EUROPEAN HOSPITAL

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

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Muhammad Ali: living with PD

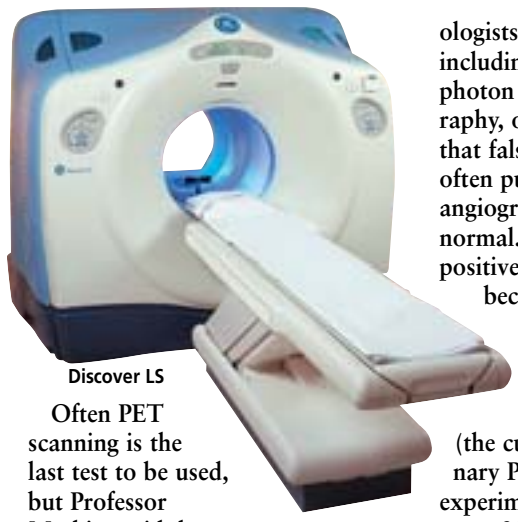
Parkinson's disease (PD) is not uncommon. It is well known that the late Pope John Paul II was afflicted, as is the actor Michael J Fox. Publicly viewing its effects helps demonstrate how debilitating the symptoms are to people otherwise sound in body and mind. To explain PD to children, Rasheda Ali (above), actor and daughter of the world famous boxer, has launched a book 'I'll hold your hand so you won't fall. ***A child's guide to Parkinson's Disease***' (Merit Publishing), which should become a valuable aid to healthcare professionals working with sufferers and their families.

See page 2

PET scanning the heart cuts costs

USA - Using positron emission tomography (PET) scanning rather than other types of imaging as the first tool to diagnose heart-vessel blockages is more accurate, less invasive and saves money, according to researchers reporting at the American College of Cardiology's Annual Scientific Session in March.

Results of the study provide a rationale for PET scanning to become the initial diagnostic test for assessing a patient's risk of heart attack, said lead researcher Michael Merhige MD, clinical associate professor of nuclear medicine, and Joseph Oliverio, certified nuclear medicine technologist and clinical instructor of nuclear medicine - both at the University At Buffalo (www.buffalo.edu), and affiliated with the Heart Centre of Niagara at Niagara Falls Memorial Medical Centre.



Discover LS

Often PET scanning is the last test to be used, but Professor Merhige said, however, he added: 'Because it is more accurate and provides a clearer picture of the state of the heart, it could decrease the use of angiograms (costing about $4,800 each) and bypass surgery by more than 50% if used as the first-line test with patients. Currently cardiologists conduct a range of tests, including stress tests and single photon emission computed topography, or SPECT.' But he added that false readings from SPECT often put patients through angiograms that turn out to be normal. 'PET avoids most false positives, as well as false negatives, because the images have higher resolution.'

There is not much peer-reviewed literature that compares PET to SPECT (the current standard), so coronary PET scanning is considered experimental in this field, although some 25 US centres are thought to use it for cardiac assessment, and one has done so for about a decade.

The researchers compared costs and results for SPECT scanning 102 patients, with PET scanning for 2,159 patients. All the patients

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Med-e-Tel 2005

'eHealth is becoming the third industrial pillar for health, behind the pharmaceutical industry and medical imaging, to reach an estimated 5% of all healthcare expenditures by the year 2010", said Professor Jean-Claude Healy, Director of eHealth Strategy at WHO, at the opening of the Med-e-Tel conference and trade show held in Luxemburg (April), which attracted over 400 representatives from healthcare, the industry, academies and government representatives from nearly 50 different countries. Several European Commission co-funded ehealth projects were also exhibited, alongside about 50 companies, projects and media showcasing vital signs monitoring, archiving and communication systems, digitisation of clinical data, electronic data capturing/sharing, medical software solutions, and decision support systems.

The conference programme covered teleconsultation, ehealth implementation in developing countries, distance education, standardization and interoperability, ethical issues, use of handheld devices in hospitals, image transfer and internet ehealth applications. A special session was dedicated to *European ICT for Health* research. The International Society for Telemedicine & eHealth (ISfTeH), presented national ehealth experiences and programmes from Brazil, Croatia, El Salvador, Finland, Georgia, Poland, South Africa, UK and Ukraine - and also represented members from Denmark, Germany, Norway, and Russia on its exhibition stand.

For details and proceedings: info@medetel.lu. Med-e-Tel 2006 is scheduled for 5-7 April, in Luxembourg. Details (available soon): www.medetel.lu or contact info@medetel.lu to register interest.

Further telemedicine reports: page 20

Drug reduces body weight plus cardiovascular risk

Professor Luc Van Gaal

The drug rimbonabant helped to substantially reduce the bodyweight, waist circumference, and risk factors for heart disease in obese people, according to results of a phase III randomised trial presented at the Scientific Sessions of the American College of Cardiology in Orlando, Florida in March and published in The Lancet (15/4/04): '*Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients*.' (The first-year results of the RIO-Europe study were presented at the European Society of Cardiology meeting in August 2004).

The RIO-Europe two-year phase III study of rimonabant involved 1,507 people from Europe and the USA, and was led by principal investigator **Luc Van Gaal MD**, Professor of Diabetology, Metabolism and Clinical Nutrition, and colleagues at the University Hospital Antwerp, Belgium. 'The RIO-Europe findings demonstrated that in addition to maintaining body weight loss, two-year treatment with rimonabant 20 mg/day compared with placebo reduced waist circumference improved metabolic profile and reduced the number of patients meeting the National Cholesterol Education Programme (NCEP) criteria for metabolic syndrome, thus diminishing cardiovascular risk factors in patients studied,' Professor Van Gaal concluded.

In an accompanying comment in *The Lancet*, Uberto Pagotto and Renato Pasquali, of the Department of Internal Medicine and Gastroenterology, Sant Orsola-Malpighi Hospital, Bologna, Italy, wrote: 'These data, and those from the other ongoing clinical trials with rimonabant, might presumably help us to better tackle obesity and related metabolic and cardiovascular disease. When additional drugs are available, we will also have the possibility to individually target the therapeutic strategies according to phenotype characteristics and to the pathophysiological mechanism inducing the disease.'

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A new training scheme for junior doctors

In the future, 80% of patient treatments will be provided in primary care settings, rather than hospitals

Sir Liam Donaldson, Chief Medical Officer for England. Role: advisor to the Secretary of State for Health, the Prime Minister, health ministers and ministers of other government departments

A Foundation Programme Curriculum for junior doctors has been launched by the United Kingdom's Department of Health, as part of its *Modernising Medical Careers* programme. In this new programme trainees will have to demonstrate competency in traditional medical areas - as well as in communication and consultation skills, patient safety and team working.

The programme includes:

- The framework for a structured two-year training programme that will give trainees exposure to a range of career placements across a broad spectrum of specialties, such as accident & emergency, obstetrics & gynaecology and anaesthetics. The programme also aims to give each trainee the opportunity to have experience in primary care and provide opportunities for experience in smaller specialties and academic medicine, not normally available at this stage of training
- Explicit standards of assessment and structure supervision for trainees, where an educational supervisor will oversee each trainee and each post will benefit from a dedicated clinical supervisor
- The requirement for trainee doctors to learn a range of skills, including communication, the undertaking and use of research, time management and use of evidence and data. Each of these skills will be assessed through an agreed method prior to completion of the programme.

'For the first time, doctors will have the opportunity to explore a range of career options, while ensuring that their acute clinical and professional skills are secure and robust,' Sir Liam Donaldson, Chief Medical Officer for England, pointed out. 'This is very much a curriculum for patient safety, ensuring that at the end of their two years of training doctors are both confident and competent and we are delighted that the UK is leading the world in innovations in medical education.'

The UK Government's Health Minister John Hutton explained that, because the country is moving to a situation where 80% of patient treatments will be provided in primary care settings, rather than hospitals, more trainee doctors need to spend time in places such as general practitioner (GP) surgeries and the patients' 'Walk-in Centres' now provided in many of them.

'The UK is at the forefront of worldwide educational practice'

One of the aims of the programme, added Dr E M Armstrong, Chief Medical Officer of Scotland, is to ensure that patients are seen and treated by '... trained doctors rather than, as at present, by doctors in training', and added that young medical graduates will need to acquire the requisite skills and competences to achieve specialist accreditation over a shorter period than previously.

Dr Ruth Hall, Chief Medical Officer to the Welsh Assembly Government, said that a second introductory year for doctors had been thought necessary in educational circles for some time. 'In introducing this now we are delighted to say that the UK is at the forefront of worldwide educational practice.'

Chairman of the Academy of Medical Royal Colleges Professor Sir Alan Craft said that the curriculum '... heralds a new era in medical training and education in the UK. As healthcare changes, the Foundation Programme curriculum will ensure that doctors going through the system are fit for the modern healthcare service."

One of those taking part in the pilot project for the programme, Dr Kate Grisaffi, explained that she had chosen to do it in order to experience a wide range of specialties. 'The best thing was developing the generic skills essential for all doctors - good acute care skills, communication and teamworking skills.'

The curriculum, which follows on from publication earlier this year of the General Medical Council's *The New Doctor 2005*, was launched in April, and will commence this August.

Until 2007, Foundation Year 1 (F1) trainees will continue to undertake a year in PRHO-approved training placements, including at least three months in both medicine and surgery. As part of F1's ongoing development, an increasing focus will be placed on assessing core competencies gained along the training pathway.

A number of assessment tools are being piloted with over 1,750 trainees across the country, to develop a robust, validated process for proving a trainee's competence ahead of full General Medical Council (GMC) registration and progression into the second year of foundation (F2).

The foundation curriculum will ensure that trainees move seamlessly from F1 into F2 following assessment and subsequent GMC registration, said the Department of Health.

PET SCANNING THE HEART CUTS COSTS

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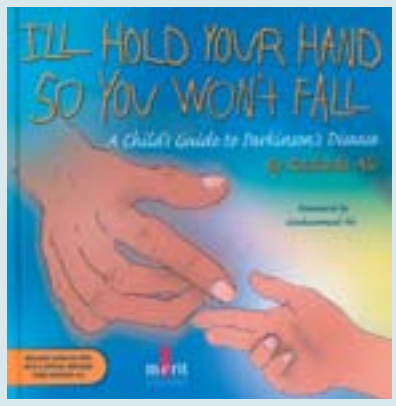
were matched by the extent of coronary artery disease. Data was also compared from the 102 SPECT patients with data from a national multi-centre trial to confirm that the team's results were valid. These showed that both the rate of heart attack and cardiac death were significantly lower after one year in patients managed by PET, as was the number of angiograms, balloon angioplasty with stenting and coronary bypass surgery. In the PET group, the average cost of management of a patient with coronary artery disease was also lower - by 25%.

Whilst Prof. Merhige said bypass surgery and angioplasty with stenting is a necessity for some patients, he believes many are done unnecessarily and medical management could be an alternative. Significant lifestyle changes - very low-fat diet, exercise, cholesterol-lowering drugs and stress management - are essential for successful medical management, he pointed out, but some people see surgery as a quicker option '...when it actually only addresses symptoms, not the underlying disease process,' he said.

Continued from page 1

A child's view of PD, written by Rasheda Ali, daughter of the great fighter, is set to help greater understanding. *Report: Brenda Marsh*

Mohammed Ali developed a shuffling walk and slurred speech, the onset of PD, in the mid-80s. But what Rasheda, one of his nine children, remembers is just accepting it as 'old age'. Gradually, she accepted what it was. 'Slurred speech certainly is an obstacle in my family,' she said, smiling. In later years, when she had her own children, she avoided the laboured phone calls with Ali, preferring to visit him, to '... have that body language - facial expressions become more important than words,' she pointed out, during her international tour in April to promote the guide. 'The majority of people with PD are very sharp, very alert,' she stressed. 'The biggest misconception is that it's the same as Alzheimer's. My father has a perfectly clear mind. He just has shaking hands and slurred speech. So he chooses not to speak. The family has developed a whole series of non-verbal ways of communicating. I was sitting with my dad at an event when a woman asked if I thought my dad would give her an autograph. "Why don't you ask him? He can understand every word you say," I told her.' He smiled and signed the autograph.



