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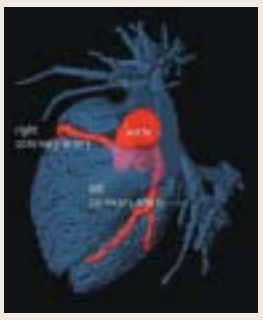

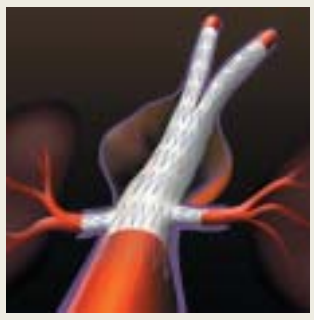

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Re-trial for Russian doctors

Illegal removal of organs

Moscow - Earlier this year four Russian doctors were acquitted of charges of murder and attempted murder. Now, however, the prosecutors have succeeded in gaining a re-trial. They claim that the four doctors were behind an organ-stealing group. The main case against them involves a man who had been treated for head injuries by the doctors, but, before this patient's death, the prosecution claimed they had prepared his body for organ removal and had even signed the death certificate.

One problem appears to be that, in Russia, doctors are allowed to remove organs for transplantation without family permission, and if no relatives object. Added to this, voluntary organ donation has not been widely accepted in Russia.

Thus, during the doctors' initial trial, with inevitably high press coverage affecting the public, organ transplantation took a huge plunge. (Surgeons had also become wary of carrying out transplants, lest they also be charged with offences). For kidney patients the situation is now dire, because Russia also does not have a sufficient number of dialysis centres to treat patients.

High flyers and high earners

€4,350 per weekend lures Europe's doctors to UK

Thousands of foreign medical professionals underpin the UK's National Health Service (NHS). In 2004, of the country's newly registered medics, two thirds of the doctors, and over 40% of the nurses, had come from other countries. In total, about 72,000 of the UK's 212,000 registered doctors are not British. That figure includes, for example, around 12,500 doctors from Africa and, from the EU, 3,764 from Germany.

Now a newer phenomenon has presented itself: 'the weekender'.

Wanting to race for a Friday night flight after a week's work in your own country, then to toil on medical emergencies through to Monday, in a foreign country where you often experience language difficulties, is not difficult to understand, if you know you will return home with €4,350 - just for *one weekend's* work. Just compare the annual income of doctors in the eight EU countries and the monthly figures presented in the boxes. The fee earned in that weekend nears what a senior physician earns in Germany *after a month's work*. No wonder an estimated 2,600 German physicians now regularly take those Friday flights.

What caused this situation? The UK is short of doctors. On top of this, last year, the NHS gave its general practitioners (GPs) the option not to work during weekends. Naturally, many do not. In addition, the British Government's move to reduce the number of doctors recruited from Africa, following pressure to prevent shortages in their own nations, may be another contribution factor.

The shortages of British doctors, and the supply and demand situation, led health recruitment agencies - which supply the NHS with doctors and nurses, for high fees - have flourished. Given the shortage of British doctors, naturally they have also trawled further for doctors. Thus, last year alone, 771 German doctors registered for the first time to work in the UK.

To work in the UK, each foreign doctor must register with the General Medical Council. This procedure involves a doctor going there in person, providing officially translated documents to prove medical qualifications, and then paying a fee of about €1,740 - less than half the fee mentioned for one weekend ahead.

Germany: Breakdown of approximate monthly incomes in euros	
Hospital doctors' salaries vary according to age/grade	
Junior doctor (aged 32, single)	3,500
Specialists or those who remain in the same grade for 5+ years	3,950
Senior physicians or heads of small departments (married with one child)	4,700
Head of large department with some head physician duties	5,300

Hospital doctors' salaries	
Country	*Salary in €*
Britain	104,000
The Netherlands	97,000
France	90,000
Italy	81,000
Sweden	56,000
Denmark	50,000
Germany	46,000
Spain	44,000

These euro sums are approximate, and based on a study by the UK's National Health Service (NHS)

Last year, the number of German doctors registering in Britain, compared with 2003, more than doubled. Frank Montgomery, Head of the Marburger Bund (Germany's biggest medical union) said that, of the country's 145,000 hospital doctors, about 6,000 younger ones work abroad permanently. He believes this is due to the working hours, hospital hierarchy, and the low income in their own country. Only after aged 28 do they earn better figures, yet their working hours can reach 80 per week. Ten years ago, he added, almost all medical students completed training, but now a quarter abandon studies, and another 25% choose different professions after qualifying.

In Germany there have been pay protests and even strikes, and difficult negotiations continue for labour agreements. However, Frank Montgomery also believes discussions should also be focused on German academic and public sector structures. Why, he asks, cannot a senior physician receive the equivalent of a private-sector salary?

Meanwhile, in Britain, some doctors have expressed concern that their foreign counterparts do not understand dialects in various areas of the country, so cannot communicate well enough with patients - nor do they understand the healthcare system sufficiently. In addition, some of the incoming doctors have spent hours in transit to the UK - too many to be alert enough to work.

Danger Inaccurate sphygmomanometers

United Kingdom - 53% of aneroid sphygmomanometers used to measure blood pressure gave inaccurate readings during a study led by Professor Andrew Shennan, the Government's chief adviser on blood pressure measurement (Pub: *Blood Pressure Monitoring*. 10(4):181-188, August 2005). Overall one in five devices was found to be of poor quality or faulty, indicating the potential for misdiagnosis that could affect treatment decisions. Professor Shennan pointed out that among over 100 models available on the market under a dozen would pass validation tests.

Currently aneroid, mercury and automated sphygmomanometers are used in general practitioners' surgeries and hospitals but aneroid devices are more frequently the choice due to their mobility, as well as recent health/environment concerns about the mercury equipment.

The study concluded that if blood pressure readings are being over-estimated by 3mmHg across the population, the number of patients diagnosed as hypertensive would increase by 24%. Underestimation by the same amount would result in 19% being diagnosed with better blood pressure than was the case.

The Department of Health is reviewing the Blood Pressure Committee's recommendations - which include calibrating aneroid devices at least once a year - and new guidance is expected shortly.

contents

NEWS

Smoking linked to atherosclerosis

Although, smoking kills so many people in the world the knowledge about pathophysiological processes is still extremely sparse, says Dr David Bernhard, Head of the Vascular Biology Working Party, in the Experimental Pathophysiology and Immunology Department, Biocentre Innsbruck, Innsbruck University. 'With the help our research we were able to shed light on how the atherosclerosis-risk factor smoking causes atherosclerosis.'

"When we started to focus our research on the interaction of smoking and atherosclerosis, the only thing that was well established, was the firm clinical and epidemiological knowledge that smoking causes/accelerates atherosclerosis. This knowledge was expanded by a study from our group (Knoflach M. Circulation; 2003 Sep 2;108(9):1064-9.), where we demonstrated that cigarette smoking is indeed *the* most important risk factor for early atherosclerotic vessel wall changes in healthy young adults. To our surprise, when we screened the literature to read about the pathophysiological processes that connect smoking with atherosclerosis, we found very few studies. Despite the existence of an enormous number of excellent *ex vivo* analyses that correlate smoking with atherosclerosis-associated factors, mechanistic studies were missing. Probably, the most likely explanation for this was the fact that good *in vitro* models to study these phenomena were missing.

This prompted us to set up an *in vitro* system that mimics the *in vivo* properties of the lung enabling the exchange of the smoke chemicals. It was our plan to set up a system with *in vivo*-like chemical transfer form the gas phase into the circulation. We designed and optimised the system in co-operation with chemists from the Institute for Analytical Chemistry and Radiochemistry in Innsbruck. Cycles of system adjustment, chemical analyses of the generated extracts, and comparison to smoker blood chemical content, finally led to the present chemically, well defined and in vivo-like system.

After having set up the 'smoking machine' we added the smoke constituent (SC) extracts to vascular endothelial cells, which are known to represent the primary site of vessel wall damage that initiates atherosclerosis. The smoke chemical concentrations were applied at 'physiologically' relevant concentrations.

The effects observed could be divided into three phases:

Damage phase: SC-mediated cellular protein oxidation followed by a fast, yet reversible contraction of endothelial cells within one hour after SC addition.

Alert & repair phase of the cells with massive up-regulation of oxidant defence and a secretion of cytokines and chemokines.

A decision phase (not starting before 12 hours of treatment) characterised by either an induction of a necrosis-like cell death or survival characterised by the return of cellular transcription activity as in cells before the addition of SC.

Further, we could show that cigarette smoke contained metals in cooperation with carbon and nitrogen based radicals oxidise endothelial cell proteins. Most importantly, this leads to damage of the structures of the microtubule system culminating in their collapse. Consequently, cytoskeletal and intermediate filaments collapsed resulting in vascular endothelial cell contraction. Electron microscopic analyses highlighted that not only gaps between cells opened, but also that transcellular pores opened. Since increased permeability of the vascular endothelium is known to constitute a prerequisite for lipid deposition and infiltration by monocytes of the vessel wall, these findings highlight for the first time a functional patho-mechanism via which smoking causes vessel wall changes known to contribute to atherogenesis.

In addition, we demonstrated that endothelial cells stressed with smoke chemicals start secreting P-selectin, cytokines, chemokines, and present heat shock protein 60 on their surface. By comparing these results with patient sera (own data and literature) it could be shown that the in vitro data accurately reflect events that occur in vivo. Finally, depending on the dose and duration of the treatment, endothelial cells underwent cell death, with clear signs of necrosis. However, this cell death did not occur before 12 hours of treatment, which is not typical for classic necrosis. Some recent evidence suggest that this cell death might be the result of the cells 'will' to undergo apoptosis, but this seems to be inhibited by smoke chemicals. As a result vascular endothelial cells switch on a rescue pathway that leads to necrosis. Necrosis is known to cause inflammation, and since inflammation contributes to all stages of atherogenesis, necrotic endothelial cell death by smoke chemicals is likely to initiate this vicious circle."

'Non-beating heart' lung transplants

The Netherlands - Two lung transplants, using lungs from 'non-beating' donors, have been successfully performed at Groningen University Hospital for the first time in this country. The hospital now expects to increase lung transplants by 25% - about 50 operations annually.

Lung transplants in the Netherlands have doubled in the last two years due to the acceptance of less severe criteria for the acceptance of donor lungs; better preservatives for the organs and the opening of the country's second lung transplant centre. Nonetheless, costs plus the shortage of donor lungs still leave an ever-growing list of patients awaiting transplants. To meet the shortage, along with its 'beating heart' donations - from brain dead donors whose breathing and blood circulation were artificially induced till the moment of organ extraction - the university hospital began its 'non-beating heart' lung donation. This means that the donor's blood circulation and heart have stopped and the patient is dead.

The first pair of lungs was transplanted in to a patient with cystic fibrosis, with extremely little lung function, whilst the second pair was implanted in a patient suffering emphysema. In both cases the donors had severe brain damage, in whom no brain death could be diagnosed. After diagnosis of the death of both donors the lungs were washed with preservatives and removed within 30 minutes. Later, the lungs were implanted in the patients.

Non-beating heart donations of kidneys and livers have take place for several years in the Netherlands, and those results are comparable with results of transplants with organs from heart-beating donors. Lungs are the last organs added to the non-beating heart donation protocol and they can be removed along with other organs from a formerly fit donor.

GP's and minister on speaking terms again

By Michiel Bloemendaal

The Netherlands - On 25 May 10,000 Dutch GP's went on strike in the Hague, blaming the minister of health, Mr. Hans Hogervorst for too little pay per patient and their fear of too much intervention from insurance companies regarding treatments. What else could they do to pressure the minister? No evening and weekend duties? Or ask for fresh negotiations?

The minister believed he had negotiated sufficiently, and said so in letters to the doctors, which many returned them unread. The minister had offered €48 per annum per patient and €7 per visit. However, the GP's feared that when, on 1st January the new health system would begin, their income would be drastically reduced and they would face far more administration to negotiate with health insurers. (In the new system, GP's would have to hand over a part of their expenses remuneration to the insurers, which they had fought against since November).

What was the reaction of their counterparts in the hospitals? They only feared extra work, but they did make arrangements and planned extra staff in first aid units during the strike. Checking on several hospitals in the region I discovered barely a problem, and patients did not suffer, except financially. (In Holland a health service patient receives a bonus at the end of the year if he/she has not visited a GP too often. Visiting a hospital reduces that bonus).

Negotiations began again. This time, it was successful. With the help of a mediator, first members of the Dutch association of GPs agreed with new financial plans. In addition, the Minister of Health said he was pleased with the result - indeed, he received the cabinet's blessing: by reshuffling a few million he has remained within the limitations of his budget. As for the insurers, although they had to accept some measures that were less attractive than those in the original plans, they too opted to accept the final propositions.

The plan: From 1st January 2006, GPs will be paid €52 per registered patient per annum and Ä 9 per visit. (Originally the doctors asked €55 and €11.56 respectively. Additionally, doctors can ask insurers for means to finance and support their practices: €49 million compensation for work in poor districts and those with many elderly patients, about €25 million and for modernisation and new local initiatives. Furthermore, there will be no alterations in the general policy in the next two years.

8th European Health Forum Gastein (EHFG)

4-8 October 2005

Austria - The politics of healthcare, specifically in Europe, will attract ever more participants from political arenas, healthcare administrators and medical companies to Bad Gastein this year. Along with the EU Health Commissioner Markos Kyprianou, Ministers and Secretaries of State from Austria, Finland, Ireland, Lithuania, Romania, Slovakia and Hungary have already confirmed their attendance.

The focus will be on e-health and personal responsibility, and a separate event will cover infrastructure investments. Pointing out that, along with plenary sessions and 14 workshops, there will be six forums, and a separate event with over 100 specialist lectures by leading experts and politicians involved in healthcare, covering the following areas:

- **Civic participation and personal responsibility**
- **Health as a burden... or as a growth factor?**
- **New impulses from the European Commission (EC).**
- **E-health**
- **Promoting investment in the framework of the EU Structural Funds.**

The EHFG will hold a separate event on 4 October, where high-ranking representatives of the EC, OECD and the WHO will be present. This aims to inform and prepare decision makers.

It has always been the most important objective of the EHFG to introduce new developments in healthcare politics and administration, and to be a think tank for these, the EHFG president Gûnther Leiner pointed out. 'With our key topics we are tackling the "hottest potatoes" in current healthcare politics - if no significant progress is made in these particular areas, the enormous scientific progress in modern medicine will be of little benefit.'

Details: info@ehfg.org
www.ehfg.org

Nominations sought for Dan David Prize

Israel - For the fifth consecutive year, the Dan David Prize, headquartered at Tel Aviv University, will award three prizes of US$1 million each for achievements having an outstanding scientific, technological, cultural or social impact on the world. Named after Dan David, international businessman and philanthropist, the prize is funded by the Dan David Foundation.

Each year, fields are chosen within three 'time dimensions' - past, present and future, and laureates for a given year are chosen from these fields. This year the selected fields are: *Preserving Cultural Heritage: Individuals' Contributions (past); Journalists of Print Media (present); and 'Cancer Therapy (future)*.

The laureates annually donate 20 scholarships of US$15,000 each to outstanding young researchers (doctoral and post-doctoral students) throughout the world in the chosen fields.

The 2006 Dan David Prize in the Future Time Dimension (Cancer Therapy) will recognise individuals' initiatives aimed at reducing cancer-related mortality and alleviating the daily suffering of cancer patients. It will honour individuals who have made outstanding contributions to the development of the field of cancer therapy in its classical aspects including surgery, chemotherapy and radiotherapy, or in more contemporary aspects such as gene therapy, immunotherapy, biological therapy and targeted therapy.

Bucharest-born Dan David founded the Prize in 2001. As president of Photo Me International PLC, which makes automatic colour photo booths and other professional photographic equipment, Mr David became a philanthropist and has since wished to aid and foster those involved in developing and advancing world knowledge of the past, present and future.

Electronic register to speed treatments

Germany - An electronic register, set up by the health fund Techniker Krankenkasse (TK) and the German Federal Association of Cardiologists (BNK), has enabled clinics and rehabilitation centres in Munich and Hamburg to gain direct access to electronic patients' records (EPRs). Doctors at the centres are now co-ordinating their work to achieve speedier responses and treatments - not just in emergencies.

TK and BNK report that the system is to be extended to further regions around Germany this year.

NEW

Filing and mailing in one smooth move

By **Michiel Bloemendaal**, our correspondent in the Netherlands

The Netherlands - Sending mail when on a train, or filing handwritten notes in the PC without carrying a laptop, seemed but a dream. To add patients' medical details directly to their files was even more of a fantasy. That is, until a new system landed in the Netherlands from Germany. I recently visited the firm Meetpapier, based in Wormer, near Amsterdam, to see the phenomenon - Dotform technology.

