursing activities and operations. 'Requirements considered are scientific innovations, the need for additional or specifically trained staff, cost of consumables, implementation and maintenance, and financial analysis,' Mercedes Mengíbar said.

AGEPS covers a network of 40 public health hospitals in the Paris/France region. According to Elisabeth Aoun, Director of Purchasing for Health Products and Equipment for the Public Hospitals of Paris, and AGEPS Co-Director Jean-Eric Lefevre, procedures are similar throughout the country because – whether public or private – eventually all comes down to the 'Appels des offres', open tenders with which all French hospitals must comply. The initial demand for new equipment comes from the end user, medical doctor, team etc. involved in its use. 'This requires a written request to the purchasing department outlining the reasons why the equipment is needed, the role it will play, numbers of patients, advantages it will bring, and so on,' Elisabeth Aoun explained. If that initial demand is considered reasonable, the end-user then explains the need orally to the purchasing committee. Jean-Eric Lefevre: 'If a purchase is authorised at this level, a request is made to the Department of Health to obtain national authorisation for the purchase.' There is no upper limit for the amount, but the hospital's individual need is weighed against the needs of the entire health service, they explain. For smaller equipment, below €20,000, the decision stays within a hospital and depends on its own budget.

Obtaining national authorisation in France is the most difficult step, but once given, the call for tenders begins. The purchasing group committee, made up of different medical and scientific advisors, and overseen by Elisabeth Aoun, decides on the equipment requirements and specifications needed and creates the tender dossier. 'This procedure follows not just national requirements but also European directives', Jean-Eric Lefevre pointed out. 'Public tenders are an open competition, published on the government's website for public scrutiny.' Once responses arrive, the same purchasing group examines them and the winner is decided – a process that can take anywhere from 6-9 months from beginning to end.

UK procurement strategies

Chris Slater, Head of Supplies and Procurement for Leeds Teaching Hospitals NHS Trust and George Anderson, senior category manager, Leeds Teaching Hospitals NHS Trust, explained that they provide a centralised function and procurement for each of these hospitals via Chris Slater's team, working in three distinct areas – purchasing and contracting; materials management service, and data management service. Some years ago procurement for Leeds was centralised into one unit rather than a division, or departments doing their own procurement. This is now common within most hospital Trusts.

Leeds Teaching Hospitals NHS Trust has five main hospitals: St James's University Hospital (Europe's largest teaching hospital); Leeds General Infirmary (a major city centre acute provider); Chapel Allerton Hospital (predominantly orthopaedics); Seacroft (renal dialysis, reproductive medicine, dermatology and prosthetics), and Wharfedale Hospital in Otley (lymphoedema, out-patients, etc.). The Trust is also part of the Yorkshire and Humber Commercial Purchasing Collaborative for the NHS at UK regional level.

In selecting equipment, the Leeds Trust works closely with clinicians. 'It's very easy to say that the cheapest, or the most expensive option must be the best. When you try to implement anything you need the buy-in and thoughts of the people who are going to use the equipment – it has to involve the business unit, clinicians and the buyer,' George Anderson emphasised.

Chris Slater: 'Procurement is not just about the purchase price of the product; it's about how we manage the product through its life cycle – how we transact for and get it to the Trust and ultimately how we get that product to the end user. Our philosophy is to release as much frontline time to patient care and not for administration of the supply chain.' NHS supply chains are highly complex because, 'We have lots of different commodities coming from different sources and ranging in values, so to release frontline services we put a portfolio of solutions together to ensure the right products are in the right place at the right time.'

Although his team covers 300 hospital departments, wards, and theatres, electronics eliminates staff worries about day-to-day products replenishment, which brings greater compliance because the procurement team decides what to buy and where. George Anderson: 'Top-up mechanisms vary from visual top-up in baskets through to bar-coded inventory control, with the Trust now looking into RFID stock control to identify and track movement of stock through the process. But with Leeds having 25,000 different stock units at any one time, what is crucial is the availability of relevant data to ensure e-Procurement and pertinent solutions are effective.' Using e-Procurement early, Leeds has worked with the Global Healthcare Exchange, for example, to implement systems to control that data.

The team tried to recreate the retail model within heathcare, despite some resistance by suppliers, but the Department of Health is now pushing suppliers to code products with GS1 barcode identifiers for tracking purposes.

IT-enhancing processes and communication is a highly dynamic field, with huge potential to optimise coordination between and within healthcare, as well as social services, said Pascal Garel, 'all the more important with ageing patients with chronic and even multiple chronic diseases.'

Undoubtedly, agreed Mercedes Mengíbar, integration of ICTs helps optimise collaboration across hospitals and beyond campuses (telemedicine, electronic imaging, EMRs etc.) and they avoid duplicate data entry. 'Overall, they allow us to move information instead of patients.' New diagnostic/therapy equipment also brings progress via alternatives to traditional hospital care, e.g., a shift from in- to out-patient care through minimally invasive procedures, and enabling patient monitoring at home.

Although state-of-the-art technologies are important in every aspect of the Leeds hospitals' care, 'We're very much budget-driven and med-tech is never one of the cheaper options', said George Anderson. 'A lot of new developments that computers offer sit outside our price bracket, so we have to tailor our use to deliver best value to the patient against budgetary constraints.'

Chris Slater: 'Outcomes are very important, but we balance what is thrown at us in terms of innovation against our budget, which is pretty much fixed almost 12 months in advance. New technology seldom costs less than the incumbent technology. The total patient pathway may cost less but, as an acute provider, we're only part of that pathway and only paid for that element of the pathway that we execute. For example, there's varying ability of orthopaedic implant technology. One may last ten years, one five years. From our point of view, we pay a standard tariff, so the commissioner would benefit longer term by us using a more expensive implant.' Presently in the NHS, the provider has the upfront cost, while the commissioner gets the long-term benefit – 'There's a mismatch between cost and benefit within the NHS at the moment.'

At Leeds, areas of outstanding dynamism are cardiology – with stenting ICD, pacemakers, and implantable heart valves; breast cancer – care and surgery; and spine, with a huge growth in surgical implants, for example to correct scoliosis with rods implanted to straighten patients' spines. 'Magnet growth rods have reduced the number of operations a patient may need but they cost five times more than standards rods', Chris Slater said. 'We have detailed negotiations with commissioners as to how many operations we can do. Surgeons want to put them in because they can see outcomes, but we are restricted because of the funding we can get from our commissioners.'

Mercedes Mengíbar - A psychologist qualified in healthcare management, she is CEO, Xanit Health Care Management (XHCM), and General Manager of the Xanit International Hospital, in Malaga, Spain. She is also President of MESTESA Healthcare Consulting and has management responsibilities at the Hospital Universitario Virgen del Rocío (Seville), Hospital de Antequera (Malaga), and the Hospital USP Marbella.

Financing: A key challenge

At Xanit, for each upcoming year and every department, the hospital management confers with the department manager to analyse investment needs. Once investments and annual budgets are approved, best-suited avenues for financing are identified – including equipment leasing contracts and long-term loans for construction.

UK hospitals can finance new technologies by ensuring they are remunerated at the right level by commissioners, as well as by negotiating with suppliers to adopt that technology in the longer term, thus perhaps not a price reduction for the device, but enabling equipment use via a long-term loan - free of charge or at a much-reduced price. Chris Slater: 'It's about trying to put enablers in place, at lowest possible cost, to allow us to use the technology and we work with suppliers wherever possible to do that. We need to think about more innovative financing options for some of the larger enabling technologies. Some more forward thinking medical device suppliers are talking about providing managed services that include not only the implant or piece of kit, but the hardware that goes with it.'

Equipment evaluation

New equipment should increase efficiency and quality or reduce cost, but investments are also legitimate where 'non-introduction would leave our hospital behind regarding clinical competence', explained Mercedes Mengíbar. 'The problem is that innovations are introduced long before any thorough examination of their real clinical impact, ethical consequences, or economic and social effects can be carried out.'

Elisabeth Aoun - Head of Purchasing for medical products for the Paris Public Hospital Group, AP-HP, she qualified in political science and hospital administration and is a working group member for healthcare purchasing within the French Ministry for Economy and Finance.

Chris Slater - Head of Supplies and Procurement for Leeds Teaching Hospitals NHS Trust, which has a non-pay spend of about £300m per annum, of which he manages a portfolio of £160m. This includes medical capital equipment purchases, but excludes: pharmacy (with its own procurement unit); maintenance and support of capital estates

To assess their value, a body of clinical evidence is often required and, with new technology, can become difficult to obtain. 'Because we have a finite budget, the cost is often not delivered at the point it is used', George Anderson explained. 'A good example is laparoscopic surgery, which may reduce the bed stay by 2-3 days, but the equipment needed is significantly more expensive. The organisation gains at the top level, but theatres are hit because the cost of the procedure has doubled or trebled; however, the patient has a far better outcome, experiences far less pain and goes home quicker. The organisation as a whole will ultimately benefit, it's just about where the budget sits – that's the difficulty.' In recent years the NHS has pushed to devolve budgets. 'While I see the logic,' said Chris Slater, 'what that has failed to address is the patient pathway issue. That pathway will probably pass through 15-20 budgets, and getting everybody aligned is actually hindering the deployment and effectively our ability to procure new technology. We are now having sensible conversations about re-centralising certain budgets – but that is only in its infancy.'

Investment budgets

At Xanit, 2.4% of the revenue budget is allocated to new fixed assets; there are currently no subsidies for fixed assets. In the UK, Chris Slater said, 'As a provider, we have capital budgets, given to buy new equipment, and we try to use that capital to buy the latest innovations. We don't have funds directly held for the development of new technology at the hospital'. However, added George Anderson, 'We do have the resource of our clinicians to help with the development of new technology, so while we perhaps don't provide funding, we've a full range of very senior clinicians who are world leaders in their areas and much sought after by the manufacturers.'

Jean-Eric Lefevre - A biomedical engineer with 29 years' experience working for AP-HP, his department at AGEPS oversees purchasing procedures and maintenance of medical equipment, covering a network of 40 hospitals in the Paris region.

Manufacturers could deliver more innovation

How? By better understanding of different hospital cultures, better understand trends in healthcare needs and demand, Pascal Garel suggested.

Cost of care matters everywhere, new technology pricing is a key aspect, Mercedes Mengíbar emphasised: 'Manufacturers should keep cost in mind – regarding device design, consumables, and maintenance. The fundamental orientation of new products has to be towards facilitating processes, enabling new services, and cutting cost of care.' Shared responsibility is her key word regarding future interaction between manufacturers and hospitals: 'The relationship has to evolve into a win-win partnership in which both parties contribute their expertise to products, for suitable use of technologies in proportion.'

For Elisabeth Aoun, equipment manufacturers should 'make themselves known to the purchasing departments via marketing materials, sales representatives, adverts, reputation etc.; to follow specifications and requirements described in the tender to the letter, not to try and sell their equipment where it really does not fit. Tender documents are carefully planned and those are the hospital's requirements, nothing else'. The ratio of quality to price is always a deciding factor, she added, but quality covers more than results the machine can give. 'After-sales service, training, technical support are all very important.'

Jean-Eric Lefevre stressed the importance of services being in French and preferably France-based. 'Manufacturers should also try and understand the healthcare system of the country, however remarkable the machine – if the exams it enables are not covered by reimbursement schemes, it can't be purchased because it won't be used'. In France, there is no customer loyalty in healthcare, he said; every public tender is an open competition so, having bought from a company one year is no guarantee for the next, 'unless of course their offer is the best'.

Chris Slater pointed out that the UK's NHS is becoming more business-like, so whilst suppliers need to involve clinicians, they must also involve the procurement and finance elements. 'We have examples where new technology has been taken straight to clinicians, bypassing procurement. We would never take a new technology and force it on clinicians, and clinicians can never take a new technology and force it on the business,' he stressed. 'Suppliers sometimes see clinicians as the key decision-makers, but actually it's a collaborative approach, and they need to understand who is in that collaborative and get the right people around the table if they want to get that product into the organisation.'

Navigating through EU funding jungle

Researchers facing a miasma of application complications need experienced support

Report: Susanne Werner

The European Union provides huge sums for science and research. The current Seventh Framework Programme for Research and Technical Development (FP7), scheduled to run until 2013, has a total budget of over €54 billion. What do scientists do to secure a piece of the funding cake? Ask Birgit Fuchs, Managing Director of Munich-based GABO:mi. She is considered one of the most successful EU funding application consultants in Germany. At EU level, she says, 'application procedures are very complex. Preparing an application is a full-time job the

National interests hamper EU cross-border research

Germany hopes for better research conditions as revision of the EU Clinical Trials Directive is nigh

The European Union invests over €20 billion a year in clinical research, in the context of Agenda Europe 2020, making an important contribution to growth politics. However, European research projects require not only sufficient funding but also a standardised framework. The EU Commission's announcement, in July 2012, about the revision of the 2001 European Clinical Trials Directive has raised hopes that the massive downward trend in the number of research applications of the last decade in Germany can be reversed. If Europe does not want to be left behind in research by international comparison, says Professor Gerhard Ehninger, Director of the Medical Clinic I and the Centre for Internal Medicine at the University Hospital Carl Gustav Carus, at the Technical University of Dresden and Executive Chairman of the German Society of Haematology and Oncology, massive efforts are needed.

'Although the 2001 Directive provides a European framework, it is interpreted very differently by the individual EU Member States and converted into national law,' he explains. Pan-European studies with participants from several EU countries are therefore hardly possible any more and the trend is definitely moving towards national studies. 'In Germany in particular, the general parameters for clinical research are very difficult. Across Europe we have the highest expense with regards to costs and staff, but only every tenth research project and every twentieth clinical study are being approved and financially supported,' he points out.

As an assessor on the Selection Commission, the professor indeed holds solid insights in this field. He sees one of the causes in the fact that the German legislator puts clinical studies with licensed drugs that have already been marketed for 20-30 years on a level with studies concerning the licensing of new drugs. This results in the same administrative expense for the Licensing and Ethics Commission and the same insurance requirements as that of the licensing procedure for new drugs, making the studies very expensive, requiring a lot of staff and making the implementation very difficult in the light of limited budgets.

'A comparison with other countries shows that working under meaningful, simplified conditions is possible, and therefore for many years we have asked AKW for studies involving already licensed drugs to be subject to other guidelines than those involving substances which have not yet been used to treat any patients,' he explains.

Overall, the DGHO Executive Chairman expresses four requirements that should make research in Germany easier. 1. In studies involving licensed drugs, the guidelines on the reporting of known side effects should not be subject to the same timing as that for new drugs; only collected reports on observed side effects should be required, with the exception of unexpected incidents. 2. For these kinds of studies, compulsory insurance should not be needed.

'Germany is the only European country that actually requires compulsory insurance for studies with licensed drugs. Why can't Germany have public accident insurance, which applies when there are problems involving blood or bone marrow donors, instead of insuring every study participant individually?' he asks, seeing an example for the implementation of the interests of lobbyists at the cost of the general public. In the other EU countries individual patients are only insured if the drug has not yet been licensed for use on humans. There is another special guideline in Germany that affects insurance: 'When we carry out an ultrasound examination, for instance to ascertain whether or not a patient is responding to a certain medication, this is being treated as if it was a full clinical study, with all the known impositions, because the ultrasound scan allegedly represents an additional risk. Small wonder then that other countries are laughing about our definition of "study". Therefore, [point 3.] we are demanding, in the case of non-risk additional exams or interventions, there should be no need to classify these as clinical studies that need licensing and insuring.'

The fourth demand relates to the Federal Office for Radiation Protection and its ineffably long authorisation requirements. With authorisation processes lasting up to a year, there is a good chance that a European study may already be finished by the time the German study partner has had the go-ahead for the implementation of procedures involving ionising radiation. In case of urgent or international studies Germany therefore brings up the rear.

Although Prof. Ehninger now has some hope that the revision will lead to an improvement of the situation in coming years, he remains sceptical: 'The national interests are still quite substantial; Germans are in fact the ones putting the biggest stops on the implementation of European guidelines.' On a national level, he sees the necessity of an increase in funding, especially in the case of the German Research Foundation (DFG).

The need to invest more money in clinical research is something of which the German Research Foundation (DFG) is also aware. With the Federal Ministry for Education and Research, the DFG has been running a development programme for large, multicentre clinical studies. With €30 million a year, the programme has the largest funding pot for open topic, non-industry funded studies.

Dr Frank Wissing, Programme Director for Clinical Studies at the German Research Foundation: 'In the last few years, we definitely stepped up our efforts, with the amount of funding (initially €10 million) as well as with the infrastructure, because there are now clearly more clinicians and networks experienced in carrying out these studies. However, our funding is only a fraction of what is invested into clinical studies in the USA and the United Kingdom.'

Last year the DFG could only support 10% of the 170 proposals submitted. 'The need for these studies is enormous, but they are very expensive,' Dr Wissing says. Although it has recently been possible to support so-called pilot studies for medical products through the Federal Joint Committee (GBA), all in all clinical research in Germany should be markedly extended, because needs will increase.

The EU has now also recognised the important role of clinical studies. 'Clinical research in the case of research projects subsidised by the EU is now far more comprehensive and more important than seven or eight years ago, although this funding is programme-controlled and the EU decides where the money goes. Moreover, reimbursement and contractual issues are clearly more elaborate than those for national studies, requiring experienced administrators for their implementation,' Dr Wissing explains. However, he also shares Prof. Ehninger's hope that a revision of the European Clinical Trials Directive will further support the expansion of clinical research.

To date, transnational research projects that are supported, for example, by the American National Institute of Health in the US and Europe, with several European countries involved, often end up not going ahead due to the enormous regulatory complexity. 'But, especially in the case of rare diseases, we cannot do without cross-border studies. Therefore, we are hopeful that the new directive will help to increasingly standardise requirements for clinical studies in Europe, and that there may be just one coordinated and central licensing procedure.'

Biologist **Frank Wissing** gained his doctorate at the University of Oxford, UK, and then carried out research in Cambridge. From 2001-2002 he was Junior Working Group Leader at the Department of Parasitology, at Heidelberg University. Additionally, since 2001 he has been Programme Director of the Group Life Sciences 1 at the DFG.

Gaining his medical degree, **Gerhardt Ehninger** initially worked as a scientific assistant in the Department of Haematology, Oncology, Rheumatology and Immunology, University Hospital Tübingen. Then, as a qualifying internist, in 1985 he became a consultant at Department II in the Medical University Tübingen. In the same year he habilitated and received his Internal Medicine teaching licence. In 1994 he was appointed Professor for Internal Medicine I at the University of Dresden and focusing on haematology/oncology, gastroenterology, infectology and bone marrow transplantation.

MAKE A NOTE:

In our next *EUROPEAN HOSPITAL* issue, due for publication in late December, the focus of our European research series will fall on the state of funding and medical research in France and the United Kingdom.

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researchers usually cannot do on the fly. It takes two to three months to finalise the documents thoroughly and convincingly'.

The EU wants to become one of the most dynamic, competitive, knowledge-based economies worldwide. Progress in medicine plays a crucial role in this endeavour. After all, healthcare is considered a key discipline to boost social development and strengthen economic prosperity. Birgit Fuchs expects large consortia to increasingly dominate European research efforts: 'In Europe, cooperation is the only way to go. As far as research funding is concerned, the trend is towards collaborative research projects with 25 to 30 partners.'

The application consultant helps scientists throughout Europe to acquire EU funding for joint research projects. Over the past five years she and her team successfully applied for and managed projects with a total volume of €200 million. 'Our application success rate is 70 to 80 percent compared to a usual rate of 10 to 20 percent. Today, on average 10 to 15 institutions participate in the collaborative research projects.'

A homogeneous application

In healthcare, one of the fields in which GABO:mi specialises, applications that focus on personalised medicine, or healthy aging, stand a particularly good chance to receive funding under FP7. 'These issues remain a major challenge,' Birgit Fuchs points out, adding, 'in the past two years personalised medicine has become a huge thing'. Other top issues in healthcare funding are systems medicine, bio-banks and biotechnology. The core competency of GABO:mi business is project management of EU research projects – which means the application is only the first step. 'In the end, the application has to be of one piece and it has to reflect the actual research process. Later on, only minor deviations are allowed. That is one of the main challenges,' Birgit Fuchs explains.

Years ago, Professor Dieter Schuster, a friend of hers and today her co-managing director, had asked her to help him with the management of a research project. 'This coincidence inspired our business idea. It had quickly become evident that there is a real gap in the market particularly in view of the fact that collaborative research, which includes several organisations, has long been favoured by the EU,' Prof. Schuster, an engineer by training, recalls. Together, in 2005, they founded GABO:mi, a spin-off from IT service provider GABO. Today 22 project managers are on the team. About 50 percent of the clients come from Germany, 25 percent from the UK and the remainder from various European countries.

Success-based compensation

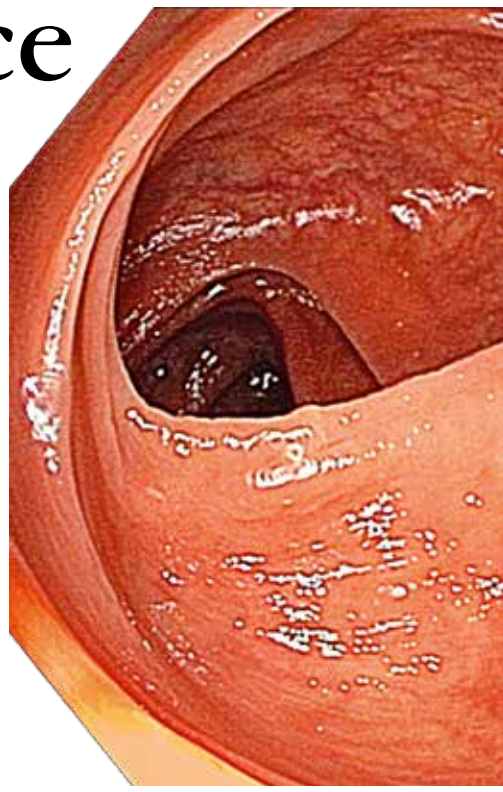
To prepare the application the Fuchs' team advises the researchers, coordinates the initial steps, fine-tunes the application text and ensures all national idiosyncrasies are taken into account and all deadlines met. This frees up time for the scientists to concentrate on their core competency – science – and to contribute the scientific content of the application. When it has been approved and funding secured, GABO:mi manages the project. This is above all people management: promoting communication between the parties, ensuring compliance with all national and European regulations, and facilitating any emerging crises. 'It does happen that project partners go off board, for example when they change jobs or, particularly with small start-ups, when they shift their focus or fail. Then it's our task to work with the major actors to come up with sustainable solutions,' Birgit Fuchs explains.

Establishing communication patterns is a core project management instrument to make sure that the information flow is smooth across all levels. A proprietary web-based platform and regular telephone conferences facilitate this process, but even more important are meticulously planned personal meetings. The stunning aspect of the GABO:mi business concept: the consultancy is compensated for their services only when funding has been granted. 'Money changes hands only if the application has been approved,' she points out. Only the actual project management fee, a funding line item, finances the firm. Approximately seven percent of the funding total is earmarked for this task. 'This concept,' she points out, 'means we carry a high risk. Therefore we only take on projects we believe in.'

After studying business information systems, in 1992 **Birgit Fuchs** became a project manager at IT consultancy and software developer GABO mbH & Co. KG. Five years later, she was an officer of the company and co-responsible for key accounts such as Deutsche Telekom AG and Siemens AG. She also headed business development. In 2004, the division *Management of EU Research Projects*, established the previous year, became the spin-off company GABO:mi mbH & Co. KG with Birgit Fuchs and **Dieter Schuster** as managing directors. Today, the Munich-based firm supports about 30 large European collaborative research projects.

The new Evis Exera III in practice

Higher quality images, pre-freeze and several other advances promise a rise in diagnostic and treatment standards in endoscopy



Dual Focus, brighter Narrow Band Imaging (NBI), and pre-freeze are key breakthroughs of the new generation of endoscopy devices – and new features such as these, embodied in the new Evis Exera III, open up a bundle of opportunities for endoscopy-based diagnoses and treatments, says Olympus. How might they benefit hospitals? **European Hospital** spoke with expert user, **Paul Fockens**, Professor and Chair of Gastroenterology & Hepatology at the renowned Academic Medical Centre (AMC), University of Amsterdam, which provides endoscopic services as a tertiary centre.

As chair of gastroenterology and hepatology at the AMC, Professor Fockens manages the department and combines clinical routine, education and academic research. 'In patient care, my focus is on advanced therapeutic endoscopy as well as some advanced diagnostics of the stomach, small bowel, large bowel and pancreas. To a large extent my cases are large colonic polyps and colonic mucosal resections, endoscopic ultrasound with drainage pancreatic fluid collections, ERCP as well as most interventions in the upper gastrointestinal tract.

'Roughly 50 percent of my cases are referrals after radiology with a requirement for interventional endoscopy, and another 50 percent are sent from other endoscopists requiring high-level endoscopic intervention at a tertiary centre. For top-quality therapeutics of these organs and regions, you need a very good diagnostic workup; neoplastic lesions are a good case in point. We can only remove superficial lesions using endoscopy; MRI merely helps in cases of large-volume lesions, which are removed surgically.'

Paul Fockens is Professor of Gastroenterology & Hepatology at the Academic Medical Centre, University of Amsterdam, and Chair of the AMC's gastroenterology and hepatology department. He is also President elect of the European Society of Gastrointestinal Endoscopy (ESGE).

Asked to outline the main differences between the new Evis Exera III and its predecessor, Professor Fockens explained that the main advantages are in the system's diagnostic capabilities. 'In many cases the images we receive from referrers prove insufficient for the preparation of an intervention. The Evis Exera III gives us more detail and images are more in focus. We'd prefer our referrers to use the new system too, in order to achieve better image quality. Currently, we invest about a third of our time in creating a more precise diagnosis; when we get really low-quality images from referrers, we schedule a diagnostic appointment first and go for therapy after our diagnosis.

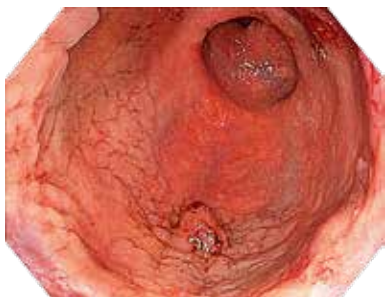
'If every physician in the care chain were to use high quality endoscopic imaging such as the Evis Exera III, this would cut down the time we take to verify a diagnosis to around 20 seconds. Better images would also make planning of the individual interventions a lot more to the point, with less need to adapt, reducing scheduling risks – meaning a significant improvement for us and the patients.'