During a visit to Ali's Michigan farm under a year ago, she watched her two sons, communicating with her father. Her younger son, Nico, had been playing with Ali, in his boxing ring, then asked her: Why is Popi shaking? 'I was stumped,' Rasheda recalls, 'All I could think was "Well, he has Parkinson's" but that means nothing to a four-year-old.' Over a period of time, some of her children's questions, included: Why doesn't he answer me? and when told it was due to PD, asked How did he get it? Is it contagious? Would they get it, too. 'I thought a lot of other parents out there probably didn't have answers for their kids, either,' she said, explaining the inspiration to write the guide.

In health, she said, 'My father has good and bad days', but he still travels to meet fans 280 days of the year. 'My father really was the people's champion, and he is still a fighter, but these days his opponent is Parkinson's disease.' One of his frequent stops is the Muhammad Ali Centre, in Louisville, Kentucky, and he is very involved with the Ali PD Data Base, into which doctors feed information about patients with the disease, to help researchers to find any common denominators that link their experiences.

Rasheda does not believe Ali's PD was caused by boxing, though feels more research is needed to fully rule it out. 'There are tens of thousands of ex-boxers out there, and I only know of two diagnosed with Parkinson's,' Rasheda pointed out. Exercise is considered vital for those with PD, and Ali uses his boxing ring, shadow-boxing and hitting punch-bags.

Ali also draws and paints, she said, showing a picture done for her sons. It depicts a boxing ring with a multitude of dots for people - it is vibrant and meaningful. 'His feeling and love for art and drawing, and my kids' love for art and drawing, is drawing them together. They almost create their own universe when they are together,' she added.

'For over 20 years I have had Parkinson's disease. Fortunately, my health has been reasonably good and I still do many of the things that I have always enjoyed. Even so, I am aware of how much this disease has diminished the quality of life I now enjoy,' Ali writes, in a foreword of the book. 'It becomes especially evident when I notice how my grandchildren and even my adult children become perplexed as the "new" me evolves. For my children the change has been gradual, but still the nuances of this disease are a challenge to us all. With my grandchildren it has been more difficult ... they find it difficult to communicate with me. They don't understand why my arms tremor or my walking is stiff and rigid, or why I don't smile as easily as they do.'

Book orders and contacts: www.meritpublishing.com

CONTROVERSY: the nurse-surgeon

Nurse-surgeon training in the UK, the lead story in European Hospital's February issue, produced a lively response because other European countries are also training nurses to undertake certain surgical procedures to address their lack of qualified surgeons. The concept is not entirely new. In the 1970s the Netherlands introduced training for 'operation assistants', and the USA has had 'registered nurse first assistants' for 15 years. A 'surgical assistant' course began in Germany in 1999, and the first course for surgical assistants in cardiology was introduced this March.

EH correspondent ***Holger Zorn*** *reports*

'The General German Medical Council, the umbrella organisation that represents German doctors, was not prepared to make a statement on this subject. However, the Marburger Bund (Marburg Association) - with 80,000+ members the largest organisation in Europe representing salaried doctors - was more forthcoming: Unfortunately, doctors (particularly hospital doctors) must carry out an increasing volume of non-medical work. But surely, the solution cannot be to remove their real medical work - particularly since it is difficult to recruit sufficient numbers of medical and nursing staff to begin with! It would make far more sense to relieve doctors of many documentation-related administrative tasks - about a third of their workload. Non-medical staff, i.e. nurses, could carry out, for example, infusion therapy, which they used to do.

Dr Udo Wolter, a member of the Marburger Bund and President of the Brandenburg Medical Council, who specialises in hand and emergency surgery, is against nurse-surgeon training, arguing that, due to the ruling by the European Court of Justice on hospital working hours (being on-call is considered time worked), assistants are left with less time to assist and learn to operate. 'Assistance through qualified doctors is the most important form of further training,' he said, adding that this must be ensured for future needs in general and specialist surgery. Although the nurse-surgeon training aims to improve and continuously ensure the quality of surgical assistance - and provide surgery at a lower cost - young doctors could miss chances to pass their medical qualification in surgery: 'No cardiac surgeon commenced his/her career with an organ transplant.'

The Catholic Institute for Nursing, Marienhospital, Osnabrück provides conventional nursing training and, since 1999, has offered a course to train as operating theatre assistants (OTA). In March, Ulrich Barlag, Head of the Institute, and nursing academic, announced that in a new course, nurses working in operating theatres will be trained as second and first assistants for surgical interventions in cardiology, e.g. removal of a leg vein or preparation of the internal thoracic artery.

Nine CAs (Chirurgie-Assistant) were trained during a pilot phase in 2001, and over 200 enquiries for places have been received for the first regular course, which will begin later this year. To qualify for acceptance, applicants must be qualified nurses or operating theatre assistants with 2-3 years experience in cardiosurgery, and must be familiar with all aspects of instrument handling.

The six-month course will cover theory and practice. Subjects: anatomy and physiology of the lower extremities, diseases of the arterial and venous systems and treatments, water and electrolyte metabolism plus blood coagulation and anticoagulation; intra and postoperative complications and wound-healing problems; the basics of HF surgery and the legal status of surgery assistants. A written exam will follow forty hours of theoretical study.

The operating theatre programme is based on that for specialist surgery training for doctors. Typical vein removal will be demonstrated and practised on dummies and the students will be taught stitching and knotting techniques. They will also assist surgeons by removing leg veins in preparation for a bypass for 80-100 cases, all closely monitored by a mentor.

Nurses who successfully complete all the categories will receive a certificate.

An unnecessary rein on medical innovations, or a wise insurance for patients' protection?

HEALTH TECHNOLOGY ASSESSMENTS


Matthias Perleth

The press says it's a miracle cure, so why can't I (or - as relevant - my brother, mother, child) have it now? The answer is not simple: although a new technology or treatment may have been the subject of successful studies, it must go through a *Health Technology Assessment* (HTA) before clinical use because, in many EU countries, medical insurers will not reimburse for procedures that have not had an HTA. We asked **Dr Matthias Perleth**, of the Department of Medicine at the AOK Federal Association, (AOK-Bundesverband, Stabsbereich Medizin) to explain how an HTA system works and its potential.

'Depending on the country, an HTA is initiated by different institutions. In Germany, for example, this it is the role of the joint federal committee - comprised of doctors', hospitals, medical insurers' and patients' representatives - which completes an application for the inclusion of a new technology,' Dr Perleth explained. 'Following various discussions in different committees, a recommendation is then made. So, initially, the HTA is a tool for health politics - used to assess whether the costs of a procedure are likely to be covered. In essence, an HTA is a data review.'

Is an HTA on for new procedures? And is it always based on existing data?

'This hasn't really been resolved. On the one hand, new technologies should be assessed as early as possible, for the potential benefit of patients. However, to carry out HTAs we need clinical studies. A good example is Kyphoplasty, which helps to repair and stabilise vertebrae affected by fractures. Because this procedure carries certain risks, the firm marketing it has imposed very limiting conditions as to who is allowed to carry it out, and also stipulates that it should only be used to treat new, recent fractures. However, because kyphoplasty is so attractive it's being used for other indications, such as for older osteoporotic fractures, but the results are not as good as those achieved with new fractures - which we hardly ever get to see.'

Couldn't a preliminary HTA be carried out, and then reassessed in a few years?

'That's something we could think about. Despite the dilemma about available data, the HTA should support decision-making, especially when a procedure is still new. If the statutory medical insurers do not reimburse for a procedure its use will be very limited, then hardly any data can be gathered. That's why differentiated decision models are increasingly discussed. Initially, a procedure can be financed within the framework of certain test trials, before a final decision about its use is made. This allows us to prevent unjustified expansions of indication at an early stage.

'How all this is being handled in detail depends on the decision-making structures in any particular healthcare system. In Switzerland, for example, there is a very differentiated range of decision-making options. Sometimes a procedure may only be allowed in certain hospitals, or a clinical study has to be carried out over a certain period of time before another evaluation is made. In Germany we have the added problem that everything is currently in a state of flow, due to the introduction of DRGs and the revision of the OPS-Code. HTA procedures must be further developed and data generated at an early stage, so that information can be updated constantly - something already occurring in other countries, at the National Horizon Scanning Centre in the UK, for example (see box). This centre produces and regularly updates dossiers when studies on certain technologies are published, and that's mostly three to five years away from them being introduced to the market.

'The classic HTA is a retrospective assessment, as existing data is being analysed. If carried out during the development of an innovation, an HTA can be completed at a much earlier stage. We can establish reciprocity between the institution carrying out the HTA and the institution developing the new technology, be it a university or a company, and use this reciprocity. There was a joint project, with the university and industry in Hanover, in which scientists at the university went to look at projects developed by companies, then gave their feedback. In this way we can ensure we have a user evaluation, as well as clinical evaluation on which to base an HTA. But quite often today's available data is just too bad for a meaningful HTA. The second, important point of doing HTAs during the development of innovations is that you can answer the question: *Is this actually potentially meaningful technology?* at a very early stage of development.

Does industry play along with this?

'Not really; they tend to want to keep things close to their chests. This is where a market economy-based way of thinking conflicts with scientific requirements. In Germany, the term *innovation brake* is used a lot - as soon as yet another great innovation has failed approval by the federal committee, and the statutory insurers decide against financing a new procedure, these bodies are automatically accused of being against innovations and of not giving enough consideration to patients. Typically, however, these tend to be technologies for which there have never been any meaningful clinical trials. This is why we need to improve communication, particularly as HTAs carried out as new procedures are being developed, give companies more reassurance about the innovations they are bringing in to the market.'

Based on an interview with Annette Bus

HOW DOES IT WORK?

The National Horizon Scanning Centre (NHSC)


Dr Claire Packer, Director

The NHSC aims to provide the Department of Health (DOH) in England and Wales with advance notice of selected, key, new and emerging health technologies (including changing applications and uses of existing technologies) that might require urgent evaluation, consideration of clinical and cost impact or modification of clinical guidance.

Its activities encompass health technologies in the broadest sense and include pharmaceuticals, devices, diagnostic tests and procedures, surgical and other interventions, rehabilitation, and therapy, public health and health promotion activities.

Two processes are used to identify advances, up to five years before their launch into the National Health Service (NHS):

1. Focused routine scanning

This is designed to identify urgent, significant advances, regardless of clinical specialty. Primary, secondary and tertiary information sources are regularly scanned, by networking with research units and commercial developers, by extensive searching of specialist and general medical and pharmaceutical literature, news and financial reports, licensing agencies, and selected internet sites and databases.

Individual health professionals and researchers are welcome to propose technologies that may need the centre's attention.

2. Specialty based work programme

A specialty review programme ensures that all clinical specialties and technology types are allocated time for an in-depth investigation of new developments. This programme involves liaison with the Royal Colleges and other professional bodies in a specialty to (a) identify any gaps in the centre's identification phase and (b) help to prioritise technologies in that specialty.

Filtration and prioritisation of technologies

Once technologies have been identified, trivial developments are discarded and related technologies are grouped together. A search for additional information, including contacting commercial developers and clinical or technological experts in the field, is then undertaken to enable an assessment of potential significance. The criteria for selection to the NHSC's final list is that the technology is:

- emerging and likely to be available to the NHS in the next 3 years, or
- it is new, or
- it represents a significant change in indication or use of an existing technology
- or it is part of a group of developing technologies that, as a whole, may make a significant impact.

In addition, if it is thought that there may be:

- significant health benefit if the technology is widely adopted, or
- a major cost impact if the technology is widely diffused because of moderate to high unit costs and/or patient numbers and/or service reorganisation or training requirements, or
- indications that the speed of diffusion of the technology may be inappropriate given the available evidence (either too slow or too fast), or
- significant ethical, social, political or legal issues, or other issues and concerns related to the use of the technology, or
- current guidelines and clinical guidance will be significantly affected if the technology is adopted.

NEW CONTROLS FOR COSMETIC CLINICS

UK - All surgeons must be registered with the General Medical Council (GMC), but not all are trained in plastic surgery. In addition, some private clinics that offer cosmetic surgery are neither registered nor regulated. On top of this, many non-surgical cosmetic treatments are not regulated - and are often carried out by non-surgeons.