Meetpapier is well known in Dutch healthcare for delivering, for over 30 years, all kinds of paper products, e.g. formulas for ECG and EEG registration. However, due to the burgeoning use of computers and printers in healthcare institutes and hospitals, Meetpapier needed to present other products. The firm's mother company, Diagramm Halbach, in Germany, had the solution: Anoto-technology, in which a special pen writes on digital paper and then those details can be filed in a PC.

The digital pen - This can store up to 150 pages of written data and, when ready, it can be uploaded from the pen to a server - automatically - whenever the pen is inserted into a docking station connected to the computer by USB cable or by Bluetooth link to a mobile phone that links to a web server. Power recharging is via the docking station or a separate power cable. The data in the pen includes all positioning co-ordinates and the time they were recorded, plus the pen's individual ID number.

Digital paper - The second component is a dotform digital form, which resembles any other form, and is printed on the same paper or substrate as a regular form. The only difference is a very fine dot grid printed on the background. The pen reads this dot grid as absolute co-ordinates, which tell it where and on which page it is writing. Diagramm Halbach is the first printer in Germany to undergo certification for this process, and they are certified to print forms with that dot grid.

Printing - A special Swedish technique is used to print the paper. The dots are placed in the matrix of 6x6 with a surface of 1.8 millimeter2 whereby a per-dot space of 0.3 by 0.3 millimetre is available. Due to the method of production, each sheet of paper printed in this way has a completely unique character, so it is always clear what information is imported to which place. Thus the pen can register what has been written, then the written text can be used in various systems, and it is also clear when the data were imported and by whom. Via a minuscule camera, the pen records written text in its own memory - storing 100 written forms. The pen not only files written text, but also registers the moment it was filed, proving the authenticity of written text, by which mailed signatures are authorised.

Hospital applications

Possibilities are enormous - there is ample need to send e-mails without a PC or notebook, but the big advantage of this system is the chance to register medical data, for example, in an electronic patient's file. The data are written on a specially developed form and could be filed immediately in the computer system, to be turned by ASCII into reports and other documents.

It is even possible to mark on a form, via a 'painline', how much pain a patient is experiencing, which can be shown immediately on a computer screen. Another option: on a form showing a drawing of a human body, the position where a pain is located could be marked, eliminating the need to describe the zone.

A further advantage is that, although each ward may design its own form, all data could be filed in a uniform way, for use in all wards, without extra handling and adaptation, thus saving considerable time.

Try it - The new system, presented by Diagramm Halbach in Europe as Dotforms, is offered as a starter kit. For six months, a hospital, ward or individual doctor can use the pen, plus a pack of paper and other necessities, to explore the possibilities, develop their own forms and develop these further with help from Dotform.

Finally: This system is not only for patients' data filing, but also for coping with statistics available online or as stand-alone.

E-mail details: geldof@meetpapier.nl

Creating

Information is as vital a resource in healthcare today as the scalpel, writes **Kevin Dean**, adding that patients also expect to have access to the same level of high-quality, timely, customer-centric healthcare services as they have for banking, insurance, travel, and retail interactions. So why, he asks, do healthcare services still lag behind other organisations? The author also outlines how far some EU countries have progressed today

In the late 1990s, the healthcare industry incubated a series of e-health initiatives but today e-health is still viewed as 'special' projects, outside of the normal day-to-day management of care, and there are powerful barriers to extending the use of IT in healthcare. However, healthcare services can no longer ignore the importance of accurate and timely information.

However, to be truly effective, that information must be securely connected across organisations, professional specialisations, and increasingly, national boundaries.

Thus e-health must evolve into 'Connected Health', meaning that we must focus on ensuring the secure and timely flow of patient-care information to its point of need. A modern health system must have a portfolio of activities that connect citizens, patients, clinicians and managers:

- Clinical information and tools dealing with complete information set on patient treatment
- Continuous retraining of professionals (and patients) in the most effective treatments and prevention of diseases
- Operational management of healthcare organisations (HR, finance, supply chain)
- Patient/public engagement to help them manage lifestyle, chronic diseases, and communications when under treatment
- Public health and performance monitoring across regional or national health systems.

Such activities must be underpinned by a secure and increasingly interactive infrastructure that allows data to be shared safely and effectively for treatment and prevention. Making this connected environment possible is a Cisco Medical-Grade Network that acts as a digital nervous system, securely and reliably carrying data, voice and video to wherever needed.

Creating Connected Health in Europe - Fortunately, many regional and national governments in Europe have recently recognised the importance of connected information in healthcare. The key change is an increased effort to move from isolated e-health projects to a systematic approach that ensures access, quality, and lower cost of care across wide communities. However, each country's individual culture, funding, and administrative systems determine very different approaches to creating a Connected Health environment.

Two countries with contrasting approaches are England and Denmark. In 2002 England's National Health Service (NHS) created a single national programme that provides standardised clinical information tools and record management. Resulting from ambitious goals and schedules, England now has a strong national IT governance structure supported by a multibillion-Euro fund, nationally led procurement and specification of information and technology services, a critical infrastructure that links regional and local organisations securely, and a newly formed organisation that creates national plans and provides resources.

TROUBLE for the world's biggest healthcare IT project

United Kingdom - The £2.3 billion National Programme for IT (NPfIT), being set up for the National Health Service (NHS), is under threat because there was so little consultation and communication from NPfIT officials and this posed a threat to the programme being successful, according to a study carried out at the London School of Hygiene and Tropical Medicine (LSHTM) and published in The British Medical Journal. The LSHTM study also suggests that, although planned to be operational by the end of 2007, the NPfIT programme is falling behind schedule in key areas.

Dr Naomi Fulop, LSHTM health policy researcher, added that, among the 23 managers and clinicians interviewed in four hospital Trusts, some clinicians felt uninvolved and wondered if the new system would actually meet their needs.

The researchers also warned that, while the new system is being developed, hospitals must continue to use their old IT systems - including, in some cases, those in radiology and pathology. 'A new patient administration system has to be installed in every Trust. While Trusts are waiting for this, there are concerns, including concerns for patient care,' Dr Fulop explained.

Although hardware/software for the new IT system will be centrally funded, managers also said they were uncertain about where funding would come from for staff training and to cope with other work changes foreseen when the new NHS system goes online.

'We are not saying the introduction of a new system is not a good thing,' Dr Fulop concluded. 'It is, and it will take the NHS forward.' However, unless these concerns are addressed, she added, 'There will be delays in implementation and a less-than-optimal use of the new system when it is finally introduced. And this will be a bad thing for all concerned.'

1,000,000 e-cards delivered

Austria - The millionth social insurance e-card has been delivered since national distribution began at the end of May.

At the Munich-based firm Giesecke & Devrient (G&D)*, which provides the card, Michael Nitz, head of the Industry and Government division, predicted that all eight million cards will have been delivered by November.

Aiming to replace Austria's current paper-based healthcare vouchers with an up-to-date electronic health card, in April 2004 the Federation of Austrian Social Insurance Organisations commissioned G&D to develop a high-performance smart card. (This e-card is also the European Health Insurance Card). By the end of that year, in an initial test phase the e-card went on trial in two practices in Burgenland, in real-time operation. When the tests had been completed successfully at the end of February this year, the trial was expanded to take in 80 medical practices with around 110,000 patients in the Eisenstadt, Neusiedl, and Rust districts. After that successful trial, countrywide delivery of the e-card began.

Connected Health in Europe

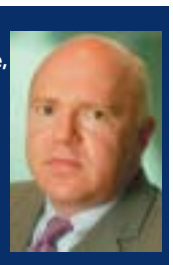
Denmark, on the other hand, has seen comparatively slow, largely user-led and modest increases in functionality over the past 10 years. Led by MedCom, a temporary project organisation chaired by the Danish MoH, the country has sustained standards for clinical messaging. With modest budgets and light staffing, direction is determined by consensus over time. Clinical acceptance has been high, and Denmark is now sharing many lessons learned with other countries (e.g. Baltic E-Health Exchange).

Alternative approaches can be seen in Germany and France. Germany, with its compulsory, highly regulated care system, has few options to encourage dramatic changes in the use of information in healthcare. However, Germany created a national smartcard programme with rapid implementation targets to give each of its 80 million citizens access to a transportable identifier and basic medical record. To increase safety and citizen mobility, the country is also taking a leading role in European interoperability initiatives.

France is looking for ways to control growing healthcare costs by transferring health records between organisations more efficiently. However, its fragmented national, regional, and local management; and its relationship to social security for payment makes for some difficult decisions in terms of budget creation, governance model, and balance between centralised and localised solutions. In the meantime, leading hospitals such as the Centre Hospitalier d'Arras are demonstrating the importance of Connected Health systems. The hospital has transformed its operation from the ground up by re-building the campus, automating administrative processes and enabling a new work culture. A state-of-the-art Cisco medical-Grade Network has provided mobile access to centralised data for hospital staff and regional health centres, helping to improve efficiency, reduce costs and enhance patient care.

Most interesting is the contrast between Western and Eastern Europe. Western European countries, with decades of legacy systems, may well proceed slowly compared to their Eastern neighbours. The new EU members Hungary, Estonia, Slovenia, as well as Bulgaria are developing remarkably sophisticated communication infrastructures, have little legacy and scepticism to overcome, and often have a more general healthcare reform programme to drive information usage. These countries have the opportunity to leapfrog to a Connected Health system in short order and, in the next few years, deliver world-leading health systems where information and knowledge are among the patients' and clinicians' most important tools.

For all European countries, the 'acid test' for their development of Connected Health is to assess the completeness of their vision and funded plans for IT in healthcare. These include clinical treatment, knowledge and learning, operational management, patient engagement and public health supported by a secure, resilient, and interactive infrastructure. Those with a comprehensive vision for Connected Health will gain immense benefits from information-transforming healthcare.



Kevin Dean, Director of Public Sector Healthcare, Internet Business Solutions Group, Cisco Systems Inc. helps public sector healthcare organisations to develop policies, strategies and implementation plans for connecting healthcare supported by IT. His team works with many governments, as well as regional and local public healthcare providers around Europe. He is editor of the IT book *Connected Health - Essays from Health Innovators* (ISBN 0-9546445-0-6. Premium Publishing, 2003/4), and he has produced, in conjunction with the Healthgrid Association, a Whitepaper discussing the use of grid technology in Healthcare (November 2004).

Along with eight million cards, G&D is delivering a complete solution that includes an electronic card management system. The numerous functions on an individual card were made possible by the Card Application Management System (CAMS), which manages all data and applications on the card throughout its life. 'A system such as this is essential if future additions to the card functionality - whether already planned or potential options - are to be managed without replacing the cards,' G&D points out.

Starting in 2006, the Austrian government is said to be planning additional applications for the e-card: it is pre-set to be used as a citizen's card and ideal for use as a high-tech ID document in e-government applications, as envisaged by the Austrian authorities, G&D says. 'Official requirements for signature functions, encryption processes and storage capacity are already met in full.'

*** In 1852, Munich-based Giesecke & Devrient began as a printer of securities, then specialised in banknote production. Since 1970, the firm has developed solutions and complete systems for automatic currency processing. Today the international company produces smart cards and provides solutions in telecommunications, electronic payments, identification, health, transportation, and IT security.**

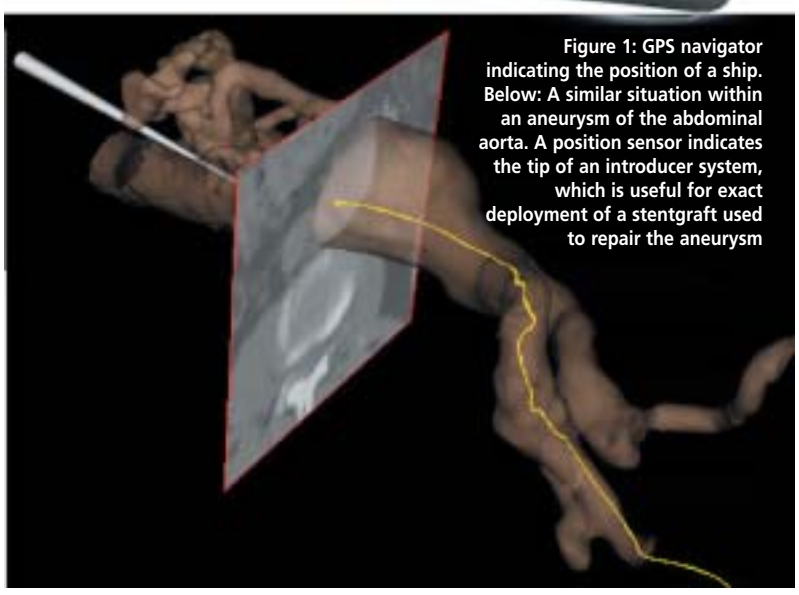


Figure 1: GPS navigator indicating the position of a ship. Below: A similar situation within an aneurysm of the abdominal aorta. A position sensor indicates the tip of an introducer system, which is useful for exact deployment of a stentgraft used to repair the aneurysm

In our last issue we featured the **Future Operating Room Project** developed at St Olavs Hospital, University Hospital of Trondheim, Norway, a collaboration between the hospital and the Norwegian University of Science and Technology. There, highly promising research on navigation is being carried out in co-peration with the research foundation Sintef Health Research. Professor of Surgery **Hans O Myhre** (above) of St Olavs and Senior Research Scientist **Jon Harald Kaspersen** PhD (below), of Sintef, describe the project's aims, their development and clinical testing of the navigation system CustusX, and the need that has now arisen for industrial collaborators to take the team's discoveries forward to expand indications for endovascular therapy in general

IGS

The GPS of arteries

Image-guided surgery (IGS) is based on an evolving technology, and is mainly developed for minimally invasive procedures. Minimally invasive treatment has expanded tremendously during recent years. It represents a decreased trauma to the patient compared with open surgery. This could again lead to shorter convalescence and hospital stay and less postoperative pain for the patient.

So far, the majority of developed systems for IGS have been designed for neuro-surgery, but other clinical applications are emerging, such as otologic procedures, hepatic surgery, orthopaedic surgery and endovascular procedures. In the most advanced systems available today, IGS provides the surgeon with a two- (2D) and three-dimensional (3D) visual 'road map' of the patient's anatomy, including the surgical instruments used during the procedure. This is similar to the situation where a ship with a GPS (global positioning system) installed can plot its position on a map (fig 1). Surgical navigation depends on a 'map' of the body, such as a CT-volume combined with information about where the surgeon's tool is located. The latter is provided by a positioning system. Prior to the development of IGS, surgeons performing minimally invasive surgery (MIS) could only see the surface area visible from the end of the imaging device, e.g. a laparoscope. IGS overcomes this limitation and provides the surgeon with real-time enhanced visualisation. Thereby the surgeon can gain access to anatomic areas that otherwise would be difficult to reach.

An IGS system combines a high-speed computer system, specialised software and tracking technology. On this computerised system the actual movements of the surgical instruments are correlated with the patient's preoperative medical images and are displayed on the system's monitor. The precision of computerised instrument localisation and navigation is critical for manoeuvring safely within concealed anatomy and for the surgeon to perform more precise and careful surgery. However, most IGS systems are based on preoperative images, sometimes acquired the day before surgery. This means that, as surgery proceeds, the images could become continuously less representative for the actual anatomy of the patient. Introducing intra-operative imaging modalities, such as ultrasound, can solve this problem.

Prior to surgery, the MR/CT images are imported into our in-house developed navigation software, CustusX, and reconstructed into a regular 3-D volume. The preoperative MR/CT images are registered to the patient. Surfaces of a few essential organs are extracted from the image data and visualised in a 3-D scene. The surgical tool controls the visualisations on the navigation monitor, and these images are updated continuously (in real time) according to both position and orientation of the pointer.

In addition it is possible to distribute the 3-D intra-operative scene to the radiology department using CustusX. Both the radiologist and the surgeon in the operating room are able to interact with the data. With this collaborative feature it is possible for the surgeon to get expert advice without having the radiologist present in the operating room.

Endovascular therapy

Endovascular techniques are increasingly used in the treatment of diseases of the main blood vessel (aorta) in the chest or abdomen. Previously, it was necessary in all cases to use large incisions and these operations were more traumatic, necessitating a longer stay in the intensive care unit (ICU) and the ward. Following minimally invasive surgery e.g. of an abdominal aortic aneurysm, the patient can get out of bed after a few hours and prepare his own breakfast the next morning.

However, so far some patients cannot be treated by endovascular technique because the disease is rather extensive without a place for fixation of the stentgraft. A stentgraft is a synthetic prosthesis consisting of a textile part with a thin metal net on the inside. The stentgraft is compressed and delivered into an introducer system. This implant is introduced into the vascular system through a small incision in the femoral artery in the groin and regional anaesthesia is applied. As soon as the proper position for the stentgraft is obtained the introducer system is withdrawn and the stentgraft expands. It is fixed to the arterial wall by radial forces, hooks and barbs. The patient is awake during the procedure. In most cases this technique is used for aortic aneurysmal disease (dilatation of the aorta) or so-called aortic dissection where the blood is running in a false lumen within the arterial wall.