What form does interaction with other disciplines take?

'Patient cases are discussed, mostly after the procedure, within the tumour board. This measure partly serves quality assurance purposes and helps confirm follow-ups, and its interdisciplinary character ensures a competent therapeutic approach. For malignant tumours, going through the board is a must.'

What about the therapeutic benefits of the device?

'For therapeutic purposes, the improved image quality of the Evis Exera III is also significantly relevant. Being able to switch back and forth using NBI is very positive; knowing exactly where to execute a cut in the region of interest is one thing; better manoeuvrability is another asset. Better vision helps to ensure that the procedure has been properly performed. In addition, motor-driven jets allow the physician to spray fluids on the lesion, which is convenient.'



Enhanced image quality.
Clinical images courtesy of Roy Soetikno, MD/Tonya Kaltenbach, MD

Is special training required?

'Well, handling endoscopes expertly has been and will continue to be largely dependent on endless routine hours spent using the instrument. Quality in what the physician does is totally tied to this expertise – and it will not change with the new instruments that have even more features.'

Where does hepatology come in?

'As far as endoscopy is concerned, portal hypertension is the key focus there. Patients with, for example, a long history of a liver disease, develop varices in the oesophagus or stomach, which tend to bleed. We treat them endoscopically using bands. Interventional radiologists will do TIPS procedures for long-term effects; these two techniques are becoming increasingly complementary today. We discuss cases with surgeons, interventional radiologists, and pathologists in hepatology and inflammatory bowel disease meetings, also for benign conditions. In-house referrals from other specialties, such as surgeons, are frequent because, in the Netherlands, there is no financial competition between specialties.'

Are there additional notable advantages?

'Apparently, acquiring really good images of the upper gastrointestinal tract present difficulties to endoscopic devices; everything in the region is continuously moving, which is a challenge to video and still frame capture. But now, with the Evis Exera III, even physicians who are not good photographers can get good results thanks to the new Normal and Near imaging modes and Pre-Freeze. The latter

100 years of suture technology

We have known since the beginning of October who will receive the Nobel Prize for Physiology or Medicine in Stockholm, this December. Since 1901, according to Alfred Nobel's legacy, the award has been given to the person(s) who 'has made the most important discovery in the field of Physiology or Medicine' – this year Sir John Gurdon and Shinya Yamanaka share that great accolade for reprogramming adult cells. A hundred years ago, in 1912, it was French surgeon Alexis Carrel, who received a Nobel for the development of a procedure for the reconnection of blood vessels and his work on the transplantation of tissue and organs – Carrel paved the way for modern vascular surgery and organ transplantation.

The precipitating event was, as so often, emotional: In 1894 the then French President Marie Francois Sad Carnot died as the result of an assassination attempt in the Silk City of Lyon – his portal vein had been severed and nobody was able to reconnect it. Carrel, aged 21 years and a licentiate of the University of Lyon, bought the finest needles and learnt the classic techniques of the Canut – the term for the respected local silk workers. He developed the Carrel suture for end-to-end and end-to-side anastomosis of blood vessels and was able to transplant thyroids and kidneys in animals, publishing his results in 1902 (Source: Lyon Med 98:859).

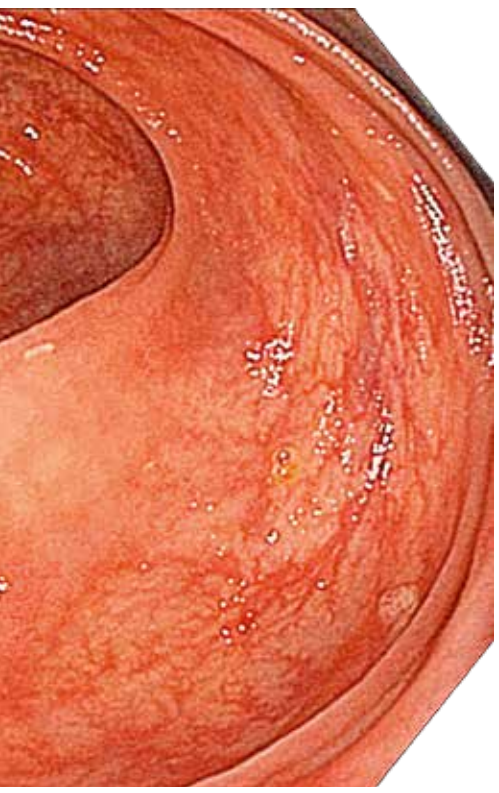
Today, vascular surgery is one of the youngest stand-alone medical disciplines and is characterised by high dynamics. Aortic surgery is one key focus. Aneurysms of the thoracic and abdominal aorta can be treated along with stenosis of the blood vessels supplying the kidneys or carotid artery.

The suture materials of the previous century were not suitable for this. Catgut, for instance, developed in 1868 by the English surgeon and pioneer of antisepsis, Joseph Baron Lister, consisted of strings from sheep guts disinfected in carbolic acid. Although made durable by tanning, these were broken down in the body enzymatically and disintegrated over time.

With the discovery of the textile fibres Polyamide 6 and Polyamide 6.6, better known as Perlon and Nylon, it was only a matter of time until these man-made fibres were also used for surgical sutures. In 1935 Synthofil AÒ, a suture made from polyvinyl alcohol, came on the market, followed in 1939 by SupramidÒ, a perlon suture especially developed for surgery. Not long after, other non-resorbable fibres made from polypropylene and polyester complemented the range. Through copolymerisation of the substances glycolic acid and lactic acid it was finally possible to develop a synthetic material (VicrylÒ) that is not broken down enzymatically like catgut, but by the body's own fluids. Plaited and coated, this material is highly tear resistant and facilitates the use of finer sutures.

For other hollow organs anastomosis can only be created through sutures techniques with great difficulty, and often not at all – the leak rate would be just too high. Here, started in 1908 by the Hungarian Humer Hültl, the staple suture technique was developed (see EH 2/2011 p. 4-5), which is actually what really made diabetic surgery possible (see EH 3/2011 p. 5-7).

A large part of suture materials is not used for the connection of tis-



helps to improve the functionality of the "freeze" button: you don't freeze exactly the last image, but the video-processor instead scans the previous images and automatically selects the last image that was well in focus. A lot more details and better, high-resolution images are the result.

'As a side-effect, the higher resolution helps us cut down on doing biopsies, which saves us costs on pathology.

'In future, with more patients referred with high-quality images based on this generation of devices, we hope to save some time thanks to better scheduling and reduced duplicate diagnostics. More importantly, however, therapeutic quality will go up because we will be able to remove neoplastic lesions completely thanks to for early indications of cancer, detecting flat lesions, or differentiating tumours.'

Mobile hybrid operating theatres

Monitor supports flexible and rigid endoscopy

Sony reports that, for medical care its PVM-2551MD 24.5" monitor is the first of its kind to harness the benefits of Sony's unique Super Top Emission OLED technology. It includes TRIMASTER EL technology to maximise image performance, a wide colour scale, and an outstanding black level. With full HD resolution (1,920 x 1,080 pixels) and 10-bit signal processing for accurate colour management it supports several colour standards and delivers optimal colour reproduction in natural shades, the firm adds. Suitable for a range of medical applications, particularly flexible and rigid endoscopy and surgical microscopy operations, Sony adds: 'In combination with modern HD endoscopy cameras, users can recognise even the smallest details, such as in screening

Details: www.pro.sony.eu/medical

Alexis Carrel

A LITTLE LESSON IN SUTURE MATERIAL

Surgical sutures can be resorbable, absorbable or non-resorbable. They are made from biological or synthetic material. Biological material can be of animal (sheep gut) or botanical origin (cotton, silk). Synthetic sutures consist either of synthetic material (polyamides, polyester, polypropylene) or steel (stainless steel). Surgical suture material is divided into monofilament, polyfilament (plaited, twisted, twined), pseudo-monofilament (sheathed individual fibres) and coated (gummed individual fibres).

sues or organs but for wound closure. However, staples, clips or glue are frequently used in place of sutures. The market is large and with an average annual growth rate of 2.2% also relatively stable. In 2007, analysts at Medmarket Diligence LLC, the Californian market research company for medical products, forecast a market volume of US$ 281 million for sutures, US$151 million for stables, US$80 million for clips and US$93 million for glues for the most important European markets in Germany, UK, Italy, France, Spain and Benelux (Source: Medmarket Diligence, LLC, Report #S180, 'Worldwide Surgical Sealance, Glues, Wound closure and Anti-Adhesion Markets 2008-2015', published: Oct 2010). France was listed in this analysis with US$ 42 million for suture materials – a multiple of the money awarded to Alexis Carrel a hundred years ago.

A trauma leader and team for every patient

Surgery means more than operating

Surgery today requires not only skilled surgeons but also a trauma leader to set up the team and manage the intervention. Thus surgery is more than operating was an apt title for a joint conference of several working groups of the German Society for Surgery (DGCH) and the German Society for Clinical Process Management (DGKP), held in Berlin. EH correspondent Susanne Werner interviewed Professor Axel Ekkernkamp MD, one of the two Conference Presidents, about the complexity of peri-operative management in trauma medicine, initially asking him to explain the conference motto.

'Professor Hartwig Bauer, long-time Secretary General of the DGCH, coined this phrase,' he explained. 'It makes it clear that surgery is a complex issue. Today in surgery the entire peri-operative process has to be planned, managed, adapted and controlled in order to be able to help the patient efficiently.

'The number of disciplines involved depends entirely on the individual patient's situation. In Berlin, the emergency hospital where I work admits about 55,000 patients per year. There are patients with myocardial infarctions or stroke as well as accident victims. We treat about 250 severely injured people per year. For those patients, we have core teams comprised of the surgeon, anaesthetist, radiologist, specialist nurses and paramedics. Depending on the kind of accidents, other specialists are needed. When there is a serious motorbike accident we might call in a facial surgeon or an ophthalmologist, sometimes we need a urologist or, for female patients, a gynaecologist.

How do you manage such a large team? Do you train for such emergencies?

'Yes, we do that among other things. At our hospital it's the core task of the Centre for Emergency Training to prepare the staff for these cases. The colleagues use dummies to go though emergency procedures. Our guidelines for an emergency are called "shock room algorithm". They map all processes and these are displayed either as posters or on the flat screen.

'The German Society for Trauma Surgery offers two-day seminars in Advanced Trauma Life Support for surgeons to become so-called trauma leaders. The participants learn to assess the status of the trauma patient quickly and precisely, to determine which treatments are to be initiated first and whether their own facility is equipped for this particular patient or whether the patient has to be transferred. The trauma leaders are in charge of peri-operative management. This means it may well be that the intern who is a certified trauma leader is the boss, rather than the university medical professor who happens to be on the team. An important tool to ensure trauma surgery quality lies in the trauma networks initiated by the German Society for Trauma Surgery.

'These networks allow close cooperation between the different care stations and provide clearly defined workflows. In a first step, the currently 1,000 participating hospitals are certified, taking stock of which competencies and care services they can contribute to the network and where there are gaps. In a second step, the hospitals negotiate cooperation agreements and define efficient procedure in quality circles and they try to anticipate the obstacles that might turn up and how they can be overcome.'

Checklists, hygiene, technical equipment – from your point of view what are the most important instruments to improve trauma care?

'All these instruments have helped to improve the quality. Documentation, however, is the core component of process quality. You have to know how long the individual process steps take, to be able to compare and to optimise them. For example, a modern hospital should be able to complete diagnostics of an accident victim within 20 minutes. This is an indicative timeframe that helps you to assess the processes in your hospital.

'Germany has a top-notch trauma care system. In no other country in Europe does the emergency physician come to the patient. An ambulance car with specially trained physician on board ensures that medical care is available within eight minutes.'

'So, our care system in Germany is highly developed and closely knit. Now we have to make sure that we can continue to finance it and maintain its quality. There is always room for improvement, be it in medical, technical or organisational terms. We have to continue to work on the system.'

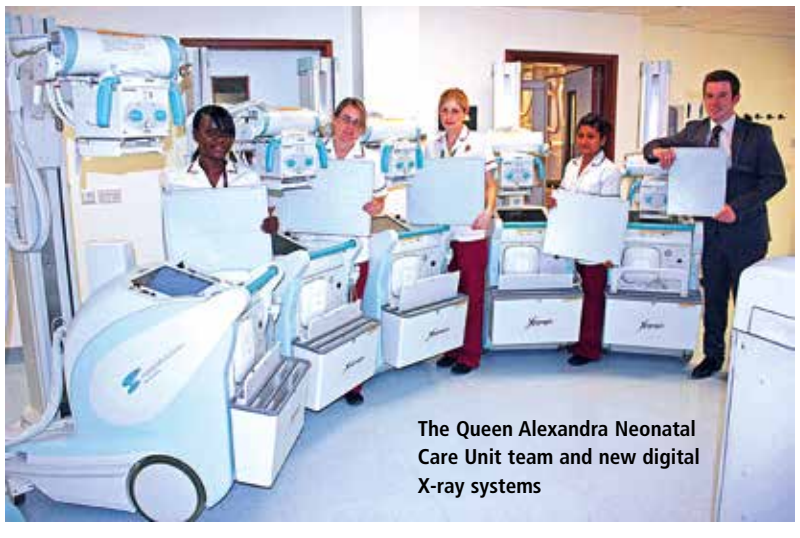
In 1997 **Professor Axel Ekkernkamp** became Medical Director and later Managing Director (from 1999) of Unfallkrankenhaus Berlin (ukb), and is a specialist in general and trauma and reconstructive surgery and orthopaedics. Following his medical and dentistry studies in Münster, Germany and Berne, Switzerland, he became a visiting physician in Vienna, a German Army physician in Cambodia, worked at Harborview Medical Centre in Seattle, USA, and became a professor at the University of Thai Binh in Vietnam. From 1984 to 1997 he was at the Surgery Clinic and Polyclinic at Berufsgenossenschaftliche Kliniken Bergmannsheil in Bochum, Germany, where he received his habilitation. He has been Professor and Chair for trauma surgery at Ernst Moritz Arndt University Greifswald, Germany, since 1999. Active in several professional associations the professor has received many awards and citations, e.g. the Order of Merit First Class of the Federal Republic of Germany.

Imaging in a major trauma unit

In Portsmouth, England, the prestigious Queen Alexandra Hospital has been using a MobileDaRt since its 2009 opening. Recently, this unit was joined by five 4th Generation siblings, three incorporating the latest CXDI-70C wireless digital imaging detector, the other with the unique CXDI-80C wireless, small format detector. Both detector types offer exceptional direct digital images within three seconds at the point of care.

With major trauma unit status, the hospital is part of a national project to improve that field of care. Thus high quality X-ray images are needed to meet and respond to the changing demands of medics in emergencies. 'Replacement of our mobile fleet required equipment that could travel the large distances in our hospital, while providing almost instantaneous diagnostic images to our clinicians,' explained Nicola Sanchez, the hospital's Advanced Practitioner Radiographer. 'We also need versatility in imaging our wide range of patients including NICU. The DaRt Evolution was the only unit that fulfilled all of these necessities.' In March 2012, Portsmouth Hospital NHS Trust appointed Gloucestershire-based Xograph Healthcare, an independent UK medical equipment provider and Shimadzu's exclusive sales partner for digital mobile X-ray in Great Britain, to supply the new mobile digital X-ray systems for rapid radiographic imaging in the ER, at the bedside and in the Neonatal Care Unit. 'It was the right decision,' Nicola Sanchez concluded.

The new mid-sized format CXDI-80C fits to modern incubators



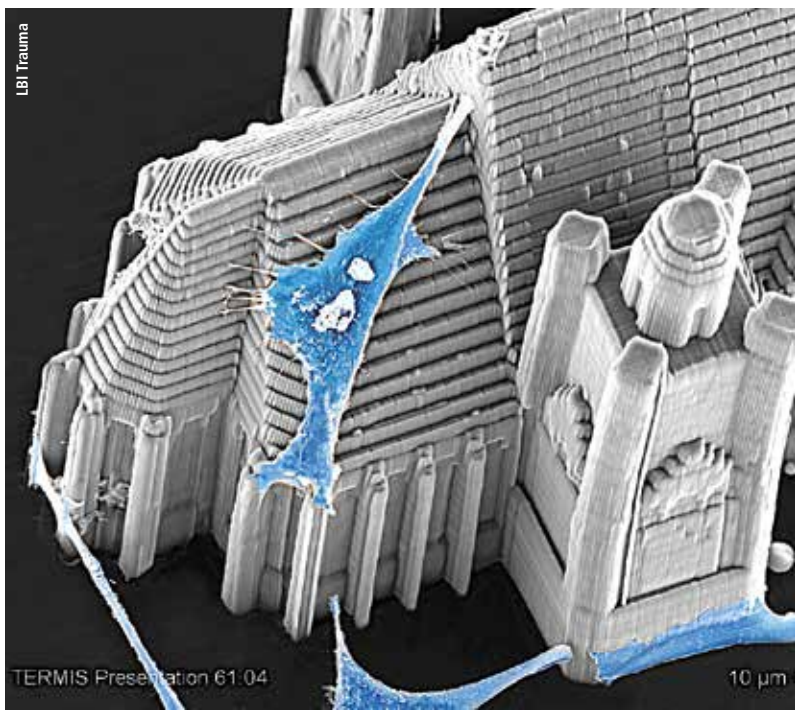
The Queen Alexandra Neonatal Care Unit team and new digital X-ray systems

Tissue reconstruction and regeneration

Embracing a nano-size silken promise

Report: Michael Krassnitzer

Artificial vascular trees, the growing of heart tissue, nerve regeneration: The World Congress of the Tissue Engineering and Regenerative Medicine International Society (TERMIS) held in Vienna this October offered an impressive display of current developments in tissue reconstruction and regeneration. The congress was also the venue for a meeting of the Who's Who in the field of silk fibroin, a protein obtained from – and one of the two components of – natural silk.



St. Stephen's Cathedral recreated in nano-size silk fibroin

DI Dr Andreas Teuschl heads the City of Vienna Competence Team Tissue Engineering Bioreaktoren, Department of Biochemical Engineering, University of Applied Sciences Technikum Wien in Vienna. He studied biochemistry at the Technical University Vienna. His PhD thesis was on Silk Fibrion – a versatile and tunable biomaterial for tissue engineering and regenerative medicine. During his studies, he worked at the Ludwig Boltzmann Institute for Clinical and Experimental Traumatology in Vienna, which forms a research cluster with – among others – the Technical University and the Medical University of Vienna.

'Silk fibroin is the best material in the world, enthused Professor David Kaplan,Director of the Bioengineering and Biotechnology Centre at Tufts University in Massachusetts, USA, and a pioneer in this field. It was he who, in a paper published ten years ago, laid the foundations for the use of silk for tissue reconstruction and regeneration. Silk fibroin is not detected as foreign matter by the immune system and is therefore not rejected by the body; it grows into the body's own tissue without any problems and is only broken down slowly. Silk fibroin is harder than steel and is therefore also used in the production of bullet-proof vests. Above all, silk fibroin can be tuned into any desired form: fibres, gels, sponges or particles. At the Ludwig Boltzmann Institute for Clinical and Experimental Traumatology in Vienna, the St. Stephen's Cathedral – the famous landmark of the Austrian Capital – was reproduced in nano-size from silk fibroin and then colonised with cells (see images) especially for this congress.

In the future, silk protein is likely to be used in this way, as a material for pedestals used for tissue regeneration. A three-dimensional silk matrix is colonised with stem cells inside a bioreactor. Growth factors integrated into this construction ensure that the stem cells develop into the desired tissue type. 'About a year after the implantation the silk fibroin will have been broken down and been replaced by the body's own tissue,' explained Dr Andreas Teuschl, Head of the City of Vienna Competence Team Tissue Engineering at the University of Applied Sciences Technikum Wien.

The procedure is suitable for the regeneration of hard as well as soft tissue. Very promising preclinical results already indicate numerous opportunities for silk protein application, particularly in the musculoskeletal system. In the USA recently, the first silk-based medical product was licensed: a fibre mesh for soft tissue reconstruction.

Prof. Kaplan is convinced that silk fibroin nano-size particles could also be used for drug delivery or drug targeting: 'Through the design of the silk particles we could determine exactly what amount of a substance is released in which part of the body under what conditions and which cell type is the objective.' Due to its unique properties silk fibroin could serve as the basis of a 'new generation of high-tech medical products' with a range extending right down to fully implantable and degradable optical and electronic interfaces, he emphasised. The concentration of silk fibroin with various proteins could give the material additional biologically effective qualities, such as anti-inflammatory ones. 'With the help of protein chemistry,' he added, 'silk fibroin could be given fantastic new functions.'

Professor David Kaplan holds an Endowed Chair, the Stern Family Professor of Engineering, at Tufts University in Massachusetts. He is Professor and Chair of the Department of Biomedical Engineering and also holds faculty appointments in the Department of Chemical and Biological Engineering, Department of Chemistry, Tufts University School of Medicine and Tufts University School of Dental Medicine. His research focuses on biopolymer engineering to understand structure-function relationships, with emphasis on studies related to self-assembly, biomaterials engineering and functional tissue engineering. He has published more than 400 papers, edited eight books, serves on the editorial boards of numerous journals and is Associate Editor for the journal *Biomacromolecules*.

FOR YOUR DIARY:
JANUARY 27-30, 2013

TERMIS-EU/Expertissues Winterschool, Radstadt, Salzburg, Austria. School Theme: "Vitro/Vivo Preclinical Models and Imaging in Musculoskeletal Tissue Regeneration"

Surgical lighting

Starled 5 LED lamp for the operating room

Starled 5 is part of the ACEM Medical Company's Starled series, 'and, as the whole range is made with LED technology (light emitting diodes),' the firm reports that this 'is an extraordinary light source which is becoming more and more popular for its reduced dimensions, duration in time, low energy consumption, high performance, lack of heat and excellent colour rendering index.'The LED technology guarantees a light beam without IR (infrared) rays hence eliminating heat under the lamp and on surgeons' heads, ACEM adds. 'The 50 LEDs are circularly positioned around the handle, generating a light spot of 21 cm at one metre, with a high illumination level of 135.000 lux (160.000 lux optional) for a steady life cycle of about 50.000 hours. Starled 5 guarantees a colour rendering index of 95 (cri) with a colour temperature of 4.900 °k. These two values allow reproduction of the exact chromatic scale of the colours of the human body.'

To achieve the necessary illumination of the surgical field, the light can produce a focused illumination as well as a uniform ambient one due to a manual focusing system in its central handle. A new light-up system (invented by ACEM), which has particular beams of light coming from the upper part of the lamp, offers perfect visualisation of the surgical field, making the lamp suitable for minimally invasive surgery, the firm adds.

Starled 5 also can be integrated with a video camera in the lamp's central handle (or on a separate arm). There are also various configurations available, according to needs.

Details: www.acem.it

Mobile hybrid operating theatres

New offering includes C-arms and operating tables

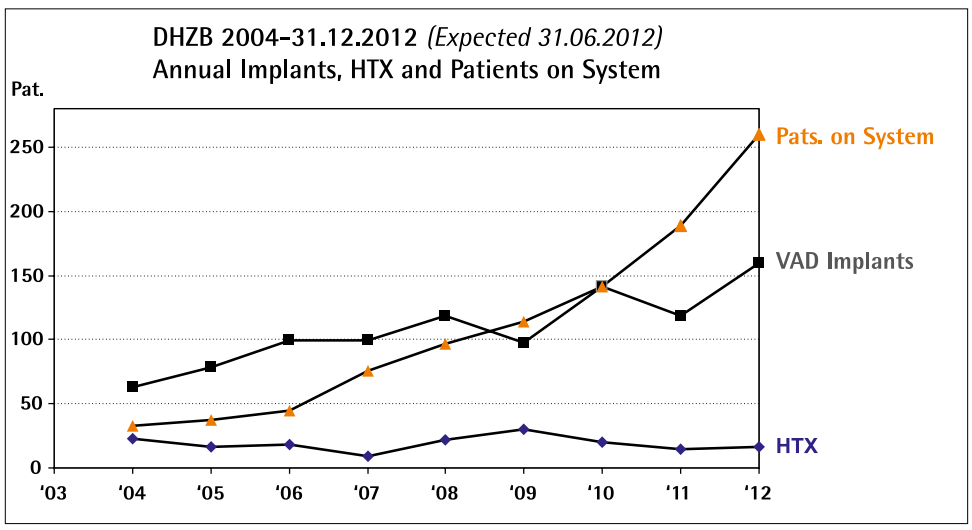
Due to a new global distribution agreement, C-arms specialist Ziehm Imaging, of Nuremberg, can now supply hybrid operating theatres with surgical tables from the Swedish manufacturer Stille to complement its Ziehm Vision RFD Hybrid Edition. 'The Ziehm Vision RFD Hybrid Edition offers a cost-effective alternative to fixed installed systems in hybrid operating rooms – excellent image resolution, a powerful 20 kW generator and an active liquid cooling system provide reliable intraoperative imaging even for complex procedures,' Ziehm reports, adding: 'The mobile C-arm and the Stille imagiQ2 OR table for vascular surgery, presented in April 2012, form a powerful duo for interventional surgery. The new OR table delivers maximum precision, reduces radiation exposure and, with its high level of flexibility, is ideal for use in hybrid operating rooms.

Treating chronic heart failure – From complementary to destination therapy

Total artificial hearts and ventricular assist devices today

Artificial hearts, originally designed to bridge the time on the waiting list for a heart transplant, in recent years have increasingly become an independent treatment option for patients with chronic heart failure (HF). Discussing this trend with Professor Roland Hetzer, heart surgeon and chairman of the Deutsches Herzzentrum Berlin (DHZB, German Heart Institute Berlin), he explained that the DHZB, a specialist centre for heart treatment, has the most comprehensive programme worldwide for the implantation of artificial hearts. In the past 23 years over 1,670 of these devices have been implanted in HF patients

Interview: Bettina Döbereiner



Annual implants, cardiac transplantations and patients on heart-lung machines

'The original concept of artificial heart developers was to create a total artificial heart (TAH) for permanent replacement of the natural heart,' he said. 'Clinically, TAHs were used for the first time in 1969 in Houston and then again in Salt Lake City in 1982, but the complications associated with TAHs were so heavy that the American government stopped their long-term use. Since that time TAHs, where the natural heart is removed, were only used to bridge the time to heart transplantation, in a so-called bridge-to-transplant therapy. As a kind of side-product of the TAH development, mechanical circulatory support systems for a heart left in place had been developed. These systems, generally called ventricular assist devices (VADs), assist either the left or right ventricle, or both at once. Because VADs were, after all, more suitable for a bridge-to-transplant therapy, they then almost replaced TAHs. Both systems, the TAH and the VAD, can only replace the pumping function of a failing heart. Regulatory and hormonal functions have not been taken into account up to now.'