Quite apart from patients' distress caused by 'bodged' treatments, the question of unfair costs on publicly funded hospitals arises. Breast augmentation*, the third most common cosmetic procedure in the USA (1st nose reshaping 2nd liposuction), is also widely used in Europe. Infection complicates 2-2.5% of breast implantations, and is the leading cause of later material illness. Then, if the augmentation was carried out in a private clinic, due to the high personal cost many patients must seek remedial care (including surgery) in a publicly funded hospital. The situation has been a vexing issue for a considerable time.

A report by The Healthcare Commission, which inspects the country's national and private healthcare providers, advised greater scrutiny of non-surgical procedures, e.g. treatments with injected fillers and Botox, and it also advised that specialist training in cosmetic surgery should become mandatory. Another report, by an expert group set up by **Sir Liam Donaldson**, the UK's Chief Medical Officer, found no firm evidence that patients were being harmed, but concluded that better regulation is needed due to the growth of new and different procedures of all types.

Sir Liam, who agreed that specialist training programmes, to be organised by surgical training bodies, are needed and that detailed information about which practitioners and procedures are accredited should be made available. 'Standards in cosmetic treatment must be as high as other areas of healthcare,' he said, announcing that non-surgical procedures will now be regulated, like surgery, by the Healthcare Commission. This means that legal action could be taken against providers who have not registered and/or followed the rules.

'The safety and quality of cosmetic and aesthetic procedures need to be kept under regular review, not least to understand and respond to new developments,' added Simon Gillespie, head of operations at the Healthcare Commission.

(* Breast implant complications: **Professor Brigitte Pittet** and colleagues at the Plastic and Reconstructive Surgery Unit, University of Geneva Hospitals, Switzerland, have described the development of breast implants and reviewed the myriad risk factors for infections, and discuss clinical features such as toxic shock syndrome, capsular contraction and late infection occurring months - or even years - after implantation. The team also outline diagnostic and management strategies for implantation problems. See: *The Lancet Infectious Diseases. February 2005, p. 94-106.*)
BM Editor

Prof Andrew Stevens, Strategic Director

Funded under contract by the Department of Health's R&D Directorate, The National Horizon Scanning Centre (NHSC) is based in the Department of Public Health and Epidemiology, University of Birmingham, which is headed by ***Professor Andrew Stevens***, whose focuses on health technology assessment, include horizon scanning in healthcare, and healthcare needs assessment. (He is also Vice-Chairman of the Appraisal Committee of the National Institute of Clinical Excellence, co-founder and vice-chair of Euroscan, and chair of the editorial board of *Health Technology Assessment*.

The NHSC is a member of and hosts the Secretariat to The European Information Network for New and Changing Health Technologies. It is also a member of the International Network of Agencies for Health Technology Assessment (INAHTA) that promotes and facilitates information exchange and collaboration among HTA agencies.

Assessment

Information is provided to the DoH as technology briefings, in about four pages, which describe the technology; patient group (with estimated patient numbers); current diagnostic or treatment alternatives; estimated unit cost of the technology (if available); current research evidence of clinical and cost effectiveness; details of any ongoing or related research activities, and an overall horizon scanning impact assessment in terms of estimated clinical, service and financial impact. (Briefings: http://pcpoh.bham.ac.uk/publichealth/horizon/technology.htm.)

Information used in writing the briefings changes rapidly and the level of evidence presented and conclusions made about a technology's potential impact must be treated with caution, the National Horizon Scanning Centre points out.

4 steps to successful staff planning

Most hospitals must now report on the origin, cost and usage of all equipment and supplies. However, far less is known about a hospital's most important and expensive* asset: employees. Despite financial pressures, DRGs, and the EuGH judgement, which aims to end stress (particularly for junior doctors) discussion of the economical and effective use of personnel is frequently avoided, or can evoke emotional reactions. Yet dialogue on demand-oriented staff planning could not only prevent job losses but also begin processes from which everyone would benefit. We know something must change. The questions are: *What?* and *How?* In an EH interview, *Dr Burkhard Scherf* and *Hans-Joachim Schütt,* of Dr Scherf, Schütt & Partner, a consultancy specialising in the effective use of hospital staff, described current research, evolving philosophies and constructive procedures that could provide the answers.

'An employee is not like a packet of plasters - we are not talking about objects - and more than just money is at stake,' Dr Scherf pointed out. 'It's about people, about a special, medical work ethic, and about status, self-respect and fears. As soon as you look into ***demand-oriented use of staff*** - i.e. the questions: What type of work arises when? and ***When do we need how many doctors and nurses with what type of qualifications?*** - you see that this addresses all key subjects in a hospital. That is, what types of services are provided, how much they cost and are those costs covered by case-based standardised lump sums paid by medical insurers. However, you cannot look at this subject from just one angle. Organisation, workflow, interdisciplinary co-operation of departments and quality of leadership are factors that all figure in demand-oriented staff planning.' SSP describes demand-oriented staff planning as a four-step process:

- Assessment of staff requirements
- Working hour models
- Time management
- Planning staff use

'Questions that arise around these four issues are: ***How can we organise this process of change? How will I win over the right people for this project? How do we generate the energy for change in all departments involved?*** Dr Scherf continued. 'In the first step, the assessment of actual requirements, the objective is to predict quantitative and qualitative curves of demand. Only when these are established can we tailor staff rotes. One thing is clear: the traditional model, where existing job head counts are filled with hours, is no longer feasible.

'The second step involves assessing which working hour models are best suited to cover staff demand. Rigid forms of working hour models are not suitable, because they entail, for example, overtime during particularly heavy periods of demand and wasted time during down periods. So we need different lengths of shifts and working hour models. Surprisingly, many hospitals still do not make use of the options offered by the BAT (A collective labour agreement covering public sector workers in Germany. Ed). We also have to examine the kind of part-time work would be feasible. Usually, part-time nurses are in a relatively high proportion, which lends itself to flexible, demand-oriented staff planning. However, part-time work is much less common for doctors, although sometimes doctors say they would prefer to work 70% or 80% of the time, rather than full-time. In that case, the loss of net income is not always so severe, because a drop in taxation offsets it.

Hans-Joachim Schütt and Burkhard Scherf (right): Change works when there is a common awareness of its need, plus the active involvement of all concerned

'The third step is about handling working hours and actively controlling working time accounts. ***What is the proportion of overtime and down times compared with other medical areas? What information is needed to establish a sensible work rota?*** Absence management is another important subject. Holidays or training days are not natural disasters; they are foreseeable. The only thing that cannot be predicted is staff absence due to acute, short-term illnesses, but this is only a small proportion of staff absence. Many of those responsible for planning staff rotas feel a little isolated. They have to work around areas of conflict between economic concerns and colleagueship. This is where any plans for the introduction of demand-oriented staff rotas tend to become stuck, particularly if not enough time has been invested in raising awareness around the need for demand-oriented staffing prior to the project's commencement.

The fourth step, the actual concept of staff planning, involves organising a flow of information that ensures that those responsible for staff planning always have the information they need: ***What demand are we likely to see over the next few weeks? Which colleagues are available? Which ones aren't?*** These questions must be answered not only from the perspective of headcount but also from the aspect of what qualifications the available staff must have. One also has to account for any particular events that may affect a hospital. A good rota means that personnel are not simply spread evenly but that over and under capacity is avoided.'

Asked about the introduction of computerisation in staff planning, SSP pointed out that it is important, but that the fourth step is initially about conceiving and establishing a flow of information that works. Then software can be used. 'Many companies that aimed to introduce a software solution before considering steps one to three of the process now say: ***Now we've landed ourselves with software which is merely automating the inefficient processes we had to begin with!'***

Asked whether staff planning software could be integrated into HIS, PACS and RIS systems, SSP pointed out that software can create work rotas, collate and evaluate working times, then translate the results into a wages and compensation system. Initially there is very little direct exchange of data. 'However,' Dr Scherf added, 'we can think about comparing data on demand and service with the actual or planned use of staff. There is a lot of potential for data collation and evaluation, but data collation must not get out of hand. Only an approximation of how many hours a doctor spends on a particular service for a particular patient can be reached, although we need some idea, otherwise we'd never be able to work out whether standardised DRG lump-sum payments are sufficient.'

In terms of economic benefits of this kind of project, SSP explained that the amortisation time is just under a year. 'A study carried out by the University of Wurzburg (Professor Nagel) found that the introduction of efficient staff planning combined with software-controlled time management in different hospitals can save between €25 and €150 per employee. The big margin between the highest and lowest savings potential results from the fact that all depended on how well these hospitals were prepared for demand-oriented staff control. However, it shows the great potential of this planning.'

Facing such massive changes, the keyword is surely change management? 'You cannot NOT have change management,' said SSP. 'Hospitals have always carried out change management, although not always consciously. Even though many of the staff in many hospitals support the process of change, hospital areas on the whole still have a very high need for professional control over change.'

Due to the strong trisection between commercial issues, care and medical services, they pointed out that there is still not the right awareness of change management. Another problem is that different medical fields may have only rudimentary, interdisciplinary co-operation. There is also a lot of catching up to do regarding leadership, they added. 'Many hospitals tend to look at the issue of co-operation from a purely medical aspect. However, to effectively introduce change, along with all other organisations, hospitals need a certain quality of leadership. There is a reason behind strong hierarchies in medicine. For example, in an operating theatre there is no room for long discussions on whether to do something this way or that way - you need clear decisions. But not all changes in hospitals relate to decisions about life and death.

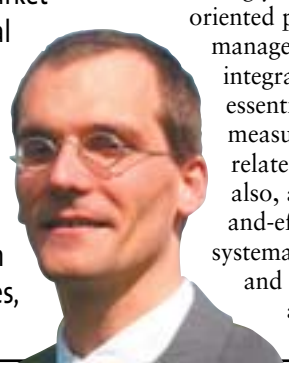
'Change,' SSP concluded, 'can only succeed if there is a common awareness of the need for it among all those who are involved - doctors, nurses, everyone - along with their active involvement in that change.'

(Amounting to 70% of hospital costs in some countries).*

Interview by **Annette Bus**

Market-oriented performance measurement

The impact of deregulation and internationalisation on the structures of healthcare systems have made market-oriented performance management and controlling a central challenge for today's hospital managers. ***Professor Rainer Sibbel***, Chairman of the Institute of International Health Management and Director of its MBA - International Hospital Management Programme for healthcare professionals, at the HfB Business school of Finance and Management,Frankfurt, describes the status quo, advises on a transfer of traditional accounting methods and approaches, and adaptation to alternative approaches



The main emphasis in hospitals is on cost-accounting and controlling, which are traditionally attached to profit quantities that are easy to collect and to measure. The internal, cost-dominated perspective leads to a mainly operational analysis, relating only to profit and cost figures. Market-oriented performance measurement and controlling concentrates on the long view and on the hard as well as soft profit-factors. The aim is a market-related positioning and navigation of the hospital, to avoid market and cost problems and to secure success on the long run.

Therefore, the following essential range of duties can be derived: The changed conditions require a consequent strategic planning and controlling. It helps to secure the success potentials for the future. Furthermore a service delivery programme must be planned actively and systematic revenue management and output controlling should be carried out. Process efficiency should be constantly questioned and improved. In such interactive and individual services, as offered in hospitals, process management and the organisation design are closely associated with capacity utilisation problems. Not to forget that quality and efficiency are decisively influenced by the staff motivation and behaviour and therefore by the incentive structures.

A high number of deficits can be recognised in the status quo. Predominantly, they often only react to changes in market and economic conditions. Mostly, only first symptoms of strategic planning, navigation and control are observable. They focus on documentation, reporting and simple variance comparison. Rough cost-object and cost-centred accounting can be found, besides the domination of full and actual costing. To fulfil the needs of market-oriented performance management and controlling, active strategic planning and navigation is necessary, just as ongoing planning and control of the service programme, market and customer oriented success analysis, process-oriented calculation and structures, intensive examination of the economic profitability as well as according organisational changes such as profit-centre-concepts, attempts of benchmarking and lots more. The basic maxims behind these are improved and long-term profitability.