In order to offer endovascular techniques to a broader group of patients, there is a need for stentgrafts with side branches or fenestrations, which can lead the blood from the main prosthesis into the major arterial branches to the head, arms, kidneys (fig 2), liver and bowel. To obtain this there is need for a new prosthesis, as mentioned. Furthermore, we need flexible introducer systems and the stentgrafts with the side branches need to be deployed accurately and easily.

The surgical tools used in endovascular therapy are guidewires and catheters. Therefore, navigation will depend on well-functioning micro-positioning sensors, which can be adapted to these small instruments. We also think it is possible to adapt micro-positioning sensors (<1mm) to the stentgraft itself. We are looking for industrial collaborators who can combine the small sensor with catheters, introducers or perhaps stentgrafts, and think that this is going to expand the indications for endovascular therapy in general. For navigation our own system CustusX meets these requirements.

We are also using the so-called DYNA CT principle (Siemens) where the C-arm of an angiography unit rotates providing us with real-time 3D-images of the vascular tree. With these techniques we think that within a few years we will be able to repair most parts of the arterial system using minimally invasive technique.

The navigation system could also be useful for re-operations where arteries and other structures are embedded in heavy scar tissue and where dissection is difficult. Development and clinical testing of CustusX will be one of the main activities within the endovascular Future Operating Room project at St. Olavs Hospital in Trondheim.

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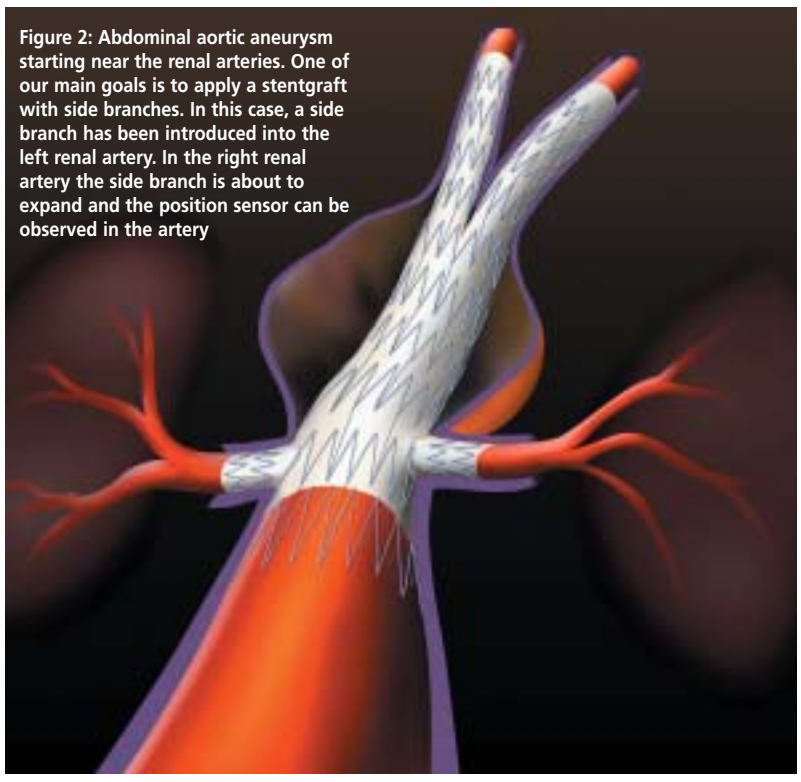


Figure 2: Abdominal aortic aneurysm starting near the renal arteries. One of our main goals is to apply a stentgraft with side branches. In this case, a side branch has been introduced into the left renal artery. In the right renal artery the side branch is about to expand and the position sensor can be observed in the artery

Mini gamma camera for radio-guided surgery

France - The first EC marked mini ambulatory gamma camera has been launched by Euromedical, which specialises in antra-operative detection and is part of the Eurorad group. Named Minicam, the system was developed for radio-guided surgery, to precisely locate radioactive-tagged tissues (sentinel node, tumour etc.) emitting gamma radiation, which allows the smallest possible incision to be made.

'With its CdTe technology detector head (camera) and a g-Cam electronics module, the Minicam system ensures very rapid detection (one minute) of the sentinel node or tumour, saving a significant

amount of time and providing a gain in precision for the surgeon,' the firm announced. 'Specially designed for small operative fields, the MINICAM also helps to ease congestion in conventional nuclear medicine departments, that can thus be reserved for examinations requiring more cumbersome equipment.'

Connected to a desktop computer, the Minicam system provides visualization of images being taken (acquisition software installation disk supplied). The detector head, made with cadmium telluride detectors (CdTe or CdZnTe), is designed for low-energy detection (30 - 200 keV). 'It has excellent spatial resolution and provides high quality pictures,' the firm pointed out.

The camera contains all necessary modules for signal processing, and the software allows selection of the kind of picture wanted for display as well as various acquisition parameters.

The system, which is installed on an ambulatory cart, is fixed and set up with a Geomed Assisto fixing arm (stand).

Currently the Minicam system is in use at the Institut Curie and Institut Gustave Roussy, and several are used in Spain, the Netherlands and the United Kingdom.

Details: www.em-instruments.com

50% more light yet cool

Germany - Chromophare D510, D540 and D660 surgical lights - newly launched by

Berchtold GmbH & Co KG, of Tuttlingen, incorporate the firm's new Reflective Illumination Technology (BRITe), providing 50% more total light while ensuring surgical site coolness. The maker reports that the halogen light technology has a unique internal bulb coating that reflects radiant energy back to the bulb filament and generates more useful light: 'Combined with our custom colour-correction filters and proven polygon reflector, the natural colour-rendering properties of the Chromophare series have been maintained. The new surgical lighting system delivers uniformly brilliant, penetrating and shadow-free lighting to surgeons performing both large-surface and deep-cavity procedures.'

Along with the Chromophare range, also produces the Supersuite Integrated OR Solution, Orics operating theatre communication equipment and Operon Surgical Tables for operating theatres.

Ophthalmology
Perforating keratoplasty

Germany - Four penetrating keratoplasties using the Femtec femtosecond laser have improved the vision of all the patients, according to a report from 20/10 Perfect Vision Optische Geräte GmbH.

Dr Mark Tomalla, of the Centre for Refractive and Ophthalmic Surgery in Duisberg-North's eye clinic, used the system to treat transparent as well as scarred corneal tissues. Apart from flap preparation during Lasik procedures, the Femtec femtosecond laser was reported as very effective in the preparation of tunnels before implanting ICRS (intracorneal ring segments) and performing cuts for AK (astigmatic keratotomy) with 'impressive postoperative results'

Drug-eluting stents

New research to be presented at the ESC Congress

By Ian Mason

Professor Sigmund Silber

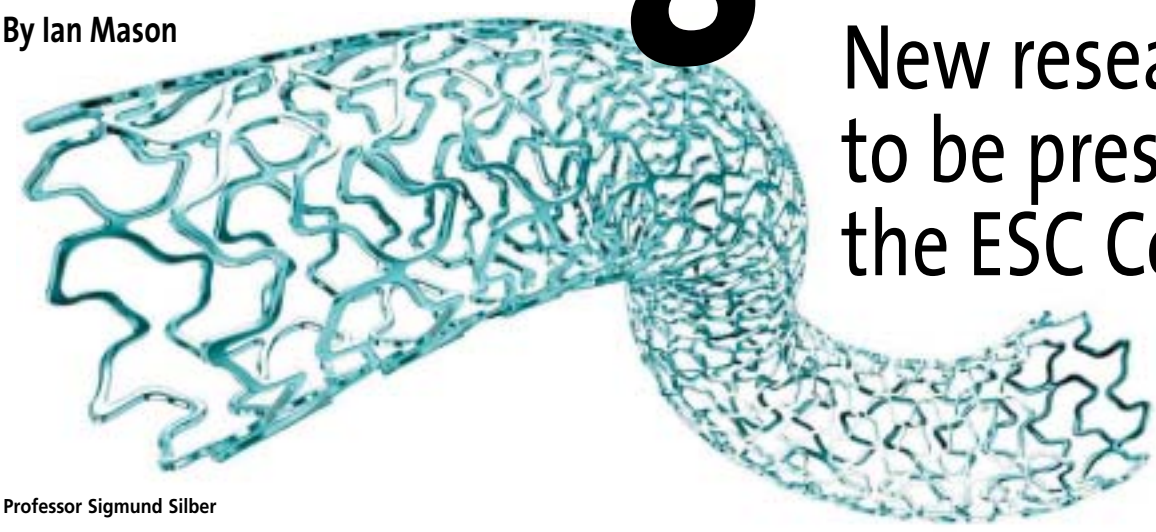


Figure 1: Taxus Liberté is expected to launch in Q3 2005 (CE mark pending; currently not available for sale in the EU or USA)

So far, 2005 has been a busy year for the rapidly evolving technique of stenting. There have been new devices, new guidelines, and the resolution of a major debate. The stent and more so the drug-eluting stent (DES) story will be taken forward at this year's European Society of Cardiology (ESC) Congress (see box) with the presentation of the latest research findings in this exciting therapeutic area.

The ESC presentations complement data presented at other recent major cardiology meetings. At the EuroPCR 2005 meeting (Paris, France, in May) an important debate amongst stent manufacturers was finally settled - at least according to the attending medical community.

At a plenary session entitled '*Direct comparison between DES: a burning issue*', a panel of leading interventional cardiologists announced a draw between the Cypher and Taxus stents, with neither showing clinical superiority and both having similar safety profiles - specifically rates of stent thrombosis.

The debate was a keynote session of EuroPCR, which although only half the size of the ESC, was nevertheless attended by some 10,000 interventional cardiologists from over 90 countries. The debate was scheduled because of claims and counter claims about competing stent systems following a number of recent small- to medium-sized single and multicentre comparative trials.

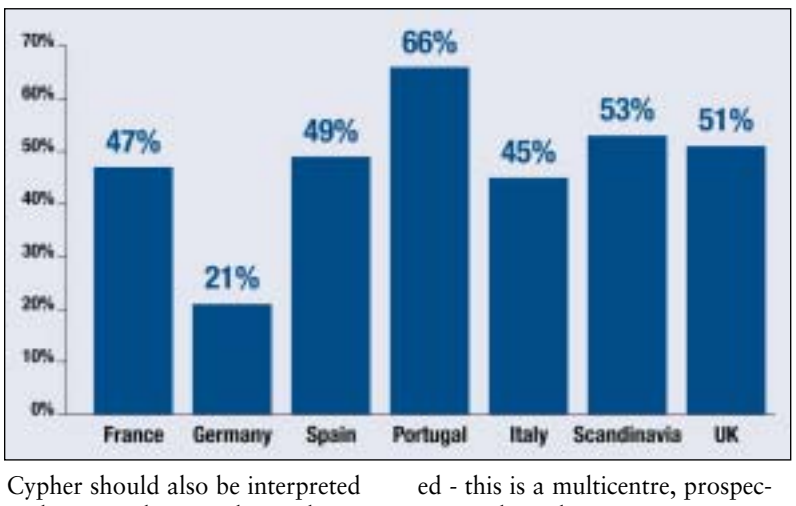
The two stents - the sirolimus-eluting Cypher stent (Cordis) and the paclitaxel-eluting Taxus Express stent (Boston Scientific) - went head-to-head in the Cordis-sponsored REALITY trial, also presented earlier this year at the American College of Cardiology (ACC) meeting in Orlando, Florida. The trial failed to meet its primary endpoint, with no difference in the rates of in-stent and in-lesion (primary endpoint) binary restenosis at eight-month follow-up. Cordis claimed a significant difference in stent thrombosis from an on-treatment secondary endpoint data analysis. However, when a nine member EuroPCR panel (Chaired by Professor Jean Marco, Director of the Interventional Cardiology Unit, Clinique Pasteur, Toulouse, France, and Professor Sigmund Silber, Gemeinschaftspraxis Hospital, Munich, Germany) reviewed the data, they concluded that the risk of thrombosis associated with the two stents could not be shown to differ, neither could the clinical outcomes.

Professor Silber, who is also Chairman of the ESC Task Force responsible for drafting the first European Guidelines on Percutaneous Coronary Interventions (PCI) (Silber et al. *Eur Heart J* 2005;26:804-47), said the REALITY trial would need to have recruited more than 10,000 patients to have been adequately powered to show a difference in rates of stent thrombosis for Taxus versus Cypher (in fact only 1,353 patients were recruited). The panel also pointed out that the recommendations regarding antithrombolytic therapy post-DES implantation varied, and that compared to previous studies with bare metal stents (BMS), DES have been scrutinised significantly more vigilantly for thrombosis and other risks.

Professor Marco added that registry data comparing Taxus and Cypher should also be interpreted with care and cannot be used to prove that one stent is better than another. 'Subgroup analyses of randomised trials and registries are severely underpowered and should therefore be interpreted with caution.'

In addition it was noted that the definitions used for outcomes and MACE (major adverse cardiac events) rates varied greatly between individual trials and registries, making it even more difficult to draw conclusions by indirect comparison of studies.

Figure 2: European conversion rates from BMS to DES



Professor Silber said that all DES must prove their efficacy in adequately powered randomised trials with a primary clinical endpoint. 'So far only three DES have accomplished their homework - Cypher, Taxus and Endeavor,' he said. The panel agreed that research should move away from trying to prove superiority of one of the current DES over the other, and should focus on new innovative developments in the field of DES. Of these there have been several. In July 2005 Medtronic announced that they had received CE (Conformité Européenne) mark approval for Endeavor, the first cobalt alloy DES. Choice of stent will be further enhanced in the coming months with the launch of the 'next generation' Taxus Liberté DES (Figure 1), which is claimed to be specifically designed for improved deliverability - a crucial consideration for small vessel stenting.

Indeed, the move towards increased use of stents for complex lesions has been a recurrent theme of 2005 developments. At the ESC Congress, the landmark SYNTAX trial, which has recently started patient enrolment, will be presented - this is a multicentre, prospective trial involving over 4,200 patients at up to 90 sites in Europe and the US. The study is comparing the performance of DES with bypass surgery in the most complex patient subsets: those with coronary artery disease in all three coronary arteries, in the left main coronary artery, or both.

SYNTAX is an important study because although DES have been proven to be superior to traditional BMS at reducing the rate of repeat procedures due to restenosis, previous studies comparing CABG and PCI using BMS or DES have been limited to highly selected patient populations. The study's primary endpoint is the 12-month major adverse cardiac and cerebral event (MACCE) rate, which includes death, myocardial infarction, repeat revascularisation and stroke. SYNTAX will also analyse the long-term health economic implication of DES versus CABG.

Economic impact

Healthcare providers are increasingly interested in the cost-effectiveness of new therapies. To date there have been no studies comparing the cost-effectiveness of DES and CABG in randomised clinical trials. Recent studies from Italy and Germany indicate that if DES could reduce the number of multi-vessel patients undergoing CABG surgery, this may reduce medical care costs (Fricke F-U, Silber S. *Herz* 2005;30:332-8; Sangiorgi G et al. *Ital J Heart Suppl* 2005;6:145-56). Within the German healthcare system, Fricke and Silber calculated that PCI of long and complex lesions with paclitaxel-eluting stents significantly reduced costs as compared to CABG (by €4,574 per patient). An economic sub-study of the SYNTAX will show how PCI with DES compares with CABG in terms of initial hospital cost as well as follow-up cost.

DES news at ESC

The symposium '*Controversies in coronary revascularisation therapy*' will take place at the ESC Congress, taking place in Stockholm, Sweden, between 3-7 September 2005. The congress is Europe's largest medical meeting and a major event in the world of cardiology, with over 25,000 attendees registered.

On **Sunday 4 September** (11.00-12.30, Budapest, Red Zone) the debate will examine whether patients with severely depressed left-ventricular function should undergo PCI, rather than bypass, and whether patients with diabetes should receive DES rather than bypass surgery.

On **Tuesday 6 September** (14.00-15.30 Athens, Blue Zone) a symposium, chaired by MC Morice (Massy, France) and E Grube (Siegburg, Germany) will review the latest clinical results for DES, including stent-to-stent comparisons, data from the MILE-STONE II (challenging patient subsets), HORIZON (DES in acute MI) and SYNTAX studies.

On **Wednesday 7 September**, a 'Featured Research' session (08.30-10.00 Oslo, Green Room) chaired by F Schiele (Besancon, France) and D Baumgart (Essen, Germany), will look at some of the remaining problems associated with DES.

A poster presentation (P3384) reviews data from an audit of more than 100,000 PCI procedures in 220 French centres (Morice MC et al). Their findings confirm that PCI can be performed safely and successfully in most patients, but the best results were achieved in centres performing the highest number of stenting procedures.

Already more than two million of DES have been implanted. DES are rapidly becoming the gold standard for percutaneous coronary revascularisation in Europe (Figure 2) as well as the US. Recently UK specialists predicted that all stents used in that country will be drug-eluting within five years (*Cardiology News* 2005;8:42-3).