If TAHs failed to permanently replace a heart, could VADs be an option to permanently replace the natural heart?

'Heart transplantation is, beyond controversy, still the best therapy for chronic heart failure. I personally oversee patients living for 28 or 29 years with an implanted natural heart. However, mainly due to organ scarcity, a heart transplant is an option only for a highly select group of patients, to a degree that I call it a casuistic therapy. In addition to this, significant improvements have been made in VAD technology. Therefore, we have increasingly used VADs for permanent therapy in recent years. I'll give you some data: At the beginning of the 1990s, we still performed 120 heart transplants at the DHZB per year; in 2011 only 34 and this year just 13, so far. By contrast, implantation of VADs has increased: In recent years we had around 170 and for 2012 we anticipate 200 implants – and I think this trend will continue.

'Why? I think the rate of heart failure will increase because the more successful we are in treating acute heart disease, such as acute infarct or acute myocarditis, the more of these patients will eventually, after further years, develop chronic heart failure. In the demographic curve you see that, in the patient group beyond 70-75 years of age, chronic heart failure is by far the most prominent heart disease, but we only perform heart transplantations up to the age of 65-70 years due to increasing complication rates beyond this age. Therefore the only way to treat this patient group even nowadays is to implant a VAD.'

Is VAD implantation difficult?

'The surgical procedure is not very demanding and I think it is so standardised that every cardiac surgeon can perform it. Particularly for older patients it's a good therapy because they don't have a great trauma and are immediately better. The oldest patient in whom we have successfully implanted a VAD is 83 years old.'

How does a VAD work?

'Nowadays, practically all such assist devices follow the rotational principle, working like a fast-running turbine with a rotor producing continuous blood flow. These small turbines are becoming smaller and smaller at present weighing about 90 to 130 grams. This year we are expecting pumps that are not larger than my thumb. The pumps are implanted into the body and only the energy source is located outside, connected by a cable running through the skin. For the patient, the energy support is relatively easy to manage and he or she can wear it in a bag on the body, which means mobility is possible.'

Isn't the continuous blood flow unhealthy?

'As I implanted the first rotational pump in humans in 1998, of course I was quite curious whether something unusual would happen because of this non-physiological blood flow, but we did not see any immediate sequel. Now, after a while, we can see that some things may develop, for instance aortic valve incompetence, some coagulation disorders, or the formation of some abnormal small vessels in the bowel that might bleed. Of course, since we only have experience over about eight years, we don't know what this type of circulation might cause in humans after 20 years. It has been speculated that arteriosclerosis or hypertension might be accelerated, but this is not proven.'

How long can patients live with a VAD?

'Patients who have had such rotational pumps the longest have had them for nine years. We estimate that the current generation of VADs technically may last around 15 years and, of course, they can be exchanged if there is technical wear. In addition the devices are being continuously improved to increase their durability. There is an energy transmission concept, for example, using plugs that are screwed to the skull to avoid infections or cable breaks. Then there's the possibility of transferring energy via induction through the intact skin. So, I think in the coming years the implantation of assist devices will probably be one of the most frequent therapy modalities we will have.'

With over 40 years' experience, **Professor Roland Hetzer** ranks among the most experienced cardiac transplant surgeons worldwide. He studied medicine in Mainz and Munich universities and then surgery at the Hannover Medical School, and was a clinical fellow in cardiovascular surgery at the Pacific Medical Centre in San Francisco and Stanford University.

Back in Germany as a senior physician at the Department of Thoracic and Cardiovascular Surgery at Hannover Medical School, he qualified as a professor and established his research in heart transplantation. He became a professor at the Free University Berlin In 1985 and subsequently established the DHZB, German Heart Institute Berlin, of which he is chairman and medical director of cardiac surgery.

Prof. Hetzer performed Germany's first successful TAH implant, the Bücherl total artificial heart, as a bridge to transplantation, in 1987. Then, in 1998, he implanted the first VAD with a rotational pump worldwide. Named after its inventor, Michael DeBakey MD, the event heralded the worldwide success story of rotational pumps.

Additionally a professor at the Humboldt University of Berlin, he is also medical director of the Heart Centre in Cottbus.

Atrial fibrillation or unexplained syncope

New implant provides long-term continuous monitoring

The BioMonitor is a 'subcutaneous implantable leadless cardiac monitor for long-term continuous remote monitoring of patients with arrhythmias such as AF, bradycardia, sudden rate drop, asystole and tachycardia,' the manufacturer Biotronik reports.

Sensitivity and specificity are essential to detect arrhythmias such as AF. Thus the firm developed ClearSense Technology which has, it explains, 'a unique three-vector signal detection that produces highly precise and reliable arrhythmia monitoring. 'The technology records three ECG channels converting them to one high quality ECG input signal to clearly distinguish, on a beat-to-beat basis, between a genuine signal and other artifacts, such as myopotentials due to body muscle contractions. This innovative technology allows for optimal arrhythmia detection independent of the device's implant orientation within the body and provides longevity of 6.4 years'.

Support Management

The home monitoring system provides daily remote data transfer without patient interaction and its 'traffic light system' streamlines monitoring by highlighting the most relevant information and providing accurate data for physicians to monitor and manage their patients effectively.

The world's first physicians to implant the BioMonitor to measure HF in patients are Professors Gerhard Hindricks, at the Electrophysiology Department, Leipzig University Heart Centre, Wilhelm Haverkamp, at the Cardiology Department, Charité Campus Virchow, Humboldt University Berlin, and Dietmar Bänsch, at the Cardiology and Rhythmology Department, Rostock University Hospital. Prof. Haverkamp observed: 'BioMonitor, with its ClearSense technology, and Biotronik Home Monitoring offer the optimal combination of reliability and efficiency.' Prof. Bänsch also commented: 'BioMonitor supports physicians in every step of arrhythmia management, from diagnosis via monitoring to individualised therapy,'

TAVI's unsung hero

The Danish inventor of an aortic valve for transcatheter implantation (TAVI) gains recognition for his achievement by colleagues within the European Society of Cardiology


TAVI inventor Henning Rud Andersen with the valve and his father, whose life it saved

A stupid idea came home to Denmark last year in a brilliant stroke that saved the life of an 86-year-old man. The idea was for a balloon-inflated aortic valve that could be implanted using a guide wire passing through the femoral artery instead of open-heart surgery.

The dying man who received the valve was Jorgen Rud Andersen, the father of the inventor of transcatheter aortic valve implantation (TAVI), Henning Rud Andersen MD. The success of that procedure, which gave back a robust life to his father, was a personal triumph that closed the circle on a journey that began for Dr Andersen in 1988 in Phoenix, Arizona. Still in training as an interventional cardiologist that year, he was inspired by a presentation of coronary artery stents. Why not make the stent bigger and place a valve inside, he asked.

No one was listening, so he built such a device himself, patiently bending wires to create a stent and buying pig hearts from the local butcher shop for the aortic valves. He then built a transcatheter delivery device inspired by the Cribier-Letac balloon catheter pioneered in France during the 1980s for balloon aortic valvuloplasty (BAV) by Alain Cribier MD. From conception to proof-of-concept took Andersen just 75 days.

Today, TAVI valves, placed in more than 50,000 patients, range in sizes from 29 French down to 18 French. Dr Andersen's hand-made valve, which he successfully placed in a pig's heart, measured an enormous 41 French with rough surgical knots stitching the porcine valve to the metal frame.

A long journey to success

Presenting a poster demonstrating the feasibility of the idea at international conferences proved to be a lonely, discouraging experience, he said, attracting the attention of no one. The rejection was complete when his paper describing the experience was turned down by the leading heart journals. Yet, this idea, most kindly described as a low priority, caught the attention of one colleague, Patrick Serruys, editor of the *European Heart Journal* who attended Andersen's presentation to the Danish Cardiology Society in 1990 and accepted the paper for publication in 1992.

For Andersen, the journey ended in 1995 when he was granted a patent, which he sold to a start-up company called Percutaneous Valve Technologies led by Dr Cribier. 'At that stage, I was convinced the idea was dead,' Dr Andersen recounted to colleagues in an article published by the University of Aarhus. 'The task was too big for us. We tried, but it was impossible.

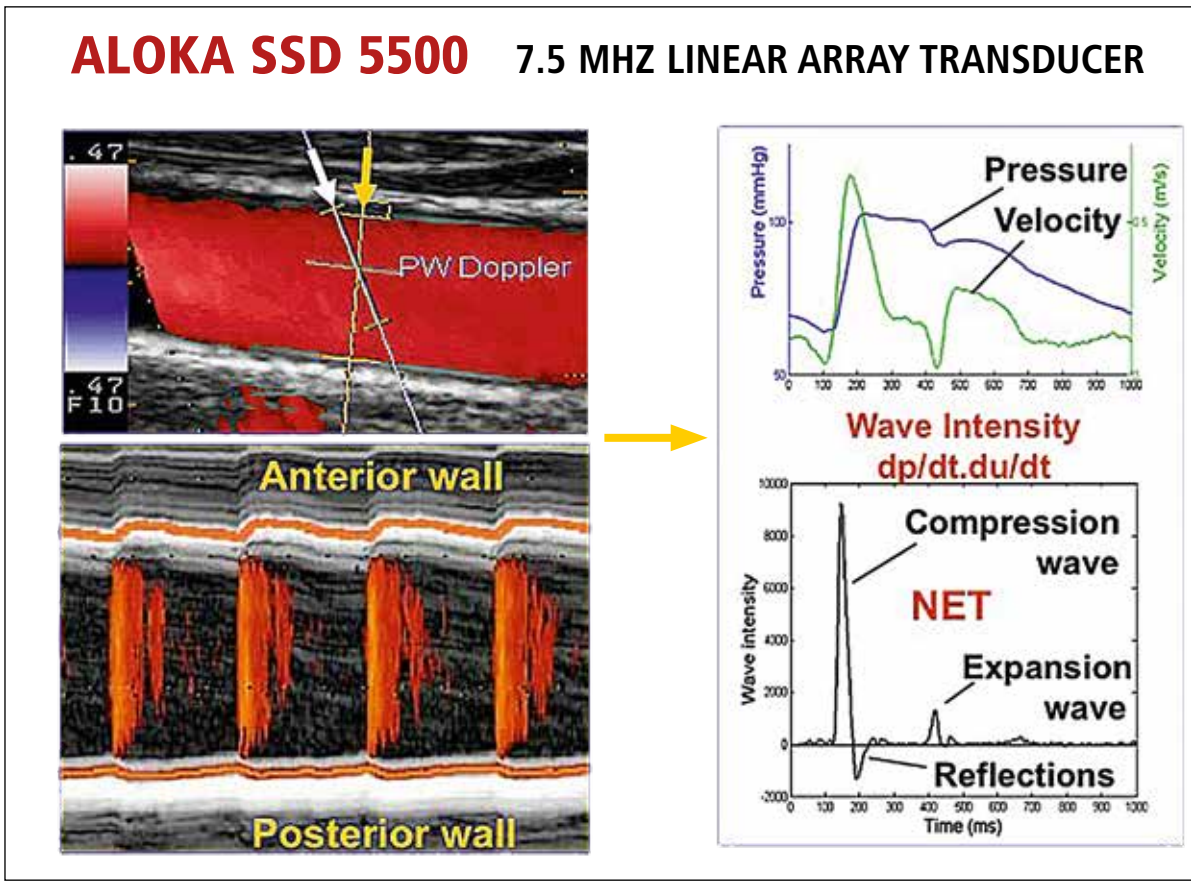
'The only thing that I regret a bit is that I did not contribute to developing the idea until it could be used in humans. I would have liked to have been part of that,' he said.

Dr Cribier's company was greeted with even greater resistance on the part of industry, with one executive famously calling TAVI 'the most stupid project ever heard of'. Nevertheless, the start-up persisted, finally finding an industrial partner to further develop the valve and its delivery system, leading to a successful first-in-man implantation in April 2002. The Andersen patent was acquired by Edwards Lifesciences and today is the foundation for the Sapien valve that won the CE mark in 2007 and approval from the American FDA in 2011.

This year a joint task force of interventional cardiologists and heart surgeons included the TAVI procedure in guidelines, recommending its use for patients like Andersen's father.

Tracking the source of heart failure

To treat heart problems, common sense says we should look to the heart. New European research based on an advanced ultrasound system suggests that stiffening of the arteries plays a key role



You can die from heart failure even though your heart seems to be pumping normally. You can take pills proven to reduce blood pressure, yet your cardiologist says you are still in danger of a stroke. With these critical conditions reaching epidemic proportions in an aging population, cardiologists are searching everywhere for answers to these mysteries.

Shifting their investigation away from the hard-working muscle at the heart of the problem, researchers worldwide in recent years have shown the complex coupling of the heart with stiff large arteries can shape the progress of heart disease.

Increased computing power has enhanced the ability of ultrasound systems to measure in a non-invasive way the a relationship between these arteries and a breakdown in the cardio-vascular performance.

On the leading edge of this investigation is the new eTRACKING system from Hitachi Aloka that for the first time can measure waves transmitted in the blood moving away from the heart in large arteries, and equally important, the speed and timing of the waves being reflected back by stiff arteries.

According to Prof. Alan Fraser of the Cardiff University School of Medicine, who led a collaborative investigation among 14 European centers with eTRACKING, cardiologists can now use these new tools to evaluate and follow the progress of a patient's condition.

"Expanding what we can measure to assess arterial function, there is a potential to tailor more precisely treatment for individual patients," he said, adding, "insights from studies using eTRACKING may provide evidence for using one drug over another that we haven't had previously."

The first applications of eTRACKING will likely be in testing which drugs are most effective in lowering blood pressure and preventing heart failure, while further collaborative studies will help to identify applications for routine clinical practice.

What is new with this system, he said, is an ability to look beyond local arterial stiffness to measure waves in the blood circulation being reflected back to the heart.

In healthy individuals, as the heart ejects blood, the aorta expands. Thanks to its elastic quality, the vessel recoils which ensures that intermittent emptying from the heart is converted into continuous flow into the peripheral arteries.

When the aorta and other main arteries stiffen, the gushing ejection is not absorbed by a stretching action, causing the speed of the waves in the blood to increase. Striking against more hard walls, and moving faster than normal, means that in the periphery there are stronger reflections of waves back to the heart. These backward waves can be two or three times faster than when the vessels were younger and more supple.

Pressure in an aging circulatory system increases. With waves coming back before the heart has finished emptying for one pulse, the heart must work harder on the next pulse.

The eTRACKING tools enable clinical researchers for the first time using a standard commercially available ultrasound system to measure this complex interplay, using wave intensity. Analysis in large arteries in different regions of the body is possible for artery stiffness, and for the velocity and amplitude of forwards travelling waves and their reflections.

These measurements in the carotid arteries were the focus for the E-tracking International Collaboration (ETIC) study coordinated by Prof. Fraser, which is now awaiting publication.

Over 2,000 patients were evaluated, a unusually high population for a study utlizing an new diagnostic imaging system. More surprising is that they were healthy people, individuals without any reported cardiovascular disease, between the ages of three years and 85 years.

ETIC is the result of an uncommon partnership between industry and the medical community. The study was funded with an unrestricted grant from Hitachi Aloka with the goal of establishing what is "normal" in the general population before focusing on patients with cardio-vascular disease. The study expands the cardiology community knowledge in what is relatively new territory.

"Many people are working in this field now," said Prof. Fraser. "Research is always a collaborative effort, so it would not be correct to claim that any one group has done something that no one else has done, or that it is independent of the work of others."

What is unusual is the approach taken by Hitachi Aloka in contributing to the investigation, he said. "The company has been very sensible in asking clinicians, the users of this system, to provide guidance to other clinicians, who will use the instrument, as to what the results mean," said Prof. Fraser.

More often, he said, manufacturers release new technologies and leave users to figure out what it means, whether it has any clinical relevance.

"Here physicists and clinicians worked hand-in-hand at a far earlier stage, during the development process, so that the hardware and the software have been developed in a way that we can use it," he said.

As the chair of last year's conference on medical devices for the European Society of Cardiology, and the lead author of the society's position paper on new technologies, Prof. Fraser said the ETIC study provides an example of how industry needs to take up its responsibility in the development of new diagnostic tools.

A Fellow of the Royal College of Physicians as well as the European Society of Cardiology, **Alan Fraser** is a Professor in Cardiology at the School of Medicine of Cardiff University in Wales. He has earned an international reputation as the head of the Echocardiography Research Group at the Wales Heart Research Institute where he has explored the pathophysiology of heart. He currently is a leading voice in discussions of European regulatory reform as it affects cardiovascular devices, having chaired an ESC Policy Conference and authored the society's policy statement.

Cardiac ergometry in an MRI

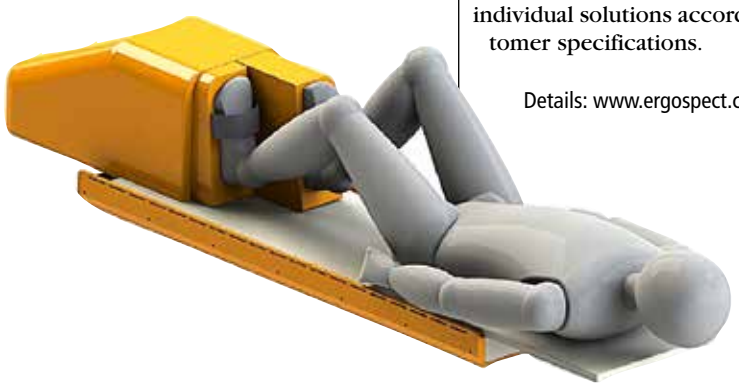
Ergospect develops ergometers for muscle exercises inside the magnetic resonance bore. The company has added two new MRI-compatible ergometers to existing devices for musculoskeletal examinations. The Diagnostic Pedal Cardio, for cardiac stress MRIs, enables examination of perfusion, motility and energy metabolism of the myocardium under stress.

Today, MRI magnetic resonance imaging of the heart during physical stress is carried out routinely. Due to the lack of suitable devices, drugs such as Dobutamin or Adenosin are usually used to stress the cardiovascular system. However, this does not reflect the physiological reality. The Diagnostic Pedal Cardio modules are suitable for MR and have been specially designed to stress the heart in an MRI bore.

Thus it is possible to investigate the performance and perfusion of the myocardium during a dynamic exercise via MRI or magnetic resonance spectroscopy (MRS), which provides an effective early diagnosis of risk patients and a more accurate diagnosis of a patient with coronary heart disease (CHD) and with myocardial infarction (MI).

All pedals are compatible with all MRI-systems (up to 7-Tesla) and consist of a basic platform to be combined with different modules. The firm will also develop and deliver individual solutions according to customer specifications.

Details: www.ergospect.com



Clinical trial

ECG analysis detects 40% more atrial fibrillation patients

***Stroke* publishes University Hospital Heidelberg study results**

More than 30 hospital stroke units in Germany, France and Austria are now successfully using SRAclinic* (SRA = Stroke Risk Analysis), a fully automated ECG analysis to detect atrial fibrillation, according to its manufacturer apoplex medical technologies GmbH, Pirmasens, Germany. Stroke, the American Heart Association journal, has published clinical trial results that 'proves a clear superiority of SRAclinic to the current standard procedures for the detection of paroxysmal atrial fibrillation,' the company reports.

Led by Professor Roland Veltkamp MD between March 2010 and January 2011, the prospective study involved about 500 patients at the stroke unit of University Hospital Heidelberg, and compared the two presently applied standard procedures in stroke units – 24-hour long-term ECG and patient monitoring with SRAclinic, to identify patients with previously unknown paroxysmal atrial fibrillation. Patients with ischemic stroke or TIA were included in the study.

During their stay at the stroke unit, in 41 from 496 patients paroxysmal atrial fibrillation was detected for the first time. 14 (34.1%) patients were found with 24 ECG recordings, 27 (65.9%) with the continuous bedside electrographic monitoring and 38 (92.7%) were identified with SRAclinic. Conclusion: SRAclinic can increase the detection rate for paroxysmal atrial fibrillation more than twofold compared to the widely used 24-hour long-term ECG recording. 'SRAclinic has clearly proven it´s superiority over the elaborate methods used in our stroke unit to detect atrial fibrillation', Prof. Veltkamp confirms. 'After the study results analysis at our stroke unit, we changed the routine diagnosis to detect paroxysmal atrial fibrillation completely to SRAclinic.' It is well on the way to become the standard procedure for the detection of paroxysmal atrial fibrillation in stroke units.

'In about 25% of all strokes in Germany the origin of the stroke cannot be identified. A substantial part of these is assumed to be caused by undetected paroxysmal atrial fibrillation, which increases the risk for secondary strokes with worse consequences for the patients,' says Albert Hirtz, Managing Director of apoplex medical technologies GmbH.

*Paper can be accessed on Stroke internet page after registration.
http://stroke.ahajournals.org/content/early/2012/08/07/STROKEAHA.112.654954.abstract?sid=53a0663e-7a28-4fb7-b841-cb9dab80d5e0

France: 61-year-old receives the first fully-biodegradable stent

A novel, entirely biodegradable device has been successfully implanted in a blocked artery patient needing a percutaneous coronary intervention

Report: Annik Chapoy

The successful implantation of a fully-biodgradable stent has been achieved in Toulouse. The surgery was the first in a clinical test called ARTDIVA (Art Remodeling Transient Dismantling Vascular angioplasty), which could lead to a revolution in coronary angioplasty. The implant used is the first truly biodegradable stent and it was developed by the French firm ART (Arterial Remodeling Technologies), founded a decade ago by cardiologist Professor Antoine Lafont and Professor Michel Vert, a leading specialist of bioresorbable polymers at CNRS-Montpellier (National Centre for Scientific Research).

ART's technology is based on intellectual property that originates from three outstanding institutions: the Cleveland Clinic (Cleveland, Ohio), the French National Centre for Scientific Research CNRS, and Necker University (Paris).

Avoiding anti-agregants

'Our stent is a completely new device, which begins to dismantle in vivo after three months, allowing the artery to recover its freedom of movement progressively, unrestricted by the presence of a permanent metallic stent. Arterial walls remodel naturally, adjusting their size for optimal blood flow. The stent gradually breaks up and will disappear completely after 18 months.' According to Professor Antoine Lafont use of this stent avoids prescribing anti-agregants for a long time.

Some thirty patients should receive such a polymer coronary stent over the next three months in five hospitals across France, and the first evaluation of these clinical tests could be available in six months for the potential complications and in one year for the evolution of the arteries, ART explains.

Since the 1990s, stents have been used by surgeons to unblock arteries during angioplasty. They are sorts of metal spring mechanisms, to which drug-eluting stents (DES), which contain medicine that is delivered in progressively, were recently added.

Research has been going on in a few countries to obtain bioresorbable stents in order to avoid the possible side-effects of traditional techniques, primarily chronic inflammation and to delay scarring, which can lead to increase thrombotic risk.

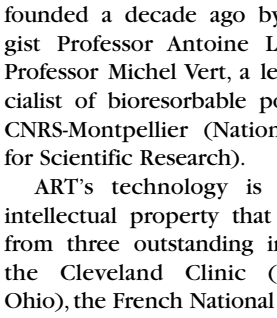
A bioresorbable polymer stent developed by US company Abbott had been clinically tested since 2009, with expected results by 2013. This particular stent is impregnated with a drug, rather than the one developed by ART.

Totally natural stents

'Our stents are designed to be both haemo-compatible and biocompatible, therein causing little or no inflammation while disappearing over time,' explains Machiel van der Leest, CEO of ART, previously co-founder and technology manager of Minvasys and, during his career, developer and successful introducer of 15 Class III medical devices, which require premarket approval and a scientific review to ensure safety and effectiveness.

To avoid any complication caused by a pharmaceutical product, 'Our stent is totally natural, and contains no active substance at all,' says Antoine Lafont MD PhD, former Chairman of the Interventional cardiology group within the European Society of Cardiology (ESC).

Since its foundation, ART has gathered €17 million from both public and private sources. The InnoBio fund, specialising in biotechnologies, has invested more than €6 million in the firm, considering that biodegrable stents represent the most promising breakthrough in interventional cardiology.



Antoine Lafont MD PhD, Professor of Medicine at the Necker medical school. University of Paris V and currently head of interventional cardiology at the European Hospital Georges Pompidou in Paris, is also Director of the INSERM unit U-849 (arterial repair).
He is the Past Chairman of the European Association of Percutaneous Cardiovascular Interventions of the European Society of Cardiology.
His research focuses on the mechanisms of restenosis and vascular healing.
He participated to the creation of the start-up ART (Arterial Remodeling Technologies), which is developing bioresorbable peripheral and coronary polymer stents.
Prof. Lafont is involved in experimental and clinical programmes for cell therapy in myocardial & vascular diseases, has been on a research fellowship at the Cleveland Clinic foundation, and was in active interaction with the departments of cardiology, cell biology, and biomedical engineering.