The Balanced Scorecard (BS) developed by Kaplan and Norton, which was broadly and rapidly accepted in industry, could strongly contribute to market-oriented performance management, by means of an integrative approach. The essential advantage is that it measures financial or output-related success factors, and also, according to the cause-and-effect-relationship, systematically considers resource and process related impacts as drivers and early indicators. So the BS combines the external market-based view and an internal resource-based view. Further on, this concept not only claims to be **a complex ratio system, it should be seen as a complete management system that helps to transfer a vision into strategy and concrete actions.**

The essential advantages for hospitals are that the basic design of the BS is flexible enough to appropriately consider specific peculiarities in market conditions and hospital service delivery. On the one hand the BS offers the opportunity and impulse to derive and implement a market-oriented strategy and to navigate its implementation. Typically, hospitals' economic as well as material goals can be combined in

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ESA THE NEW EUROPEAN SOCIETY OF ANAESTHESIOLOGY

60,000 members predicted

Brussels - The former European Sn Academy of Anaesthesiology (EAA) and the Confederation of European National Societies of Anaesthesiologists (CENSA) have been amalgamated into a single organisation - the European Society of Anaesthesiology (Details: www.euroanesthesia.org President: Hans-Joachim Priebe). Although predominantly a European Society, ESA has Affiliate Members in many countries and, due to a new Society Membership category, ESA's 5,000+ individual members are expected to swell to over 60,000 anaesthesiologists.

The Society aims to raise standards in this field by promoting education, research, scientific progress and data exchange between European anaesthesiologists. A further aim is to improve safety and quality of care for patients undergoing anaesthesia.

ESA Annual meetings - Euroanaesthesia meetings are accredited by the American Medical Association and the Union of European Medical Specialists (UEMS) for continuing medical education (CME) credits. Some 5,000 members and non-members attend, from over 65 countries.

ESA publishes the *European Journal of Anaesthesiology* (EJA), provides research grants, fellowships and awards programmes (e.g. grants for ten young lecturers from East European countries to attend the annual meeting), and organises the examination for the European Diploma in Anaesthesiology and Intensive Care, as well as a hospital visitation programme.

The society is linked with the Society to the European Union of Medical Specialists (UEMS) and the European Board of Anaesthesiology (EBA), to promote and protect its members and, through its National Anaesthesia Society Committee (NASC), ESA is also linked with the World Federation of Societies of Anaesthesiologists (WFSA).

Administration is handled by an Executive Director and seven staff members based at the society's Brussels HQ. An Interim Board of Directors, Interim Council and the General Assembly will govern the Society in 2005. However, a new Board of Directors and new Council will be elected later this year, to take office in 2006.

MARKET-ORIENTED PERFORMANCE MEASUREMENT

continued from page 7

the highest level of strategic objectives. From the perspective of customers, many different groups of clients e.g. patients, doctors or other external stakeholders, can be considered and judged separately. Specific requests and conditions for offering such interactive services can be considered completely on the process level. The potential perspective reflects, in particular, the interests of employees, as well as the relevance of infrastructure or even of modern information and communication technologies. The integrative role is attached to the BS in market-oriented performance management based on the feature of translating vision and strategy and linking strategic and operational management level. The BS is connected to various operational systems and instruments, especially in accounting and controlling. It unifies traditional and modern concepts and methods by perspectives and cause-and-effect-relationships and directs them to strategic critical factors of success. So it offers a promising integrative approach to support and implement market-oriented performance management.

However, the main success factor and premise for implementation is a qualification of management and its perception of hospitals as market-driven, competitive and complex service providers in a very important growth market.'

Details - MBA - International Hospital Management Programme: www.hfb.de

Money and mammography

Could a fully digital breast imaging service be financially viable?

USA - North-Western Medical School has used Activity Based Costing (ABC) to analyse five major services provided by its mammography section: screening, diagnostic, breast ultrasound (US), interventional procedures, and reviews of external mammograms.

The ABC analysis revealed that only two services showed a profit, screening mammography and intervention procedures. There was no consistent relationship between the financial contribution of the service and the total mammography volume and therefore no economy of scale. This suggested that the more a service is provided, the greater the financial loss. When indirect costs were included in the cost structure all the mammography programmes in the survey registered losses.

The report pointed out that the term 'mammography' refers not to a single examination but to a set of diagnostic procedures, the most common and familiar being screening mammography, in which the examination consists of two standard views of each breast interpreted by the radiologist. The ACR-published standard for diagnostic mammography defines it as a problem-solving breast evaluation, which is indicated by a particular concern. However, using computer-aided diagnosis in screening mammography may increase the inexperienced image reader's sensitivity to breast cancer and so give more false-positive interpretations. This leads to an increase in the number of diagnostic mammograms and a reduction in productivity.

Diagnostic mammography on the other hand is a much more comprehensive examination and consists of customised views of the breast depending on the findings of concern and may involve tailored or comprehensive imaging analysis. Often associated with diagnostic mammography the interpretation of outside mammograms can be time-consuming. In a negative financial outcome for diagnostic mammography these three examinations, each with a loss per procedure, were often grouped in delivering comprehensive breast imaging services. In addition, the volume of different procedures was interrelated; growth in screening mammography being followed by growth in diagnostic mammography, breast US, and interventional procedures. Breast centres with a good reputation, due to referrals, have a higher proportion of diagnostic mammograms and difficult outside mammograms, and because these are provided at a financial loss per examination, there are economic disincentives in concentrating high-quality mammography talent.

The new digital mammography environment promises to change the entire practice of mammography in terms of who and how and where digital mammograms are acquired, interpreted, and stored. But migrating from a film-based examination to a fully digital one will require substantial capital investment. Clearly a financially self-supporting mammography service would facilitate this transition. The report concluded that, to realise the real benefits of a fully digital breast imaging service, a different financial environment would be needed.

Report by *Peter Howieson*

Superheat system success

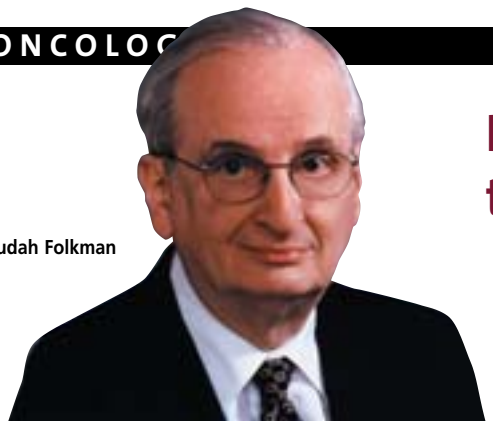
Boosting the effects of radiation and chemotherapy

Germany - Interest in a therapy system named BSD-2000 has increased significantly since a Phase-III European trial, involving patients with advanced cervical cancer, showed that radiation combined with the system resulted in an almost a 50% higher survival rate than for the patients treated with radiation alone. To date, six systems have been installed in Bavarian clinics alone and, in April, the seventh BSD-2000 system will become operational at the Schlossberg Clinic, in Oberstaufen.

The system's manufacturer, the US-based BSD Medical Corporation, which develops microwave and radio frequency systems for thermal medicine applicable to the treatment of cancer, benign diseases and other medical conditions, explained that its cancer treatment systems are used to superheat and kill cancer cells and to boost the effectiveness of radiation and chemotherapy. 'The BSD-2000/3D employs a revolutionary annular phased array of 24 dipole radiofrequency (RF) antennae placed around the patient to focus RF energy steered in 3D on the cancer. Cancers targeted are primarily those located deep in the body, such as colorectal, bladder, ovarian and prostate cancer.'

The firm added that the Schlossberg Clinic (a member of the Munich Comprehensive Cancer Centre, and holder of a clinical co-operation contract with the LMU Munich University Medical School at Klinikum Grosshadern, which specialises clinical cancer research) will use the system in combination with chemotherapy and radiation, in a pilot project that could lead to use of the BSD-2000/3D in other centres owned by the Humaine Kliniken Group.

Details: www.BSDMC.com



Dr Judah Folkman

Biomarkers lead the way - and may even trigger a preventive treatment approach to cancer in the future. ***Report by Karen Dente, our US correspondent***

Early-stage cancer detection

In 2003, the US-Food and Drug Administration (FDA) stated that '*...one cannot prove the existence of a tumour that can't be seen*'. But with biomarkers indicating disease detectable in the blood or urine before full-blown cancer becomes visible, researchers hope that cancer can be treated long before it becomes noticeable by conventional means.

Dr Judah Folkman, the founding father of angiogenesis - the theory that tumours rely on the sprouting of new blood vessels to survive and grow - has been advocating anti-angiogenic therapy to treat cancer for 30 years. Anti-angiogenic therapy relies on the principle that blood vessels feeding a tumour are inhibited from growing, thereby cutting off the vital supply of nutrients and oxygen needed by the tumour cells. These agents have been approved for use in treating cancer along with chemotherapy, radiation and surgery, as a fourth arm of treatment. Due to their lack in causing major harmful side effects commonly seen with chemotherapy, Folkman has proposed the use of these agents in treating patients before the tumour is actually seen, but when certain biomarkers indicating disease become prominent.

There are several known biomarkers indicating disease, but many remain elusive and much more research is needed to understand when a tumour switches from a small harmless entity to a lethally growing cancer. A few years ago only a small number of conferences worldwide discussed biomarkers. Today, there are many, many more, and, last December, the FDA acknowledged the demand for biomarkers by establishing a new agency - the *Critical Path Initiative*.

Why all the sudden fuss and interest in biomarkers? In order for novel therapies to be approved for useful application in humans, pharmaceutical companies must first jump through some hoops at the FDA, whose guidelines require that a drug is shown to be efficacious in what it sets out to achieve. A cancer drug must lead to an improvement in outcome, be it in a prolonged duration of disease-free survival following a cancer diagnosis, or an increase in overall survival time, often measured in months.

But how does one measure the success of a new drug in preventing cancer that has not even grown to a stage at which it can normally be detected? This would require knowing certain markers that indicate the growth of cancer before it becomes visible. This principle has been applied to statins - the cholesterol-lowering group of drugs used to prevent heart attacks. Cardiologists are already well aware of certain precursors that are detectable in blood before disease becomes pronounced. Physicians prescribe Lipitor, a statin, to treat levels of LDL, HDL, cholesterol and C-reactive protein visible in blood, to avert the possibility of a future heart attack in at risk individuals. They would not wait until a heart attack occurs. In oncology the available option is to wait until it is often too late, i.e. when the cancer is at an advanced stage and even surgery cannot lead to a definite cure.

Judah Folkman has been advocating finding biomarkers for cancer to facilitate a possible preventive treatment approach to cancer in the future. One of the best-known biomarkers indicating the presence of cancer is calcitonin, a hormone seen in increasing amounts in the blood of people with medullary thyroid cancer before the cancer actually becomes pronounced. Since first proposing his theory that cancer needs blood vessels to grow in 1972, much has been learned about what factors are involved. Since angiogenic factors are involved in most, if not all types, of cancers at some stage, Dr Folkman has been focusing on these as potential biomarkers for disease, and recently, with his colleague Dr Giannoula Klement, at the Boston Children's Hospital, has collaborated with Ciphergen Biosystems Inc, to develop a protein-chip platform that can help detect a 'platelet angiogenic profile'. The SELDI TOF-MS chip has successfully detected cancerous agents present in the blood platelets of mice. Scientists have found about two dozen angiogenic regulatory proteins, including VEGF, bFGF, PDGF, PF4, and endostatin sequestered in platelets. The platelet angiogenic profile is more inclusive than a single biomarker, because it can detect a wide range of tumour types and tumour sizes, and Drs Folkman and Klement believe that this proteomic analysis of circulatory platelets can be potentially useful for early cancer diagnosis, since a relative change in the platelet profile permits tracking of a tumour throughout its development. If the observations seen in mice can be effectively translated into humans, the chip may offer an ultra-early indicator of disease at the in-situ stage.

Last year four new anti-angiogenic agents were approved by the FDA, and Avastin (bevacizumab), an anti-VEFG factor and potent inhibitor of angiogenesis, manufactured by Genentech, has been shown to be effective in treating colon cancer that has spread beyond the confines of the large intestine. This was FDA-approved in February 2004, and by all European countries in January this year.