New ESC PCI Guidelines

Earlier this year the European Society of Cardiology (ESC) released the first European Guidelines on Percutaneous Coronary Interventions (PCI). According to these guidelines, PCI can now be regarded as the first option for a larger group of patients with acute coronary syndromes than before. Recent technical and pharmacological improvements have developed PCI into a procedure that can be safely and effectively applied to patients with various types of coronary lesions and patients with and without myocardial infarction.

The guidelines can be viewed at: http://www.escardio.org/knowledge/guidelines/PCI-Guidelines.htm?1703

Seeking cardiac stem cells

Stem cells have been found in many organs, including the brain, but many researchers are not convinced that the heart contains any. However, leading stem cell researcher Dr Pierro Anversa, Professor of Medicine and Director of the Cardiovascular Institute at New York Medical College, has suggested that heart cells undergo an ongoing turnover fuelled by stem cells, and in June he published a study that identified cardiac stem cells in animal models that repaired tissue damaged by an adverse cardiac event.

Steven Houser PhD (above), Director of the Cardiovascular Research Centre at Temple University School of Medicine, Pennsylvania, USA, whose own research had focused on cardiac reaction to hypertensive diseases that can lead to congestive heart failure, recently joined Professor Anversa, and the team has received a NIH grant to study whether there are autologous stem cells in the heart.

Early in this disease, heart muscle increases and chambers stretch in an attempt to increase contracting power. Part of this enlargement is due to increased muscle mass, but how the chambers grow is less certain. Traditionally it is thought that cardiac cells simply grow larger to accommodate the increased need, but Dr Houser and Prof. Anversa have developed a different theory: spurred by cardiac stem cells, cardiomyocytes actually increase in number in response to the heart's traumatic condition. In their study, after inducing hypertension in an animal model to distress the heart, the team will study the heart tissue and count cells, first in the normal heart, then in the harder working heart. If, according to their theory, there are more cardiomyocytes in the heart, rather than simply larger cells, they could conclude that stem cells are attempting to repair the heart.

Based on a report by Eryn Jelesiewicz at Temple University.
Source: www.medicalnewstoday.com

BALTIC SUCCESS

Lithuania - 'A country's overall development level is demonstrated by the level that cardiac surgery has reached,' said Valdas Adamkus, President of the Republic of Lithuania (right) at the opening of the 15th Congress of The World Society of Cardio-Thoracic Surgeons, held in Vilnius this June.

Lithuania, which gained EU membership about a year ago, has three public and one private heart centres. Performing interventions from coronary surgery using the Ross procedure to organ transplants, the country provided 794 heart operations per million people in 2002, positioning it between France (635) and the UK (636), and Austria (868) and Denmark (882).

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Professor Paul Pepe and **Dr Jane Wigginton** discuss current research and concepts that will affect the future of basic CPR

BASIC cardiopulmonary resuscitation

For over forty years, basic cardiopulmonary resuscitation (CPR) has been performed by laypeople and health professionals with significant life-saving effects. Today basic CPR training also includes training in the use of automated external defibrillation (AED). Along with early defibrillation, research has shown that CPR is the only well-proven life-saving procedure for sudden cardiac death. Although they may very well be effective in aggregate, to date, none of the drugs and no other advanced cardiac life support techniques currently in use have been proven explicitly as contributing to long-term survival with intact neurological function in the clinical setting. Therefore, although it is still infrequently performed in many communities, basic CPR remains a critical component of community-wide life-saving efforts.

Basic CPR also has regained centre-stage in resuscitation research efforts. In addition to evaluating the concept of markedly abbreviating the time to provide effective training, recent investigations suggest that current CPR procedures can be modified easily to significantly improve outcomes beyond what they can do today. Specifically, renewed focus has been directed at not interrupting chest compressions and on a de-emphasis of rescue breathing, especially in the first few minutes after collapse. In addition, evidence has been growing steadily for deferring initial defibrillation attempts until a brief period of chest compressions can first be performed.

Here we briefly highlight each concept and provide some insight to the future of basic CPR.

Abbreviated Training - Research has confirmed that the average person is less likely to learn CPR unless they are compelled to do so for a job or school requirement. One of the rate-limiting steps toward implementing workplace and school-based requirements is being able to make the requisite time commitment considering that several hours of work would need to be interrupted to train all employees using current courses.

Fortunately, recent research has indicated some hope for expanding the numbers of persons trained in CPR. Specifically, new initiatives and teaching techniques that involve video-based adult learning have demonstrated the effectiveness of 20-30 minute training [8]. More recently, resuscitation researchers in Dallas have begun to test a combined CPR-AED training course that is less than 30 minutes. Preliminary information demonstrates that immediate retention and effectiveness of performance are at least similar. This new training technique may eventually prove to be even better because the abbreviated course focuses on the actual skills used and not didactics. It is also less intensive in terms of trainers, allowing large-scale classes to be conducted by a single instructor

Uninterrupted Compressions - Research has confirmed that interrupting chest compressions to perform defibrillation or to provide rescue breaths, causes abrupt falls in coronary perfusion pressure (CPP) and that restoration of a reasonable CPP will take at least 10-15 seconds after resumption of chest compressions. This means that CPP is inadequate throughout the majority of the resuscitation effort. Also, exacerbating this concern, rescuers actually take longer to provide mouth-to-mouth breaths and defibrillation than one would presume. Furthermore, even a 10-15 second delay in delivering the

The recently convened ESC Policy Conference titled *Women at Heart* was chaired by Professor Marco Stramba Badiale, of the IRCCS Istituto Auxologico Italiano, Milan, Professor Silvia Priori and Professor Kim Fox. We asked Professor Badiale about progress in the understanding of women and heart disease

Prof. Marco Stramba-Badiale

Women and heart disease

The Policy Conference was convened by the European Society of Cardiology. ESC President Professor Michal Tendera

Clinical manifestations of ischaemic heart disease in women may differ from those commonly observed in males and this factor may account for under-recognition of the disease,' the professor pointed out. 'Some diagnostic tests and procedures may not be as accurate in women, so physicians may avoid using them and a heart attack or stroke may not be detected in women until later, with more serious consequences. An exercise stress test, commonly use to diagnose ischemic heart disease, may be less accurate in women: in young women with a low likelihood of coronary heart disease, an exercise stress test may give a false positive result. In contrast, single-vessel heart disease, which is more common in women than men, may not be picked up on a routine exercise stress test. These important differences in clinical manifestation of heart disease in females are not familiar to physicians who may therefore under treat their female patients.

Symptoms - Women have a greater tendency to have atypical chest pain or to complain of abdominal pain, dyspnoea, nausea and unexplained fatigue. Since women tend to have heart attacks later in life than men, they often have other diseases that can mask heart attack symptoms. Furthermore, ischemia may be more often silent in women and the proportion of unrecognized myocardial infarction is greater in women than in men.

Therapies - Women have been under represented in randomised clinical trials and only recently has there been a significant increase in the number and proportion of women who participate in these studies and, even more recently, trials have been targeted solely on females patients. Most progress in this direction have occurred in the USA, as a direct consequence of the commitment of funding agencies that have provided economic support to clinical trials only when a balanced gender presence was assured in the design of the trial. In Europe, there is no regulation of this type and therefore there is less sensitivity to the issue. Once again, scientific societies should play a major role in ensuring that gender specific issues are sought and, when identified, gender specific response to therapy should be investigated in clinical trials.

What doctors need to know - Coronary artery disease is the leading cause of death for men and women in the western world. About 40% of all female deaths are caused by cardiovascular disease, especially coronary artery disease and stroke. However, unfortunately women, and their physicians, underestimate the risk of heart disease because of the perception that women are 'protected' against ischemic heart disease. What is not fully understood is that women, when fertile, have a lower risk of cardiac events, but this protection fades after the menopause, leaving women with untreated risk factors vulnerable to develop myocardial infarction, heart failure and sudden cardiac death.

shock (after the order to 'halt CPR' has been given), will lead to dramatically diminished rates of resuscitation. Therefore, recent efforts have gone into developing AED devices that can analyse the cardiac electrical activity without interruption of compressions and deliver the shock at the moment the rescuer backs away from the chest. Also, to maintain continuous chest compressions, scientists are investigating the efficacy of deleting rescue breaths during the first minutes after cardiac arrest, particularly when gasping is present.

Compressions-only CPR - As mentioned, recent studies have confirmed that compressions-only CPR may be even more effective than traditional CPR that includes mouth-to-mouth ventilation, particularly in the first few minutes following a sudden cardiac arrest. Not only do the rescue breaths frequently interrupt compressions and thus the maintenance of adequate CPP, but it also can add to inhibited venous return because of the positive intra-thoracic pressure generated by the positive pressure ventilation.

In fact, significant gas exchange still occurs without rescue breathing. Chest recoil after release of the compression tends to move air into the airways (assuming the airways are open). Also, most people likely to survive a cardiac arrest will be gasping, a unique respiratory event that not only can rapidly expand a larger volume of dependent lung spaces, but also generates a stronger intra-thoracic vacuum than a normal breath. In turn, this generates better pulmonary oxygenation and more CO2 clearance, while also generating better venous return. In addition, by not interrupting chest compressions, perfusion to the brain and respiratory apparatus is better sustained, thus prolonging gasping and, in turn, better oxygenation, CO2 clearance and circulation. Paradoxically, by not stopping to breathe for the person, respiratory functions are actually prolonged and improved.

The problem is that gasps eventually deteriorate and, also, not all patients gasp and not all cardiac arrests are sudden. Therefore, some lung inflation will need to be provided sooner or later. Nevertheless, even when breaths are provided, they are not needed as often as previously thought. The traditional 15:2 compression-ventilation ratio may be better at 100:2 or 50:2 for many of the reasons stated previously and because ventilation should match perfusion. In low blood flow states like CPR situations, CO2 is not produced as readily and, even when it is, it is not circulated back to the lungs for removal. Therefore, ventilatory demands are low until full circulation and strong pulses are restored. Although theoretical models indicate that children should receive breaths more often, the need is much less than the current 5:1 ratio proscribed for children.

CPR Before Defibrillation - Growing evidence has indicated that once ventricular fibrillation (VF) has been prolonged beyond four or five minutes, remaining cardiac energy supplies will become depleted and a relatively de-oxygenated heart is less apt to respond to defibrillation. It has become apparent that, once several minutes of VF have elapsed, preparing the heart for defibrillation with basic CPR and/or certain medications, will make a heart more amenable to successful defibrillation with return of spontaneous circulation. Although it is clear that immediate counter-shock is the most effective strategy in the first few minutes after onset of VF, laboratory studies support the use of vasopressor drugs to enhance CPP during CPR conditions prior to defibrillation. Furthermore, two recent clinical studies demonstrated the probable value of providing a brief period (1.5 to 3 minutes) of basic CPR prior to defibrillation. While these studies have their limitations, they are the best available data and clearly indicate the value of chest compressions prior to defibrillation unless it is a witnessed collapse in the presence of a defibrillator. Combined with the information previously discussed, it is clear that a re-focus on chest compressions must be emphasized in CPR training and performance.

Caveats - Although the research discussed here is compelling enough to indicate a need to change current CPR techniques, there still is no worldwide consensus on these issues nor, in some cases, is there conclusive enough evidence to effect worldwide changes in CPR training. Nevertheless, it remains clear that many of these proposed changes will eventually become mainstream as the evidence grows and more data are accumulated. There is little doubt that more emphasis should be placed on the performance of aggressive, continuous chest compressions that are interrupted only infrequently, if at all. Most importantly, this discussion again portrays the critical importance of basic CPR and our need to ensure that every person is trained and knows how to perform this life-saving intervention when it is needed.

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Progress

Our raison d'être

Scientific meetings held since 1998 at Alpbach, Germany, have attracted the sponsorship of leading associations and companies such as the Philip Morris External Research Programme, the Donors' Association of German Science, Swiss National Fund, the German Heart Centre Foundation, Berlin, and Philips Medical Systems. At the 4th Alpbach Meeting, which focused on *Magnetic Resonance, Contrast Mechanisms and Molecular Imaging of Coronary Artery Plaques*, Daniela Zimmermann spoke with **Professor Eckart Fleck** of Berlin's German Heart Centre (*Deutsches Herzzentrum Berlin*) about the constantly increasing importance of this event and its current aims

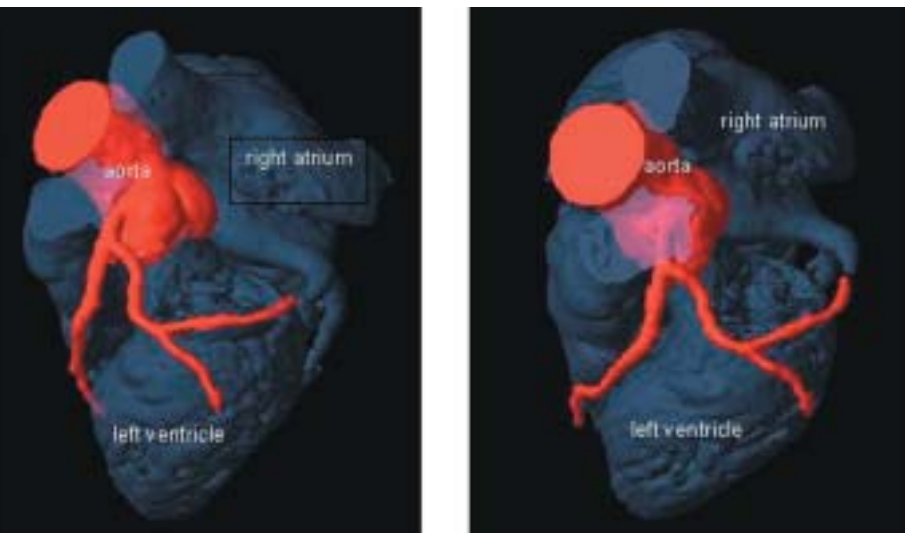


Fig 1. Coronary magnetic resonance angiography (MRA) visualising the left system of the coronary arteries originating from the aorta (red). Cardiac chambers (blue transparent)

Cardiologists, radiologists, physicists, vascular biologists, and other specialists arriving at Alpbach, Germany, could not fail to admire their surroundings. 'Alpbach is very beautiful and has a long tradition as a place for universities and the European Forum, which seemed a particularly attractive combination for our meetings. It provides the atmosphere you need to concentrate on topics, combined with a chance to relax in pleasant surroundings,' said Professor Fleck, explaining the choice of venue.

Here, the present and future issues to be faced in cardiology are discussed, centred on two approaches: 'First, the enhancement of diagnostics to detect potential dangers at an early stage - meaning not just in time,' the professor explained. 'Second: What treatment? If one bears in mind that arteriosclerosis will not only continue to persist but also increasingly prove a general health problem, then of course diagnostic considerations of this nature are of paramount importance. In 2020 cardiac diseases, and particularly coronary heart disease, will be the number one cause of death, worldwide, and not just in industrialised countries as at present. At the moment, infectious diseases hold that position, but, as pointed out, this will change worldwide, mainly because of changing dietary habits and that people are living increasingly longer. Arteriosclerosis will ultimately affect us all, if we live to be old enough.'

At the Alpbach meeting the convergence of imaging and treatment was constantly demonstrated. 'The critical areas of interest to us are plaque formations, that is deposits on local vascular wall sites, something that we cannot really detect from the outside. We need in vivo information about this. To date, imaging is conducted within the vessel itself; not only angiographically showing the internal volume but attempts are made to depict the wall. This is possible, for example with ultrasound and new modalities that can produce slice images of adequate resolution. As such, this could diagnose millimetre structures in the vascular walls.