Top billing for cardiac MRI

Today, magnetic resonance imaging receives top billing in cardiology next to the co-star computed tomography while much hailed single-photon emission computed tomography (SPECT) plays but a minor role. *Professor Stefan Schönberg MD*, Director of the Institute for Clinical Radiology and Nuclear Medicine at the Medical School Mannheim, University of Heidelberg explains the new imaging star's rise – functional and perfusion analysis in a single examination offers a marker for clinical endpoints and thus increases the predictive value of diagnostic imaging

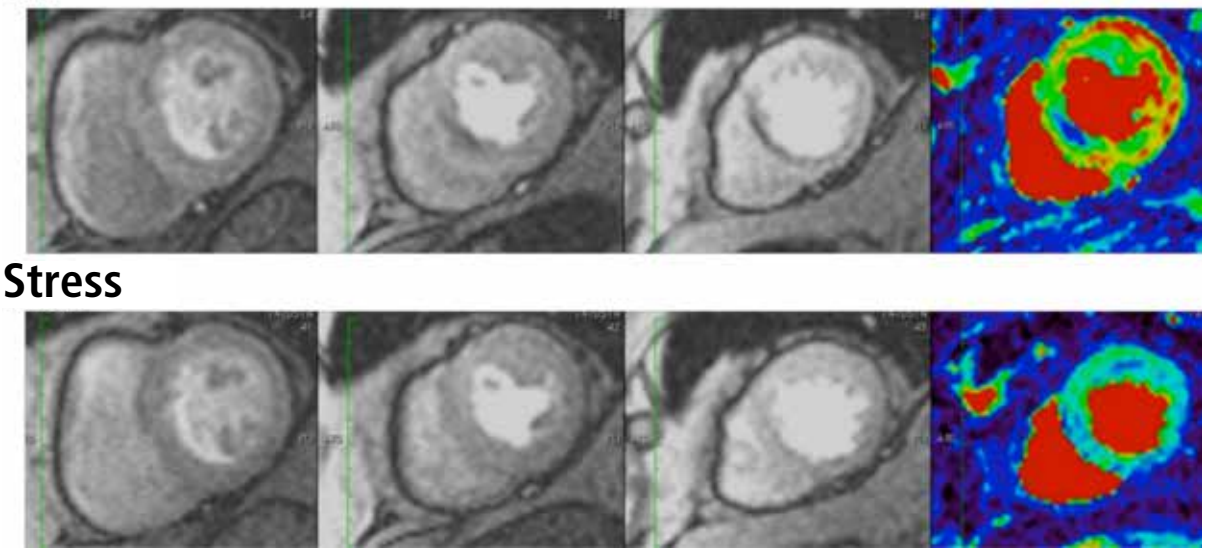


Fig. 1: Adenosine-induced MR stress and rest perfusion with 3-T in a patient with VA stenosis in the ramus interventricularis anterior in coronary CTA: Detection of a haemodyamically relevant stenosis with stress-induced perfusion deficit (septal and inferior-septal mid-ventricular to apical)

'While ECG triggered computed tomography allows us to completely exclude a coronary artery stenosis', Professor Schönberg explains, 'despite all technological progress, we can determine the degree of a stenosis only with 70 to 80 percent precision'. Indeed it is the radiologist's job to determine the degree of stenosis as precisely as possible and adenosine stress MRI, Prof. Schönberg adds, can provide important information on the haemodynamic relevance of a stenosis prior to elective revascularisation (Fig. 1).

Today, MRI, which has been improving technically over the last decade, 'offers better results than SPECT, the competing functional modality that many cardiologists nevertheless still consider the gold standard'. Research results corroborate the professor's thesis.

More sensitive than SPECT

For example, lead investigator Juerg Schwitter, associate professor at the University Hospital Lausanne, recently published the results of the MR-IMPACT trial, which analysed 515 patients in 33 centres who underwent SPECT as well as MRI to detect ischemic coronary artery diseases (CAD). The prevalence of CAD in the sample was 49 percent. With a score of 0.67 MRI had a higher sensitivity than SPECT (0.59) while in terms of specificity SPECT (0.72) yielded better results than MRI (0.61). Superior sensitivity and lower specificity confirm MRI as safe alternative to SPECT to detect perfusion deficits in coronary arteries [Source: Eur Heart J (2012), doi: 10.1093/eurheartj/ehs022].

More than an ischemia detector

With the help of suitable MRI sequences, MR contrast agent enhancement in a cardiac structure can be visualised after 10 to 15 minutes. It has been known for some time that this so-called delayed contrast enhancement (DCE) can show myocardial infarction scars no matter how old they are. Moreover, the analysis of the DCE distribution pattern in the heart provides vital information to differentiate CAD from other forms of cardiomyopathy.

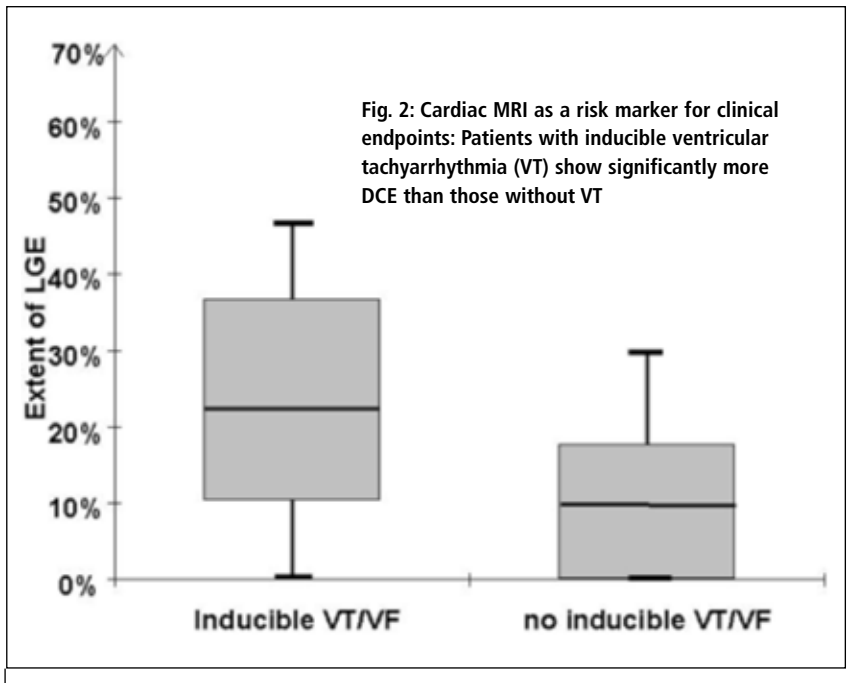


Fig. 2: Cardiac MRI as a risk marker for clinical endpoints: Patients with inducible ventricular tachyarrhythmia (VT) show significantly more DCE than those without VT

Prof. Schönberg is even going one step further: 'In cooperation with the cardiologist Professor Martin Borggrefe, a specialist in structural heart diseases, in Mannheim we were able to show that in hypertrophic cardiomyopathies (HCM) the extent of DCE, and thus the anomalies of the myocardial structures, correlates with risk factors of sudden cardiac death and with the likelihood of inducible ventricular tachyarrhythmia under programmed stimulation.' [Source: J Cardiovasc Magn Reson 2010;12:30] (Fig. 2). Furthermore, Professor Papavassiliu et al found that in 87 patients with HCM with (n=37.42%) and without atrial fibrillation (AF) HCM patients with AF displayed significantly more DCE than those without AF [Source: J Cardiovasc Magn Reson 2009;11:34]. While this method is not as reliable in predicting AF than measuring the left atrium, Prof. Schönberg points out: 'in imaging we have to learn to not only use phenomenology for differential diagnoses but also to look at predictive values with regard to clinical endpoints.' Severe ventricular tachyarrhythmia, for example, is such a parameter, which means that MRI is increasingly becoming a marker for patient outcome.

High evidence

'Coronary stenoses which are not relevant do not require stenting – a simple guideline which also saves costs,' Prof. Schönberg says and emphasises it is 'crucial for us radiologists to understand these clinical endpoints. A young athlete who has severe arrhythmia for the first time requires a cardiac MRI scan because it tells us more about the risk of life-threatening tachyarrhythmia. This is the kind of endpoint we have to use in order to convince the payers.'

What he is concerned about is the exclusion of severe events, of the evidence implied in the radiological finding: 'In many cases cardiac MRI helps us to recognise and delineate the proarrhythmogenic substrate, which allows us to risk stratify each patient and initiate a suitable therapy. When I can safely say that a patient shows a certain DCE, which indicates a significantly increased risk of severe arrhythmia and thus requires a defibrillator for prevention purposes we clearly prevent mortality, which is quite legitimately evidence grade I.' A single important precondition: radiologists and cardiologist must work as well together as they are doing at Mannheim University Hospital!

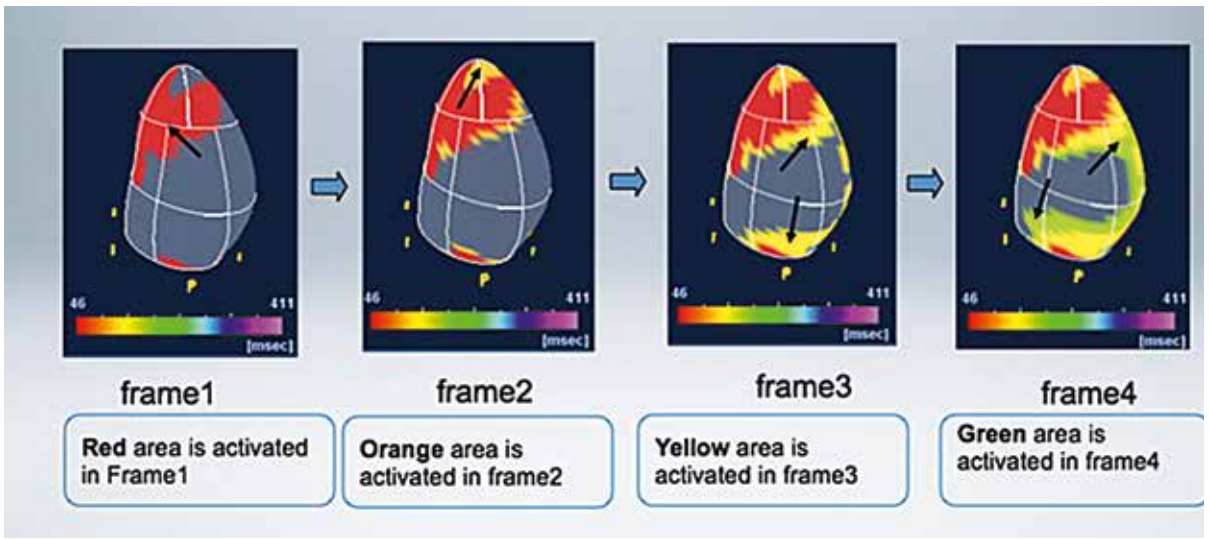
The future?

Preliminary studies with 7-Tesla systems indicate that MRI might even become more precise and might be able to show even more minute structural changes. Sodium imaging, for example, is becoming a routine procedure with 3-T scanners. Developed in the 1980s, diffusion tensor imaging provides increasingly better insights into the deeper structures of the heart. Prof. Schönberg is convinced: 'We do need high standardisation with good precision and robustness before new methods can be integrated into clinical routine in a meaningful way and can be widely used. We have now reached that point. Today 3-T can generate high-resolution perfusion maps' – a fact that secures top billing.

Professor Stefan Schönberg MD began his career in Heidelberg, where he studied medicine and worked as Assistant Physician at the German Cancer Research Centre (DKFZ). In 2001, after his transfer to the Institute for Clinical Radiology, at Ludwig-Maximilians University in Munich, he became Senior Consultant, managing the MRI Division. The professor has directed the Institute of Radiology and Nuclear Medicine at the university hospital of Mannheim since 2007. In 2006, he received the Herrmann-Holthusen-Ring award from the German Radiology Society (DRG) for his scientific research published in national and international publications.

3-D ultrasound reveals heart function in ways cardiologists have never seen before

Hearts in motion



Ultrasound is enthusiastically embraced by cardiologists in guidelines as essential for evaluating a patient's heart. Now visualisation of 3-D wall motion takes ultrasound to a higher level, opening a new understanding of heart mechanics

Captured in a single heartbeat with high-end CT, images of the human heart are breathtaking and suitable for framing. Which is actually a problem. For clinicians these frozen images have a limited value for diagnosis, for helping to understand how a patient should be treated. On the other hand, the truly useful images of a beating heart created by ultrasound have been impossible to understand, let alone interpret, except for a highly expert elite. Practicing cardiologist are left scratching their heads after examining scattered dots in black and white, or strange colour patterns that resemble modern art abstracts.

Thanks to the same advances in computer processing power and software that allow CT to show snapshots, ultrasound signals today can also be filtered and displayed as video-like images that cardiologists instantly recognise. In the same way that you might wipe the fog off a window on a rainy day to suddenly see the world outside, cardiologists for the first time are looking into the workings of the heart.

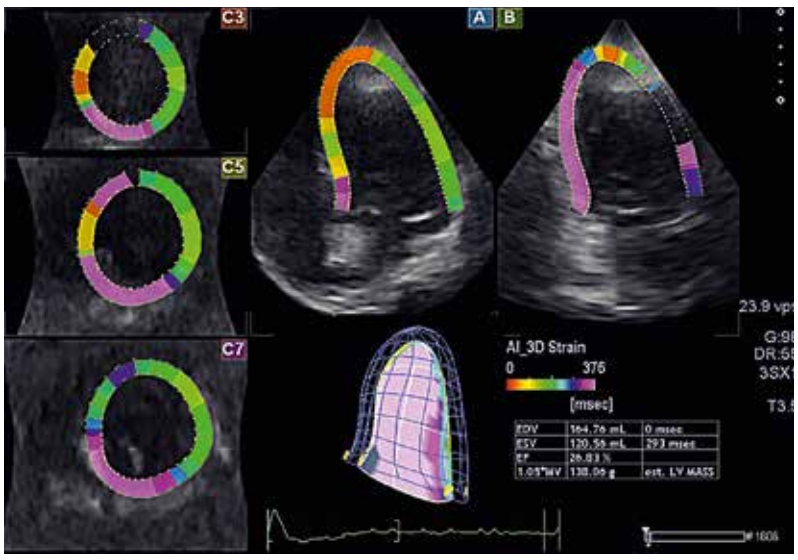
Hans-Joachim Nesser MD, a professor affiliated with three Austrian university teaching hospitals, is one of the elite experts in echocardiography who can actually interpret the arcane images of two-dimensional speckle tracking and the wavy colour blotches of Doppler ultrasound. He is also a pioneer in the emerging visualisations of 3-D ultrasound that are rapidly revolutionising the way cardiologists can diagnose a patient's condition while at the same time challenging the cur-

continued on page 18

Hans-Joachim Nesser MD, Vice Medical Director of the Teaching Hospital Elisabethinen in Linz, Austria, lives on the leading edge of developing technologies for ultrasound. A pioneer in speckle tracking and tissue Doppler echocardiography, he introduced 3-D motion tracking to the world in the 1990s at an Advances in CardioVascular Ultrasound and Intervention conference he had organised. Dr Nesser is the co-editor of the Atlas of Real-Time-3-D Transoesophageal Echocardiography and has written or contributed to 363 scientific abstracts, books and supplements. A professor affiliated with universities in Graz, Vienna and Innsbruck, he also taught as an Adjunct Associate Professor of Medicine at Tuft University Medical School in Boston.

Hearts in Motion

continued from page 17



rent understanding of how the heart works. 'The truth is that physicians like things that are easy to understand and they tend to shy away from physiology,' he said, adding that practicing cardiologists are busy working with patients and want to know how to treat that patient. The new generation cardiovascular ultrasound, Prof. Nesser said, makes diagnosis understandable immediately: 'For the first time we can display the motions of the heart in three dimensions, in a way that is immediately understood, not just the volume but the longitudinal, circumferential or radial strain, the rotations, twists and torsion.' One eye-catching feature of this new visualisation is the 'dancing bag', a dynamic 3-D representation of the left ventricle. 'On the surface of the ventricle you can now see the changes, or abnormalities of strain,' he explained. 'This instantly shows colour changes to identify areas where there is a problem, an area of infarction where there is reduced strain.'

Dr Nesser's current application of the new technology is for studies of myocardial ischemia, a close examination of where heart muscle has been damaged, reducing its ability to pump efficiently. Recently Toshiba Medical Systems introduced a break-through technique called Activation Imaging, which builds on the potential of 3-D speckle tracking to study specific segments with delayed contraction or movement of the wall. A direct application of the technology is for cardiac resynchronisation therapy (CRT) enabling cardiologists to define quickly and easily changes of delayed muscle activation or even to analyse, frame by frame, the extent of dyssynchrony.

Dr Nesser is also applying the technology for refined research of ischemia, identifying sub-endocardial infarction, areas where necrosis is less than 50% of the muscle tissue thickness, potentially providing an early indication for a vulnerability to heart attacks. 'Activation Imaging is providing cardiologists with a new parameter for assessing the patient condition at an earlier stage with a potential to influence therapy decisions,' he said

The future of 3-D speckle tracking echocardiography appears bright and its potential is clear, he added. The challenge now is to validate findings, because a gold standard for strain imaging does not exist. 'We are collecting a broad range of information making it difficult to compare those findings with other techniques. It puts echocardiography out ahead of other imaging modalities,' said Prof. Nesser. 'There is highly advanced software that can demonstrate strain using MRI, but this technique is also in a pioneering phase,' he added, and the output remains in two dimensions. The ultimate advantage for ultrasound in cardiology, he believes, is that it is immediately available from the first office consultation with a patient to a post-procedure follow up at the hospital bedside.

To win support for motion tracking in the cardiology community, he thinks an enthusiasm as strong as the endorsement in guidelines for ultrasound in other applications will require multicentre studies of the new technology.

'Ultrasound is increasingly giving cardiologists the ability to only intervene in patients where we have a very clear picture of what the problem is,' he said. 'Taken together with the symptoms of the patients and the clinical examination, a heart team can make a decision on treatment strategy. This is the future for cardiac patients.' Enthusiasm, he added, 'will increase with evidence.'

Diagnosing from a distance

An echocardiography system that conveniently slips into a coat pocket, this kind of miniature device is now commercially available. Portable ultrasound has been around for about a decade, but until recently the machines were about the size of a laptop rather than that of a smart-phone

Report: René Lindner

Sirsa, India – 250 km northeast of Delhi. Twelve million men, women and children have gathered for the Dera Sacha Sauda meditation camp. However, meditation is not the only technique that participants employ to care for themselves – more than 1,000 people also preregistered to undergo cardiovascular screening using a pocket echocardiography device. While the patients in this remote rural Indian district await examination by a team of American radiographers and cardiologists, 75 physician volunteers in the USA, Canada, Bulgaria, Georgia, and Saudi Arabia stand ready in their respective time zones to read the incoming images.

Organised by Dr Partho Sengupta from Mount Sinai School of Medicine, New York, and physicians at Medanta Medicity, in March 2012 the examinations in Sirsa were part of one of the largest trials carried out with miniature ultrasound – and highlights the technology's promise for application in the developing world.

No substitute for full echo

As the study carried out in India shows, one of the most promising areas of application of the miniature echocardiography machines are remote places, which previously have had no access to this technology. 'The image quality rendered by the device is average and it lacks spectral Doppler imaging capability,' explains Jens-Uwe Voigt, Professor of Cardiology at the University of Leuven. Voigt co-authored a study comparing the pocket echo to the gold standard, i.e. the full-featured system. Compared with the gold-standard full-featured system, the pocket device underestimated, for example, aortic-stenosis severity in half of the patients. Nevertheless, Voigt and his co-author Dr Christian Prinz concluded it was 'possible to perform adequate imaging and quantitative assessment of heart function in every case of our study population'. Distinguishing between the diverse ways in which the new technology can be used is important. Just relying on the image visible on the pocket-sized device itself can serve a number of important purposes, even though it cannot replace a complete echo exam. 'A pocket-sized echo device allows initial assessment of ventricular and valvular function, pericardial and pleural effusion or extravascular lung water,' explains Dr Ivan Stankovic, who spoke on this topic at the ESC conference in Munich. All these features may be useful in different clinical scenarios, from emergency settings, for example, to rule out cardiac tamponade. Another application is the standard physical examination, enabling a physician to rule out depressed left ventricular ejection fraction in a patient with exertional shortness of breath, for instance. In this way, the devices may be useful even in well-equipped hospitals since they can solve certain clinical questions on the spot, Prof. Voigt adds.

Sending images from Honduras

'When full echocardiography is not available, images obtained with pocket-sized devices can be extremely valuable,' says Dr Stankovic. He emphasises the fact that echocardiography is a highly operator dependent technique and the level of knowledge and training of the echocardiographer plays a major role in establishing an accurate diagnosis. Hence, the combination of obtaining images with pocket-sized devices and expert interpretation, as in Sirsa, has great potential for diagnosing patients who have never had access to echocardiography before.

Dr Stankovic points to a study carried by Choi et al. The results were published under the title 'Interpretation of Remotely Downloaded Pocket-Size Cardiac Ultrasound Images on a Web-Enabled Smartphone: Validation against Workstation Evaluation' in the Journal of the American Society of Echocardiography in December 2011. The study was to test the hypothesis that remote interpretation on a smartphone with dedicated medical imaging software can be as accurate as on a workstation.'

Eighty-nine patients in a remote Honduran village underwent echocardiography by a non-expert using a pocket-size ultrasound device. Images were sent for verification of point-of-care diagnosis to two expert echo cardiographers in the USA reading on a workstation. The author of the study concluded that they 'found that expert interpretation of echocardiograms on a smartphone has minimal loss of accuracy over traditional workstation methods'. There are, however, several important limitations to take into account. Transmission of data over the public internet raises questions about data privacy, if there is a possibility to connect to the World Wide Web at all. This might often not be the case in remote rural settings. The study carried out in Honduras came with other important limitations, too. The authors point out that 'the indications for echocardiographic evaluation were heavily weighted toward arrhythmia, cardiomyopathy and syncope, indicative of the nature of cardiovascular disease in rural Honduras, where Chagas disease is endemic.'

In Europe and the US, many pocket size devices have already found their way into 'many white coat pockets', Dr Stankovic says. Pocket-sized echo devices are used by general practitioners, internal and emergency medicine specialists, anaesthesiologists, and other medical professionals. 'There is a risk that widespread use of pocket-sized devices by non-experts lead to a rising number of inaccurate diagnoses or lull patients into a false sense of security,' he points out. While the small devices are useful to exclude major cardiac pathology mentioned above, it is not often the case that patients are referred with a clear diagnostic question. More often than not, patients come in with nonspecific complaints, such as light-headedness or shortness of breath, for which there are a large number of possible causes and then it needs the expertise of a cardiologist to find an explanation.

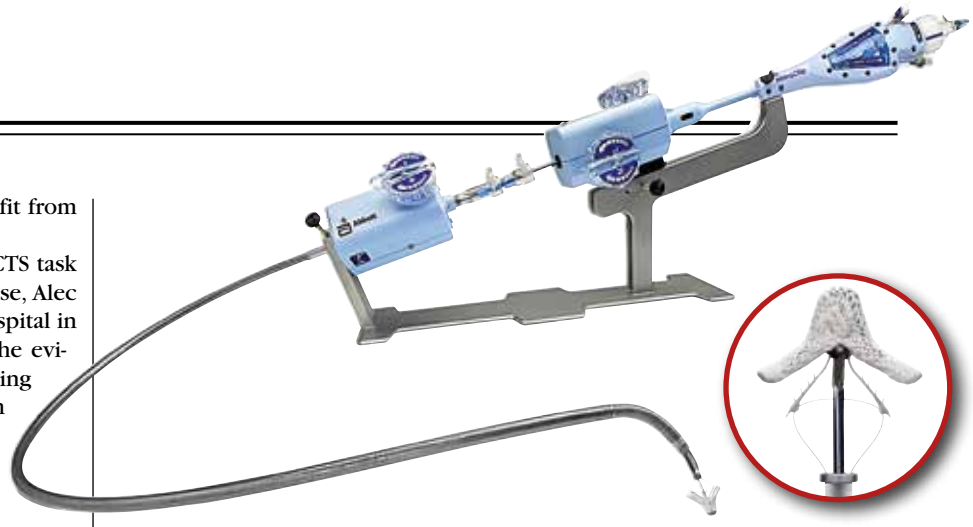
While accredited echo cardiographers don't need additional training to use pocket imaging devices, other medical professional should undergo at least basic echocardiographic training. The European Association of Echocardiography (EAE) is developing a certified training to fill exactly this gap. Professor Voigt leads the committee in charge of developing the training. 'The training consists of a combination of online and practical modules,' he explains. Physicians interested in using a pocket-sized device will first acquire the basic knowledge via the online module. After they have successfully demonstrated their knowledge in a multiple choice test, they must spend a number of days in an accredited echocardiography laboratory, shadowing an expert and eventually delivering their own diagnosis for a pre-defined number of cases.

Jens-Uwe Voigt studied medicine in Germany, the UK and USA and is professor of cardiology at the department of Cardiovascular Diseases of the university hospital Leuven, Belgium. He heads the echocardiographic laboratory and a science group for non-invasive diagnostics, which focuses on image based methods of metering the myocardfunction. He also initiated and runs the reference laboratory for different European multicenter studies. The professor is a board member and head of the further education commission of the European Association of Cardiovascular Imaging, fellow of ESC and a member of the German and Belgian Societies for Cardiology, and has edited several echocardiographic textbooks and international guidelines.

Ivan Stankovic graduated from the Faculty of Medicine, University of Belgrade in 2005 and, following postgraduate studies in Advanced Medical Imaging, from the Catholic University Leuven in 2012. He then became an internal medicine resident at the Department of Cardiology, Clinical Hospital Centre Zemun, Belgrade, Serbia, and is now a research fellow at the Medical Imaging Research Centre, University Hospital Gasthuisberg, Leuven, Belgium. In 2011, Dr Stankovic was the Research Grant Winner of EAE. His special interests lie in advanced echocardiographic techniques, emergency and stress echocardiography.

Mending Hearts

A new device promises minimally invasive repair of a failing mitral valve for patients who cannot withstand surgery



Report: John Brosky

There is nothing magic in mitral valve repair. Yet, for a select group of patients suffering from mitral regurgitation, cardiologists agree there is potential for relief and a higher quality of life with a new procedure.

Patients at a high risk for open-heart surgery who have heard of the success achieved in replacing aortic valves using a minimally invasive technique might think the mitral valve could be fixed in the same way. Unfortunately, this is not the case. A device to replace the mitral valve is still off in the future due to anatomical challenges. What is possible today is a repair of the valve using the MitraClip from Abbott Laboratories to treat both functional and degenerative mitral regurgitation.

Based on experience with 6,000 patients at 150 heart centres worldwide, cardiologists have found the device, which mimics an edge-to-edge repair technique perfected by surgeons, provides a nearly equivalent outcome.

When updating guidelines in August 2012, a joint task force for the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) issued a Level IIb recommendation MitraClip for severe symptomatic patients suffering primary or secondary mitral regurgitation. The recommendation is comparable to the level of confidence given to surgery.

In its 2012 Heart Failure guidelines the ESC also considers the MitraClip to be a suitable option on functional mitral regurgitation for patients judged inoperable or at unacceptable high risk for surgery.

Further evidence for the success of the procedure was provided at the ESC 2012 congress by Abbott in the ACCESS-EUROPE real world registry that followed 487 patients, the largest group of patients evaluated to date. A multicentre study of the MitraClip system, the study showed a high rate of procedural success and reported mortality at 30 days was 3.4%, which compares quite favourably with transcatheter aortic valve procedures.