Dr Folkman hopes that, with the advent of anti-angiogenic agents such as Avastin, which do not have the adverse side effects of conventional chemotherapeutic drugs, patients with cancer might have a good treatment alternative with less harmful side effects, which may even be combined with reduced doses of the traditional cancer treatment. 'Patients that are on less toxic therapies do not have bone marrow suppression, nausea and diarrhoea, they travel, gain weight up to 20 pounds, keep their jobs, and have a wholly different lifestyle,' he observed

ELECTROCHEMOTHERAPY

Professor Gregor Seröa, of the Institute of Oncology in Ljubljana, and ***Professor Damijan Miklavcic***, of the Faculty of Electrical Engineering, University of Ljubljana, Slovenia, describe this effective local tumour treatment and the launch of a new medical device

Prof Damijan Miklavcic

Prof Gregor Seröa

Electrochemotherapy is a combined treatment of chemotherapy and high voltage electric pulses for local tumour treatment. The effectiveness of some chemotherapeutic drugs, with an intracellular target like DNA, which also have difficulties in crossing the cell plasma membrane (e.g. cisplatinum and bleomycin) can be greatly potentiated by simultaneous application of high voltage electric pulses. High voltage electric pulses, which can be as short as 100 microseconds, are delivered locally to the tumour via appropriately designed electrodes. The electrodes and voltage pulses have to ensure electric field distribution in the tumour tissue that triggers cell membrane electroporation (see European Hospital vol 14 Issue 1/05, page 9 - Electroporation by D. Miklavcic and A. Macek Lebar). Namely, the cell membrane that is exposed to a sufficiently high electric field undergoes structural changes that increase its permeability. These changes thus allow introduction of molecules (drugs, DNA/RNA) that otherwise cannot penetrate, or have difficulties in penetrating the cell. It has been demonstrated that electrochemotherapy is an effective local treatment and can be used for local control of tumours, irrespective of their histological origin. Recently, a medical device called Cliniporator has been developed, with the support of European Commission under the 5th Framework Programme, and standard operating procedures are being prepared for treatment of skin and subcutaneous lesion (www.cliniporator.com). However, further technical development is needed for the treatment of deep-seated and endoluminal tumours.

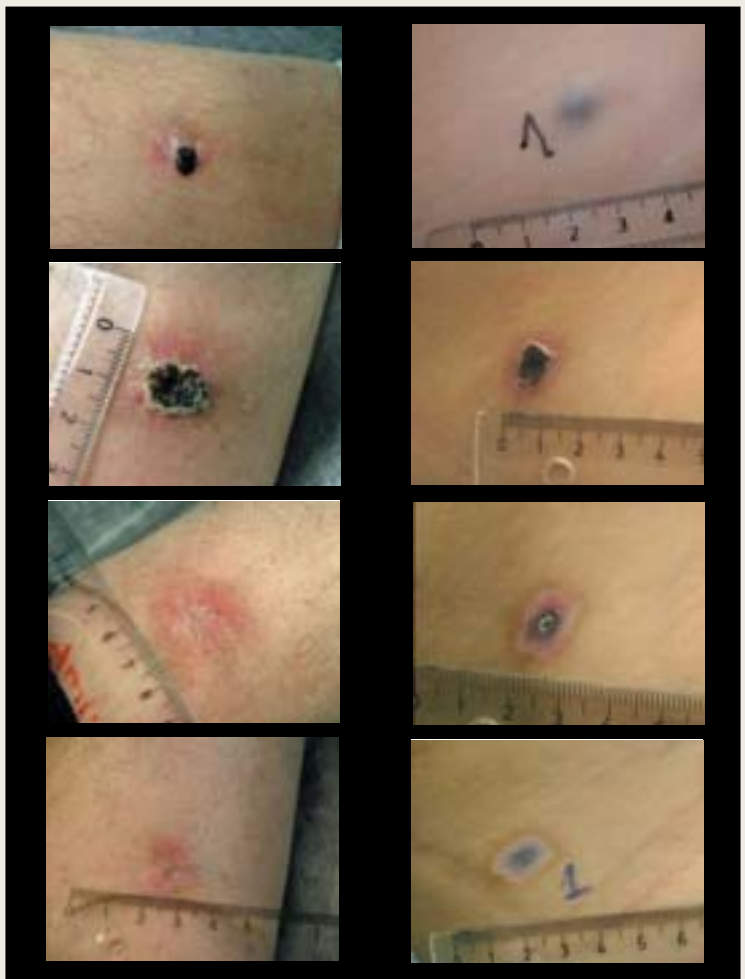


Figure 1. A cutaneous tumour nodule of malignant melanoma (1.8x1.6 cm in diameters) was treated by electrochemotherapy with bleomycin. Bleomycin was injected intratumourally and immediately thereafter electroporation of the tumour nodule was performed by four applications of electric pulses, using needle electrodes. The tumour nodule responded with complete regression. Superficial scab was present up to eight weeks after treatment, and the tumour nodule is in complete response nine month after treatment

Figure 2. A cutaneous tumour nodule of malignant melanoma (0.9x0.7 cm in diameters) was treated by electrochemotherapy with cisplatin. Cisplatin was injected intratumourally and immediately thereafter electroporation of the tumour nodule was performed, using plate electrodes. The tumour nodule responded with complete regression. Superficial scab was present up to eight weeks after treatment, and the tumour nodule is in complete response 12 weeks after treatment

Further reading

1. Mir LM, Glass LF, Sersa G, Teissie J, Domenge C, Miklavcic D, Jaroszeski MJ, Orlowski S, Reintgen DS, Rudolf Z, Belehradek M, Gilbert R, Rols MP, Belehradek JJr, Bachaud JM, DeConti R, Stabuc B, Cemazar M, Coninx P, Heller R. Effective treatment of cutaneous and subcutaneous malignant tumours by electrochemotherapy. *Brit J Cancer* 77: 2336-242, 1998.

The first extensive study on electrochemotherapy with bleomycin that reported good antitumour effectiveness of this therapy on 291 cutaneous and subcutaneous tumour nodules of basal cell carcinoma, malignant melanoma, adenocarcinoma and head and neck squamous cell carcinoma. Objective responses of tumours were obtained in 85.3%, out of which 56.4% were complete responses. The article summarises results obtained in independent clinical trials performed by five cancer centres.

2. Sersa G, Stabuc B, Cemazar M, Miklavcic D, Rudolf Z. Electrochemotherapy with cisplatin: Clinical experience in malignant melanoma patients. *Clin Cancer Res* 6: 863-867, 2000.

The article reports results of electrochemotherapy with cisplatin on 10 patients with malignant melanoma where, in 82 electrochemotherapy treated nodules, a 77% long-term control rate was obtained. The results demonstrated, for the first time, that electrochemotherapy with cisplatin is highly effective in treating cutaneous and subcutaneous malignant melanoma nodules.

3. Gothelf A, Mir LM, Gehl J. Electrochemotherapy: results of cancer treatment using enhanced delivery of bleomycin by electroporation. *Cancer Treat Rev*. 29: 371-387, 2003.

This review article summarises basic principles of electrochemotherapy with bleomycin and all clinical data that were published so far. Detailed report on anti-tumour effectiveness of electrochemotherapy is given, summarising data on 96 patients with altogether 411 malignant tumours.

4. Sersa G, Cemazar M, Rudolf Z. Electrochemotherapy: advantages and drawbacks in treatment of cancer patients. *Cancer Therapy* 1: 133-142, 2003.

A review article, this summarises data on clinical trials published so far and presents the latest clinical experience on electrochemotherapy with cisplatin at the Institute of Oncology Ljubljana. Results from the study confirm results of the previous study, which was published in *Clin Cancer Res* in 2000. Based on the clinical experience authors are pointing out the advantages and drawbacks of this treatment.

New initiative aims at clarification and education

CVD and women

Professor Silvia Priori

There appears to be little medical, or public, awareness or understanding of cardiovascular disease (CVD) in women, because CVD is often still viewed as a 'male disease', and cardiologists frequently under-diagnose and under-treat women because the symptoms may differ between women and men.

Cardiovascular disease (CVD), which includes coronary heart disease and stroke, kills more people of both sexes than all cancers combined. However, according to public awareness surveys, women think cancer - particularly of the breast - is a greater risk for them. The truth is that CVD kills a higher percentage of women (55%) than men (43%) in Europe and accounts for more deaths than all cancers combined. It is also notable that although men suffer strokes, women are more likely to die as a result of a stroke.

To address this, at a recent meeting of its 49 national cardiac societies the European Society of Cardiology (ESC) launched the Women at Heart initiative, aimed at medical professionals, because, the ESC points out, women are under-represented in clinical trials and their CVD clinical manifestations are less well charted and outlined to the medical professional in their initial or ongoing training.

Apart from increasing awareness across Europe, among many other activities will be an analysis of ESC Euro Heart Survey databases to obtain specific data on women and CVD, such as the differences between women and men in specific disease and treatment areas. Results from these analyses will be presented at the Euro Heart Survey Symposium at the ESC Congress in September.

Professor Silvia Priori, of the Fondazione Salvatore Maugeri, Pavia, Italy, Chairperson of Women at Heart, and a member of the Board of the ESC, said: 'The analysis of our Euro Heart Survey databases will be extremely interesting, as these are large databases on extensive European populations without the artificial representation so often seen in clinical trials. We have all the data at our fingertips and can reassess them in a relatively short time. These data are likely to give us important insights into manifestation, treatment and co-morbidity patterns, as well as hints on treatment and response trends, in women as compared with men. I am very much looking forward to the release of these data at our Stockholm Congress.'

What is already known is that women with heart disease are up to ten years older than men and present with much less obvious and stereotypical symptoms. They tend to have heart disease later than men due to the cardio-protective effects of oestrogen, which plays an important role up to the menopause. However, after the menopause, risks increase significantly and need delicate management.

In many women, the onset of heart disease is more gradual, accompanied by tiredness rather than the more commonly recognised symptoms predominant in men - e.g. sudden violent chest pain. Furthermore, women with CVD are more likely to die or suffer disability from a further attack or heart failure. Professor Priori said: 'The issue is not simply that men and women are different per se, but rather that there are specific differences between the genders in symptom profiles and responses to treatment that must be taken into proper account.'

Physicians' training is dominated by male data and trends, and guidelines focus on such data in recommending drug dosages and procedures. Thus women are being treated as if they are men, despite the notable differences in their disease elements.

- The ESC's Women at Heart initiative is supported by an unconditional educational grant from the Bristol Myers Squibb Foundation.
- Information: www.escardio.org/initiatives/WomenHeart/

Device minimises ventricular pacing

Italy - A new pacemaker has been launched that promotes a patient's natural cardiac activity by pacing the right ventricle only when AV blocks occur. ELA Medical reports that its second-generation pacemaker, Symphony AAIsafeR 2, is now available in Europe.

The new device promotes the patient's intrinsic electrical conduction by drastically limiting the amount of unnecessary, often deleterious pacing delivered to the right ventricle, the firm said: 'This is also the primary objective of Medtronic's Managed Ventricular Mode (MVP). AAIsafeR 2 manages to reduce ventricular stimulation to 0.1% in patients with intermittent atrio-ventricular conduction. This represents as little as 1 min 30 sec ventricular pacing per day or 9 hours per year!

Permanent checks on a patient's natural conduction allows the pacing system to deliver right ventricular pacing when normal conduction of the cardiac impulse to the ventricle does not occur. When intrinsic conduction resumes, the system automatically switches back to physiological AAI pacing.

ELA Medical also reports that its next Implantable Cardiac Defibrillator (ICD), which will also feature the advanced pacing mode, will be launched later this year.

Cryoablation

A safer therapy for children with arrhythmias

Italy - Freezing abnormal electrical pathways in the hearts of young patients may be a safer alternative to zapping them with powerful radiofrequency probes to treat tachycardias and other arrhythmias, according to Dr Fabrizio Drago (above), of the Bambino Gesù Hospital, Rome. 'If you have a child with a supraventricular tachycardia due to a re-entry circuit, or a target very close to the atrioventricular node, or the His bundle, try to do a cryoablation first. Then, if it is unsuccessful, you can do a radiofrequency ablation, if there are no other alternatives,' he advised in his paper published in the Journal of the American College of Cardiology (5/4/05).