This is possible using CT, but there are major problems - even to be able to see wall thickness and calcification. Conversely, by using MRI one can determine the different quality of tissue and obtain a resolution of practically microscopic quality, without using radiation. Imagine how exciting it is to conduct histology in a body that is completely penetrated by light. This is possible not only thanks to the resolution but also by marking those sites that you seek. The combination of these two approaches is the focus of the Alpbach meeting. The scientists ponder what are the potential binding possibilities and what

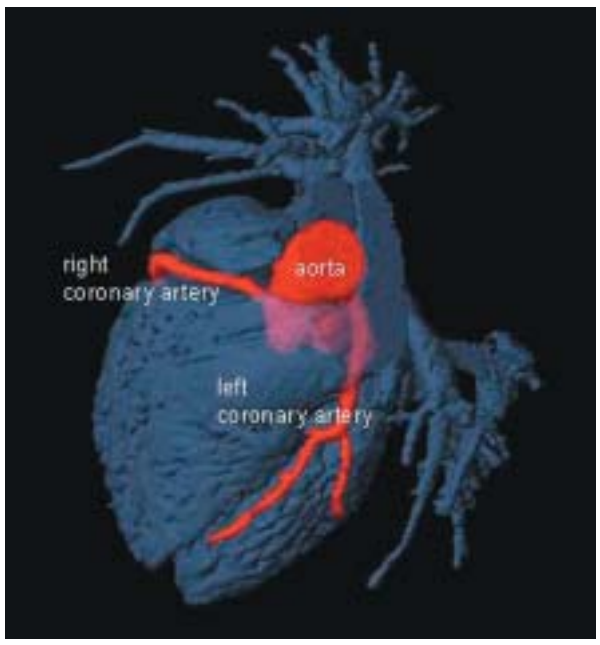


Fig 2 (left). Coronary magnetic resonance angiography (MRA) visualising the coronary vessels and the aorta (red) as well as the large thoracic vessels and the chambers (blue transparent)

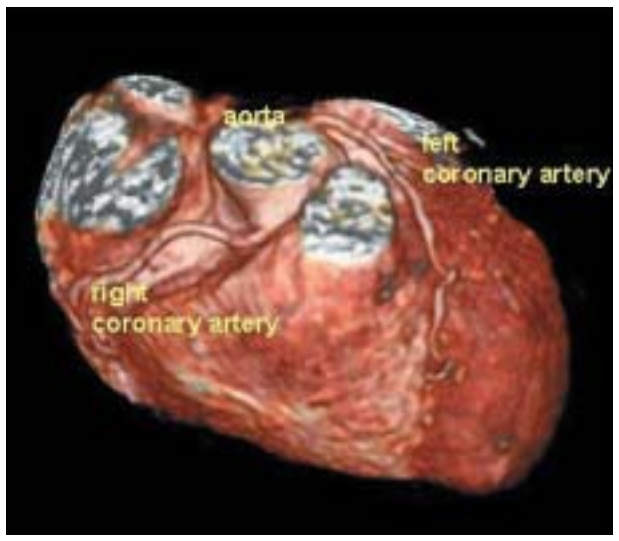


Fig 3 (below). Reconstruction of a 3D data set (whole heart coronary angiography), visualising the surface of the heart, the descending large thoracic vessels and the coronary arteries on the heart

individual proteins or other enzymes are known and could be considered as a target for specific binding sites, because this has implications for the combination of contrast media. In future it is even conceivable - should it be possible to identify such proteins and enzymes - to also use these for treatment, because you can see where and how the therapeutic agent acts at a specific site. This conjures up futuristic images and is based on the assumption that we work at obtaining high resolution of local visualisation and on identification of receptor proteins.'

Multidisciplinary research such as this, drawing together biologists and chemists as well as medical not made aware of the context and cannot understand what it's all about - and, of course, vice versa. What do you do with an image when you do not know how it was generated and thus misinterpret? So we must know relatively a lot about the local circumstances, not only about diagnosis of disease. We should know what specific particles are used and whether these really do bind as selectively as desired. Or is the receptor - a good early marker of small, non-magnetic iron particles. If we could bind these beads to specific molecules, which, in turn, would dock on to receptors, then you would have created a permanent link at this site, which could be visualised with MRI - assuming that a sufficiently large quantity is available. If all that is possible, you could localize a particular site.'

Professor Fleck agreed that the MRI-PET scanner would be a useful machine is such a situation, '... because it appears to be much easier to establish the special binding forms I spoke of earlier - in nuclear imaging. It would work very well with PET, but the only drawback with PET is that it does not at all have the kind of local resolution we need. If MRI could be used here, for example, in combination with specific contrast media, then one would probably not need PET anymore. Perhaps PET can be used as a general investigation system, while selectively using MRI to generate the high resolution needed. However, we believe that in future using MRI alone we will be able to visualise specific binding forms and thus achieve the requisite precision.

'We have been aware for years that conventional diagnostic modalities were not enough and that we would have to achieve higher quality using less invasive approaches. Our insights to date come from relatively highly invasive procedures. This is something that we would like to change - particularly in preventive medicine. We do not want to subject healthy, or potentially healthy, individuals to a battery of tests that, in some cases, could cause disease themselves. We therefore need data that will, a priori, assure equal, if not better, precision. Indeed, medicine has always explored such investigation procedures, be it nuclear medicine procedures or ultrasound, etc. But all the procedures mentioned suffer the drawback that local resolution is not good enough. For that reason we began working in this field as soon as the technology- fast computers for image reconstructions and strong magnets that can acquire the required signal - became available.'

THE ARTIFICIAL PATIENT

Holger Zorn reports on a new dimension in medical training

Pilots train on simulators and so do doctors who specialise in emergency care, because, in extreme situations, doing the right thing is not something that can be learned from books - it requires practice, without endangering passengers or patients respectively. However, although paramedics and anaesthetists have used simulators during their training for several years, one of the most complex treatments - extracorporeal circulation, i.e. taking over the cardiovascular functions of a patient - had not attracted that much interest. Now, the first simulator for extracorporeal circulation during heart surgery- has been introduced.

Named *CardioSim*, the world's first Perfusion Simulator was introduced to clinical users during the 34th Annual Meeting of the German Society for Cardiovascular Engineering in May this year. CardioSim simulates critical situations that can occur in a patient or the heart lung machine during extracorporeal circulation. For example, tubes might kink, cannulas twist, air might enter the venous system, cooling water could enter the bloodstream, blood filters become blocked, gas membranes leak, the pH-value move. All these are extremely rare incidents but require immediate action to avoid damage to a patient. Every action is recorded and evaluated. Using CardioSim, the trainers can step in at critical moments and analyse any incorrect reactions, because the system offers real-time control. The simulator is not only being used for safety training but also to train cardiac technicians.

CardioSim was developed under Professor Gerd Haimerl MD Dipl-Ing. (BA) at the Centre for Applied Simulation, Technical University Furtwangen, Department Villingen-Schwenningen, in co-operation with the Department for Cardiac and Vascular Surgery at the University Hospital Freiburg. The project, which to date has cost around €500,000 is funded by the Ministry for Science, Research and Arts in Baden-Wuerttemberg and by the German Society for Cardiovascular Engineering.

The simulator is to be used as a platform for research and innovation in extracorporeal circulation. Additionally, Prof. Haimerl believes that, one day, it will be able to simulate all organ-preserving systems, from dialysis to the artificial heart.

Ingredient in cocoa may combat CHD

Cocoa may be beneficial for those suffering heart disease and stroke, according to researchers at the Southampton University Hospitals NHS Trust, UK, whose study was presented in August, at the 20th Congress of the International Society on Thrombosis & Haemostasis, in Sydney, Australia, by consultant haematologist Dr Denise O'Shaugnessy. According to the research, cocoa inhibits platelet function, so it has been suggested that drinking a cup of cocoa could prevent potentially fatal blood clots. 'Cocoa contains flavinoids, which are also present in red wine. These can be preventive for coronary heart disease. However, our research uncovered another ingredient in cocoa that may be responsible for platelet inhibition.' The finding, she added, may lead to important new therapies to prevent heart disease and stroke.

Interventional Cardiac 3D Imaging

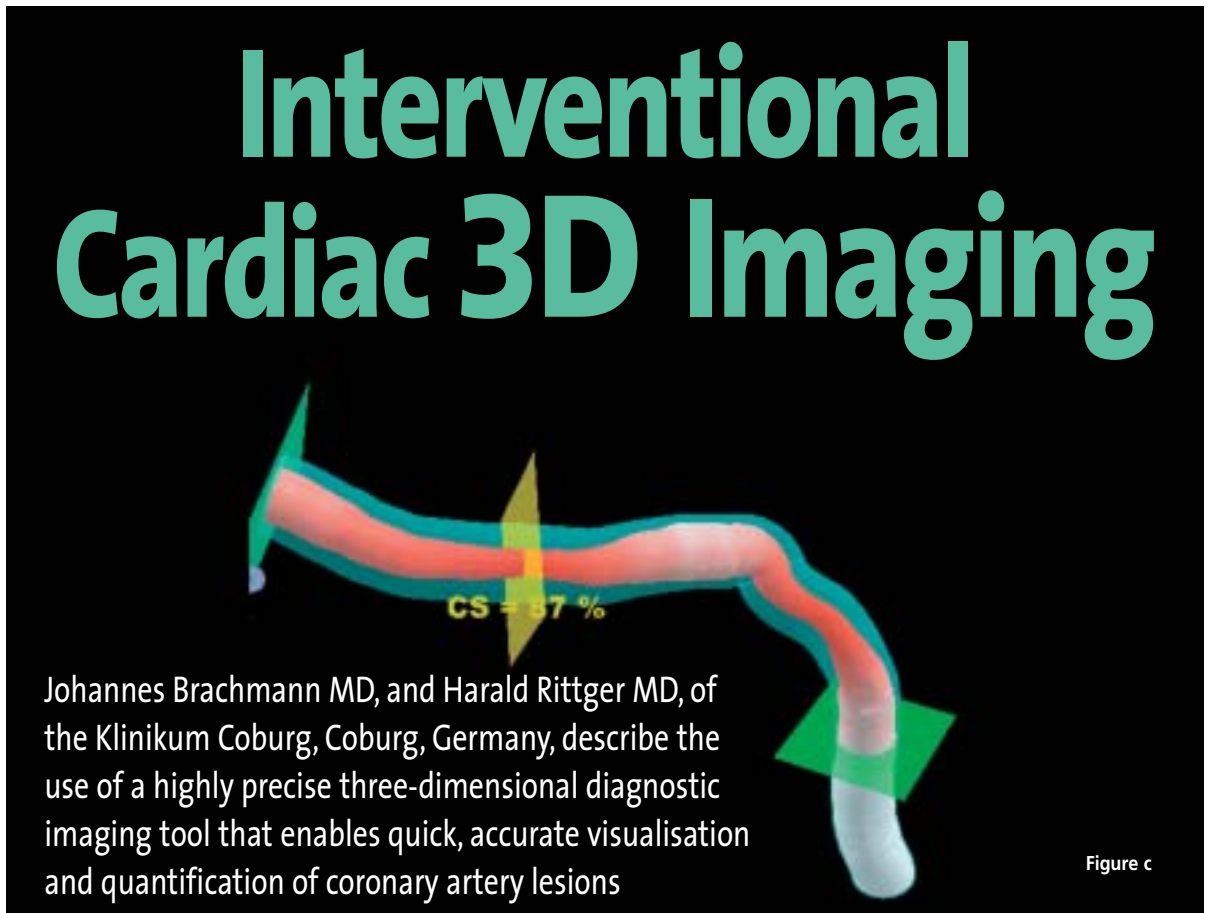


Figure c

Improved therapy planning for LAD lesion patients

Johannes Brachmann MD, and Harald Rittger MD, of the Klinikum Coburg, Coburg, Germany, describe the use of a highly precise three-dimensional diagnostic imaging tool that enables quick, accurate visualisation and quantification of coronary artery lesions

In interventional cardiology, accurate lesion assessment plays a vital role, particularly when determining the appropriate stent size and length. Interviewing Cardiac Imaging (IC3D), a highly precise three-dimensional diagnostic tool, increases diagnostic assessment capabilities.

IC3D involves selecting a lesion of a certain coronary vessel segment with as few as two standard angio images. From those two different projections, a three-dimensional volume image is created that can be visualised from any chosen angle.

One of the reasons for the accuracy of this application lies in the fact that a three dimensional reconstruction is not subject to the so-called foreshortening effects, thereby enabling length measurement with a higher degree of accuracy. Another reason is the greater precision with which the diameter profile and related parameters can be assessed - making IC3D a particularly valuable tool for selecting appropriate stent lengths and diameters. The IC3D model can be freely rotated in space and viewed from various angles, allowing a selection of optimal working projections for use during the intervention.

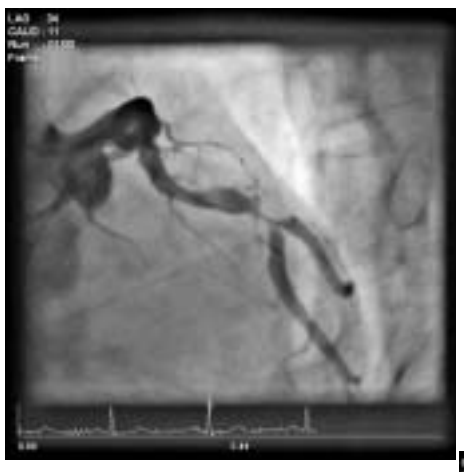


Figure a

Patient History

81-year-old male; weight 75 kg; height 175 cm; history of renal failure; the patient was diagnosed with three-vessel disease including moderate left main (LM) disease. The patient refused to undergo CABG (coronary artery bypass surgery). Therefore PCI (percutaneous coronary intervention) of RCA has been performed. After intervention, moderate increased serum creatinin level and ongoing stable angina CCS III.

Concerning renal failure, an optimal therapeutic strategy with a minimum dose of contrast medium is necessary for the planned treatment of the LAD lesions.

Diagnosis

Three-vessel disease: 50% LM stenosis; RCA 25% re-stenosis after stent placement; LAD proximal 85% stenosis with severe calcification continuing to the mid LAD; in the distal part of the LAD bifurcation 70% stenosis; normal left ventricular function; EF > 60%.

Treatment

PCI of LAD: Balloon angioplasty and implantation of two stents in the proximal two LAD lesions; stent implantation in LAD bifurcation lesion*.

LAD Proximal Two Lesions:

With Interventional Cardiac 3D (IC3D), precise three-dimensional vessel reconstruction was possible, supporting an optimal therapeutic strategy for this 81-year-old man with renal failure.

In the angiographic scenes [1A-C], the lesions are difficult to evaluate. Foreshortening effects complicate exact lesion length calculation with QCA. 3D-reconstruction with IC3D

Figure b

[2A+B] shows the morphology and length of the proximal two stenoses, with 37.6 mm in total. With regard to the supposed calcification, especially in the proximal long lesion, balloon angioplasty is performed. Due to the difficulty in inserting the balloon through the two difficult lesions and the total lesion length of 37.6 mm, the decision was made to implant two proximal stents.

LAD Bifurcation Lesion

IC3D [2C+D] provides excellent knowledge of the bifurcation morphology*. The angle of the side branch is close to 90∞ and not as acute as estimated from the angiographic data [1A-C]. Treatment of a bifurcation lesion with an acute angle of the side branch requires a 'kissing balloon' procedure to ensure that the side branch will remain open and will not be closed by a plaque clot. The kissing balloon procedure is very time-consuming and requires a lot of angiographic scenes, including a lot of contrast medium and radiation exposure. Because 3D-reconstruction verified that we were dealing with an open angle, we decided in this case that no kissing balloon procedure was needed to ensure that the side branch would remain open.

Due to knowledge of the morphology of the three lesions with IC3D, the optimal stent sizes and lengths, as well as the method of implanting the stents, had been chosen. Using IC3D was ideal in this case. The patient benefits are various: exact lesion calculation enabled us to keep the procedure time, radiation exposure and usage of contrast medium at a minimum. Additionally, the complete coverage of the lesions reduces the risk of re-stenosis.

** Information about this product is preliminary. The product is under development and not commercially available in the USA.*

IC3D INVOLVES selecting a lesion of a certain coronary vessel segment with as few as two standard angio images (see a and b) to create a three-dimensional (see c) volume image of the segment of interest. The IC3D reconstruction enables highly accurate quantitative measurements and can be visualised from any chosen angle.

Exclusive HDMR images presented at ESC 2005

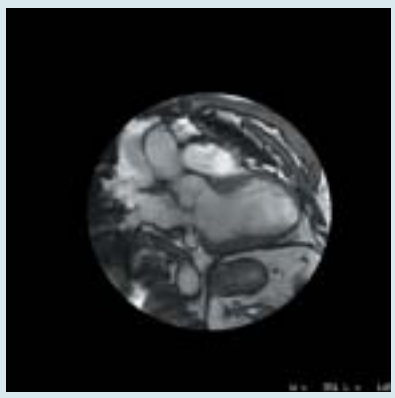
Sweden - GE Healthcare at The European Society of Cardiology (ESC) in Stockholm will present exclusive cardiac imaging techniques produced via the world's first high-definition magnetic resonance (HDMR) system. 'GE's HDMR is an extremely fast data processing engine coupled with high-density surface coils and extremely accurate gradients. The result is unique balanced acquisition architecture; with individual receive channels connected to dedicated reconstruction engines. This allows us to develop entirely new applications available only with HDMR,' said Stefano Vagliani, General Manager MR Europe at GE Healthcare.

The 'only-GE' cardiovascular imaging techniques include:

1.5T EXCITE HD MR Echo Cardiac Imaging - Real-time cardiac imaging with the resolution of MR at the speed of ultrasound, without the need for breath-holding or ECG gating.

One in three cardiac patients cannot hold their breath long enough for an image to be made. Frequently, cardiac patients are too ill to hold their breath and have weak or arrhythmic heartbeats, resulting in special imaging challenges. GE's MR Echo produces high-definition cardiac images in real-time, from the most unwell patients, providing clinicians with the contrast detail of MR with the real-time speed and ease of use of echocardiography, the firm reports.

'It's the ease of echo with the detail of MR,' said Steven D Wolff,



MD, PhD, Director of Cardiovascular MRI & CT, Cardiovascular Research Foundation and Chief of Cardiovascular MRI, Lenox Hill Hospital. 'Real-time image quality is robust even in patients with irregular cardiac rhythms who cannot breath-hold.'