After one year 82% of the patients were still alive

The procedure is performed under general anaesthesia without the use of a heart-lung machine, and post-procedure recovery is typically one to three days.

As for effectiveness, co-principal investigator Wolfgang Schillinger MD, from the Göttingen University Medical Centre in Germany, reported that at one year 79% of patients were free from mitral regurgitation above Grade 2, where all patients were rated at Grade 3 and higher before the procedure. In a six-minute walk, these patients improved an average of 60 metres, a small but significant victory among this elderly and ill group.

Improvements in quality of life were shown to be a median improvement of 14 points between baseline and one-year scores on the Minnesota Living with Heart Failure Questionnaire. Professor Schillinger concluded that given the 'abundant co-morbidities of these patients,' the MitraClip presents a viable therapy option fulfilling an unmet clinical need. 'Where the benefits of surgery do not outweigh the surgical risks, the MitraClip treatment is an important alternative for patients with mitral regurgitation,' he concluded.

In a follow up discussion, Simon Ray MD, from the Wythenshawe Hospital (Manchester, UK) agreed that ACCESS-EUROPE 'demonstrates that, in expert hands, the MitraClip is feasible and safe with acceptable risk for a complex patients.' Key to further investigations will be better quantification of valves, and thereby better patient selection the better to assure that patients will benefit from the procedure, he said.

A co-chair for the ESC/EACTS task force on valvular heart disease, Alec Vahanian, from the Bichat Hospital in Paris, praised the quality of the evidence in ACCESS-EUROPE noting that edge-to-edge repair with the MitraClip is appropriate for a select group of patients and that it requires a high level of experience and skill.

'The study shows a treatment exists for these patients, and that it is feasible in the right hands,' he said, adding, 'the alternative is not to treat the patient, or to experiment with other techniques that are perhaps more challenging.' Beyond repairing the mitral valve a recent study suggests that improved valve performance may help mend the heart.

Salvatore Scandura MD, reported in a recent issue of the Journal of the American Society of Echocardiography that at six months after implantation 77.3% of MitraClip patients showed reverse remodelling, in other words, a positive reshaping of the left ventricle with significant improvement in ventricle size and function.

Dynamic Nuclear Polarisation

UK researchers are working on a new MRI technique

UK researchers are working on a new MRI technique called hyperpolarised MRI – or Dynamic Nuclear Polarisation (DNP) – that can utilise more of the available nuclei than traditional MRI, helping to overcome some of its limitations by increasing sensitivity 10,000-fold or more. DNP is part of a longer-term aim to improve cancer mortality with the help of novel cancer imaging tools.

Report: Mark Nicholls

Dr Ferdia Gallagher, Cancer Research UK Clinician Scientist Fellow at CRUK Cambridge Research Institute & the University of Cambridge, said that MRI has the power to distinguish different molecules non-invasively within tumours. 'The concentration of these can report on how metabolically active the cancer is and its rate of growth – both of which are important for predicting survival and for determining appropriate cancer therapy,' said Dr Gallagher. 'However, the great weakness of MRI is its lack of sensitivity: a typical MRI image utilises only a few nuclei in every million to produce the image that we are familiar with in radiology.' His work on DNP, in collaboration with Professor Kevin Brindle of the CRUK Cambridge Research Institute, is focused on overcoming this problem and increasing sensitivity by considerable magnitude. The end result, he added, is a technique that can probe carbon metabolism non-invasively using MRI in patients; naturally occurring molecules can be labelled with a non-radioactive form of carbon, hyperpolarised using DNP, and then injected into an animal or patient.

'The spatial distribution of the injected molecule can be imaged as well as the molecule(s) formed when the substrate is metabolised,' he said. 'This approach is similar to the use of a radiolabelled tracer in PET imaging but, unlike PET, the metabolites formed can be differentiated from the injected substrate using MRI, albeit with a lower sensitivity than with PET.' The lead molecule is called pyruvate, a breakdown product of glucose, and both it and the lactate formed from it in a tumour can be imaged following intravenous administration. The first clinical trial involving this technique has taken place in the USA with prostate cancer patients and the UK team will be undertaking its first clinical trials in Cambridge shortly.

Dr Gallagher: 'There are many unmet needs in clinical oncology where imaging is likely to play a role in helping patients of the future. For example, MRI can be used to give an early marker of successful response to treatment: patients who fail to respond to a drug therapy could be detected sooner using molecular imaging techniques, and then the patient could be quickly commenced

Complementary m diagnostics

Ultra-synthesis deciphers bits and bytes of the breast

Much, if not even everything, may have been said already about the multimodal approach in breast diagnostics. However, Professor Rüdiger Schulz-Wendtland at the Institute of Radiology, University Hospital Erlangen, says there is still surprising news from this field – innovations in multimodal breast diagnostics, for example. Asked to explain, he said: 'A future-oriented multimodal diagnosis visualises a joint conclusion achieved based on various examination methods. This can be successfully achieved in the form of a hybrid, where two modalities are combined. In practice, this may be the transfer of MRI images to an ultrasound scanner to reconstruct the MRI information with the help of ultrasound. Another option is to amalgamate both methods, known as fusion. This fusion of both procedures has not yet been quite successful, but this is precisely what we are working on, so far with promising results. With Siemens, the Fraunhofer Institute Erlangen and the Fraunhofer MEVIS in Bremen, we've succeeded in developing a prototype that combines tomosynthesis and ultrasound in one examination.'

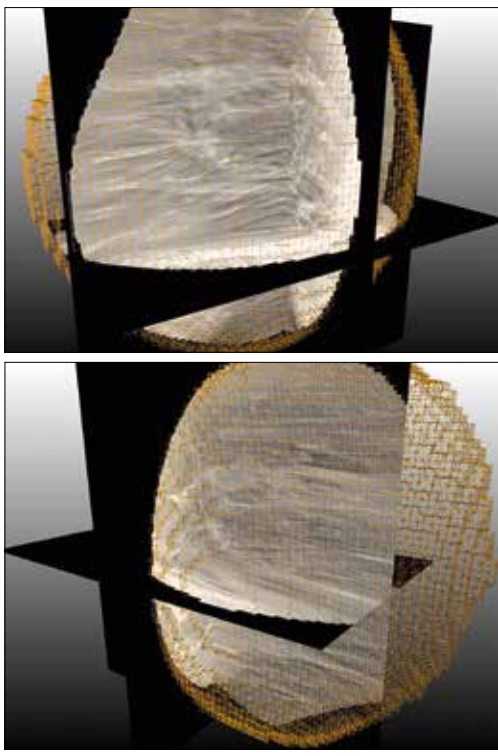
Is tomosynthesis carried out first, followed by an ultrasound scan?

'Yes, but done in one examination procedure and therefore with the same compression. The technical prerequisites are 3-D mammography, i.e. tomosynthesis, and volume ultrasound. In order to carry this out directly after mammography, a gel pad is placed in the compression window and, just after the tomosynthesis scan, the flat volume scanner moves over the breast. This procedure only extends the examination time by about four to six seconds. When images from these two procedures are combined this delivers a fused volume image – and this is our objective. As said, we are currently still working with a prototype, but this example perfectly illustrates which way breast diagnostics is going, i.e. toward a combination of modalities to generate real 3-D images.'

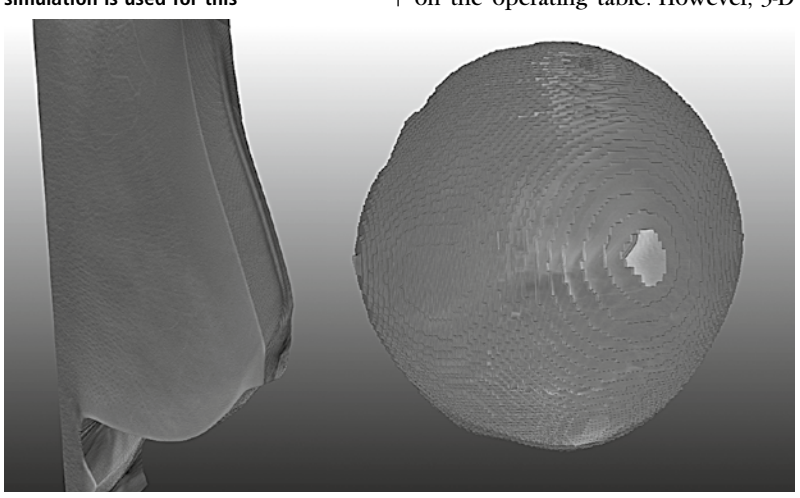
What diagnostic benefit does such fused imaging present?

'For one, it means that the ultrasound data becomes reproducible. Previously this procedure was maligned as having a high level of subjective validity. However, it is much more important that the fused volume images allow us to produce more precise anatomical references. We achieve realistic images of the breast and can make this information available to the surgeon during an operation.

'Nowadays, diagnosticians have a lot of technology at their disposal to help generate their diagnoses, which cannot actually be presented to the surgeon in the right way. Up to now, we've been able to supply images that require a high level of imagination to transfer the information to the patient on the operating table. However, 3-D volume images, that can be rotated and zoomed, facilitate the imaging of the tumour according to the patient's position on the operating table.'



Imaging of orthogonal layers of a non-deformed breast. The finite element grid used for this simulation is shown in orange



Decompression of a tomosynthesis data set to show image information in a non-compressed breast. A finite element simulation is used for this

The image is of a compressed breast, but the surgeon is working with a flat breast. How can they be comparable?

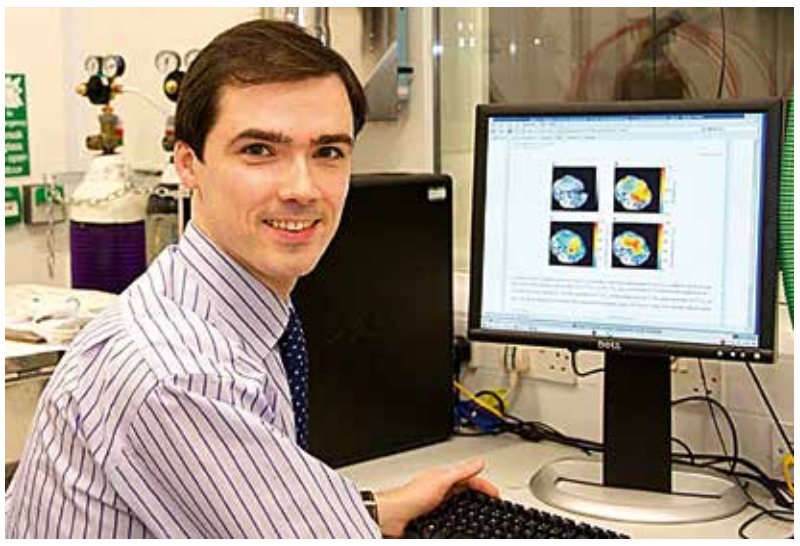
'The key word is decompression. The Fraunhofer MEVIS in Bremen is doing a lot of work with this. Numerous sensors record data during the examination, which are then measured and processed in a way that also makes the image of a non-compressed breast available. Tomosynthesis and ultrasound do not recognise the breast as such. These procedures collect data that are used to make up an image – bits and bytes, which are brought together by algorithms. We have to prepare this dataset in such a way that we can make it available to the surgeon as a real benefit. 'To what extent this is already possible these days will be shown in a small experiment to be carried out at the 17th International Training Course in Breast Diagnostics and Therapy next spring. A patient will have a tumour removed in a live operation, which will then be pathologically prepared and compared with a model of the tumour. Fraunhofer MEVIS will create this model based on a data packet consisting of mammo-

on a more effective therapy. By probing specific and fundamental biological properties of tumours (such as how acidic the cancer is, or the surface expression of specific proteins), we may be able to stage cancers more easily and predict patient outcome more accurately in the future. The long term aim of molecular imaging in oncology is to improve cancer mortality with the help of novel oncological imaging tools.'

What continues to motivate Dr Gallagher and collaborators is that, while radiology has made great advances over the last 40 years in improving morphological imaging, the limits of anatomical resolution that can be achieved with conventional imaging methods such as CT and MRI has largely been reached. 'We are therefore increasingly turning towards functional and molecular imaging techniques to provide new information about our cancer patients,' he said. 'The expectation is that these methods will be more sensitive and specific than morphological information alone. For example, hyperpolarised MRI could help us to reveal early changes in tumour metabolism following treatment, as well as predict the best form of treatment for patients.'

For patients – as medicine becomes more personalised and tailored to the individual - molecular imaging will play an increasingly important role in this by revealing some of a tumour's molecular signature. 'Functional and molecular imaging could also be used to detect tumours earlier,' he added, 'which is likely to have an impact on patient survival.'

Dr Ferdia Gallagher is CRUK Clinician Scientist Fellow, CRUK Cambridge Research Institute & University of Cambridge, and Honorary Consultant Radiologist at Addenbrooke's Hospital. He studied medicine as an undergraduate at the University of Cambridge before completing clinical studies at the University of Oxford and training as a radiologist at Addenbrooke's Hospital. His main area of interest is in developing molecular imaging techniques for oncological radiology and how these can be translated for humans. The focus of this work is to develop new molecular biomarkers to detect cancer, as well as methods to assess the early response of tumours to chemotherapy.



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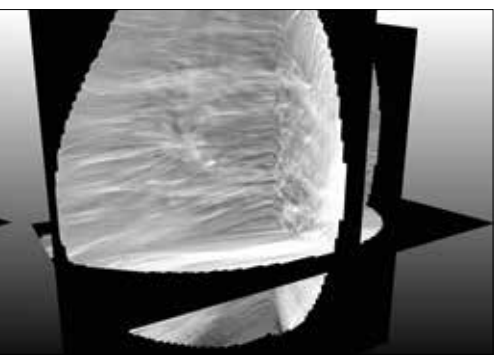
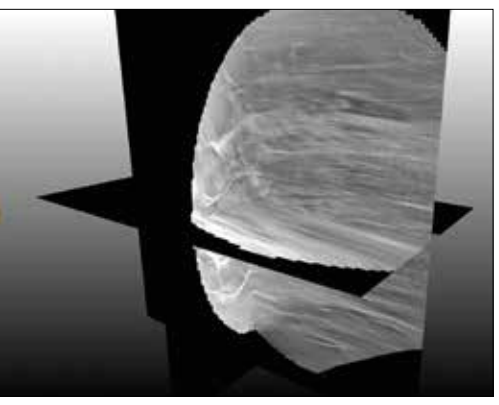


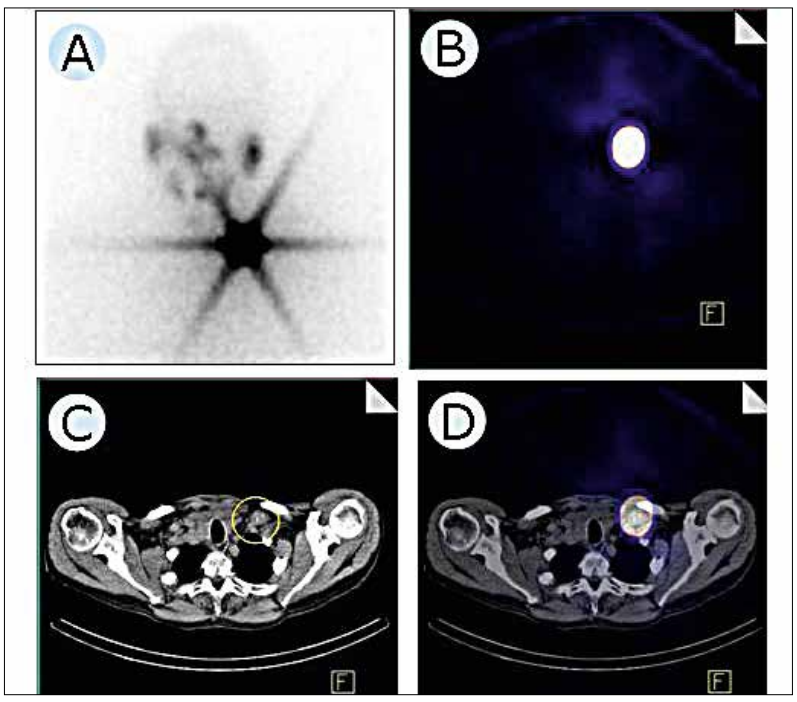


graphy, tomosynthesis, volume ultrasound and MRI images, which are used to calculate the size and diameter of the tumour. This will be very exciting and heralds the future of multimodal breast diagnostics.

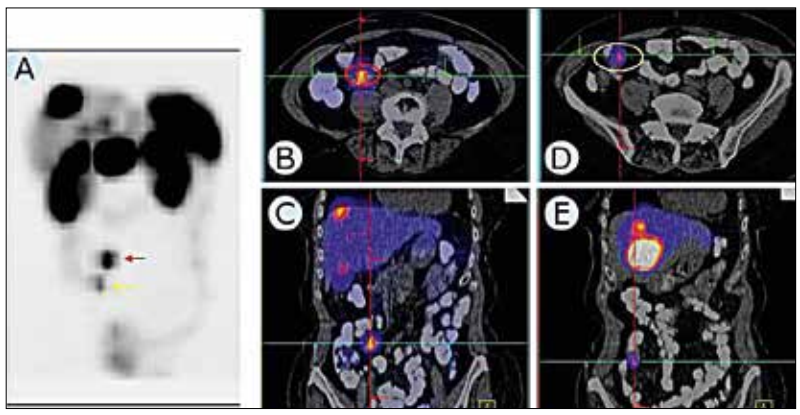
Professor Rüdiger Schulz-Wendtland is a consultant at the Institute of Diagnostic Radiology at the University Hospital Erlangen. The radiology and radiotherapy specialist has been Secretary of the German Society of Senology since 1999 and a member of numerous Assessment and Advisory Boards for breast diagnostics. A working group under his management is considered the first diagnostic unit in Germany that succeeded in introducing digital mammography to clinical routine. Further studies in which he is involved are investigating interventional procedures for breast diagnostics, particularly the experimental new development of minimally invasive procedures.

Single photon emission computed tomography

New tracers and hybrid systems enhance applications for SPECT



Scintigraphic image of a patient with thyroid cancer after radioiodine treatment. In the planar images (A) one can see a focal concentration of iodine left vertically and in the upper mediastinum respectively. A SPECT (B) alone does not allow better classification of the focal lesion. Through the complementary CT (C) and the fusion of both imaging modalities (D) one can see that the radiopharmaceutical product concentrates in an enlarged lymph node. The resulting diagnosis is iodine positive lymph node metastasis.



Octreotide scintigraphy for identification of the primary tumour in a patient with liver metastases of a neuroendocrine tumour. The focal tracer concentrations in the planar images (A) in the right abdomen localise in the fusion images of the SPECT/CT on the primary tumour in the bowel (B/C) and a mesenteric lymph node metastasis (D/E).

Although most nuclear medical examinations using SPECT (single photon emission computed tomography) take place beyond hospitals, two to three times more SPECT exams than PET-CT exams are carried out within hospitals. Thanks to new tracers, SPECT-CT is also expected to present new prospects for examination and treatment in the future and, if those promising approaches work, they could be ground breaking in the treatment of prostate cancer, for example. Among other questions, EH asked the Director of the Nuclear Medicine Clinic at Erlangen University Hospital, Professor Torsten Kuwert, why there is little talk of the SPECT procedure and whether this indicates PET is superior

'The PET procedure is a relatively new method which, from a technical point of view, is certainly better than SPECT,' Professor Kuwert explained. 'The attention of the research community is therefore focused on this innovation, which can be seen by the number of habilitation treaties written on this subject. Nowadays PET only exists as PET-CT, which enhances the opportunities of application for this procedure. Although SPECT is also now available as SPECT-CT, for example, its use is largely limited to university hospitals in Germany, but the trend looks different worldwide because every other machine sold is a SPECT-CT, so there's a trend towards a fusion of both procedures.'

'SPECT-CT represents a clear improvement in diagnostic imaging. Just as in the case of PET-CT, two examinations are carried out directly after one another without the patient having to shift position. The nuclear medical CT image can be overlaid with a radiological CT image and the concentrations of a radioactive tracer, visible in a SPECT-image, can be correlated with the CT image. This results in two distinct advantages: first, concentrations can be characterised better than before; in the case of an iodine SPECT-CT, we can see faster whether a concentration in the neck is benign or malignant, i.e. whether it corresponds with a normal thyroid rest or for instance with a lymph node metastasis.

'Studies have shown that the precision of diagnosis could the increased by up to 30% through this. Secondly, the changes can be better localised by overlaying the two procedures, for instance to see if they can be surgically removed. This was not previously possible because the resolution for nuclear medical images is much weaker and the tracers only show the disease process, but not the rest of the organs. Through the combination with CT, the SPECT-CT now also shows the anatomy and therefore delivers a significantly better effectiveness for many indications.'

PET-CT also shows the anatomy, so where is the boundary between SPECT-CT and PET-CT?

'The difference is mainly with the tracers. Whilst we largely work with F-18-Deoxyglucose as a universal oncological tracer, there is no such substance for SPECT. Here we work with the classic nuclear-medical radiopharmaceutical products, such as iodine scintigraphy after thyroid cancer. Bone scintigraphy is also among the classic procedures where the conclusion can be clearly improved with SPECT-CT, and cardiac scintigraphy, where the procedure is used for the attenuation correction of images. Then, of course, there's tumour scintigraphy – although this works with specific tracers for SPECT, such as the octreotide scintigraphy, which facilitates the detection of neuroendocrine tumours, or the MIBG scintigraphy to diagnose neuroblastoma. With SPECT in particular, there are some promising approaches for new tracers. In my view a new tracer for prostate cancer is simply ground breaking. This tracer, developed by an American company and already trialled in studies, can be used for diagnostic as well as therapeutic purposes.'

What does treatment with tracers mean in practice?

'During therapy the organic, basic molecule is combined with iodine 131, which – put simply – allows us to treat metastasised prostate cancer with 'radioiodine therapy'. Moreover, there are other radiotherapeutic products for prostate cancer, such as the alpha emitter that's currently being trialled in a multi-centric study. All in all, more is happening now in the field of tracers than over the entire past decade. The problem with tracers is that they fall under the pharmaceuticals law and their market is much smaller than with other pharmaceutical products. However, the costs of clinical trials are on a similarly high level to those for a non-radioactive therapeutic agent, which obviously hinders developments in nuclear medicine significantly. Nonetheless, there are still reasons to be hopeful.'

Could there be a SPECT-MRI in the future?

'It's certainly conceivable, although the development costs of such a scanner also need to pay off. The examination time would be longer because the MRI sequence is definitely longer than that of a SPECT. Moreover, there is the difficulty of integrating the detectors into the magnetic field. For PET this became possible after a few years of development. However, it's debatable whether we should continue to follow this path for SPECT because PET-MRI is already available as an alternative, and besides it's possible to fuse the MRI data with the SPECT retrospectively. With SPECT-MRI we can probably expect high acquisition and running costs whilst only being able to carry out a limited number of examinations due to the length of examination time.'

Following his medical studies at RWTH Aachen University, **Professor Torsten Kuwert** trained as a specialist at the Nuclear Medicine Clinic at the Research Centre Jülich. He then became a consultant at the university hospitals in Düsseldorf and Muenster and was Director of the Institute for Molecular Biophysics, Radiochemistry and Nuclear Medicine at the Heart and Diabetes Centre NRW, from 1987 – 1988, and Professor for Nuclear Medicine at the University of Bochum. Since 1998, he has directed and been Professor for Clinical Nuclear Medicine at the University of Erlangen. In addition, from 1998 – 2011 he represented the Committee for Radiopharmaceuticals of the German Society of Nuclear Medicine. The professor has cooperated with Siemens Medical Solutions in the development of the SPECT-CT since 2005 and from 2009 he has been Clinical Assessor of a PET/MRI whole body scanner.

In their infancy but new PET tracers have a rich future

Dr Peter Choyke, Chief of the Molecular Imaging Programme at the National Cancer Institute in Bethesda, USA, who believes that new tracers will have an evolving role to play and represent an exciting development in the imaging of cancers, will outline the potential of new PET tracers in a session at the ECR 2013 congress in Vienna next March. In an interview with European Hospital he explained why he believes they represent such an advance.

Due to the sensitivity of PET (nano-pico molar sensitivity vs. micromolar for MRI) it is possible, he said, to image cell membrane based receptors responsible for the abnormal growth associated with cancers and detect subtle changes in the integrity of cancer cells. FDG-PET/CT has been the trailblazer agent, demonstrating unique sensitivity for cancers, but he said while FDG uptake does reflect glycolysis, it is relatively non-specific and, to date, has not dictated the choice of therapies.

'The promise of new PET agents is that they will aid clinicians in adding or deleting therapies depending on the pharmacodynamics of the imaging biomarker,' he added. 'For instance, classes of agents have been developed to investigate angiogenesis, proliferation, hypoxia, apoptosis, hormone sensitivity and amino acid transport. Each of these provides a unique window on the biology of each cancer and will hopefully guide therapies in the near future.'

In the specific example of metastatic prostate cancers, he said, Sodium Fluoride PET is proving far more sensitive than conventional bone scans. Agents such as F-ACBC (amino acid transport) F-DCFBC (Prostate Membrane Specific Antigen PSMA) F-DHT (androgen receptor) and F-Choline (cell membrane turnover) are proving efficacious in the detection of metastatic disease and reflect actual tumour burden in contrast to existing methods that only indirectly image tumour (bone uptake).