The use of a catheter probe chilled to -75° Celsius to destroy or ablate abnormal electrical circuits in adult heart arrhythmia patients is becoming increasingly popular, but Dr Drago's work is the first study of its type to involve children. Currently, radiofrequency ablation, which uses a probe emitting very powerful electromagnetic energy, is the treatment of choice for these patients.

While usually effective, ablation of electrical pathways in the heart can create new problems, including atrioventricular block - an impairment in the transmission of electrical signals from the upper to lower chambers through the atrioventricular node. Whilst radiofrequency ablation is permanent, cryoablation has the potential advantage of being reversible during the procedure. Cardiologists can set the freezing probe to -30∞ Celsius and test its effect on the patient. If a problem appears in the heart's electrical pattern, the probe can be removed and the chilled nerves can recover. If the test freeze appears successful, the probe temperature is then lowered to -75° Celsius to achieve a permanent ablation.

Twenty-six paediatric patients (age range 5 to 20 years) were treated; 16 had tachycardia and 10 had Wolff-Parkinson-White syndrome, a condition in which electrical signals to the heart's pumping chambers arrive too early, thus interfering with normal pumping action. No permanent cryo-related complications or adverse outcomes were reported. The procedure was successful in 24 patients (92 percent). However, during follow-up (range: 1 to 22 months), arrhythmias returned in seven of these 24 patients.

'This report is important because it describes the first single-institution experience about the use of cryoablation in a paediatric population in an attempt to eliminate re-entry circuits located near the atrioventricular junction without any complications. This is the critical point,' said Dr Drago. 'Our acute success was very high, but we had many recurrences, maybe more than those reported in adult patients.'

However, Dr Drago considers the higher rate of recurrences is an acceptable trade-off for increased safety in young patients, compared with the usual experience with radiofrequency ablation. 'We think that, when dealing with children, it's better to do a procedure with a little lower success rate and no risks, than to carry out a procedure with a higher, long-term success rate, but with the risk, even if low, of severe complications,' he explained.

The study was not a randomised, controlled trial, he added, and it did not directly compare cryoablation to radiofrequency ablation. It also reports the experience of only one hospital.

Cardiovascular screening

USA - A guideline to help identify patients at risk of a heart attack in the near future, but who show no signs/symptoms of cardiovascular disease, was presented in a symposium at the 54th Annual Scientific Session of the American College of Cardiology. The concept is based on identification of subclinical atherosclerosis, then it incorporates additional information derived from traditional risk factors for heart disease, with the option of incorporating additional new and emerging biomarkers, explained Dr P K Shah, chair of the SHAPE Task Force Editorial Committee, which devised the guideline. Almost all males aged 45+ years, and women of 55+ years are encouraged to be screened for subclinical atherosclerosis. Only 'very low risk' people, i.e. non-smokers with cholesterol lower than 200(mg/dl), blood pressure under 120 over 80 (mmHg), and no history of diabetes or family history of heart attack would be exempted. However, Dr Erling Falk, a leading cardiovascular pathologist from Aarhus University, Denmark, who led the Writing Group of the SHAPE Task Force, said very few people in the industrial West fall into that category.

Two methods are widely available to help evaluate any subclinical atherosclerosis: coronary calcium score via a CT scan, and ultrasound used to measure plaque build-up in coronary arteries, and assess thickness of the carotid artery wall and presence of plaque, which correlates with an individual's total burden of arterial plaque build-up or atherosclerosis.

The guideline defines a negative test as a coronary calcium score (CCS) of zero or carotid intima-media thickness (CIMT) lower than 50th percentile. If the person has no established risk factors, he/she is categorised as Lower Risk and advised to re-test in five years. If any traditional risk factors exist, those people are categorised as Moderate Risk and treatment is recommended, according to existing guidelines as well as a further test in five years.

Those with a CCS greater than zero, or a CIMT higher than the 50th percentile, are classified as positive for subclinical atherosclerosis, and fall into three subgroups:

Moderately High Risk - With a CCS greater than zero but less than 100 and less than the 75th percentile, or a CIMT between the 50-75th percentile and no discernable plaque build-up.

High Risk - With a CCS greater than the 75th percentile or over 100 - aggressive lifestyle modifications are recommended to lower target low-density lipoprotein (LDL) cholesterol. If the CCS is greater than 400 or over the 90th percentile, additional testing for myocardial ischaemia is recommended. High Risk patients with no evidence ischaemia are still given an even lower LDL goal than patients with less extensive atherosclerosis (LDL less than 70).

Very High Risk - Those who present an abnormal test for ischaemia. Recommendation: coronary angiography, and very aggressive therapy.

'We are not saying we've discovered a magic wand to eradicate heart attack,' said Dr Morteza Naghavi, founder of the Association for Eradication of Heart Attack (AEHA), and chairman of it's the SHAPE Task Force. 'The initiative calls to foster an environment of searching for more cost-effective and simplified approach to identify those at different stages of progression toward a future heart attack, long before one occurs. We are not there yet.'

Drug reduces body weight plus cardiovascular risk

The RIO-Europe two-year phase III study of rimonabant (see page 1), led by principal investigator **Luc Van Gaal MD**, Professor of Diabetology, Metabolism and Clinical Nutrition, and colleagues at the University Hospital Antwerp, Belgium, involved 1,507 people from Europe and the USA. Participants had a body mass index (BMI) of 30 kg/m2 or greater, or a BMI greater than 27 kg/m2 with abnormal blood fat levels, high blood pressure, or both. They were randomly assigned 5mg or 20mg of a drug called rimonabant, rimonabant (the first in a new class of therapeutic agents called selective CB Blockers) or a placebo once daily, in addition to a calorie controlled diet. The treatment groups had similar characteristics. 920 patients (61%) completed the one-year follow-up: 379 in the rimonabant 5mg group, 363 in the rimonabant 20mg group and 178 in the placebo group. Weight loss at one year was greater in patients treated with 5 mg or 20 mg of rimonabant compared with placebo. More than 67% of patients who completed treatment with 20mg of rimonabant achieved 5% or more weight loss, and 39% achieved 10 % or more weight loss.

Patients on 20 mg of rimonabant had greater improvements than placebo in waist circumference (average reduction of four cm), and cardiovascular risk factors including cholesterol, insulin resistance and prevalence of metabolic syndrome. The pattern of weight loss seen with rimonabant was sustained for around 36-40 weeks.

Side effects - The most common side effects leading to study discontinuation were depressed mood disorders in all treatment groups; withdrawals due to nausea, vomiting, diarrhoea, headache, dizziness, and anxiety were more frequent in the rimonabant 20 mg group than in other groups. Serious adverse events did not occur more frequently in patients treated with the drug than in those on placebo.

The trials were funded by the Paris-based pharmaceutical company Sanofi-Aventis, where researchers had worked on the premise that, because cannabis smokers experience extreme hunger bouts, cannabinoids stimulate appetite, a means of blocking the brain's central cannabinoid (CB1) receptors could reduce hunger. The researchers cloned the human cannabinoid receptor then expressed this in cells. Compounds with potential inhibitory activity against this receptor were then screened for inhibitory activity, and rimonabant was identified as a CB1 receptor antagonist. Pre-clinical animal studies later indicated that rimonabant reduced consumption of fats and sugars.

Links: Luc.Van.Gaal@uza.be

Cardiac progenitor cells isolated

Researchers at the University of California, San Diego, have identified human cardiac progenitor cells - 'Very rare cells, explained research team member Dr Kenneth Chien, 'which accounts for why they haven't yet been reported' - which might one day lead to novel treatments to repair damaged hearts.


Kenneth Chien

Unlike mature cardiac cells, progenitor cells retain the ability to reproduce themselves. But only a few hundred of these cells remain in the heart after birth, and that number decreases with age.

Reporting in the journal Nature (Laugwitz K L, et al. Nature 433, 647 - 653. 2005), the researchers said they traced products of a gene named islet-1, which is expressed in progenitor cells and, by tracking cells in developing mice, they linked adult cells expressing islet-1 with a population of embryonic cells that can produce heart muscle. In the lab, hundreds of progenitor cells, which had been removed from the animals after birth, produced millions of cardiac-muscle cells. The team reported they had also identified the same cell types in the human heart - mainly in its pumping chambers.

Both stem cells and these progenitor cells have potential use in repairing cardiac damage. Although stem cells appear to have an unlimited capacity for self-renewal, and progenitor cells undergo a finite number of divisions, progenitor cells have a big advantage over stem cells: they can be prompted by scientists to become fully specialized cells without the use of chemical or hormonal stimuli.

In theory, if progenitor cells could be collected from a cardiac patient, then grown and transplanted back into the patient's heart, regeneration of a damaged heart could result. However, for now, isolating a substantial number of progenitor cells is the biggest technical challenge.

Advancing diagnostic skills

New workshops for post-processing images

The Imaging processing team of radiologists and application specialists: 10 dedicated post-processing workstations were used during the 3-day course

Germany - Eleven participants, who took part in a new seminar held in Heidelberg, this April, were awarded 22 CME credits and a certificate.

Explaining their motivation for setting up the three-day course, radiologists Hendrik von Tengg-Kobligk, Sebastian Ley, Julia Zaporozhan, Frederik L Giesel, and Hans-Ulrich Kauczor, director of the Radiology Department, at the German Cancer Research Centre (DKFZ), pointed out: 'With the mushrooming of Multislice CT installations across Europe, radiologists are challenged to include a large number of high spatial resolution images (up to 2,500 images per patient), and sometimes functional data, in a diagnostic reading. Whole body MRI examinations are also on the horizon. All this information needs to be put together and visualised in a 'condensed' form for a fast and target-oriented interpretation. Even if a Picture Archiving and Communications System (PACS) is available, it is still primarily a viewing station, lacking dedicated 3-D visualisation and segmentation capabilities. Furthermore, some diagnostic tools lack performance for advanced processing of imaging data. Within a clinical environment, PACS offers several viewing stations to facilitate the handling of digital data load and interaction with clinical partners. However, to answer more detailed or complicated questions, and to satisfy the interest from clinical partners offering 3-D and functional analysis, additional hard- and software is needed. Therefore, an increasing number of radiologists purchase dedicated workstations that allow fast creation of maximum intensity projections (MIP's), curved MIPs, axial, coronal, sagittal, oblique or curved multi-planar reconstructions (MPRs), volume rendering (VR), fly-through and segmentation of vessels and bone. Additionally, overlying soft-tissue can be removed with 'one-click' and measurements on segmented 3D volumes can be performed. Frequently, once a workstation has been installed, there is not enough time for the staff to read the manual (often 500 pages), thus the more advanced applications and complicated post-processing steps cannot be routinely used. Since many new post-processing applications can improve image quality and facilitate diagnostic interpretation by the radiologists a higher acceptance of the results by the clinical partners might be achievable today's radiologist need to adhere to upcoming standards.'

The participants worked on ten dedicated post-processing workstations in a mix of theory and skills training. Talks focused on the acquisition of Multislice CT, challenges of optimal contrast media injection, dosing, theories behind different post-processing techniques, as well as IT and the legal aspects of image archiving.

Hardy Schumacher and Dittmar Boeckler, from the Vascular and Endovascular Surgery Department, University of Heidelberg, lectured on the relevance of imaging and post-processing for surgical planning and follow-up, and short lectures, delivered by Benedikt Pruemer, of Clemenshospital, Muenster, and the organisers, covered relevant post-processing steps for clinical applications in the lung, heart, head and neck, vascular system, colon and bone.

Next 'hands-on' workshop:
6-8 October 2005
Language: German
Details: www.dkfz.de

Report by
Dr Hendrik von Tengg-Kobligk

Here – and the far horizons

Dr Hanns-Joachim Weinmann, Diagnostics and Radiopharmaceuticals, Magnetic Resonance Imaging & X-Ray Research, Schering AG, examines what is feasible and what still lies only at a tantalising distance

What is molecular imaging? Is it a buzzword to stimulate the imaginations of researchers, managers and analysts, or something real - a part of a daily routine in imaging departments? Honestly, nobody really knows. If we understand molecular imaging as the in vivo characterisation of biological processes at cellular and molecular levels, we are already fully in the future.