ReportCARD - This innovative tool significantly reduces review, analysis and cardiac MR reporting time. 'ReportCARD is an integrated tool for reviewing, analysing, and reporting Cardiac MRI studies. There is nothing else like it. I can't imagine doing cardiac MR without it,' Dr Wolff observed.

HDMR: Overcoming current technology limitations - GE's HDMR, available on GE Signa 1.5T and 3.0T MR systems, enables massively simultaneous imaging in multiple channels in increments of 16. HDMR features unique balanced acquisition architecture, with individual receives channels connected to dedicated reconstruction engines.

As channels are added (in units of 16, 32, 48, 64 and more), image-processing power increases in proportion. The coil elements that detect the signal, the receivers that digitise it and the array processors that perform calculations are scaled together, so that massively simultaneous imaging can be performed without image processing delays. This technology sets a new standard for acquisition, gradients and the human interface.

GE's exclusive *Excite* technology has already enabled three exclusive, targeted MR applications with meaningful clinical benefits: *Vibrant* for bilateral breast imaging in a single exam; *Tricks* for MR angiography of the legs; and *Propeller* for high-quality brain imaging that is extremely resistant to motion artifacts. *Excite HD* brings each of these new applications into high definition.

'HD technology paves the way for an extremely wide range of targeted applications,' Stefano Vagliani pointed out. 'The possibilities are limited only by clinicians' imaginations. This new technology now allows physicians to image patients where it was previously impossible to consistently obtain diagnostic images.'

FULL SERVICE CONCEPTS

In 1995, the Hamburg-based firm Life Systems Medizintechnik-Service GmbH (part of the Krauth Group) was formed to develop a new, multi-supplier, full service concept for cardiac-perfusion units for cardiology and radiology departments. The company explained that the structure has three independent modules:

- medical supplies and disposables
- capital equipment
- specialised personnel (40 perfusionists among its 50 employees)

and that the advantages for clinics include:

- cost transparency through changeover from fixed to variable costs
- free financial resources through avoidance of capital commitment
- planning reliability for all the modules
- cost reduction by realisation of synergistic effects.

'With this innovative full service concept, Life Systems gradually increased its market shares. Today, approximately 20% of all perfusions in Germany are provided by an external service. In this market segment, Life Systems is not only established, but is also the market leader,' the firm added. The company is currently negotiating with several German and other European clinics to strengthen that market position and internationalise the business.
Details: www.life-systems.com

Walk run *jump!*

25 Sept 2005 World Heart Day

This day's activities in a 100 countries include health checks, walks, runs, rope jumps, fitness sessions, public talks, stage shows, scientific forums, exhibitions, concerts and sports tournaments to emphasise physical fitness to reduce body weight. Men with waist sizes above 94cm (37 inches) and women above 80 cm (32 inches) are considered at significant risk of developing heart disease and stroke. 'Waist size is like blood pressure and cholesterol level, another one of those numbers that we should all know, understand and watch closely,' explained Dr Sidney Smith, Chairman of the Scientific Advisory Board at the World Heart Federation, through which the international member organizations arrange the events.
Details: www.worldheartday.com

SPY SYSTEM GAINS US PATENT

Canada - The US Patent and Trademark Office has granted Novadaq Technologies Inc, of Toronto, a patent for its SPY Intra-operative Imaging System, which also has 510(k) clearance from the US Food and Drug Administration (FDA) for use during CABG surgery.

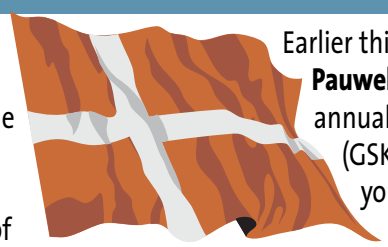
Picture courtesy of Novadaq Technologies, Toronto

The patent, titled 'Method and Apparatus For Performing Intra-Operative Angiography', describes SPY as an intra-operative fluorescent imaging system that enables cardiac surgeons to confirm the location of coronary arteries during coronary artery bypass graft (CABG) procedures and visually assess and validate the functionality of bypass grafts. Novadaq adds that the system allows the surgeon to view, record, replay, print and archive high quality real-time images of the coronary arteries and bypass grafts.

SPY's core imaging technology is also used in Novadaq's OPTTX System, for the diagnosis, evaluation and treatment of wet age-related macular degeneration (AMD). OPTTX is currently being evaluated in clinical trials.
Details: www.novadaq.com

The European Respiratory Society (ERS) 15th Annual Congress


ERS President Ronald Dahl



Denmark - In the year of his Presidency of the ERS, Ronald Dahl was pleased that, by coincidence, the congress was to take place in his homeland, also coincidentally celebrating the 200th anniversary of Hans Christian Andersen. 'The ERS Annual Congress has become a major event in respiratory medicine and science, and has developed from a European event into a conference that attracts delegates from all over the world,' he pointed out. However, this expansion, Dr Dahl added, would progressively limit venues able to host the growing number of participants. Others, he suggested would visit Copenhagen's many cultural sites - as well as join in some of the many Andersen festivities.

Earlier this year, the ERS launched the **Romain Pauwels Research Fund**, worth €50,000 annually and sponsored by GlaxoSmithKline (GSK), to help support up-and-coming young researchers in their quest to understand and treat respiratory illnesses. This was named after the late Professor R Pauwels, who had said, before his untimely death this year: 'Having spent more than 30 years in respiratory research, I am proud to have contributed to our present understanding of respiratory diseases and can see just how far this understanding has improved the way clinicians treat patients. However, we still have a lot to learn, and with increased mortality predicted for respiratory disease like COPD, it is vital that we continue to support respiratory research.'

Facing the future

A European perspective by **Dr Philip Tønnesen** (Dr Med. Science), Chair of the pulmonary medicine department at Gentofte University Hospital, Copenhagen, Denmark; President of the Danish Respiratory Society and Vice-Chair of the European Respiratory Society Annual Congress 2005 (17-21 September)

Respiratory diseases have an important negative impact on morbidity and mortality and this impact appears to be increasing, mainly due to smoking-induced disorders such as COPD and lung cancer. Also, during the last decade, and mainly in western Europe, an increasing incidence of asthma patients has appeared.

During coming decades we will have to deal with an increase in COPD patients as well as patients with other chronic diseases, and patients in the future will demand far more of us, all of which will challenge healthcare systems in many ways. Co-operation between hospitals, general practitioners and primary healthcare groups must be optimised, harmonized and we need to use similar clinical guidelines. Prompt exchange of patient health information's calls for fast implementation of the electronic patient record (EPR) and in a few years it will probably be customary, during discharge from hospital, for a patient to have personal health information downloaded on to his or her own pocket computer. The EPR will be a very big step forward in terms of the availability of health information and quality control.

In hospitals, an increasing burden will be more COPD patients of greater age. Until now the monitoring of acute admitted COPD patients have been relative sparse and in many departments not optimal. A simple comparison can be done with patients with acute myocardial infarction and in fact the mortality is as high in patients admitted with COPD. There is a need to increase the quality of monitoring of COPD patients and other patients with acute respiratory distress. In the next decade continuous monitoring of oxygen, carbon dioxide, respiratory rate, etc. should be standard during the first days of hospitalisation and easier ways to assess pH is strongly wanted.

Non-invasive ventilation (NIV) will also be standard in all departments who receive acute COPD patients and this therapy will not only decrease acute mortality but also increase the prestige of respiratory medicine among our colleagues in internal medicine.

New studies will show whether long-term home NIV will be effective or the use of NIV should be used to prevent exacerbations in COPD.

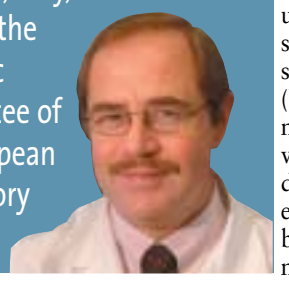
Long-term oxygen treatment (LTOT) will be demanded by many more COPD patients than today, and our role will be to prescribe oxygen according to clinical guidelines. Ambulatory oxygen will have an increasing use and further development of lightweight portable oxygen with long duration will be demanded.

In the next decade, I suspect a dramatic increase in the quality of care for patients with respiratory diseases and a demand for more optimal monitoring and treatment equipment.

Last but not least, we must not forget that smoking cessation is of major importance to prevent COPD and lung cancer.

From burden to therapy
Respiratory diseases

By **Andrea Rossi MD**, Director of the Respiratory Division at Bergamo General Hospital Bergamo, Italy, and Chair of the Scientific Committee of the European Respiratory Society



Thousands of diseases challenge human survival on our planet. However, a few of these represent a major cause of mortality and morbidity worldwide. Respiratory diseases are among the leading health problems for human beings. In particular, respiratory tract infections, including tuberculosis and lung cancer, account for a large portion of human suffering and death. Chronic inflammatory disorders of the airways, such as bronchial asthma in infants and chronic obstructive pulmonary disease (COPD) in adults, embody the highest prevalence, respectively, in Europe. The former is mainly related to the 'allergy march', whereas the latter is strongly related to tobacco consumption, though other factors such as occupational and environmental pollution also significantly contribute to the overall prevalence. It has been estimated that the total financial burden of lung diseases in Europe amounts to nearly €102 billion.

The prevalence of COPD is rising worldwide, and it has been estimated that, in 2010, COPD will be the 4th leading cause of death in Europe, immediately after cardiovascular diseases and lung cancer. Asthma is the most common chronic disorder in children in Europe. There is no fundamental therapy for asthma. However, inhaled corticosteroids are effective to control symptoms and to reduce the risk of exacerbations substantially. Inhaled bronchodilators are also helpful.

In COPD, smoking cessation is the most effective measure to slow down the progression of the disease. However, the inflammatory process does not reverse after smoking cessation. Therefore a treatment for COPD is needed. Regular therapy with long acting inhaled bronchodilators is effective to reduce dyspnoea, as well as to improve exercise tolerance. The addition of inhaled corticosteroids may help to reduce the frequency and severity of exacerbation in severe patients.

Although available asthma and COPD treatments, inhaled corticosteroids and long acting bronchodilators respectively, are effective to reduce symptoms and to improve the quality of life, the lack of a real, prime therapy for those diseases stimulates a lot of basic and clinical research aimed to elucidate the fundamental bio-cellular mechanisms as well as to find new drugs active at that level. It should be mentioned that both asthma and COPD are widely under-treated because they are underdiagnosed due to the limited use of spirometry as a diagnostic tool. Spirometry should become part of the routine assessment of health status.

A major problem in clinical respiratory medicine is acute respiratory failure; namely hypoxemia often associated with hypercapnia and respiratory acidosis. An extraordinary advance in the management of acute respiratory failure is a worldwide success, as well as the use of non-invasive positive pressure ventilation (NPPV). This is a mode of artificial ventilation that does not require endotracheal intubation, because mechanical assistance is delivered through a face mask. NPPV dramatically reduces mortality in critically ill patients because it decreases the frequency and severity of complications, particularly infections, associated with the endotracheal tube. NPPV can be delivered in the intensive care unit as well as the ward for less severe patients (pH <7,30).

Although there are some promising prospectives and new treatments are under evaluation, the mortality remains high for patients with lung cancer and for patients with interstitial lung disorders. There is a lot of effort in those areas, but until now success is minimal.

In conclusion, respiratory diseases are among the leading causes of mortality and morbidity in Europe as well as worldwide. There is a need for more basic research as well as for more epidemiological data. Some effective treatments are available and they should be more widely used. New, more effective therapies are expected in the next years.

New features and a colourful design

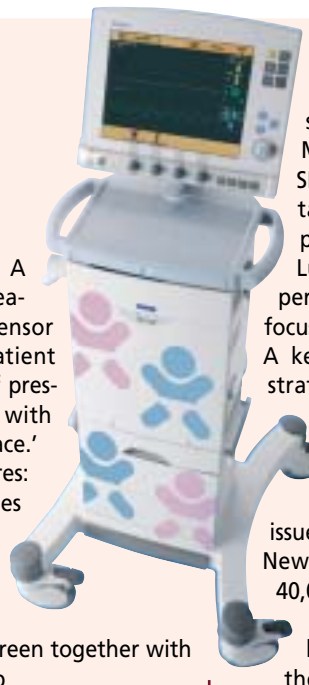
The SERVO-i Infant

Belgium - A new version of the SERVO-i Infant neonatal ventilator, featuring additional treatment functions and an optional colourful, child-friendly design, is to be launched by MAQUET Critical Care at the European Society of Paediatric and Neonatal Intensive Care (ESPNIC) Annual Conference in September. The equipment will also be on show at the European Society of Intensive Care Medicine (ESICM) Congress in Amsterdam (25-28 September, booths 77-79 and 82-84).

New features in the neonatal ventilator include nasal continuous positive airway pressure - Nasal CPAP - an option that can be used with a variety of patient interfaces, Maquet reports. 'New hardware has also been introduced. A new Y-piece measurement sensor allows near-patient measurements of pressure and flow with minimal dead space.'

Other new features:

- FiO2 trend values can be stored and viewed
- Reference loops can be presented on screen together with the current loop
- The patient circuit can be tested independently of the pre-use check
- Alarms for airway pressure upper limit can be muted
- Apnea alarm limit is extended from 15 to 45 seconds



MAQUET Critical Care's SERVO-i offerings for neonatal, pediatric and adult patients will be on display at Lung recruitment and clinical performance will be the major focus of MAQUET's presentation. A key highlight will be demonstrations of the system's outstanding transport capabilities.

The company also reports that the September issue (number11) of Critical Care News (distributed globally to 40,000 physicians, therapists and nurses in intensive care) will highlight ICU centers around the world where changes in ventilatory care procedures have had an impact on staff treatment routines and patient outcomes. These include the Prince of Wales hospital ICU in Hong Kong, which implemented new precautions and routines after the SARS outbreak, and developed a comprehensive strategic planning process for future crisis management scenarios.

'The magazine also features a presentation of post-graduate lung recruitment workshop activities in Sweden and the Netherlands, which look at the mechanisms of atelectasis and lung recruitment strategies in order to provide more optimal ventilation procedures.

'The special needs of the CICU environment are also highlighted, examining the benefits one CICU has experienced from implementing a fast-track extubation procedure,' Maquet adds. 'The feature article focuses on the challenges of refining ventilatory care processes in the paediatric intensive care environment. We visit Arkansas Children's Hospital, a private non-profit paediatric medical centre that offers a range of ventilatory treatments, and one of the largest of its kind in the US.'

Today's treatments
and training tomorrow's specialists

Dr Christiane Eickelberg, of the University of Giessen Lung Centre (UGLC), outlines the centre's research projects, aims and academic offerings

Science can be breathtaking at UGLC: The 'Giessen Everest Experiment', a challenging high altitude study organised by a team of physicians (pictured above), is an extreme example of clinical research; it is also a milestone in the recent approval of Revatio, better known as Viagra, by the US Food and Drug Administration (FDA) as a treatment for pulmonary arterial hypertension (PAH).

At sea level, in the heart of Germany, interested members of the public and patients can more easily benefit from and share in UGLC's collective research spirit, for the centre constitutes a busy scientific network that incorporates 20 research groups with over 120 basic scientists and clinicians.

Close interaction on the Giessen University Hospital campus ensures that UGLC members can work effectively to meet patient's needs and match capabilities. 'We believe in translational science,' says Professor Werner Seeger, chairman of the renowned centre, 'and we aim to deliver our research directly from bench to bedside.' With the orchestrated pursuit of clinical, research and training activities in pulmonary medicine, UGLC members seek a new approach to understand, treat, and ultimately prevent lung diseases. The clinical departments of medicine, surgery and paediatrics offer modern patient care and services to juvenile and adult patients suffering various lung diseases. The UGLC also has emergency and intensive care units with adjoining wards, including facilities designed especially for treatment of rare and specific lung diseases. Additionally, the centre hosts highly specialised ambulatory care facilities for all general lung diseases, as well as specific pulmonary infections (i.e. HIV/AIDS, avian influenza), juvenile and adult mucoviscidosis, lung cancer, fibrotic or chronic obstructive lung diseases including asthma, pulmonary hypertension, and sleep related disorders. Some of these facilities, namely those focusing on pulmonary hypertension and lung fibrosis, care for the largest patient groups in Europe.

Daily, UGLC clinicians are supported by the skilled diagnostic experts in the Institutes of Microbiology, Virology, Pathology and Pharmacology.

With a continuous emphasis on research and innovation, the centre looks back on long traditions of inventive treatment strategies, vaccines, diagnostic tests, and other technologies that have improved health. The exchange of complementary scientific knowledge, skills and experience of the cardiopulmonary system is fertilised by a joint dedication to education. UGLC faculty members actively engage in a conjunctive concept to integrate young scientists and clinicians from all over the world in clinical fellowships and a PhD training programme specialised in pulmonary medicine and molecular biology.

Details: www.uglc.de

DRUG EASES LUNG FUNCTION

The Netherlands - A randomised trial of roflumilast, led by researchers at Leiden University, has shown that the anti-inflammatory drug improved lung function in patients with moderate to severe chronic obstructive pulmonary disease (COPD), according to the results published in *The Lancet* in August.