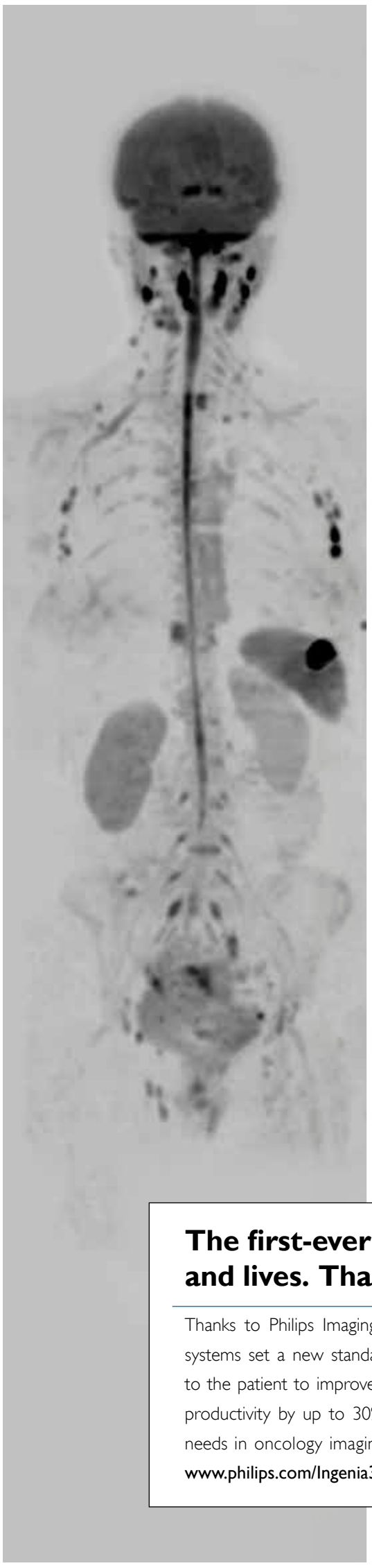
The new tracers he will mainly focus on at ECR 2013 will be F-18-FLT, F-18 Fluciclitide, F-18 FACBC, F-18 DCFBC, F-18 Estradiol and F-18 Sodium Fluoride - newer agents that are more specific and target receptors on cancer cells – and they have a clear application for oncology with F-18 Fluciclitide being useful in identifying tumours with high integrin expression or angiogenesis, possibly suggesting that an anti-angiogenic agent or anti-integrin agent would be a useful adjunct to the treatment. 'Similarly,' he added, 'F-18 Estradiol (FES) shows whether the oestrogen receptor is active in a tumour. This can be useful in determining which drugs targeting ER are appropriate for a specific tumour.'

Some of the agents may also be useful in determining whether inflammation is present (e.g. in inflammatory bowel disease) or if there is ischemia (vascular disease).

The major benefit of the newer tracers to clinicians/radiologists, he pointed out, will be in selecting the right drug for the right patient. 'Currently, oncologists use the same kinds of drugs in all patients for first and second line therapies. Using new tracers it will be possible to select the best drugs for a patient and to anticipate when drug resistance is beginning, thus providing an opportunity to switch to more effective therapies before subjecting the patient to needless toxicities. Moreover, these tracers will allow earlier assessment of the benefit of particular therapies. Ineffective drugs can be dropped earlier while more effective drugs can be added to the regimen.'

For the patient, he pointed out, molecular imaging provides the opportunity to treat each tumour individually and monitor for success or failure by using specific markers expressed by the tumour, and be accomplished without invasive biopsies. They also may change the approach to diagnosis and treatment.

'Molecular imaging, along with new tissue and serum/urine based biomarkers,' Dr Choyke confirmed, 'offer the possibility of customising treatments based on individual tumour molecular expression profiles.'



Dr Peter Choyke, Chief of the Molecular Imaging Programme of the National Cancer Institute, Bethesda, graduated from Jefferson Medical College and trained in Diagnostic Radiology at Yale University and the University of Pennsylvania. His research focuses on the development of new imaging methods, principally PET, MRI and optical, that result in improved outcomes for cancer patients. His special interest is prostate cancer for which he has an active research programme involving MRI, PET and optical imaging.

Spectral Mammography

It's like switching from black and white to colour TV

Study suggests a new method to measure breast density can help determine cancer risk

Breast density is a key risk factor for breast cancer. Accurate measurement may be made possible by a new approach to mammography, according to early research presented at the 54th Annual Meeting of the American Association of Physicists in Medicine (AAPM). That new method, spectral mammography, could also reduce the radiation dose of mammography by up to half, said Sabee Molloi PhD, professor and vice chairman of research for the department of radiological sciences, University of California at Irvine. Dr Huanjun Ding, who is a member of his research group, presented results of a feasibility study last July in Charlotte, N.C.

The denser a woman's breasts, the higher her risk is for breast cancer. Less dense breasts are fattier, while denser breasts have more connective tissue. Denser breasts are more difficult to read on a mammogram because tumours are harder to see; standard mammography therefore is not suitable for precise measurement of breast density.

Spectral mammography provides precise measurement of breast density.

The group, led by Prof. Molloi, Dr Ding, and Dr Justin Ducote, used a photon-counting spectral mammography system and applied both computer simulations and physical phantom studies. They imaged four models of breasts, which represented various configurations including thickness and density. The results suggest that spectral mammography could measure volumetric breast density in a screening exam with an error rate of less than two percent. This could help identify women at higher risk of breast cancer incidence at an earlier time in the screening process. The researchers now plan to conduct pilot studies of women as part of regular screening programmes.

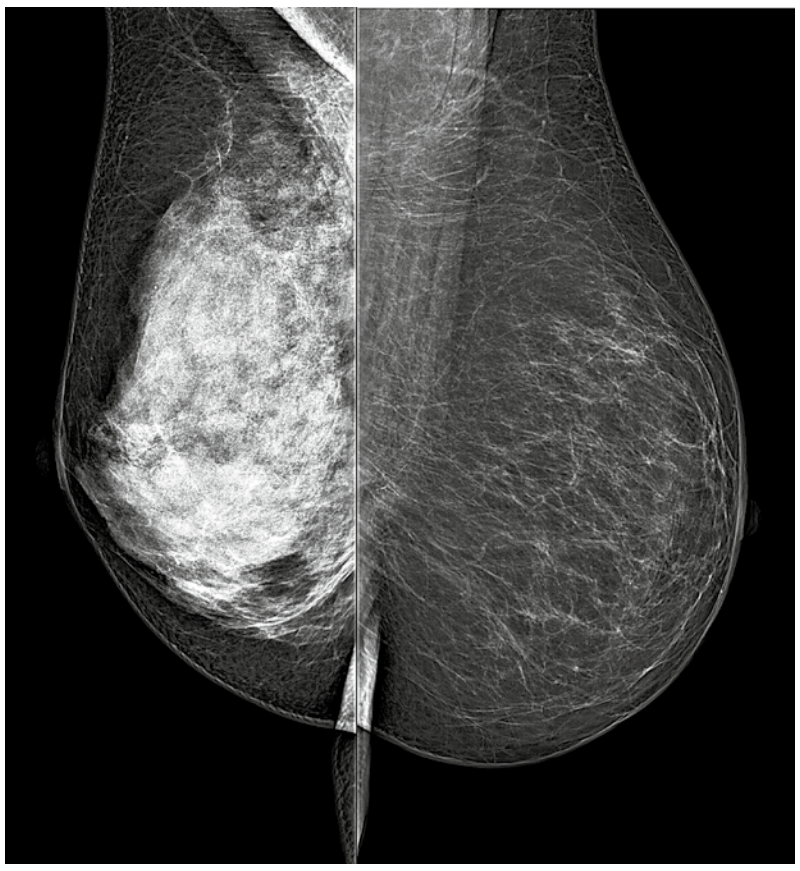
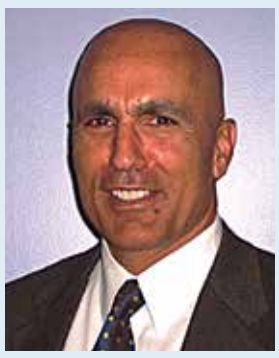


Image shows a high-density mammogram (left) and low-density mammogram (right). (Image courtesy of AAPM, Sabee Molloi PhD.)

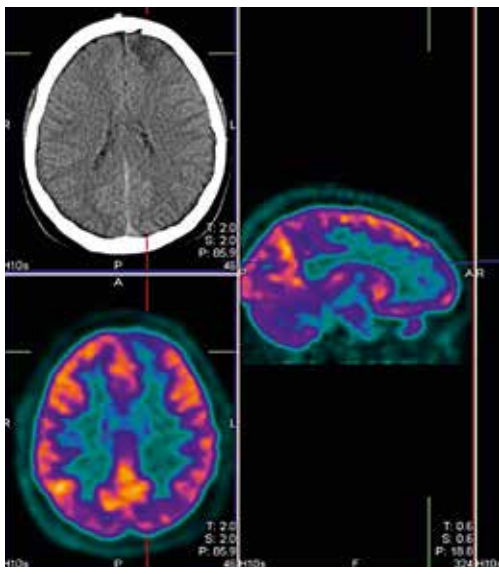
'Spectral mammography vs. standard mammography is like comparing colour television to black and white TV,' summarised the expert. 'Although the object represented is the same, the colour image has more information inside. Spectral mammography allows the image to be viewed at two different energy levels, instead of just one, helping quantify the density of a woman's breasts and, in turn, her relative risk.' There are no significant drawbacks to this approach, Prof. Molloi emphasised. Radiologists will not need to adapt their workflows to apply this technique. The vendor underlined as offering suitable devices is Philips. According to the researchers, dose exposure is cut by up to half in comparison with standard mammography.

The method may evolve into the standard of care

If further validated and approved, spectral mammography could become the standard of care for breast cancer screening. It could help define a woman's appropriate mammography frequency and any need for further testing. A woman with denser breasts might benefit from having regular screening mammograms more frequently, or at a younger age. Women with extremely dense breasts, a family history of cancer, and genetic predisposition to the disease might benefit from having a more sensitive test such as MRI.



Sabee Molloi PhD is Professor of Radiology, Medicine (Cardiology), Biomedical Engineering and Electrical Engineering and Computer Sciences, and Vice Chairman of Research, at the Department of Radiological Sciences, University of California at Irvine. His research focus is on medical X-ray imaging.



Keep up-t with deve

Radiologists should know the indications for PET/CT scanning

In recent years PET/CT has proved a versatile and promising examination procedure, especially in oncology. Thus, according to Professor Christoph Eilles, head of the Nuclear Medicine Department at University Hospital Regensburg, 'Radiologists should know the indications for carrying out PET/CT scans, be aware of what the procedure can deliver and when it makes sense to schedule or recommend such a scan.' Also, although all indications are not yet known, because their number has grown continuously it is important that radiologists keep abreast of developments.

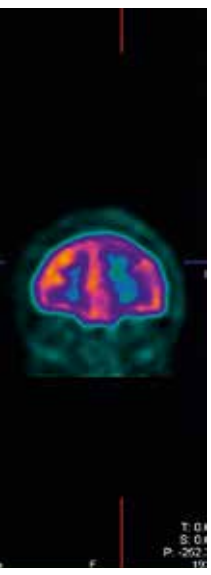
An important prerequisite to be able to assess PET data is radiologists' knowledge of metabolic processes and opportunities for different tracers. 'There are different substances, although currently only the FDG tracer is licensed, which delivers information about the glucose metabolism – ideal for imaging most tumours,' he points out. There are, however, also tumour entities that need different tracers, e.g. prostate cancer where

Intensity m radiothera

UK's cancer innovation fund will share trea

A new £15 million Cancer Radiotherapy Innovation Fund, announced in October by Prime Minister David Cameron and Health Secretary Jeremy Hunt, could provide nearly 8,000 more cancer patients with access to Intensity Modulated Radiotherapy (IMRT) during the rest of 2012-13. 'Radiotherapy is one of the most clinically and cost-effective treatments for cancer and this funding will bring our additional investment in radiotherapy over the Spending Review period to £165 million,' Jeremy Hunt pointed out.

Most of the 50 radiotherapy treatment centres in England presently do not provide IMRT to every patient who could benefit from this technique. Under a new NHS system, cancer treatments will be planned and paid for on a national basis, so that patients do not miss out on certain treatments because of where they happened to live. Thus, for example, brain tumour patients needing stereotactic radiosurgery will have the same access to this treatment as



Staging and treatment planning with FDG-PET/CT for a female patient (aged 65) with head and neck tumours, hypopharyngeal cancer (cT4 cN2b), primary radiochemotherapy (cisplatin/carboplatin)

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Choline is used, or brain tumours where Tyrosine is utilised. For some problems PET/CT is now regarded as the procedure of choice, e.g. for staging bronchial carcinoma. 'If the radiologist discovers this type of tumour PET/CT is the best procedure to deliver an overview of the extent to which the cancer has spread in the body,' he explains. The procedure is also very important as a follow-up examination for unclear diagnoses. Here PET/CT can be very helpful in achieving a differentiation between metastases, benign tumours and the presence of infections. As PET/CT is a different procedure to that of a radiological examination, the nuclear medicine specialist must always be informed about medication and previous treatment. Dynamic processes must also be considered, such as the behaviour of the tracer over time. 'Time can play an essential role, for instance in the differentiation between a radiation necrosis and tumour recurrence in the case of brain tumours, where it's important to determine whether the tracer accumulates in the focal lesion or whether it is quickly excreted.' For brain tumours the basic examination is an MRI scan, with images later fused with those of the PET/CT. 'But, PET/CT can also initially be utilised pre-operatively as extensions of the brain tumour may not be visible on the MRI scan and the exact localisation of particularly malignant parts is particularly practicable with this procedure. This is of especial importance for a biopsy,' he says, also adding his appreciation that PET/CT image data can be directly transferred into the radiation devices.

Now, next to PET/CT are devices for a hybrid application of MRI and PET. 'Whether or not this combination of the modalities in one machine will be as successful as that of the PET/CT, however, is still unclear and is currently being examined in studies. Anyhow, the separate MRI and PET images can be fused easily through software. However, MRI/PET could be helpful for brain tumour diagnoses because PET/CT is mainly used for attenuation correction and the MRI for tissue imaging. With all other tumours, apart from the head, PET/CT is used for localisation, often even together with a contrast medium examination in one process.

Professor Eilles welcomes a rapprochement between radiologists and nuclear medicine specialists – facilitated by the use of the PET/CT, along with the formation of working groups by their specialist associations, and talk of a partly combined medical specialist training. 'In Regensburg we already have some radiologists who spend a year with us in the department of nuclear medicine to learn how to better assess PET images. Beyond the question of which modality is the best procedure, it's the experience and expertise of the person operating the machine that's decisive.'

Trained in medicine at the Friedrich-Alexander University, Nuremberg-Erlangen **Professor Christoph Eilles**, in 1977 he gained a doctorate at the university's Eye Clinic. Following his habilitation at the Julius-Maximilian University of Würzburg, in 1989 he received the Bavarian State Ministry teaching licence. In 1992 he became Professor of Nuclear Medicine at Regensburg University Hospital and, a month later, became head of the Department of Nuclear Medicine. Professor Eilles is a member of various specialist associations and on the advisory board of several publications.

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anyone else. Dr Harpal Kumar, chief executive of Cancer Research UK, commented that the new fund would help to place the country as a world-leader in cancer therapy since radiotherapy cures more cancers than drugs and IMRT presents a higher chance for survival. The already operating Cancer Drugs Fund has so far assisted more than 21,000 patients.

IMRT is a very precise technique that uses hundreds of collimators to shape the radiotherapy area. The collimators can move during treatment and vary the beams intensity as they are aimed at a tumour from different directions during each treatment dose. IMRT can also create a dipped area to avoid structures that would be damaged by radiotherapy, such as the spinal cord or salivary glands.

An oncology team uses a patient's 3-D CT images to plan treatment, based on computerised calculations to ascertain the dose intensity pattern to match closely to the tumour shape and thus spare surrounding tissue.

The Southampton Traffic Light test

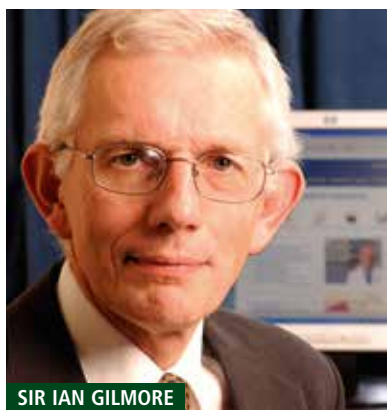
Doctors aim to spot hidden liver fibrosis and cirrhosis far sooner

Report: Mark Nicholls

Dr Nick Sheron and colleagues at the University of Southampton and Southampton General Hospital hope to use a test they are developing for the earlier identification of people in need of hospital treatment from liver disease – a condition that develops silently and presents late, often with fatal complications. The team also hopes it will help reduce unnecessary hospital referrals.

The Southampton Traffic Light (STL) test combines several different tests and clinical markers, which are given a score that indicates the patient's likelihood of developing liver fibrosis and cirrhosis. A simple algorithm transforms this into a red, amber or green rating: red means the patient has liver fibrosis and may even have cirrhosis; green suggests there is no cirrhosis, and amber indicates at least a 50:50 chance of scarring with a significant possibility of death within five years, and patients are advised to stop drinking to avoid further disease.

The test is part of the Alcohol and Liver Disease Detection Study (ALDDeS) and comes at a time that liver disease mortality in the UK has doubled over the last 15 years, with 25% of the population drinking above recommended guidelines. Additionally, many patients are arriving at hospital liver clinics for the first time with liver disease that has been entirely unsuspected and sometimes with end-stage liver disease – and liver disease survival rates have not improved in the last 15 years.



SIR IAN GILMORE

Dr Sheron, who heads Clinical Hepatology at the University of Southampton and is consultant hepatologist at Southampton General Hospital, said that while altering people's behaviour by reducing alcohol intake was important, the ability to go out into the community to detect people with liver disease and reach them before they develop end-stage liver disease is also crucial. Historically, liver disease diagnosis relied on referral to specialist services, often based on an elevated level of alanine transaminase (ALT), he said, but such tests were of little help in predicting which patients have liver fibrosis or cirrhosis. 'As a result, from about the year 2000, we've been trying to find a test that would reflect the scarring process and would enable us to detect liver disease earlier.'

The aim was to develop a liver disease 'traffic light' suitable for community use to enhance liver risk assessment and allow rational referral of more severe disease to specialist care. That led to the use of fibrosis markers (procollagen-3 N-terminal peptide [P3NP] and hyaluronic acid) along with routine liver function tests to create the Southampton Traffic Light test.

In trials the test, from a routine blood sample, was given to over 1,000 patients and proved to be accurate in severe liver disease detection. It was also shown to provide GPs with an objective means to accurately assess the potential severity of liver fibrosis in high-risk patients such as heavy drinkers, type II diabetics, or obese people.

Dr Nick Sheron, Head of Clinical Hepatology at the University of Southampton and liver unit at Southampton General Hospital, is involved in a clinically based research programme on various aspects of alcohol-related problems. With Royal College of Physicians President Sir Ian Gilmore, he co-founded the Alcohol Health Alliance, consisting of 27 organisations including Royal Colleges, NGOs and charities, to lobby for evidence-based policies to reduce alcohol-related harm in the UK. He is also a founder member of the European Union Alcohol Forum and an Adviser to the House of Commons Health Select Committee on Alcohol.

As part of on-going research, the Local Care and Treatment Evaluation (LOCATE) study funded by the British Liver Trust, aims to further assess the test in primary care settings but Dr Sheron said there are clear benefits for hospitals too. 'A large number of referrals to hospital liver clinics are completely unnecessary and patients with fatty liver disease but no underlying fibrosis could manage their condition in the community,' he added. 'The test would reduce unnecessary referrals but also increase necessary referrals and lead to a reduction in the number of people developing liver disease.'

Professor Sir Ian Gilmore, chair of the Alcohol Health Alliance, said the work of Dr Sheron and his colleagues 'may prove really useful for guiding the right patients towards specialist care in a timely way'.

TB and HIV di national borde

The World Congress for Biomedical Laboratory Science (IFBLS 2012) in Berlin yet again emphasised that infections require safe and low-cost diagnostics worldwide

Report: Susanne Werner

How can effective yet low-cost diagnostics be ensured worldwide? The question was among those raised at the IFBLS Congress 2012. In Africa, diseases such as HIV or Malaria present the biggest dangers, in Eastern Europe the number of TBC cases is on the increase and resistance rates are increasing dramatically, and Western Europe is scared of sudden epidemics such as the EHEC outbreak in 2011. Around 800 participants from 58 countries attended the Berlin congress, held in Germany for the first time in 46 years and hosted by the International Federation of Biomedical Laboratory Science (IFBLS) with the German Association of Medical Technologists e.V. (dvta).

'Pathogens can change very quickly. Diagnostics must be able to react to this and doctors need to know about the dangers so they can brief the laboratories accordingly,' says Annette Artelt, who works at the veterinary medical laboratory, University Hospital Giessen, represents the dvta within the IFBLS and was among the congress organisers. 'Although colleagues from many other parts of the world found our modern tests interesting,' she said, 'they made it clear that what they need is something different, meaning cheap solutions that will work under different local conditions.'

Diagnostics gains global importance

How can diagnostics be developed and utilised worldwide to ensure it really helps with solutions to local problems? One person who knows the answer is Dr Sabine Rüsch-Gerdes (see box), congress speaker on infections. She heads the National Reference Centre for Mycobacteria at the Research Centre Borstel, which is among the Supranational Reference Centres of the World Health Organisation (WHO). The microbiologist is pleased that diagnostics is gaining in importance: 'For decades, it has been neglected. Patients were just being treated without clarification of the resistance situation. The large number of antibiotics resistances is one of the consequences,' she explains. She constantly travels the world to develop standardised diagnostics and treatment based on local quality control and assurance.

Increased automa speeds up results

Siemens platform provides tracking, biochemistry, haematology, serology and coagulation services in a single automated laboratory solution

Report: Mark Nicholls

As automation eases the logistics of laboratory operation, new systems enable clinical laboratory scientists to provide clinicians with a quicker and more robust results service. Dr Bill Bartlett, Joint Clinical Director of Diagnostics at NHS Tayside, Scotland, believes automation will also enable lab staff to better educate clinicians to 'ask the right questions' to enable the correct choice of tests 'at the point of care', in turn leading to more focused results and potentially improve patient outcomes.

NHS Tayside is deploying the Siemens Aptio Automation, a platform that will see the introduction of state-of-the-art tracking, biochemistry, haematology, serology and coagulation services on to a single automated laboratory solution.

It sees a shift away from the conventional departmental approach and separate analytical lines towards an integrated service, further facilitated by the formation of a Department of Blood Sciences headed by Dr Bartlett. 'This,' he said, 'will provide us with opportunities to deliver new ways of working, new ways of applying knowledge and skills and a new way of managing the delivery of the service.'

The department provides laboratory services for a population of about 475,000 people in Tayside and North Fife and includes routine blood science and biochemical inves-

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Currently she mainly concentrates on Eastern European countries such as Azerbaijan, Armenia, Kazakhstan and Moldova, as well as African countries. 'In countries of the former Soviet Republics the TB resistance rates are extremely high; south of the Sahara there's a dangerous co-existence of HIV and TB. In Western Europe, TB appears to be clearly on the increase among children,' she reports. The result: There cannot be just one treatment concept for the entire world.

Dr Rüsch-Gerdes recommends a range of interventions to fight infection effectively: The affected countries must initially be sensitised and must realise that these infections represent dramatic dangers for the population. Therefore, the first objective must be interrupting the chains of transmission at as early a stage as possible. In turn, facilitating this requires local diagnostics that can be utilised under the respective circumstances.

TB infection rates in Germany have continuously fallen in recent years. In 2010 the Robert Koch Institute registered 4,330 TB cases; in 2009 there were 4,419 cases. However, Western Europe and Germany, Dr Rüsch-Gerdes said, should still not play down the dangers. She is not reassured by these figures: 'TB only tends to be detected at a very late stage in Germany. The only thing that helps is to be particularly vigilant and to correctly interpret the first symptoms.'

Worldwide training and education

The second central question at the congress was: *How good is training in laboratories globally?* 'Germany is the only country that does not provide academic training for medical and laboratory technologists,' Annette Artelt pointed out. 'From our point of view, this needs to change urgently.' There, training to become an MTLA requires three years' attendance at technical college.

For three years the dvta has asked for academic degree courses to be created. 'The quality of our work and care of patients in Germany are of a high standard, but there is a lack of formal recognition with academic titles,' Annette Artelt explained. Many MTLAs in Germany already work independently and hold managerial roles in hospitals. The dvta therefore changed its name in spring. Instead of medical-technological assistant the job description is now medical technologist – in line with the terminology of neighbouring European countries. This should be a signal to German politicians to also change the job description respectively. 'We are,' she added, 'running the risk of falling behind in scientific work if Germany does not promote the "academisation" of this profession.'

Having begun her career at the National Reference Centre for Mycobacteria at the Research Centre Borste in 1977, in 1993 microbiologist **Dr Sabine Rüsch-Gerdes** became its head. Her research has focused on the diagnosis and treatment of pathogens that cause tuberculosis (TB), and she advises international organisations such as the WHO, 'Médecins Sans Frontières', the German Agency for International Cooperation and the International Red Cross. The microbiologist is particularly active in Eastern Europe and Africa, where she works to develop the infrastructure to combat and treat TB. Since 2010 she has been the WHO speaker for all Supranational Reference Centres, as well as head of External Quality Control for all 30 European countries. In December 2005 Dr Rüsch-Gerdes was awarded the Federal Republic of Germany Order of Merit for her significant commitment.

ation service

Dr Bill Bartlett is a Clinical Scientist and Joint Clinical Director of Diagnostics, NHS Tayside, based at Ninewells Hospital, Dundee, Scotland, and the authority's clinical lead for Blood Sciences. He is also honorary senior lecturer in College of Medicine, Dentistry and Nursing at the University of Dundee.

tigation ranging from U and E (urea and electrolytes) and liver function tests to tumour markers, therapeutic drug monitoring, haematological parameters, cell counting, haematinic investigations, coagulation studies and a number of serological services, amounting to almost seven million tests annually in support of routine medical care.

'We chose Aptio Automation because it can handle increasing workloads while enabling us to use our staff better,' Dr Bartlett explained. 'We expect that the implementation of this new platform will allow us to provide a state-of-the-art service that

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Assisted reproductive treatment

Under the microscope: Embryos are monitored minute by minute

Fathers as well as mothers provide a fertile field of study for Unilabs-Eylau Centre for Assisted Reproduction in Paris

Report: John Brosky

You may have seen the results of Eylau Laboratories work – a happy couple holding a miracle, their newborn baby, or perhaps walking a toddler in a park – without realising the connection. For behind the parents' joy lies a history of anguish before the child could be born.

Regularly, in medical journals, the Eylau Laboratories publishes articles describing the techniques used to assist would-be parents to realise their dream of creating a child.

The people from all backgrounds, from ordinary to famous, pass discretely through Paris seeking the services of the Eylau Centre for Assisted Reproduction, which since 1954 has built an international reputation in the field of assisted reproductive medicine and in-vitro fertilisation.

Each day more than 180 hormonal or semen analyses are conducted at the Eylau facilities for couples referred by their physician, or those who have found the clinic on their own through recommendations of friends, or increasingly, social media.