This article mainly reflects Schering's view on the clinical imaging techniques (CT, MRI, and US). It is not an evaluation of SPECT, PET and NIR in detail.

Today's MRI is far more than just another imaging modality; it offers not just morphological or anatomical details, it also gives physicians detailed information on the physiological status of the area of interest. An area of long T_2 relaxation time, what does it mean? Because of our accumulated knowledge in reading such images, it could be an inflammatory process. Why do we see brain metastases as bright as a star after dosing gadolinium? The exobiotic contrast agent clearly delineates the breakdown of the blood-brain barrier, or an area without a blood-brain barrier, for example, a malign tumour. Following the first marketing authorisation for an MRI contrast agent (Magnevist) additional new indications are being investigated. How does it work that a so-called unspecific contrast agent elicits a specific contrast enhancement? The delayed enhancement in the myocardium is a sensitive marker of viability - obviously not too fancy, is it? We are already seeing changes at the cellular level, but we are simply not used to accepting this.

Targeting a plasma membrane bound protein or receptor has become a reality after the introduction of Primovist and Multihance. The gadolinium chelates bind specifically to a transporter located on the sinusoidal and bile canalicular surfaces of hepatocytes. To this day, the binding kinetics and the window to functional studies are just a little open - and by no means divulged.

Another example of today's molecular imaging in MRI is superparamagnetic particles (SPIO), for example, Resovist. Those tiny aggregates, a product from nanotechnology, stimulate mononuclear phagocytes (Kupffer cells), the few nanometer large aggregates will be engulfed. Mononuclear phagocytes include the monocytes (in the bloodstream) and lymphocytes (mostly resident in lymphatic tissues); that's why SPIO accumulate in the liver and also in the lymph nodes: *in-vivo* targeting of very specific cells. Using these superparamagnetic iron aggregates in stem cell research is just at the beginning. Stem cell can be labelled by SPIO *in-vitro*. When injected into the blood stream, cell trafficking can be monitored by MRI. *In-vivo* labelling of other specific cells, benign or malign, will be the next step into molecular imaging.

Researchers at Schering AG demonstrate that Gd-labelled antibodies can be used as highly specific tumour-seeking agents for MRI. However, such magic bullets didn't make it into real medicine. Not because they where not specific enough, the commercial aspect still dominates its practicability. MRI is not a very sensitive technique so far as contrast efficacy is concerned. Micromolecular concentrations of gadolinium ions cannot be achieved after dosing just a few milligrams; consequently, the amount of antibodies becomes too large. Biotechnology is quickly developing and single chain fragments or small polypeptide will pave the way for disease-specific MRI agents.

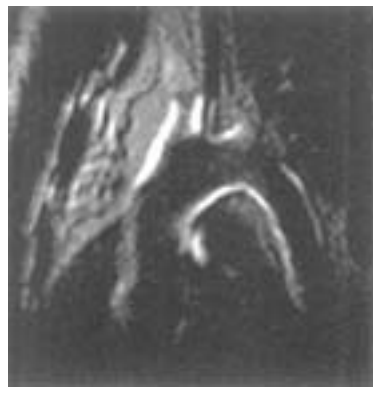
EPIX, a small Cambridge/USA based pharmaceutical company just finished the phase I study of such a peptide-based gadolinium chelate. Equipped with a couple of high-relaxivity gadolinium chelates, the agent targets fibrin. This new compound is designed to detect pulmonary embolism, deep venous thrombosis and blood clots in the coronary and carotid arteries, to name a few relevant indications. Recently, water-soluble gadolinium endohedral metallofullerenes have been synthesised. Such Gd-fullerenols, with one or even two Gd atoms, exhibit the highest relaxivity ever measured per paramagnetic atom. Are these the tools we are looking for to make MRI molecular imaging even more specific?

Cell tracking in the living organism, using magnetically labelled cells, is under active investigation, and this research will open new opportunities in molecular imaging and contrast-enhanced MRI.

Ultrasound (US) is the most common imaging technology in medicine. Phospholipid-encapsulated, liquid perfluorodichlorooctane is the basis of a new, targeted ultrasound agent. When these submillimetre-sized particles were combined with a fibrin-seeking antibody, they could identify blood clots. Several groups showed that microbubbles could be guided to intravascular receptors of inflammation, atherosclerosis, and angiogenesis. Antibodies were linked to the coating material of the US microparticle.

One of the latest preparations, which contains gas entrapped in cyanoacrylate particles, produces a strong contrast when administered intravenously. Highly effective imaging techniques, such as stimulated acoustic emission, require only small quantities of this agent to produce pathology-specific enhancements.

Dr Hanns-Joachim Weinmann



Detection of atherosclerotic plaques by a gadolinium compound in an animal model (WHHL rabbit, aortic arch)

New developments in nanotechnology will further improve the efficacy and potential of target-specific imaging agents. However, at least for the next decade classical small water-soluble agents will be the gold standard for most daily studies in CT and MRI. Other more sensitive imaging techniques, such as SPECT, PET or newly emerging near infrared imaging modalities will reach different levels of molecular imaging within coming years.

The potential for earlier diagnoses of diseases and monitoring, at a molecular level, their response to therapies, promises a revolution in medicine. We interviewed *Bill Clarke*, Executive Vice President and Chief Technology & Medical Officer at GE Healthcare, about DatScan, a molecular imaging agent that is already influencing physicians' decisions about therapies for Parkinson's patients

A MOLECULAR IMAGING AGENT AT WORK

'To see in days, weeks or, in some cases, a month, whether a disease is actually responding to therapy, means a profound change in medical care,' Bill Clarke explained. 'We are absolutely confident we can use this new paradigm of early diagnosis and then follow the response to therapy of a number of important diseases, such as Alzheimer's or early congestive heart failure. And we have an answer right now! In Europe we've introduced DatScan, a molecular imaging agent for Parkinson's disease. It examines the Dopamine uptake system in the brain's neurons. In Parkinson's these begin to die and they do so very early in the course of the disease - long before clinical symptoms start to be evident. In addition, the symptoms of Parkinson's disease, which is progressive, resemble those of a non-progress type of tremor. It is thus important to be able to differentiate between these two diseases. Using the molecular imaging of DatScan, a physician can differentiate Parkinson's disease from the non-progressive disease with similar tremors and thus choose the right treatment.

'Then the physician can follow the progress of Parkinson's disease by repeated scans. So, it's a very good way to diagnose whether or not some movements lead to Parkinson's disease or other types of movement disorders. We are studying this right now, and it is far more precise and reproducible than even the best physicians at saying whether or not a patient's disease is progressing and whether or not they are responding to therapy. This is a true molecular imaging agent!'

Given that this is an Amersham/GE Healthcare product, does the agent only work with a GE SPECT scanner?

'No, DatScan works with any SPECT system. Many physicians do not have GE equipment, and there's an ethical obligation to make molecular imaging agents available to everybody. However, because we understand what is possible in chemistry or biology, we can design new generations of equipment that improve upon the utility of molecular imaging agents. Or we can make big bets in chemistry, biology and pharmaceuticals, because we understand what is going to happen in hardware and software.

'That was a significant impediment for Amersham and GE, before we merged. We have had several recent examples of things we wanted to do with Amersham, but did not know if there was technology that would allow that. At the same time people at GE were creating that kind of technology without knowing if there would be any use for it.'

So, given the educational implications the merger has for both parties, how do you think this progress?

'Neuroradiologists will learn to use

molecular imaging just as they've learned to use very sophisticated MR imaging. There is a real change in the way medicine is done. I think all of companies that sell hardware and software - GE, Philips, Toshiba, Siemens - nobody is better at staying in touch with their physician and technologist customer base than GE. We have a huge set of television studios where every day we produce education programmes - not just about our equipment but about advances in medical imaging, science and technology. We have the opportunity and the ability and commitment to educate physicians and technologists about this new brand of imaging in medicine.

'Also, people easily forget informatics. GE has a very strong IT healthcare business and we are in the process of finalising several products that will improve our understanding of how molecular imaging agents - like DatScan - work. They enable us to take critical data from hundreds of patients and make these available to physicians to help them understand if they have obtained a good quality image, or to show them the best way to read an image and the use very sophisticated computer systems.

'In our initial trials we found out that we could raise Parkinson's diagnosis to almost 96% sensitivity and specificity by adding our software to the process of reading DatScan images. So, whilst I'm aware that this is a big change in medicine, I'm sure we can not only help to educate physicians, but also help them actually read images and make a diagnosis.'

THE COMING ERA OF GENETIC MEDICINE

By ***Stefan G Ruehm*** MD PhD, Associate Professor of Radiology, at the ***David Geffen School of Medicine, UCLA***, California

With advances in radiology over recent years medical imaging has become more precise, meanwhile even allowing for functional and metabolic analysis. It can be expected that imaging with genetic and molecular markers will play an important role in the foreseeable future. New developments in contrast media research, with the design of biologically specific contrast agents for a variety of imaging techniques, and for magnetic resonance imaging in particular, are expected to further contribute to the accuracy of medical imaging.

Molecular imaging may be characterised as the in vivo visualisation of specific biological processes at the cellular or even molecular level. It aims at the detection of early underlying biochemical and genetic alterations responsible for various disease entities rather than late changes as demonstrated by most current diagnostic imaging tools.

Excellent soft tissue contrast, high anatomical resolution and multiplanar imaging capabilities qualify MRI for molecular imaging. Compared with positron emission tomography (PET), with or without computed tomographic imaging (PET/CT), MRI does not require coregistration of molecular activity with anatomical structures. In addition, the lack of radiation exposure further favours the use of MRI. However, relatively large and potentially toxic concentrations of imaging markers are commonly necessary to visualise molecular events, representing some of the challenges faced by molecular MRI.

For a successful implementation of molecular MRI the following criteria should be fulfilled:

- sufficient MR contrast to depict changes on a cellular or molecular level
- favourable safety features of the contrast agent / molecular probe; and
- usefulness of the probe with proven validation for basic science or clinical application.

The current probes for molecular MRI combine either a paramagnetic or superparamagnetic contrast compound with a ligand. The ligand binds with high affinity to a molecular target or receptor, which usually serves as an imaging biomarker, allowing assessing the presence or severity of disease. Targets may range from copies of DNA to multiple intra- or extracellular proteins or metabolites. The capacity of a probe to detect the target molecule follows the rules of classic pharmacology. Therefore, the route of administration, distribution and delivery to the target, followed by elimination through metabolism or excretion, need to be considered. As the ligand-receptor interaction is dynamic in nature, the correct timing of the imaging data acquisition is crucial. Usually molecular contrast agents require a 24-hour period after administration until a significant amount of the probe has accumulated at the target to provide sufficient signal for MR imaging. Therefore, registration of pre- and postcontrast data sets is usually required. Image resolution and speed of data acquisition are further important determinants for the depiction of signal changes.

A substantially different means of imaging molecular events is MR spectroscopy. This relies on the detection of a spectroscopic peak at a certain location, generated by a metabolite that is produced by, or heralds, alterations on a molecular level.

Clinical Applications of molecular MRI include oncologic imaging, detection of thrombosis as well as imaging of inflammatory and/or rheumatoid disease. In addition, genetic and cell-based therapies are likely to benefit from molecular imaging.

Molecular MRI holds promise to enhance tumor detection, to provide accurate staging, to monitor therapeutic response and to survey for recurrent disease. The primary goal in oncologic imaging is to improve the detection of malignant cells, both at the primary site of origin and at locations of metastasis. As a common characteristic tumor growth is paralleled by the *de novo* formation of blood

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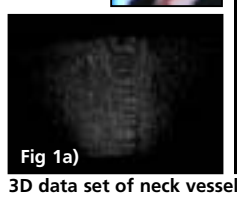

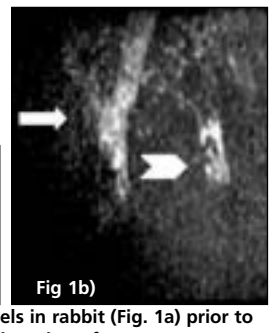

3D data set of neck vessels in rabbit (Fig. 1a) prior to and (Fig. 1b) post administration of contrast agent targeted to bind to fibrin identifies clots with high signal intensity in jugular vein (arrow) and carotid artery (arrowhead). Courtesy of Epix Pharmaceuticals, Cambridge, MA, USA

High-field MRI catalyses new diagnostic approaches

By Karen Dente MD

USA - The Biomedical Imaging Center of New York University has formed a seven-year collaborative agreement with Siemens Medical Solutions USA, Inc, bringing the university's radiology department to the forefront of medical imaging.