The investigators, Klaus Rabe et al, tested for effects of the drug, a phosphodiesterase-4 inhibitor, on the lung function and health-related quality of life in 1,157 COPD patients, in centres in 11 countries. These had been randomly prescribed 250 mg of roflumilast, 500 mg of roflumilast or a placebo. When compared with the placebo, roflumilast was found to have improved lung function and reduced worsening of respiratory symptoms. The researchers also found that patients on the drug had greater improvements in health-related quality of life than those given the placebo. 'Roflumilast was effective in improving lung function and reducing exacerbations in a population of patients with moderate to severe COPD. The phosphodiesterase-4 inhibitor class shows promise as a new therapeutic strategy for patients with COPD,' Dr Rabe concluded.

40th ANNIVERSARY for the Annual Meeting of the German Society of Neuroradiology

As the German Society of Neuroradiology 40th annual meeting approached (Venue: Dresden. 31 August - 3 September), **Professors Martin Schumacher** (Freiburg), President of the German Society of Neuroradiology (GSN) and **Rüdiger von Kummer** (Dresden), the meeting's President, examine the history and potential in this medical field

"The programme in Dresden reflects the unbelievable development of neuroradiology worldwide. It impressively shows the enormous upswing in diagnostics and therapy of central nervous system diseases and particularly in brain research.

Neuroradiology in Germany is older than the 40 years in which regular annual meetings have been held. The earliest publications, in 1905 (Schüller: *The skull base on the radiogram*) and in 1906 (Fürnrohr: *X-rays in the Service of Neurology*) witness that Wilhelm Conrad Roentgen's discovery was already in use in neurodiagnostics only 10 years later. Arthur Schüller was also the first to introduce the term Neuro-Roentgenology in 1913. For over half a century it was the neurosurgeons and neurologists who practiced and developed neuroradiology, including famous names such as Dandy, Forrestier, Moniz, Djindjian, Krayenbühl and Serbinenko. When the German Neuroradiological Working Group was founded, in 1963, and well beyond the founding of the German Society of Neuroradiology (1970), neuroradiology departments were embedded primarily in neurological and neurosurgical hospitals. Not until the 1970s did the use of the same techniques result in greater co-operation with radiology, leading to the successful recognition of neuroradiology in 1987. German Neuroradiology led the way, with a status that even now still has to be attained in many European countries. It was outdone only by Portugal, which first established the speciality of Neuroradiology.

In evolution, those creatures survive which have solid basic endowments which they can use for their own further development and profit additionally from favourable environmental conditions. Apparently neuroradiology possesses these prerequisites, since it has managed to show further decisive developments in the last two decades, despite increased pressures. This is confirmed by a quick look at the summaries of the scientific contributions to the 40th Annual Meeting.

In diagnostics, magnetic resonance imaging (MRI) has provided insight even into microscopic areas to reveal pathological cell functions. Just to name a few: cellular layer composition of the cerebral cortex or the hippocampus and populations of the same cells in core areas of the brain stem or the basal ganglia can be differentiated, previously only histo-anatomically demonstrable fibre tracts become visible. Foci only millimetres in size, which generate epilepsy, no longer remain hidden and can be neurosurgically excised if they are resistant to medication therapy. Metabolic brain function disorders can be classified by imaging and spectroscopy, sensory and aphasic deficits in the function-MRI can be revealed (**Fig. 1**).

The early diagnosis of stroke, so vital for therapeutic decisions, is provided in minutes by diffusion-weighted sequences and enables differentiation of tissue at risk, which may survive under rapid treatment, from those ischaemic areas (core infarction) in which the transition from functional damage to a structural lesion has already occurred (**Fig. 2**).

In therapy, a not inconsiderable number of surgical procedures has shifted to interventional methods of neuroradiology. Minimally invasive therapies are now considered standard, such as endovascular embolisation of arteriovenous malformations and endovascular elimination of aneurysms by coiling (**Fig. 3**). After the International Aneurysm Study ISAT, involving over 2,000 patients, brought convincingly better results than surgical clipping, standard treatment of aneurysms shifted from operative to endovascular techniques, so that currently ca. 2/3 of the patients are treated with coiling. By embolisation alone of AV-malformations or in combination with surgery or stereotactic radiosurgery, the complication rate could be reduced and malformations treated that could not be removed earlier due to their size or localisation. Likewise in recanalisation of acute vascular occlusions, sophisticated endovascular techniques have created completely new treatment paradigms. Re-opening, using drugs for intra-arterial fibrinolysis, has been increasingly supplemented by mechanical recanalisation procedures, whether as clot retriever systems, vacuum-rinse systems or ultrasound and laser procedures. Their application areas range over the entire central vascular system, including ocular arteries. There has also been a shift in indication for the treatment of vascular stenoses, which are increasingly treated by endovascular procedures with stent-protected percutaneous transluminal angioplasty (PTA)(**Fig. 4**).

In a ranking of the 30 most-important innovations of the past 30 years, MRI and CT-Scanning were at the top, followed in third place by balloon angioplasty of vascular stenoses, whereby application of these imaging modalities play a key role in the central nervous system and the supra-aortal vessels (Fuchs VR and Sox HC, Health affairs, 2001; 20: 30-42). This impressively underlines the importance of neuroradiological diagnostics and therapy.

What will research bring? The decade of the brain flows without a break into the century of brain research. Our high expectations of progress in the neurobiological examination of the brain and its functions are fully justified. Imaging procedures will depict the highest organisational level of cognitive functions, memory processes and even the experiencing of emotions in ever-greater detail, and even portray the function or coupling of neuronal networks in their complex highly dynamic relationships. Neuroradiology stands at the middle of the co-ordination of research work in the clinical partnerships between neurologists, neurophysiologists, neurosurgeons, neurobiologists, psychologists, psychiatrists, microbiologists, informatics and microsystem researchers.

Fig. 1 (below): fMRI of a left handed female suffering from a large temporal low-grade glioma on the right side. Language fMRI with semantic decision tasks for localisation of language areas. Due to the patient's left-handedness a right dominance of language has to be ruled out by fMRI. The fMRI showed clear left sided dominance, thus the patient could be operated on without any risk of speech arrest after surgery

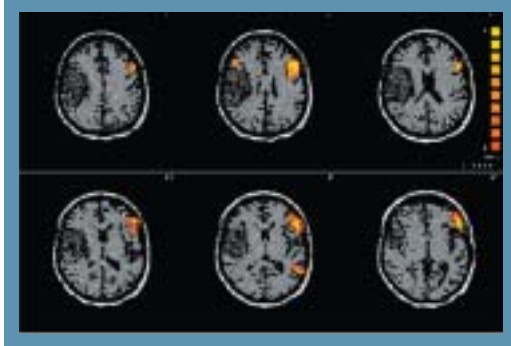
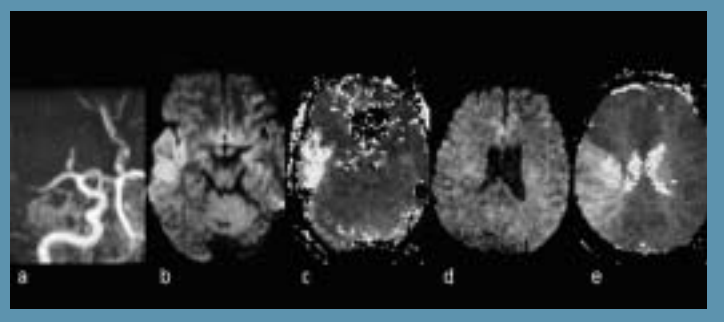


Fig. 2 (below): 58-year-old patient with acute occlusion of the right middle cerebral artery (a). DW-image (b) 45 minutes after stroke shows an ischaemic lesion in the right temporal cortex and subcortical area with a corresponding perfusion deficit (c) in the same area. At a higher level there is no diffusion disturbance (d) but a distinct perfusion deficit (e) indicating a diffusion-perfusion mismatch standing for the penumbra area (tissue at risk)



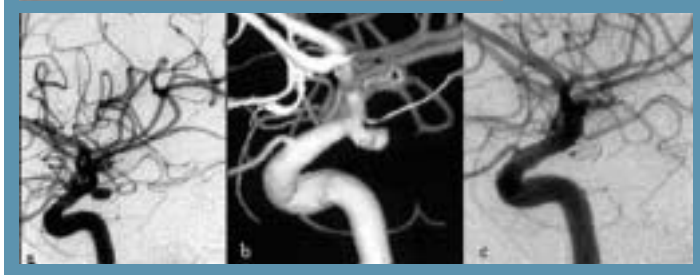


Fig. 3 (above): 40-year-old male with acute rupture of an aneurysm at the origin of the right posterior communicating artery (conventional DSA [a] and 3D reconstruction [b]). Complete occlusion of the aneurysm by 2 GDC-Coils (c) using remodelling technique

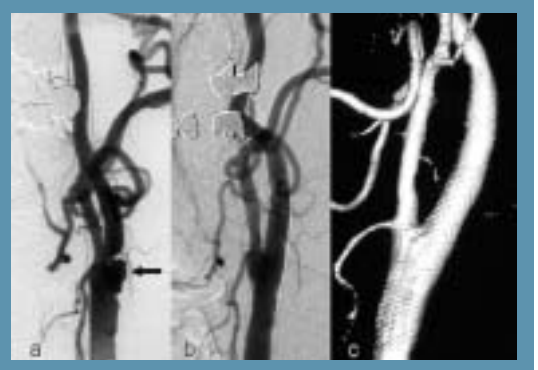


Fig. 4 (right): 66-year-old patient with ulcerous stenosis at the origin of the left internal carotid artery (arrow in a). Angiographic control after stenting with regular vessel lumen (b) well demonstrated in 3D reconstruction (c)

Belgian clinic offers TomoTherapy

Brussels - The Radiation Oncology Department at the Vrije Universiteit Brussel has become the first Belgian and second European facility to install the TomoTherapy Hi-Art System, which is the first commercial system specifically designed for IMRT (intensity-modulated radiation therapy). Chosen to complement the department's oncology treatments the system is expected to reduce side effects (e.g. dry mouth in neck cancer) without compromising a cure.

The TomoTherapy Hi-Art System, which fuses a computed tomography (CT) imaging system with a dedicated system for helical tomotherapy, or slice therapy, combines treatment planning, patient positioning and treatment delivery in precise treatment doses - to all body parts - without increasing radiation deposited on healthy tissue.

Planning - Before beginning this treatment, the doctor uses 3D images (e.g. CT) and special software to establish precise contours for each region of interest (tumour) and any regions at risk (sensitive organs or structures). A decision is then made about the amount of radiation to be given to the tumour, and acceptable levels for surrounding structures are defined. Then the TomoTherapy Hi-Art System calculates the appropriate pattern, position and intensity of the radiation beam to be delivered, to match the doctor's prescription as closely as possible.

Patient Positioning - A special CT scan can be made just prior to each treatment, so the tumour's position can be verified and the patient's position adjusted if necessary (between treatments a patient's tumour can move).

Helical Treatment Delivery - The TomoTherapy Hi-Art System combines IMRT with a helical (or spiral) pattern to deliver radiation treatment. Photon radiation is produced by a linear accelerator (or linac), which travels in multiple circles all the way around the gantry ring. Meanwhile, the couch also moves, guiding the patient slowly through the centre of the ring, so each time the linac comes around, it directs the beam at a slightly different plane.

Report by Michiel Bloemendaal (above) our correspondent for the Netherlands and Belgium

Poland's $1 billion national cancer programme

Two CT laser mammography systems purchased

Following the setting up of a US$1 billion National Cancer Programme to cover a 10-year period and provide screening, diagnostic and therapeutic programmes, two CT Laser Mammography (CTLM) systems, made by Imaging Diagnostic Systems Inc (IDSI), have been installed for clinical research projects in the Institute of Oncology, Maria Sklodowska-Curie Memorial Institute, in Gliwice.

'The research projects we began with the Institute of Oncology, with currently over 400 cases completed in six months, will now continue to conclusion,' said Tim Hansen, IDSI CEO. 'We expect that our global commercialisation programme will follow this pattern, one of regional clinical investigations followed by local area sales.'

IDSL reports that the CTLM system is the first patented breast imaging system to utilise state-of-the-art laser technology and patented algorithms to create 3-D cross-sectional images of the breast. 'It is a non-invasive, painless examination that does not expose the patient to radiation or require breast compression. IDSI has received CE Marking, CMDCAS (Canada), Canadian License, China SFDA approval, UL listing, ISO 9001:2000- 13488 certification and FDA export certification for its CT Laser Breast Imaging system. The Company is seeking PreMarket Approval (PMA) from the FDA for its CTLM(R) system to be used as an adjunct to mammography.'

Interdisciplinary concepts in the fight against breast cancer

At the German, Austrian and Swiss Societies for Senology joint annual meeting (Stuttgart. 8-10 September), experts will discuss the interdisciplinary treatment of diseases of the female breast. **Professor Diethelm Wallwiener MD**, Chairman of the German Society for Senology and Managing Director of the University Women's Hospital Tübingen, points out that this is only the second time that the subject has been aired at the meeting, but adds: 'Only the transfer of knowledge between experts of different medical disciplines will ensure optimum treatment results.'

SENOLOGY

"Interdisciplinary treatment in the context of senology is not an attractive buzzword - it stands for life-saving structures. For a woman with breast cancer, interdisciplinary treatment means that at each stage of her treatment all competencies that she may need are available, to ensure her best possible care. Hormone and chemotherapy are some of the focal points of this year's joint annual meeting in Stuttgart. Psychological aspects of the therapy of mamma carcinoma, as well as the use of new procedures in early diagnosis, will also be discussed.

In the last few years there have been significant changes in the diagnosis and treatment of breast cancer. Ductoscopy, for instance, is one of the forward-looking new procedures for early diagnosis. This imaging procedure would be even better if, in addition, it could help to differentiate between benign from malignant growths. How to achieve this is precisely what experts at the meeting will introduce - a novel concept. There is also news from the neo-adjuvant chemotherapy. The smaller the tumour is at the point of surgery, the more likely the surgeon is to be able to save the breast. Many women feel a great deal of relief when the tumour already becomes markedly smaller during that phase in the treatment. Experts will discuss the advantages and disadvantages of neo-adjuvant chemotherapy during the joint meeting.

These days, breast-preserving therapy is becoming possible for an increasing number of patients. However, it is not the end of treatment for those patients. Rehabilitation of a patient after the operation, and ensuring her quality of life after breast cancer, are important steps in the fight against cancer. That is why we will also bring up these aspects of senology at our Stuttgart meeting. Furthermore, we will discuss the needs of patients whose desire for surgery is only aesthetically motivated. Experts will be introducing the latest operating procedures during lectures and seminars on aesthetic breast surgery.

We expect around 1,800 participants at the meeting, who will discuss these and many other current topics. Over 200 speakers will introduce the latest findings on diagnosis, therapy and aftercare of breast cancer. The objective of our annual meeting is to convey evidence-based findings, which doctors can then put into practice.

The registration fee is based on the date of registration, status, length of visit and membership. Registration is possible online at *www.senologiekongress.de* or through the congress organisers. Current information and the programme can be found on the society's home page (www.senologie.org).

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Prostate cancer

European trials of HIFU treatment are underway

High-Intensity Focused Ultrasound (HIFU) converges at a selected distance from the transducer elements, and the curvature of the transducer determines the distance to the focal length. Although the intensity of the ultrasound is relatively low at the face of the transducer (30 Watts), the site intensity at the focal zone can reach levels greater than 2,000W/cm2. This is a sufficient intensity to raise the tissue temperature in the focal zone to 70-100°C in less than one second, making it a perfect energy for non-invasive therapy - which is real-time image-guided.

Francis and William Fry, researchers at the Indianapolis Centre For Advanced Research (ICFAR), based in Indiana, first used HIFU in the early 70's to treat inoperable brain tumours at the Indiana University Medical Centre. Later, under the direction of Dr John Donahue, Department of Urology, Indiana University, researchers began to pioneer the prostate treatment application for HIFU. From this, ICFAR founded Focus Surgery Inc (FSI) Indianapolis, developer and producer of the Sonablate HIFU-system. In Europe, studies from the early 90s, by Drs Gelet and Chapelon, showed significant success using HIFU for prostate cancer. Those first results have been backed-up by other scientific research (e.g. *3D contrast enhancement after HIFU*, Sedelaar et al: *Eur Urol* 2000). In 1994, the Sonablate HIFU-system was used in Europe for the first time to treat prostate cancer (Dr Michael Marberger: *Effect of High Intensity Focused Ultrasound (HIFU) on Human Prostate Cancer*, 1994).

At the end of 2001, FSI introduced Sonablate 500, a HIFU-system that offers a revolutionary state-of-the-art technology that makes the use of HIFU for prostate cancer treatment more precise, safe, and effective.