Over 5,000 in-vitro fertilisation procedures are performed each year, and the number of analyses at Eylau surpasses the combined volume of private and public clinics in France. The centre also performs highly advanced tests from profiling of the viability of sperm and eggs to a minute-by-minute monitoring of embryo development.

'We present a global solution for couples to explore the causes of infertility, and then propose a full palette of techniques and tools that can be applied to bring the best possible result,' said Thierry Leclerc, vice-president for Unilabs-France who is responsible for the reproductive medicine operations of Eylau Laboratories.

Thierry Leclerc, vice president at the french laboratory of Unilabs, Paris

Eylau clinicians and scientists are on the leading edge of infertility studies, drawing more than 200 participants every year to the conference updates in infertility, which features their research.

The group publishes between 10 and 15 papers each year, said Leclerc, 'not fundamental research or science for the sake of science but results-based, applied science focused on obtaining the best results for couples.'

A study from researcher's at Unilabs' Eylau Centre for Assisted Reproduction made headlines internationally last year reporting at the congress of the European Society of Human Reproduction in Stockholm that a study of nearly 2,000 young, obese men showed they had a higher chance of producing infertile sperm than men of normal weight.

It was the largest study of its type ever conducted according to the scientific director of Eylau-Unilabs, Paul Cohen-Bacrie MD, who added that, while the risk of infertility for overweight women had been established, there had been less evidence about the impact of obesity on men.

Leclerc said the statistical strength of Eylau studies for reproductive medicine comes from the fact that the specialised services of the Centre for Assisted Reproduction are part of the larger operation of Unilabs-Eylau that conducts more traditional laboratory analysis.

More complete and comprehensive analyses across a larger population enable findings to be carefully corroborated.

Eylau researchers and clinicians also take a more comprehensive view of problems of infertility, including especially a close examination of the father. Studies by researchers from Eylau, for example, established that men have a biological clock as well as women, showing that there was a decrease in pregnancy rates from 12.3% with fathers 30 years of age or younger to 9.3% in fathers older than 45 years of age.

Miscarriage rates also increased where the father was over 35.

Eylau was the first in France, and among the pioneers in Europe, to directly introduce morphologically selected sperm into the oocyte, greatly increasing the success rate for couples affected by infertility.

The centre also utilises the newest technology, an embryoscope, an image capture system that allows an enormous amount of specific and objective information to be collected for each embryo from the moment of in vitro fertilisation.

Monitoring the dynamics of a developing embryo aids clinicians in identifying the most viable candidate to be transferred into the uterus.

Genetic profiling of embryos is highly controversial in assisted reproduction for ethical and moral reasons. Yet genetic profiles of the sperm or ova before fertilisation, called karyotyping, responds to essential clinical questions of reproductive biology.

In 2008 the Eylau centre opened a genetics unit that serves the wider Unilabs network.

The European scope of the larger Unilabs group across 11 countries represents a significant opportunity for expanding the specialised services of the Eylau Centre for Assisted Reproduction.

Currently, Thierry Leclerc added, Unilabs is studying the potential to establish a reproductive medicine group within a larger laboratory operation in Spain.

C. difficile test guidelines are being ignored

Inadequate testing may mean one of the most common healthcare-acquired infections could go undiagnosed

New data presented at the international ID Week 2012 conference in the U.S. showed that over three quarters (78%) of healthcare professionals surveyed in Europe believed that they may not be following guidelines for the testing of Clostridium difficile infection (CDI). This is despite survey respondents believing that CDI is increasing with a large number of cases going undiagnosed.

CDI is one of the most common healthcare-acquired infections in Europe and the leading cause of antibiotic-associated diarrhoea in adults. CDI has become an increasing problem in hospitals. It is estimated that as many as one in 50 people with CDI will die within three months as a result of the infection.

Current European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines recommend a two-step approach for the diagnosis of CDI involving two different tests detecting both the presence of C. difficile bacteria and the toxins produced by the bacterium. Just 22% of surveyed healthcare professionals understand that their laboratories

MARC WILLCOX

regularly used a two-test diagnostic algorithm for CDI that detects both the presence of C. difficile and the presence of toxins.

"It's concerning to see that there appears to be confusion about which CDI tests are actually being used. The findings suggest that the recommended CDI diagnostic tests may not be being conducted systematically across Europe. This could lead to under-diagnosis or misdiagnosis, ultimately meaning that patients may not receive optimum care", said Professor Mark Wilcox, Professor of Medical Microbiology, Leeds Teaching Hospitals & University of Leeds. "The net effect of this non-standardised approach to testing could also mean that the true incidence of CDI across Europe is underestimated."

The survey was conducted by GFK and commissioned by Astellas Pharma Europe Ltd. A total of 868 questionnaires were completed by healthcare professionals from France, Germany, Italy, Spain and the UK that included hospital physicians, infectious disease specialists, surgeons, primary care physicians and microbiologists.

The survey found important discrepancies between the tests requested by physicians and those actually performed in the laboratories. While 64% of physicians requested a stool culture, only 42% of microbiologists reported using this method in the laboratory. Conversely, 44% of physicians requested an enzyme immunoassays (EIA) toxin A+B+ test, while 75% of microbiologists used these tests in the laboratory. This discrepancy may be due to the fact that stool cultures can be labour intensive and slow when EIA tests are simple and quick to perform. However, EIA tests are less sensitive and may lead to cases being undiagnosed if used alone.

"These findings reveal important variations in knowledge regarding CDI diagnosis among healthcare professionals and suggest that a significant educational effort is required to address this", said Wilcox. "Physicians need to familiarise themselves with locally available tests and establish a dialogue with laboratories to optimise their diagnostic approach."

The results of this pan-European survey highlight the need to standardise testing in line with recommendations to minimise the under-diagnosis of this distressing and sometimes life-threatening infection.

For references and more information please go to www.astellas.eu

Increased automation

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aligns the lab function with Tayside's overall goals for organisational sustainability and improved patient outcomes. It will provide opportunities for multi-skilling, improve turnaround times, and provide a more complete range of test results to the requesting clinicians within a shorter time window.'

Aptio Automation's circular track and modular design means it is adaptable to a range of lab or testing environments and also offers connectivity to Siemens' portfolio of automation-ready analysers, facilitating a multi-disciplinary approach to testing. It also delivers comprehensive analytics via powerful, centralised IT, while having the flexibility to provide pre- and post-analytical capabilities.

Dr Bartlett suggested that laboratory medicine is undergoing a revolution with lab staff working closer with clinicians to 'enrich' the reports they produce to offer more impact at the point of care. With finite staff, space and financial resources available, he said advances in IT and analytical technology will help lab managers to better deal with the complexities of testing and allow staff to more effectively deliver those 'value added' elements of the service, which go beyond producing reports and extend to providing the right testing profiles, contributing to research and development, training and playing a role in translational medicine.

'Siemens, and companies like them, can take the pain out of delivering the bulk of the work,' he added, 'so we can start using our resources to focus more on these effectiveness issues.'

Finding the quicker route to test results

Nine UK hospitals participate in a red cell immunohaematology electronic reporting pilot

Nine British hospitals are working with National Health Service (NHS) Blood and Transplant (NHSBT) on an electronic reporting pilot that may offer quicker access to patient test results and data. When rolled out nationally, hospitals will no longer receive traditional printed reports and antibody cards from NHSBT. The implementation of a web browser will also make access to results more secure and, where appropriate, enable sharing of information and patient results between hospitals

Report: Mark Nicholls

The current pilot is for requests for Red Cell Immunohaematology (RCI) results; NHSBT also plans a similar project for Histocompatibility and Immunogenetics (H&I) in January 2013, a system to become available across England and North Wales early next year.

NHSBT, the NHS Special Health Authority responsible for optimising the supply of blood, organs, and tissues, has been working closely with Sunquest and the pilot hospitals to implement the initiative known as Sp-ICE.

Hospitals in the electronic reporting pilot: the Freeman, Newcastle; Manor, Walsall; Poole General; Russells Hall, Dudley; Southampton General; Royal Bournemouth; Birmingham University; Coventry University and North Staffordshire University. 'These nine were chosen because they expressed an early interest in NHSBT developing and rolling out an electronic reporting system,' explained Dr Carol Ash, who leads the project for NHSBT. They are also hospitals that send a large number of samples to NHSBT every year and early adopters of the NHSBT OBOS (Online Blood Ordering System), which allows them to order blood electronically. 'For a number of years, users of our diagnostic services have been telling us they want more rapid access to patient results and their preference would be to have these results electronically,' Dr Ash added. 'So, the drive has come very much from the hospital users of our services.'

Dr Carol Ash is Head of Strategic Delivery for Specialist Services at NHSBT with ultimate responsibility for delivering the project and is supported by a team that includes a project manager, scientists within RCI and H&I, IT, finance and customer service support.

The project aims to deliver a reduced risk of transcription errors, results within one hour of authorisation, a full audit trail of report access, access to historic test results and the ability to search and display reports for a single patient or requesting location.

NHSBT say early feedback indicates that hospitals would like the ability to view test results from other Trusts, to help with the care of patients who move between different healthcare providers. If all organisations taking part in the project give permission for all other organisations to view their results, NHSBT will be able to provide a national antibody database for NHSBT-generated results. 'Sp-ICE has functionality that can control that level of access,' she said. 'Some hospitals have a pathology network where they may wish for their results to be visible only within that network but hospitals have seen the benefit of patient data being visible nationally.'

Security protocols are in place through the NHS Caldicott Guardian system to protect patient and service-user information.

The ICE web browser was originally developed for use in single hospitals, NHSBT has worked with Sunquest to implement software changes so it will function in a national environment, with access provided via a secure N3 connection.

The benefits to NHSBT and hospitals in terms of efficiency, speed, accuracy, patient safety and security are clear but, as Dr Ash added, 'The real benefit is to patients because Sp-ICE is about rapid access to patient data.'

Ben Wilson, Sunquest Product Manager for ICE, said Sunquest already has the ICE system in more than 100 UK hospitals, as well as in the USA and the UAE. 'Traditionally ICE has been installed in a single organisation, with patient results being delivered electronically to only users within that organisation. The NHSBT asked us if we could develop it to help them provide an electronic reporting system for their clients to save them sending over 150,000 paper results a year to 300 organisations.'

With improvements in functionality to enable ICE to work in a cross-organisational model, he said a large number of hospitals and tertiary care organisations can now access patient records in ICE - without compromising security, patient confidentiality or data issues.

Molecular diagnostics platform

Second cartridge on the way to detect pathogens and antibiotic resistances in implant and tissue infections

Curetis has developed its CE-marked Unyvero molecular diagnostics platform to provide clinicians with crucial information on infectious disease pathogens and their antibiotic resistances within four hours - saving up to several days compared to conventional microbiology culture.

The first application, the P50 Pneumonia cartridge, is already available. The second, to detect pathogens and antibiotic resistances in implant and tissue infections (ITI), is being developed with Heraeus Medical. One key application area will be orthopaedics, e.g. to diagnose infections after knee and hip replacements. 'Wound and surgical site infections are increasingly caused by bacteria carrying multiple antibiotic resistances,' explained Oliver Schacht, CEO of Curetis. 'In orthopaedic indications, infections often involve biofilms, i.e. communities of microorganisms that are very hard to open up and cultivate. Presently, it may take 7-15 days to obtain results from biofilm samples. This often leads to prolonged empiric treatment, follow-on surgery and increased morbidity and healthcare costs.'

The partners have teamed up with key European clinical opinion leaders to determine the pathogens and antibiotic resistances that need to be included in the ITI panel. 'The ITI cartridge is likely to include more than 40 and possibly up to 50 analytes,' he said. 'We expect an EU launch by the end of 2013.'

Curetis is also completing a European clinical trial to further substantiate the clinical benefit of its P50 Cartridge. By the end of September, enrolment was complete, with over 800 patient samples collected. The trial will compare the cartridge performance with conventional microbiology culture, the current standard of care. The primary endpoint will be clinical sensitivity and specificity for the identification of 17 pathogens covered by the P50 panel. Curetis will systematically resolve discrepant results by PCR and sequencing.

As of October, the Unyvero products are distributed in Germany, Austria and Switzerland by Curetis, in The Netherlands by Mediphos, Russia by Bioline LLC, Turkey by Mikromed, and the Middle East by ATC.

Accolades for London 2012 Olympics doctor

No one who had the good fortune to be at the London 2012 Olympics could argue that the organisation and volunteers were exemplary. Due to these 'behind the scenes' people, the entire period was a dazzling success – not least for the emergency care system for all Olympic and Paralympic venues, covering all athletes, officials, Olympic and Paralympic families and spectators, estimated to be over 200,000 people per day in the Olympic Park alone. Who pulled off this successful medical coverage?

In September, consultant anaesthetist David Zideman MD, the Clinical Lead for Emergency Medical Services of the 2012 Olympic and Paralympic Games, was awarded an Honorary Membership of the Association of Anaesthetists of Great Britain and Ireland* (AAGBI), to reflect his highly distinguished career in the fields of anaesthesiology and emergency care. 'This award,' said Dr Andrew Hartle, the association's Honorary Secretary, 'is one of the AAGBI's highest honours and recognises David Zideman's substantial contributions to anaesthesia, emergency care, resuscitation and the success of the London 2012 Olympic and Paralympic Games. He has played and continues to play an important part in UK medicine and is a worthy recipient of this honour.'

As the Clinical Lead for the Emergency Medical Services, Dr Zideman was part of a team that recruited more than 4,000 medical volunteers (2,000 in the emergency medical teams) from all parts of the health service. 'I planned an emergency medical service that included the recruitment of volunteers, the selection and provision of equipment, and undertook the training of all our volunteer staff,' he explained. One significant need was to match the professional skills of his team members carefully to each individual sport, to ensure an effective and efficient service, for example, in the boxing arena compared with swimming at the Aquatics Centre. 'It was,' he added, 'all about having the best possible system for optimising pre-hospital care for anyone in an Olympic or Paralympic venue who became seriously ill or was injured.'

Comprehensive training system for volunteers was an essential element, he said. 'The very simple message is that our system worked thanks to our trained volunteers. Each volunteer received around 18-20 hours training in total. This included teams arriving before their shifts and practicing various scenarios thereby familiarising themselves with the venue and pieces of equipment they might not be familiar with. Most importantly it ensured that they got used to working as a team with other volunteers who might change on a daily basis.'

During the Games Dr Zideman visited up to four venues per day, and participated and provided clinical support and advice to his volunteer teams. 'It was a great pleasure providing the structure for our tremendous emergency medical volunteer teams,' he said. 'I'm delighted to report that across the entire Olympic and Paralympic games, we did not have to perform a single general anaesthetic or emergency tracheal intubation.' He hopes that the lessons learnt from London 2012 will be carried forward to the Olympics in Sochi and Rio.

AAGBI President William Harrop-Griffiths MD (left) presenting the association's award to David Zideman, who says his Olympics role was a 'pinnacle of my work in pre-hospital medical care'

** The Association of Anaesthetists of Great Britain and Ireland (AAGBI) has over 10,500 anaesthetists in the UK and Ireland. Details: www.aagbi.org*

A renowned international lecturer, **David Zideman MD** was a consultant anaesthetist at Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, from 1980 to 2010, when he retired from the UK's National Health Service, although he still works in an honorary capacity for the Trust. He has been an honorary senior lecturer at the University of London since 1981 and was Chief of Service for Anaesthesia at the Hammersmith from 1995 until 2008.

His appointment as Clinical Lead of Emergency Medical Care for the 2012 London Games was among the most senior medical positions of the Olympics.
An Honorary Physician to the Queen, he became Lieutenant in the Royal Victorian Order (LVO)) in the 2008 Queen's Birthday Honours list. In 2012 he gained an Honorary Fellowship of the Royal College of Physicians, London. A founding member of the Resuscitation Council (UK) he chaired the European Resuscitation Council from 2004 to 2008, and has been a member of the International Liaison Committee on Resuscitation (ILCOR) since 1994 and its Treasurer since 2002.
From 2003 to 2009, Dr Zideman also chaired the British Association for Immediate Care (BASICS), which plays a fundamental role in the provision of pre-hospital resuscitation and trauma care in the UK. As a volunteer, he regularly undertakes pre-hospital medical shifts for London BASICS, the London Helicopter Emergency Medical Service (HEMS) and the East Anglia Air Ambulance.

Cutting risks to surgical patients

Anaesthetist advises expansion of post-operative high-dependency services

A leading UK anaesthetist has said many hospitals could significantly reduce risks to patients undergoing surgery by expanding and developing their post-operative high-dependency services.

Report: Mark Nicholls

Dr John Carlisle explained there are a number of indicators that can identify and quantify risks to patients facing an operation, and steps that can be taken to reduce post-operative mortality. That includes managing patient expectation, fully informing a patient as to those risks – with the patient even opting not to undergo the surgery – and striking a balance between 'hazardous cure and less hazardous partial cure.'

However, Dr Carlisle, who is consultant in preoperative preparation, anaesthesia and critical care at Torbay Hospital in S-W England, said: 'Probably more important is postoperative monitoring and care, partly because this phase lasts much longer than surgery and is associated with greater physiological demands. To deliver this safely, we need to expand the provision of postoperative high-dependency services and for many hospitals this might mean trebling or quadrupling their current HDU beds.'

The subject of 'How to identify a high risk patient and quantify their risk' is on the agenda at the annual congress of the Association of Anaesthetists of Great Britain and Ireland in a presentation by Dr Carlisle. 'Anaesthetists have an ethical duty to quantify harm and benefit to patients to help those undergoing surgery make better informed decisions about the procedure they may be having,' he said. 'Failing to do so risks people making decisions based upon false assumptions. We also have a clinical or organisational duty to quantify these risks, because the safe perioperative care of patients depends upon us recognising how much hazard each patient faces and distributing scarce resources – such as intensive care and Monday morning lists – appropriately.'

When it comes to surgery, Dr Carlisle said patients who are older, male, less mobile, under-weight or already have a life-threatening disease are most at risk of dying, along with those undergoing emergency surgery because they are acutely unwell and more likely to undergo surgery outside normal working hours.

'Most people having scheduled surgery don't die or become infirm because of the surgery, but substantial proportions can be unhappy with the results,' he pointed out. 'Therefore an important part of patient preparation is the assessment of their expectations and if necessary realigning them with reality. This process can contribute indirectly to a reduction in postoperative mortality and morbidity, because about a quarter of patients fully-informed of postoperative outcomes decide to decline surgical treatment.'

Anaesthetists can quantify that risk for mortality by factoring in the average mortality risk for a person of a given age and sex, and adjusting it for all known factors that independently affect this risk. However, to simplify the process Dr Carlisle has developed a calculator that can work out the risk at *https://sites.google.com/site/informrisk*

An anaesthetist also needs to ensure his colleagues are 'in the loop' as the role of other clinicians around the anaesthetist, and effective communication with them, is crucial in reducing that risk.

In helping reduce the risk of surgery, anaesthetists should look to strike a balance between hazardous cure and less hazardous partial-cure or palliation. 'The risk of dying will often be higher for a year-or-so after hazardous curative treatment, for instance complete resection of a colorectal tumour, compared to, say, stenting of a colorectal cancer that threatens bowel obstruction,' he said and added that the safety of perioperative care increases through ensuring that 'the right patient has the right operation at the right time, delivered by the right team' and that the relevant equipment, such as intra-operative cardiac output monitoring is in place. Patient risk can be further reduced by ensuring their fitness for surgery, they are taking the prescribed drugs and are of sufficient weight to undergo a surgical procedure.

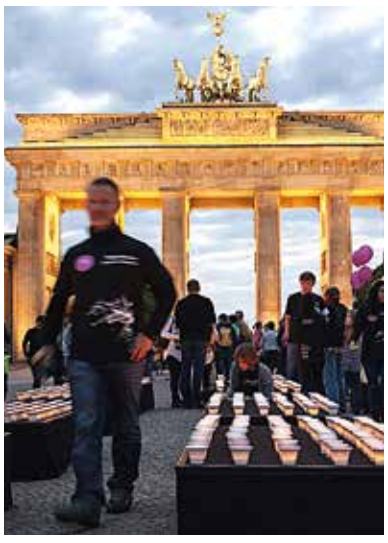
Key learning points: Understanding and communicating risk is important; risk quantification is an ethical and

Mounting systems for anaesthetic units

Intelligent mounting systems featuring CIM med GmbH's integrated data and power lines for anaesthetic technology increase hygiene in operating theatres and protect cables from damage, the manufacturer reports.

'The flexible carrier mounts can be adjusted for height and moved laterally. This enables ergonomic positions for personnel. The mounts are made of eloxised and powder-coated aluminium and are resistant to disinfectants and cleaning products. They have been equipped with the necessary component grounding for special connections with anaesthesia units. Cables with large 24-pole DVI connectors can be easily integrated to support imaging with PDM systems. The mounts, which have been tested by the TÜV, are designed for carrying heavy weights and hence ensure the needed stability.'
Details: www.cim-med.com

Height-adjustable carrier arm for monitors, connected to the anaesthesia unit.



World Sepsis Day aims to raise awareness

13 September 2012 was the first World Sepsis Day initiated by the Global Sepsis Alliance and supported by hospitals, professional associations and individuals from 93 countries. More than 100 events took place in 40 countries, inter alia in the cities Berlin, London, New York, Houston, Orlando, Beijing, Seoul, Delhi, Mumbai, Sao Paulo and Lima. It aims to raise awareness among physicians, nursing staff and the general public about this devastating disease which, despite medical care, kills about one third of all infected patients.

Dr John Carlisle is consultant in preoperative preparation, anaesthesia and critical care at Torbay Hospital, South Devon NHS Foundation Trust. His main areas of interest are perioperative risk compared to 'at home' risk; cardiopulmonary exercise testing; evidence-based medicine including systematic reviews; detection of data fabrication. He is editor & author for the Cochrane collaboration, editor for the journal Anaesthesia, author for Oxford Handbooks of: anaesthesia; day surgery; vascular surgery and an instructor on the biannual CPET workshop course. At the Association of Anaesthetists of Great Britain and Ireland annual congress, this September, he presented the session *How to identify a high-risk patient and quantify their risk.*

practical imperative, and anaesthetists should not only estimate mortality risk but other outcomes of postoperative damage and patient dissatisfaction.

Hospital Design

Giving the tiniest patients a chance

'An environment that promotes development improves the survival chances of premature babies'

The number of premature births increases continuously in all European countries – with the exception of Sweden. Every year around 500,000 children – every 10th baby – in Europe are premature, i.e. born before the end of the 37th week of pregnancy and with a birth weight below 2,500g. Along with these 'near term babies', the number of 'extremely low birth weight infants', who can now survive from the 24th week of pregnancy, has also been increasing. However, premature babies are at risk of future health problems.

Erna Hattinger-Jürgenssen MD - Gaining a medical degree in Vienna and Innsbruck, and then pursuing a specialty in paediatrics, in 2000 she became a consultant at the Neonatology Centre Salzburg and a senior consultant in 2005, frequently deputising at the Centre. To a large extent the Centre is the result of her efforts and bears her marks.
In addition to her clinical work she founded the association 'früh-R-leben' (literally 'live- and experience - earlier') for premature and newborn infants and their parents.

The parents' refuge, very near the ICU, to help them relax as well as exchange experiences with other parents

At a symposium held by Dräger during the 108th Annual Congress of the German Society of Paediatrics and Adolescent Medicine experts explained how the neonatal ward environment and parental involvement can positively impact on the neurological development and growth of a baby's brain.

Since its inception in 2008, the European Foundation for the Care of Newborn Infants (EFCNI) has lobbied for the causes of newborn and premature infants and their parents. For Silke Mader, founder member and chairwoman of the foundation, the promotion of better neonatal care is something very close to her heart as much as it is a purpose. Based on her own experience of giving birth prematurely she is raising awareness of this topic amongst the public and even with the European Parliament. The benchmarking report compiled by the foundation in 2010, which compares neonatal standards across Europe, uncovered alarming differences and a north-south divide. The EFCNI White Paper on Maternal and Newborn Health and Aftercare Services: *Caring for Tomorrow*, published last year, based on the findings of this report, is the first evidence-based paper to substantiate demands for improved care of pregnant women and newborns. The fact is that, so far, there are no unified standards across the EU, no standardised documentation systems and no obligatory hygiene guidelines for the care of newborns. This leads to very different quality standards and outcomes for those affected. The main demand is the implementation of family-orientated care, parents' rights are not acknowledged in many countries: 'Instead of viewing them as the guarantors of the children's wellbeing, they are often treated as guests on the special care baby unit,' says Silke Mader. The foundation is also lobbying for high, unified standards for the care of children and for the working conditions for staff.

Room on the ICU in the Perinatal Centre, University Hospital Salzburg, providing comfortable furniture and two incubators per room maximum

Oliver Hantke, Architect for the Federal Association 'The Premature Baby' e.V. is currently developing a website *(www.neoträume.com)* that will from 2013 provide inspiration for the professional design of neonatal intensive care units. Based on the premise that 'everything revolves around the child' he is introducing building blocks for the design of the different areas on the ward, ranging from the patient area with a protected environment for babies and parents via a buffer zone to a zone with a normal, adult-appropriate environment. Professional groups have defined ideal case standards for this purpose. Apart from conceptional approaches, examples of recently built or refurbished wards are to inspire the viewers' imagination and also to show decision makers what can actually be achieved. Neoträume considers itself as an open-ended, continuous project and a place to record dreams and wishes.

Care concept with parents

Dr. Erna Hattinger-Jürgenssen, Consultant at the Neonatology Centre of the University Hospital Salzburg, spoke of her experiences with the implementation of a type of environment and care that promote the development of premature infants, the first ward of this kind in German speaking countries. She was no longer content with the fact that, whilst physical closeness between parents and newborns is now considered to be a matter of course, it is often not possible to realise this for premature babies due to various technological limitations. After a planning stage lasting seven years, two years' building and overcoming many prejudices, the Parent-Child-Centre and Perinatal Centre opened in Salzburg in June 2010.

Based on Scandinavian ward designs, parents are automatically integrated into the care concept. A maximum of two incubators are in a sufficiently large room, with comfortable beds, along with five parent-children rooms to enable parents to carry out frequent, long sessions of 'kangaroo care', i.e. direct skin-to-skin contact with their babies. Families also have a lounge and respite area on the ward in the immediate vicinity of the intensive care ward, with bedrooms, kitchen and play area for siblings. The design of the egg-shaped new building incorporates the latest findings on noise and light reduction.

According to Dr Hattinger-

Silke Mader - After a premature birth and the demise of one of her twins, in 1999 the former nursery nurse became involved with the Parents Initiative 'Unsere Frühchen' (Our Preemies) in Munich. In 2003 she became the organisation's Federal Chair and, in 2006, its Executive Chairwoman. Two years later she was a founding member of the European Foundation for the Care of Newborn Infants (EFCNI). Silke Bahr is still its Executive Chair.

Jürgenssen, the objective of optimum care for premature babies is to continue the neurological development begun before birth, within the context of intensive care medicine. This obviously cannot be identical, but the differences compared to development in the womb should be kept as little as possible.

Silke Bahr, Marketing Manager Neonatology for Central Europe at Dräger introduced the technical opportunities that can help achieve an environment that promotes development. Apart from a lighting concept based mainly on indirect lighting, the noise level can also be monitored with the help of a noise-display. If noise levels around the incubator rise too much, an 'ear' lights up in red and visually alerts for noise reduction.

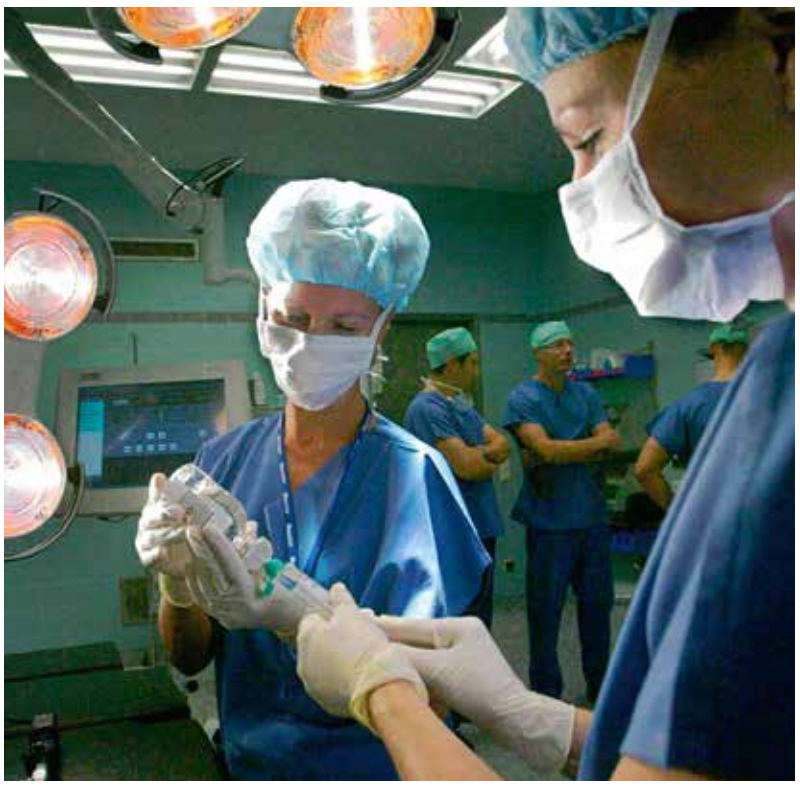
Improved incubators

The incubator design has also undergone many improvements in recent years. Dräger incubators can be closed quietly, the motor supplying warm air runs on as quiet a noise-level as possible and light from the monitors is minimised via a day-night mode setting. Potential false alarms during Kangaroo care sessions, which stress babies and parents, can be excluded. Customers can see 3-D visualisations when planning the design of a neonatal ICU. At the Dräger design centre in Lübeck the entire plan can be reconstructed true to scale and inspected for evaluation.

Silke Bahr - Following her role as Product Manager and Business Development Manager for Australia and Asia-Pacific, in 2010 she became Neonatology Marketing Manager for the Central European region for Dräger Medical Germany. With over 18 years of neonatology experience at Dräger she has accumulated comprehensive knowledge of the clinical environment and requirements for the care of premature babies.

Pre-operative risk stratification

Anaesthetists are part of a team providing optimal peri-operative care for the patient



Report: Mark Nicholls

A key part of pre-operative risk stratification must include cognitive and frailty assessments of patients in order to help identify those who may be most at risk of post-operative cognitive dysfunction, according to a leading anaesthetist. Dr George Djaiani MD, Associate Professor of Anaesthesia at Toronto General Hospital and the University of Toronto, warns that post-operative cognitive dysfunction (POCD) and delirium are relatively common after major surgery, particularly amongst elderly patients.

He said anaesthetists could play a key role in highlighting those who may suffer POCD and as a consequence must be given an influential part in planning the surgery and treatment. 'Anaesthetists are often perceived as physicians who put people to sleep. However, the first patient encounter occurs in the pre-operative clinic, well before surgical intervention takes place, except for emergencies. Furthermore, anaesthetic care extends to the postoperative period as well.

'Consequently, anaesthetists assume a role of peri-operative physicians being part of the team providing optimal peri-operative care for the patient. Identification of patients at risk of POCD and delirium pre-operatively, choosing the optimal anaesthetic and cerebral monitoring techniques during surgery, and provision of best analgesia after surgery is pivotal in improving cerebral protection peri-operatively.'

Figures show that POCD and delirium occurs in 6-30% of patients after cardiac and major non-cardiac surgery, while one year after surgery it is around 5-15%. With POCD more common in elderly patients, he said that the peri-operative team would face growing challenges to offer better outcomes as the elderly population presenting for surgery increases. 'Pre-operative risk stratification models should include some cognitive, frailty, and daily living activity assessments to establish baseline and determine brain reserve,' he points out. 'Impaired cerebral auto-regulation, and altered cerebral reactivity may get recognised during the pre-operative "brain stress testing".'

'Sometimes, for patients at high risk, less invasive surgery or at times even medical management might be a preferred option. If it is decided to proceed with surgery, more rigorous cerebral monitoring may be required and certain pharmacological agents should be avoided. Anaesthetists have been in the driving seat for years testing different hypotheses, including pharmacological agents as well as different equipment and anaesthetic techniques to minimise POCD and delirium after surgery.'

Among the pharmacological agents he suggests should be avoided are benzodiazepines, and opioid use should be minimised, though continuing the use of statins during the peri-operative period.

At Toronto General Hospital there are currently five anaesthesia-driven trials looking at reducing delirium after surgery. However, as there is no known treatment for POCD at this stage, Dr Djaiani said, it is important to continue POCD and delirium research to 'better understand the pathophysiology of these complex conditions and develop new prevention and treatment strategies.'

Teamwork is paramount in helping to improve outcomes, with the patient's family, psychiatry, surgery and nurses working together to achieve best outcomes but Dr Djaiani said that less invasive surgery and further development of interventional radiology and cardiology techniques will also have an impact and modify the type of anaesthesia used for procedures. 'Recently,' he added, 'we reported that endovascular repair of abdominal aortic aneurysm was associated with less delirium after surgery compared to the open approach.'

Dr George Djaiani is Associate Professor of Anaesthesia, Director of the Cardiac Anaesthesia Fellowship Research, and Associate Director Anaesthesia Research Cardiovascular Anaesthesia and Intensive Care at Toronto General Hospital and the University of Toronto. An authority on post-operative cognitive dysfunction (POCD), the current focus of his research team is directed at identifying risk factors, managing perioperative care, and reducing short- and long-term adverse outcomes after cardiac surgery. The main area of his research concentrates on brain injury and cardiac surgery, as well as perioperative coagulopathy and thrombosis identifying aetiology, pathophysiology, prevention, and treatment.
As a key speaker at the recent Association of Anaesthetists of Great Britain and Ireland, Dr Djaiani presented the session *Postoperative cognitive dysfunction - How much is down to the anaesthetist?*

Personalised cancer medicine

It's not a done deal yet, says expert, but it's absolutely where we are heading!

Personalised cancer medicine is much discussed, with high expectations for biomolecular decoding of various tumours and the global pharma industry developing targeted drugs to attack tumours at a biomolecular level. However, during EFO 2012, *Alexander Eggermont*, Professor of Surgical Oncology at Erasmus University, The Netherlands and General Director of the renowned Institut de cancérologie Gustave Roussy (France) warned that personalised cancer medicine its 'not a done deal yet' - nor will it be in the near future. *Bettina Döbereiner* asked this pathophysiology and immunotherapy research specialist what makes him sceptical.

'Personalised cancer medicine is still in its infancy,' Prof. Eggermont pointed out. 'By now we indeed have some targeted drugs to treat certain tumours, for example the agent Trastuzumab (trade name Herceptin) to treat breast cancer. This drug is very successful – if it's a HER2 positive tumour. It's important to understand that, for the same reason, the drug is also effective in HER2 positive gastric cancer. Thus it's less important which organ is the origin of the tumour (e.g. breast, gastric, lung) but which molecularly defined target is present at the tumour. Most tumours have multiple derailments and are very complex and therefore personalised cancer medicine is not a simple one-target/one-drug approach, but will face many complex hurdles in its development.

'For these complex tumours we are still analysing which are the driver mutations, which are the most important ones, effecting the so-called signalling pathways – pathways that guide the cell and consequently the tumour. The knowledge of this - is of course the precondition to develop targeted drugs. A major problem is that most tumours, right from the start, have different cancer cell populations, with different molecular characteristics or profiles. We call this heterogeneity, and it's an important reason why parts of many tumours are resistant to various treatments, right from the start. Besides the heterogeneity of the primary tumour itself, we have two further parameters that increase complexity. First, the profile of a metastasis differs from the primary tumour and may also differ from other metastases – depending on the location; secondly, the tumour will acquire in time more and more mutations, because of its genetic instability; so, all in all we have three levels of heterogeneity. That is to say, personalised cancer medicine only fits in very specific conditions: you need the right drug for the right patient with a right tumour in the right time.'

What possible solutions might there be to cope with this immense diversity of tumours, metastases, or even in different parts of one tumour? Why not simply combine those particular drugs that proved effective?

'We have to take a combination of different inhibitors causing a multiple pathway blocking to get an effective response to have a chance to eradicate the tumour in the end. However, not all drugs can be combined, it could be toxic. So, the question is - Which drugs should or could be combined? So far this isn't studied very well and we're trying to find out.'

Could a combination then suffice to guarantee successful treatment?

'No, this is very unlikely. There is a growing understanding and appreciation of the fact that if we do not simultaneously engage the patient's immune system then achieving cures will be very difficult. Only killing tumour cells will not cure any patient. The activation of the immune system is indispensable to ensure a successful treatment. My colleagues Drs Kroemer and Zitvogel discovered that chemotherapeutics and other tumour cell killing drugs could create immunogenic cell death or tolerogenic cell death. With immunogenic cell death cancer cells die in a way that they present their antigenes to the immune system and thus mobilise it. So immunogenic cell death is essential for engagement of the immune system and for success. In experimental systems, we could demonstrate that all the targeted drugs fail that don't present their antigenes to the immune system. Thus the question remains of how we can optimise our immune system to cooperate with all these targeted drugs, so that we get the synergy of both systems.'

If the cost of a single targeted drug causes financial problems, how can there be a realistic prospect for a combination of multiple targeted drugs?

'True – with current drug prices we cannot pay for personalised cancer medicine. We have to change the system that will lead to reasonable/affordable pricing of new cancer drugs. The current situation is not sustainable for any society and will only increase enhanced inequality of access to new drugs. We need a new type of drug development system, first with much earlier decisions about which drug to develop and which to abandon. This includes acting against 'defensive patenting', which is a way to block the development of drugs that are in competition with your own drug, even if they have the potential to be better.

'Secondly, drugs that are of essential value, and which mechanisms of action we understand well should be able to be approved more rapidly than in the current system. For instance, a drug in the BRAF-Inhibitor Vemurafenib category, used to treat late-stage melanoma, should be approved much earlier than today. A study of ours, related to Vemurafenib, showed identical data of response within 32, 130 and 650 patients. Therefore, this kind of super early efficacy-signals in phase 1 and early phase 2 studies should be sufficient for drug approval. As a complement to that, we would need more safety-evaluations, once the drugs are in the market to evaluate if the safety data remain the same and if not, to intercept and withdraw marketing authorisation. To shorten drug development is indispensable, otherwise we'll just produce things for which we later cannot pay.

'Thirdly, we need to focus on the combination of targeted drugs with host-immune-modulators. If you only develop drugs that will give a short response and only a small impact on survival, society will never pay for that. However, if you find a way how, on top of these responses, the immune system can control it for years - then you have a model. This would render a treatment for which society would be running to pay.'

How will things stand in 2020?

'We'll have a whole number of additional drugs like Vemurafenib, and then will be held up for a while due to the increasing complexity level, and hopefully we'll understand and know more about how to activate the immune system. That's why I had to qualify personalised cancer medicine as not being "a done deal", because it's not yet, but it is absolutely where we are heading!'

Barcelone: 3-4 December 2012

Conference on personalised cancer therapy

The organisers of the IDIBELL Cancer Conference (ICC) on Personalized Cancer Medicine – Manel Esteller, George Thomas, Cristina Muñoz-Pinedo and Sara Kozma – will present 21speakers for the event, all leading oncologists and cancer researchers, particularly those working in the study of genetic and epigenetic defects leading to the selection of cancer patients for new drug therapies. The meeting aims to highlight the latest understanding of biological mechanisms and natural history of cancer, thus providing novel targets for therapy, as well as to discuss the molecular mechanisms involved in the stratification of oncology patents according to the recently described molecular markers. Special focus: Epigenetics and DNA Repair and the metabolism and cell signalling areas with the updated clinical applications.

Details: http://bocemtium.com

EUROPEAN HOSPITAL

EUROPEAN HOSPITAL Publisher, Theodor-Althoff-Str. 45, 45133 Essen, Germany
Phone: +49 (0)201 87 126 850
Fax: +49 (0)201 87 126 864
E-mail: info@european-hospital.com

www.european-hospital.com

Editor-in-Chief Brenda Marsh
Art Director Olaf Skrober
Managing Editor Brigitte Dinkloh
Senior Writers John Bosky, Michael Reiter
Executive Director Daniela Zimmermann

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Austria: Michael Kraßnitzer, Christian Pruszinsky.
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USA: Kerry Heacox, i.t. Communications.
UK editorial address
55 Wey Meadows,Weybridge, Surrey KT13 8XY
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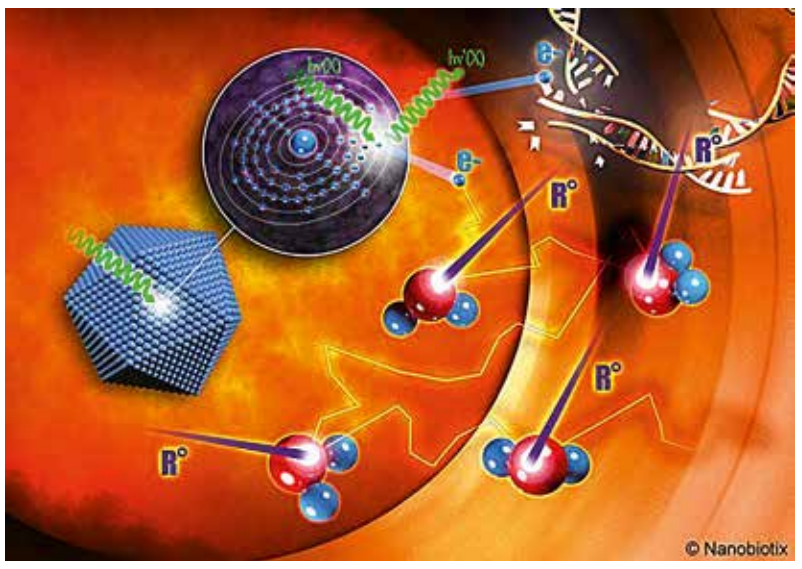
Representatives
China & Hongkong: Gavin Hua, Sun China Media Co, Ltd, Room 802, 15th Building, BinJiang Residential Quarter, Dongyuan Road, Futian District, Shenzhen, Guangdong, China, Code: 518031
Phone: +86-0755-81 324 036
E-Mail: gh@european-hospital.com
Germany, Austria, Switzerland:
Ralf Mateblowski, Hintergasse 1, 55234 Hangen-Weisheim, Germany
Phone: +49 6735 912 993
E-Mail: rm@european-hospital.com
France, Italy, Spain: Eric Jund, 2264 Chemin de Sainte Colombe, 06140 Vence, France
Phone: +33 493 58 77 43
E-Mail: ej@european-hospital.com
GB, Scandinavia, BeNeLux: Simon Kramer, Willem Alexander Plantsoen 25, 2991 NA Barendrecht, The Netherlands
Phone/Fax: +31 180 6200 20
E-Mail: sk@european-hospital.com
Israel: Hannah Wizer, International Media Dep. of El-Ron Adv. & PR Co., Ltd., 7, Leteris street, Tel-Aviv 64166, Israel
Phone: +972-3-6 955 367
E-Mail: hw@european-hospital.com
South Korea: CH Park, MCI, Room 103-1011, Brown Stone, 1330, Baekseok-dong, Ilsan-Ku, Goyang-si, Gyunggi-do, Korea 410-360
Phone: +82 2 730 1234
E-Mail: chp@european-hospital.com
USA & Canada:
Hanna Politis, Media International, 8508 Plum Creek Drive, Gaitherburg, MD 20882, USA
Tel: +1 301 869 66 10
E-Mail: hp@european-hospital.com

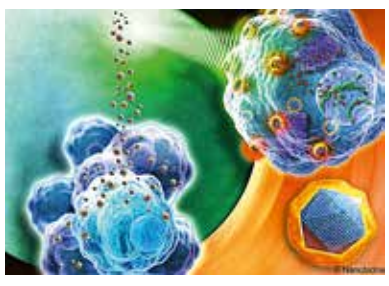
Nanomedicine

Inert inorganic particles reach selected tumour cells

Radiotherapy is a treatment of choice for six million (60%) of cancer patients annually. However, it has a crucial deficit: its therapeutic window is limited. The reason is simple. While radiotherapy is very efficient in killing cancer cells, it inevitably also damages surrounding healthy tissue. Therefore, in many cases doctors need to restrict the dose - a compromise that prevents the effective eradication of tumour cells.

For decades, radiotherapists have not been able to greatly improve the situation. They believe that even a 5-20% increase in the therapeutic window could drastically change clinical output. French nanomedicine specialist Nanobiotix has developed NanoXray, a formulation of inert, inorganic particles with a size of 50nm that can be delivered selectively to tumour cells. Consisting of hafnium oxide, they react to a standard radiation dose by emitting a shower of electrons. This is the identical physical mode of action of radiotherapy – except that hafnium oxide emits far more electrons than a water molecule, the usual target, and thereby locally increases the effective dose by a factor of nine. The radiotherapy dose in the surrounding healthy tissue is unaffected because it is not loaded with nanoparticles.





NanoXray particles made from Hafnium crystals (enlarged particle, lower right) are entering cancer cells

NanoXray can be administered without the need to invest in novel devices; it does not even require changes in standard radiation procedures. NanoXray is applied either via intra-tumoural injection (NBTXR3) or by deposition of a gel-formulation in the tumour bed during surgical resection (NBTX-TOPO). A formulation for intravenous injection (NBTX-IV) is also in development.

Upon X-ray radiation (hν(X)), NanoXray particles emit electrons (e-) that in turn lead to the formation of radicals (R°) that damage DNA molecules and other cell components

EU regulated as a medical device, NBTXR3 is in a Phase I study in soft tissue sarcoma patients. Preliminary results are expected at the end of 2012.

Today's antibiotics misuse threatens future patients

Poor quality medications also play a role

A situation has evolved that places future patients at serious risk: resistance to antibiotics has risen drastically. 'Microorganisms such as Escherichia coli and Klebsiella pneumoniae, which are commensals and pathogens for humans and animals, have become increasingly resistant to third-generation cephalosporins,' according to Jean Carlet and colleagues at the 2011 3rd World Healthcare-Associated Infections (HAI) Forum. 'Moreover, in certain countries, they are also resistant to carbapenems and therefore susceptible only to tigecycline and colistin,' they added in their call for action. The causes are numerous; overuse has been identified as a root problem.

At the Forum, 70 experts endorsed the *Pensières Antibiotic Resistance Call to Action* globally. Among them was Professor Dilip Nathwani, who chairs a successful programme in Scotland designed to implement antibiotic stewardship, an approach that he outlined for EH reporter Michael Reiter.

'Antimicrobial use and consumption in Europe continues to rise, and is a key driver for antimicrobial resistance,' he explained. 'In the UK it has been estimated that 80 percent of human antibiotic use takes place in the community, of which up to 50 percent may be inappropriate; 20 percent of use is in hospitals, out of which up to a third may be inappropriate. The consequences of this are antibiotic resistance, *Clostridium difficile* infection (CDI)-associated diarrhoea, and subsequently an increase in patient morbidity and mortality as well as in healthcare costs.' The reasons behind this, he explained, are, 'Misuse – defined as the wrong choice or spectrum of antibiotic, the wrong route, dose, or duration – and increased antibiotics prescribing is driven by a range of factors that include suboptimal clinical and laboratory diagnostics to diagnose bacterial infection, sociocultural and economic influences, defensive medicine, self-medication and poor regulation. Additional factors include poor education both of prescribers and the public, with antibiotics used to counter common viral infections, and the poor quality of the actual antibiotics also plays a role – particularly in antibiotics available in developing countries.'

Professor Dilip Nathwani MB FRCP (London, Ed. Glasg.), DTM&H, is a Consultant Physician in Infectious Diseases and Honorary Professor of Infection, Ninewells Hospital and Medical School, Dundee, UK. He chairs the Scottish Government Funded Scottish Antimicrobial Prescribing Group (SAPG), which has been tasked by the Scottish Government to take forward a national clinical antimicrobial stewardship programme. He also chairs the European Study Group on Antibiotic Policies (ESGAP), one of the study groups of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).

Describing the aims of the programme, Prof. Nathwani said, 'Antimicrobial stewardship is the term used to describe a set of interventions aimed at optimising the quality of antibiotic prescribing and improving the management of infections. In Europe, and globally, a number of initiatives are being implemented to do this. In Scotland, since 2008, there has been a government-funded multi-stakeholder antimicrobial stewardship programme – the Scottish Antimicrobial Prescribing Group* – which I chair. The programme has led to a significant reduction in the number of antibiotics prescribed in the community and hospitals that are associated with CDI, with a substantial reduction in the prevalence of this serious infection at a national level. We implemented it through organisational support and clinical leadership; through the introduction of hospital and community antimicrobial management teams; measures for improvement, and accountability targets for prescribing linked to national targets for disease reduction, such as CDI. Stewardship was also a component of external inspection by the Health Environment Inspectorate.

'The programme included the development of an integrated framework for surveillance of microbial resistance and measurement of antibiotic consumption and quality and a blended approach to educational support for all prescribers. Presently, the programme has not led to 'unintended consequences, such as worsening of resistance in key pathogens or evidence of increased mortality due to the change in the types of antibiotics used,' he pointed out. 'The measurement of other unintended consequences [e.g. aminoglycoside related toxicity] remains a key component of the programme.'

Summing up the role of the hospital's activities in this field, he said: 'The multi-disciplinary stewardship team at Ninewells has been at the forefront of this national work and instrumental in developing & using robust scientific methodology in the evaluation of the impact of the stewardship interventions on core clinical outcomes. We continue to work with other NHS Boards in Scotland, with the Scottish National Patient Safety Programme – the Sepsis Collaborative – as well as European and international collaborations to measure the intended and unintended impact of our stewardship interventions. We remain committed to sharing our experience and learning with other European and international groups.

* http://www.scottishmedicines.org.uk/SAPG/Scottish_Antimicrobial_Prescribing_Group__SAPG_

Infections in ICUs

Study proves simple soap and ointment cuts serious infections

Lead researcher
Susan Huang

California, USA – The use of antimicrobial soap and ointment will reduce bloodstream infection among patients in intensive care, according to a large study on antibiotic-resistant bacteria presented by a group of researchers at *Infectious Disease Week* 2012 in San Diego (17-21 October). 'This trial,' stated lead researcher Dr Susan Huang, an associate professor at the University of California, Irvine School of Medicine and medical director of epidemiology and infection prevention at University of California, Irvine Healthcare, 'provides strong evidence that removing bacteria from the skin and nose is highly effective at preventing serious infection in high-risk ICU patients.'

The project involved almost 7,500 patients from 43 different community hospitals throughout 16 States. The researchers randomly assigned the participating hospitals to different groups, one to focus on continual routine care by screening ICU patients and isolating patients with bacteria; another to also screen patients, but offering them chlorhexidine soap and nasal mupirocin ointment to help remove MRSA. The last group didn't screen any patients, but treated every patient admitted with a daily chlorhexidine bath and a five-day treatment of mupirocin ointment in the nose.

To better understand routine medical care in each hospital researchers spoke with the quality improvement team and patients. Working with these teams enabled important questions to be answered during routine medical care. As such, the study's findings about 'universal decolonisation' for methicillin-resistant *Staphylococcus aureus* (MRSA) may have widespread applicability to hospitals across the country.

Of the strategies tested, the one that proved to be most effective, was arguably the simplest and most straightforward – the one in which all patients were bathed daily with chlorhexidine antiseptic soap for the duration of their ICU stay, and all received mupirocin antibiotic ointment applied in the nose for five days.

Investigators found that the number of patients harbouring MRSA – not sick because of it, but at risk for later illness and for spreading it to others – dropped by more than a third. Bloodstream infections caused by MRSA and other pathogens decreased by nearly half. 'This trial provides strong evidence that removing bacteria from the skin and nose is highly effective at preventing serious infection in high-risk ICU patients," said lead researcher Susan Huang MD MPH. 'A 44 percent reduction in infection is very promising for improving medical care and protecting highly vulnerable patients. It suggests that treating all ICU patients with this strategy is beneficial. This approach may make screening for drug-resistant organisms unnecessary.'

The scientists believe that the findings of the project could help implement changes in bedside clinical practice. However, the results come with a warning: those winning measures should only be applied in ICUs, so that the bacteria do not develop resistance to the antimicrobial soap and ointment.

The study, conducted between 2010 to 2011, involved various universities, the Hospital Corporation of America (HCA); the Agency for Healthcare Research and Quality (AHR), the U.S. Centres for Disease Control and Prevention (CDC).
IDWeek was the first combined meeting of four organisations: The Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), HIV Medicine Association (HIVMA), and the Paediatric Infectious Diseases Society (PIDS).

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