The main advantages of this technology include:

- the multi-focal length probe (3.0/4.0) using the same confocal transducer for imaging and treatment - with visualisation during the whole treatment process
- 3D planning software to precisely define the treatment zones
- pre-treatment reference pictures for each image during treatment
- RIM (Reflexivity Index Measurement) for continuous real-time rectal wall monitoring, automatic temperature control, and continuous measurement of rectal wall distance to avoid rectum damage
- a flexibly controlled power output interface that allows the adoption of power intensity to special given tissue situations (e.g. radiologically pre-treated prostates)
- treatment in lithotomy position, which makes a special treatment-table unnecessary. This enabled the development of a compact and mobile device.

The treatment is performed under spinal or sacral anaesthesia. After insertion of the transrectal probe, the prostate is visualised and treatment areas are defined according to the shape of the individual prostate. During treatment, the transducer fires and moves under computer-controlled real-time visualisation until the entire pre-determined volume has been treated. Benefits of the Sonablate 500-system are that it is truly non-invasive, safe and physician controlled, effective, adaptable to the physician's and patient's therapeutic goals, repeatable, and there is no therapeutic impasse (alternative options still allow post Sonablate 500 therapy).

Worldwide clinical studies show up to a 90% CR (complete response=neg. biopsy and no PSA increase), an average nadir PSA lower than 0.45ng/ml and a re-treatment rate of approx. 10% after one year. These data are backed-up by a European MC-study, as well as a few additional, smaller studies done with another HIFU system (success rate 84%, with 5-year follow-up).

So far, over 7,000 patients have been treated with HIFU, and more than 2,000 of these with the Sonablate 500-system.

Furthermore, the Sonablate 500-system shows multiple-use potential - prostate diseases including cancer and BPH, liver and kidney carcinoma applications under development, and testicle carcinoma in clinical evaluation (first clinical results from Prof. Marberger, at the AKH/University hospital, Vienna - presented by Prof. Schatzl of AKH in June 2003 at the 3rd International Symposium on Therapeutic Ultrasound (ISTU).

Source: Misonix

EU challenge to worldwide BRCA2 gene patent

Recently an unparalleled legal challenge has been underway in the European Union (EU) regarding the number of human gene patents held by US-based corporation Myriad Genetics, for sequences of two genes, BRCA1 and BRCA2, mutations that indicate a predisposition to breast cancer. This type of legal challenge is commonly known as an 'opposition' to a granted patent

By our USA correspondent
Karen Dente

Dr Karen Dente

under European patent law. 'Third parties are allowed to challenge the validity within nine months from the grant of the patent,' explained Siobhan Yeats, the European Patent Office's director of Examination and Opposition in Biotechnology, in an interview with European Hospital.

On June 29 the European Patent Office (EPO) upheld a patent licensed to Myriad Genetics of Salt Lake City, Utah. European clinical groups launched an opposition to the worldwide monopoly rights over the breast cancer BRCA2, saying that it should be dismissed on the basis of ethical and legal reasons. Myriad has been pushing for licensing expansion in Europe.

Between 2001 and 2003, the EPO has granted several patents to Myriad Genetics on familial breast cancer genes BRCA1 and BRCA2. These patents have permitted the US firm to gain and retain monopoly on BRCA1 and BRCA2 testing. Although Myriad has exclusive rights to commercialise tests based on BRCA1 and BRCA2 in the United States, European clinics have been opposed to signing up for licenses. The European genetics community has adamantly resisted Myriad's monopoly for breast cancer screening as they see it as an interference with national policies surrounding DNA-based diagnostic services.

Furthermore, the basis for the breakthroughs in breast cancer research that led to the initial patent claims by Myriad in 1994 and 1995, was made possible as a result of a collaborative effort on behalf of worldwide academic research groups. Geneticists and healthcare providers criticise the fact that Myriad spent minimal funds discovering diagnostic tests that, in addition to having inaccurate results, are offered at very high costs. While Myriad offers patients a test for a fee of about €3,800, similar tests are offered by German universities at a cost of around €1,800.

Whereas opposition to some of Myriad's claims over the gene BRCA1 was successful, to the extent that it no longer provides any considerable threat to diagnostic practice in Europe, it is Myriad's licensing rights on the second breast cancer gene, BRCA2, that has recently met with disapproval among European physicians and researchers. Before facing opposition at the EPO, Myriad rephrased its claims for the patent to cover the use of a certain DNA probe that compromises a single mutation for 'diagnosing a predisposition to breast cancer in Ashkenazi Jewish women in vitro.' The mutation 6974deIT, described in the patent, is somewhat more common among Ashkenazi Jews.

'This is definitely not the way to go,' said Geert-Jan van Ommen, a human geneticist from the University of Leiden, in the Netherlands. Seeking ownership of a mutation in an ethnic group '...is not acceptable to most geneticists,' said Gert Matthijs, of the University of Leuven, Belgium.

The patent dispute over the BRCA2 gene is being followed closely by researchers, physicians and policymakers both in the European Union and the United States, where the permission of exclusive monopoly rights over human genes in dereliction of healthcare and scientific research runs contrary to the public interest and the goals of the patent system. The growing debate over gene patent domination over both patient care and research illustrates the need for prompt modification of the US patent law.

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THE BALKAN CLINICAL LABORATORY FEDERATION
Success through collaboration

By Manole Cojocaru MD PhD, President of the 2004 BCLF Meeting

Founded in 1993 to promote the advancement of clinical laboratory medicine in the Balkan region, the Balkan Clinical Laboratory Federation (BCLF) encourages the affiliation of clinical laboratories with leading international organizations, such as IFCC and FESCC.

In 2004, I was president of the BCLF. This September the 13th BCLF Meeting will be held in Tirana, Albania, under the presidency of Professor Todor Gruev, of Macedonia.

After the successful 8th BCLF Meeting with international participation in 2000, in Sinaia, I had proposed that the 12th Meeting of the BCLF should be organized by the Romanian Society of Laboratory Medicine (RSLM), and it was organised under the auspices of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and Forum of the European Societies of Clinical Chemistry and Laboratory Medicine (FESCC). The event, in Neptun in September 2004, attracted over 300 laboratory medicine workers from Balkan countries, and the rich scientific programme included 24 main topics. Professor H Reinauer (Germany) delivered an excellent plenary lecture on *Laboratory diagnosis and monitoring of diabetes mellitus*, and the following research studies contributed to numerous new and interesting observations, studies, and discoveries in all laboratory medicine branches. Within the scope of this review, however, only a few can be mentioned (see box).

BCLF must remain basically a Scientific Society, as quoted in its name, and consider the role and importance of scientists in the future orientation and developments.

The link with IFCC and FESCC and recognition of a full speciality in all Europe are the keys to attract more members and enlarge our field. Specialists in clinical laboratory must also be aware of laboratory medicine, to maintain a strong harmonized European speciality in all the countries, with common training and CME, and free circulation.

Member societies of the BCLF and of the Executive Board of the Federation are from Albania, Bulgaria, Greece, Macedonia, Romania, Serbia and Montenegro, and Turkey; additionally, from 2004, the Sarajevo-based Association of Medical Biochemists of Bosnia and Herzegovina (founded 2003, and with about 50 members) became a full member of the BCLF.

The 12th BCLF Meeting was a successful congress, where the participation of professionals and the societies of Balkan countries joint efforts continue to improve the quality of the profession. I am deeply indebted to many people who worked together to achieve that very successful meeting.

Research presented at the BCLF Meeting

A world priority of the Romanian science from the discovery of the first water channel protein (later called aquaporin I) in Cluj-Napoca in 1985 to the 2003 Nobel Prize in chemistry and the medical implications of aquaporins **(Gh. Benga, Romania)**; External quality assurance and the detections of autoantibodies **(M. Bluthner, Germany)**; Infection surveillance and control programmes in preventing nosocomial infections in French hospitals: national programme 2004-2007 **(B. Gouget, Chair IFCC Communication and Publications Division, France)**; Transforming growth factor beta system in kidney diseases **(T. Gruev, Macedonia)**; Quality control of genome detection in virus diagnostics **(H. P. Grunert, Germany)**; Molecular investigations of the hereditary cancers **(Ch. Kalogera, Greece)**; Traditional and novel biochemical markers of cardiovascular disease risk prevention **(E. Bairaktari, Greece)**; From analytical to clinical quality in laboratory medicine **(S. Ignjatovic, Serbia and Montenegro)**; Metabolic syndrome and risk of CVD **(A. Tzontcheva, Bulgaria)**; Oxidative stress and antioxidative defence in type 2 diabetic patients with cardiovascular complications **(E. Colak, Serbia and Montenegro)**; Clinical relevance of antikeratin antibodies in rheumatoid arthritis and symmetric polyarthritis associated with hepatitis C infection **(M. Cojocaru, Romania)**; New IgE myeloma case report **(Z. Mijushkovich, Serbia and Montenegro)**; Etiologic agents of urinary tract infections and their susceptibility to antibiotics **(S. Berbecar, Romania)**; Quality control in the clinical microbiology laboratory **(R. Papagheorghe, Romania)**, etc.

Advanced ADME/Tox technologies and drug development

Approximately 90% of drugs fail in their development stage due to poor absorption, distribution, metabolism, elimination (ADME) or toxicity properties. The estimated cost to pharmaceutical firms is US$50-$70 million.

'It is increasingly clear that the ability to detect issues with pharmacokinetics before the drug moves into clinical testing will ultimately save considerable resources in time and money for pharmaceutical and biotechnology companies,' says Frost & Sullivan Healthcare Analyst at Frost & Sullivan, a global growth consulting company, Dr Amarpreet Dhiman, in his report 'Strategic Analysis of the ADME/Tox Technologies Markets in Europe (B512-55).

ADME/Tox tests had been deployed in the later stages of drug development, he points out. However, with the number of drug targets as well as the volume of assay points performed in high-throughput screens expanding, it has become critical to rapidly and efficiently triage 'potential hits', having significant ADME and toxicity profiles.

Innovative technologies and solutions are already facilitating ADME/Tox optimisation

earlier in the drug discovery pipeline. 'This will help yield compounds with good target affinity, reasonable drug-like properties and ensure greater likelihood of acceptable ADME/Tox properties. Moreover, it is likely to accelerate the selection process, reduce the cost of preclinical and clinical studies and boost overall prospects of success,' he points out.

Sophisticated informatics is widely deployed to manage data for analysis and interpretation. Advanced software with the ability to distil compound leads with promising drug development potential, as well as predict biological properties, have been designed. Complete solutions that include tools are also poised to amplify their presence within the ADME/Tox tools market.

In-silico techniques - complex and accurate models for rationalising and predicting ADME properties - are allowing enhanced prediction of complex systems (for hepatoxicity and cardiotoxicity).

Such computational technologies and predictive solutions are likely to enhance the scope and speed at which drugs develop from a research to clinical stage. At the same time, however, in order for ADME/Tox studies to be truly beneficial, data generation needs to be of high quality, reliable and accurate. 'The key would be to develop tools that facilitate data consolidation and information sharing,' Dr Dhiman advises 'Standardised systems and solutions that integrate data from numerous tools and experiments need to be developed while manufacturers should develop opportunities to offer services in data management, training, tool maintenance and others, functioning as both a service providers and product developers.'

'As companies try to decrease costs by increasingly outsourcing drug development functions, failure rates become more controlled, in-silico technologies become more widely adopted and a better understanding of ADME/Tox and pharmacokinetic properties motivates the use of innovative solutions and early ADME/Tox screening, the European ADME/Tox technologies market will grow from its current size of $384.0 million to $776.0 million by 2011. Currently, ADME/Tox services comprise the largest market segment in Europe for ADME/Tox technologies, accounting for nearly three-fourths of overall market revenues. It is followed by ADME /Tox tools (including systems & consumables) and in-silico ADME /Tox.

One key global trend is likely to be the rising uptake of in-vitro screeningtechnologies (for screening toxic compounds), he predicts. A stream of novel compounds moving through the clinical process is likely to support the rapid development of assays for ADME/Tox properties, creating, in turn, significant long-term market growth opportunity for in-vitro screening technologies.
Details: http://healthcare.frost.com

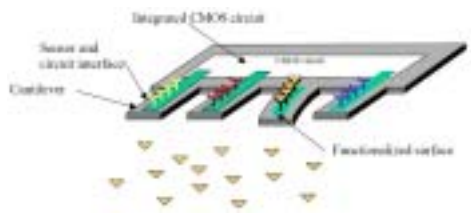
Micro and nano–technologies

Spain & Ireland - Working on the BioFinger Project funded by the IST Programme, a team of researchers has begun testing a small molecular detection tool amid expectations that a commercial product will become available within two to three years. 'We are creating a generic, highly precise and highly versatile tool to detect and analyse molecules in the blood, and other fluids, using nano and micro cantilevers,' explained project coordinator Joan Bausells, of the Consejo Superior de Investigaciones Cientificas, Barcelona, Spain.

Nanocantilevers, smaller than the surface of a fly's eye, and their larger counterparts microcantilevers, function as sensors to detect molecules. When coated with antibodies they bend and resonate to changes in surface tension and mass when fluids containing disease-related protein molecules attach to them. By seeing whether or not the cantilevers react, doctors should be able to determine whether or not a disease is present.

Though much research has been carried out on cantilevers, this has focused principally on creating large-scale tools for use inside laboratories. But, said Joan Bausells, 'You can't carry those around with you. What we're developing is the first portable device that will allow doctors to diagnose diseases on the spot, almost immediately.'

During the present trials at Cork University Hospital, Ireland, the microcantilever ver-



sion of the system is being used to detect a protein associated with prostate cancer, while the nanocantilever system, said to detect a single molecule, is being used to test blood samples for interleukin 6, a protein associated with inflammation.

BioFinger incorporates the cantilevers on a microchip that is disposable after each use, allowing it to be reconfigured with new on-chip cantilevers to detect different substances, the team explained, adding that analysis can be performed anywhere, anytime, and takes only 15-20 minutes. 'In addition, the system is likely to be considerably cheaper than traditional diagnosis techniques with each disposable chip expected to cost around 8 euros. It is also extremely versatile,' Bausells observed. 'It could be used to detect virtually any disease, or as a pregnancy test or even to determine blood types. Outside of the medical field,' he added, 'it could be used to analyse chemicals, detect bacteria in food or test for water pollution.'
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Grants for pain researchers

The European Federation of IASP Chapters (EFIC) Grünenthal Grant 2005 has been awarded to young scientists and their research projects on pain therapy (see photo caption).

The EFIC Research Committee, which decided on the purely scientific projects to be sponsored, reported that this year sees a variety of different approaches ranging from imaging of chronic pain processes in the brain to the psychological management of pain patients following cervical spine injuries.

Four of the five sponsored scientists - from the UK, Denmark and Germany - have received a grant of 20,000 Euros each for their research project. The fifth prize winner is receiving 15,000 Euros to learn a special research technique at a different institute.

Grünenthal GmbH, a research-based, family-owned, pharmaceutical company that focuses on pain therapy, gynaecology and new technologies, donated the 100,000 grants. The firm has production sites in seven countries, representation in 25 countries, affiliates in virtually all European countries, and employs around 1,800 people in Germany and 4,800 worldwide.

The firm's managing direct, Rob Koremans, said: 'Traditional research prizes consider the results of work already performed and therefore often tend to be awarded to specialists in established research centres. In contrast, the EFIC Grünenthal Grant (EGG) sponsors planned projects before they start. In particular EGG focuses on sponsoring young scientists and the dissemination of innovative pain research throughout Europe.'

From left: Rob Koremans, member of the Executive Board of Grünenthal, with EGG 2005 winners Dr Christina Liossi (Great Britain), Dr Helge Kasch (Denmark), Dr Anthony R Hobson (Great Britain), Professor Jens Ellrich (Germany) and Harald Breivik, chairman of the EFIC Research Committee and immediate former president of the EFIC. The fifth laureate Dr Irene Tracey (Great Britain) could not attend the ceremony

€1.5 million prize for scientific research

Prof. René Bernards

The Netherlands - The Spinoza Prize, worth €1.5 million, is awarded annually by the Dutch Organisation for Scientific Research NWO to four top researchers for their 'outstanding, groundbreaking and inspiring research'. Professor René Bernards (52) has been named by the NWO jury as one of the prominent leaders in biomedical research. The professor uses innovative technologies to study fundamental processes in cells, and was among the first to measure patterns of gene activity by applying DNA micro-array technology, which predicts accurately whether a breast cancer patient will develop metastases. More recently, he worked with RNA interference technology (RNAi), a new method that - using a library of 24,000 RNA fragments - enables shutting down of human genes one at a time, thus revealing their function.

Prof. Bernards is also co-founder and chief scientific officer of Agendia BV, a spin-off of the Netherlands Cancer Institute (NKI). Agendia's MammaPrint, a prognostic test for breast cancer patients, is based on parts of the professor's work that was honoured by NWO. The professor, with over 100 papers published in peer-reviewed journals, is head of the division of Molecular Carcinogenesis at the NKI, which he joined in 1992 after a six-year assistant professorship at Harvard University.

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