A 7-tesla magnetic resonance imaging unit - one of only a few worldwide - is helping researchers at the institution to redefine the frontiers of disease detection in areas such as multiple sclerosis and Alzheimer's disease. Developments of new diagnostic approaches are catalysed by the increased power of the new high-field MR machine.

The dynamic core of the unit is the machine's massive 'motor' - an enormous magnet that weighs 30 tons, and holds some 420 kilometres of superconducting wire. It has a magnetic 'field strength' of 7-tesla. Tesla is named after the famous inventor Nikola Tesla, and is a unit of magnetic flux density that describes the strength of the magnet. A 7-tesla magnet is 140,000 times stronger than the earth's magnetic field. To put this into perspective, the earth's magnet is strong enough to turn a compass needle with a strength of 0.00005 tesla.

'The total amount of stored energy in this magnet is about 80 mega joules and 80 mega joules is about something in the order of 40 pounds of TNT,' said Joseph Helpern PhD, Professor of Radiology and Director of the Center for Biomedical Imaging. In 1991, Dr Helpern built the first 3-tesla magnet in the world, and he explains that the size of the magnet is crucial to MR technique, where bigger units equate to more detailed images.

To produce their minutely detailed images, MRI machines detect the movement of atomic nuclei in a magnetic field. Lower-field-strength magnets mostly detect variations in the physical characteristics of hydrogen atoms in water molecules. Since water makes up about 70% of the body, it tends to override the weaker signals from other tissue substances. Physicists have now found out how to mask the signals from water. With the 7-tesla magnetic strength, scientists can measure other elements that make up central compounds in the body, such as phosphorus and carbon. This allows them to detect metabolism in action, such as the movement of chemicals used to transmit nerve signals.

Dr. Helpern viewing the steel shield that was put in place to prevent damage from the high-power MRI in preparation for the Magnet's arrival from England (above)

The 7-tesla unit, with 30-ton magnet, was built in England and delivered by boat, then flatbed truck. Traffic was stopped on Manhattan's 38th Street to allow delivery at the medical center. To support its massive weight, and provide a shield to contain the magnetic field, a bed of concrete 14-feet-thick had been laid on the ground floor of the Center. 420 tons of steel were needed to build the octagonal shield that now surrounds the 7-tesla, to protect other technology and people in the building. (It could even demagnetise the credit cards of pedestrians passing on the street).

Funding for the enterprise was received via a $2 million grant from the National Institutes of Health and a contract with Siemens Medical Solutions USA Inc, that exceeds $110 million. The strategic alliance with Siemens came about through the efforts of Robert I. Grossman MD, Louis Marx Professor and Chairman of the Department of Radiology at the NYU Medical Center.

A multiple sclerosis (MS) researcher, Dr Grossman hopes that high-field strength machines, such as the 7-tesla MRI, will help researchers find answers to some of most challenging questions facing the medical profession. The increased power of the novel imaging machine has provided novel insights into understanding the aetiology of MS. Since the advent of high-field MRI, MS diagnosis and treatment has undergone a major shift from a purely clinical diagnosis to one that now uses imaging in conjunction with clinical diagnostic evaluation, enabling earlier-stage diagnoses and earlier entry to clinical trials.

Cutting-edge MRI and other technologies have developed to the point where they can render extremely detailed pictures of what is happening in the brain on a molecular level. 'MRI is non-invasive and allows us to make diagnoses we couldn't make before, and it allows us to see whether the treatments we are giving are effective or not,' Dr Grossman said. The tool he and his researchers used to discover that MS is a whole-brain disorder, as opposed to only a white-matter disease, was MR spectroscopy. The technique allows scientists to look at specific neuronal markers in the brain. One such chemical clearly reduced in the brains of MS patients is NAA [N-actetyl aspartate], a metabolite found in neurons and axons. This means that neurons are being lost, and that MS is destroying the cell, not just the myelin (the cell's white insulating sheath). 'NAA is four times more sensitive in diagnosing MS than clinical reporting of brain shrinkage,' Dr Grossman points out, adding that looking at NAA in elderly patients could potentially provide a window on aging in the brain.

At the Biomedical Imaging Center, Georgeann McGuinness MD, Associate Professor of Radiology, is also benefiting from the high-field MR machine. She is researching lung disease using hyperpolarised helium. One of her studies involved looking at the lungs of firemen, involved in the 9/11 World Trade Center attacks, who had symptoms of cough and chest pain. While the normal CT images indicated normal lung anatomy, MRI with helium indicated that large sections of the men's lungs were actually not functioning at all.

Dr Helpern compares 7-Tesla MRI to the discovery of the electron microscope.

It is to the regular X-ray what the electron microscope is to the original bench light microscope. To him MR technology is nothing less than revolutionary, and he is proud that NYU is at the center of this rapidly growing technological advance

PACS:

Once upon a time, in Vienna, a radiologist worked with a group of sweet tempered radiological-technical assistants (RTA), making many, many X-rays of many patients. The assistants prepared the X-rays on the light board, where after scrutiny, the radiologist prepared the diagnosis. The typing pool was so busy writing reports of the findings that their fingers went numb. Only after reports were typed were patients allowed to collect their X-rays and reports at the office. When needed, the referring physician was given the reports and X-rays. Lots of other people - e.g. mailmen and archivists - searched for and distributed large bags of reports and letters. Everyone lived happily, until PACS destroyed this heaven on earth ...

In October 2003, a PACS - AGFA's IMPAX combined with a RIS by Siemens (Magic SAS) - went into routine operation at Vienna's University Hospital for Radiodiagnostics at the Allgemeine Krankenhaus. IMPAX is an application that runs on UNIX servers and includes a list of advantages (a central database, all examinations saved in one system) and disadvantages (very complex and not always the desired response time).

Presently PACS has been partially implemented in three of the clinics:

- university hospital for radiodiagnostics
- trauma surgery
- X-ray therapy

Over 70 modalities are connected to the PACS network. In addition, approximately 30 diagnostic stations with two flat screens each

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vessels. MRI probes aimed to specifically detect molecules mediating the process of angiogenesis have been employed to assess tumor growth and malignant potential.

Similar to FDG-PET, an imaging modality which measures increased tumor metabolism to highlight areas of tumor, a contrast agent based on (Gd)-encapsulated liposomes has been developed with ligands bearing glucose conjugates at the liposome surface. **Targeting of tumor cells with liposomes is attractive for two reasons. Firstly, high concentrations of the MRI contrast material can be delivered in the liposomes, secondly, liposomes can be used to deliver drugs. Thus, the simultaneous detection of malignancy and delivery of chemotherapeutic agents appears feasible. Possible drawbacks, however, include the relatively large size of the liposome challenging the access into the extracellular compartment, and the immunogenic potential of the liposomes.**

An approach to monitor tumor progression and response to treatment has been developed based on a superparamagnetic probe specific to cells expressing a molecule (Synaptotagmin I) that binds to apoptotic cells. Since the degree of programmed cell death after radio or chemotherapy has been shown to correlate with impediment of tumor growth and cure, the superparamagnetic compound conjugated to synaptotagmin showed good correlation with apoptosis both *in vitro* and *in vivo*.

Potential benefits of lymphotropic superparamagnetic nanoparticles have been extensively discussed in the radiological and oncologic literature. They show the potential for widespread clinical application in order to stage nodal malignant disease, particularly in the presence of prostate cancer. Clinical investigations have demonstrated that MRI with superparamagnetic nanoparticle contrast agents may improve the diagnostic accuracy. The application of these iron-based contrast agents allow the detection of malignant lymph nodes smaller than the threshold size of 10 mm that is commonly used to identify nodal disease on conventional cross-sectional imaging.

In addition to oncologic applications molecular MRI based on the use of superparamagnetic iron particles has been investigated for the diagnosis of inflammatory disease such as in antigen-induced arthritis or for the early detection of atherosclerotic disease. It has been shown that activated macrophages, which are part of the disease process, can be labeled with iron particles, presumably by macrophage phagocytosis. These initial results suggest that molecular MRI might play a role for the advanced detection of inflammatory disease, the characterisation of the degree of macrophage infiltration, and to monitor treatment response.

Current MR techniques aimed at the detection of arterial or venous thrombosis would benefit from a more specific approach to depict clot. As many clinically significant thrombotic events occur in small arteries that are below the resolution of current fast MR sequences, for example distal coronary vessels or peripheral pulmonary arterial branches, a targeted probe to provide a specific marker to improve the detection of small thrombi would be desirable.

With the development of clinical applications for gene therapy molecular MRI may play an important role for monitoring and quantifying the amount of gene delivery to an area of interest and to survey the efficiency and duration of gene expression. For that purpose 'intelligent' molecular imaging probes have been developed. In the presence of a common reporter gene product such as _-galactosidase (_-gal), these probes undergo an irreversible transition from a weak to a strong relaxivity state. Cells that express the therapeutic gene generally also express the reporter gene _-galactosidase. Thus a high signal detectable by MRI is generated.

Molecular MRI may also permit quantification and localisation of gene expression. For this purpose the transgene for tyrosinase has been incorporated into cells. The activity of the transgene can then be measured by its production of melanin. Melanin reveals a high binding capacity for metal. It has been shown that as a result of the tyrosinase expression bright signal of iron containing melanin can be detected on T1-weighted MR images.

Comparable to gene-therapeutic approaches, cell-based therapies are used with increasing frequency. Molecular MRI might provide substantial support to establish these recent treatment options by offering strategies to monitor the success of treatment. Bone marrow transplantation is widely employed and might benefit from in vivo tracking of transplanted haematopoietic cells, particularly when modified treatment regimens are evaluated. Transfection techniques allow increasing the amount of contrast agent delivered to cells. This enables even the visualisation of single cells. With the further advancements in the development of cell-based therapies, e.g. the transplantation of cardiac myocytes to restore myocardial function, the demand for specific and non-invasive imaging strategies is likely to increase.

The enormous potential for molecular MRI is based on evidence that most diseases are caused by alterations on a molecular level that may be detected by sophisticated imaging modalities. In contrast to current diagnostic imaging algorithms molecular MRI moves far beyond the structural foundation of traditional imaging techniques. Molecular MRI aims to reveal the biochemical and genetic sources of the disease in addition to the mere display of anatomy and physiology. The synergy of refined MRI techniques and new, targeted contrast agents will determine the success of molecular MRI in the future. It is likely that molecular MRI will open a wide range of novel applications, not only for the assessment of disease, but in screening for pre-disease states, which might be commonplace in the upcoming era of genetic medicine. In the consumer-driven health care environment imaging faces a bright future. However, more research is necessary to prove the value of these high tech imaging techniques with regard to overall patient outcome and cost.

Links: sruehm@mednet.ucla.edu

the never ending story

Helga Fischer (right), radiographer at the University Hospital for Radiodiagnostics at the Allgemeine Krankenhaus, Vienna, and former Vice-President of Austria's RTA Association, which focuses on MR, lectures and workshops for imaging processes, describes experiences, covering a year and a half, with a PACS system, and suggests ways forward

(resolution between 1 and 3 mega pixel) are also installed in the hospitals.

The layout of the PACS is designed and dimensioned to include:

- Images saved in the short as well as long-term archive after acceptance by the server.
- The short-term archive allows relatively fast loading of archived images.
- The long-term archive is designed for 10-year storage. Data are only rarely retrieved.
- Pre-fetching should mainly take place from the short-term archive.
- For security reasons, data must be present at least twice, whereby one copy should be stored 'remotely'.

Present workflow - This practically depends on people and the 'green folder', a collective folder used to transport all findings, images, language cassettes and task lists for the examinations. The RIS and PACS are presently used as passive systems.

Even though workflow is presently very smooth, there are three sources for errors and time-consuming complications:

Time pressure at central planning - Because processes at central planning are so fast but the IT input does not happen synchronously (capture KIS - RIS), the patient index numbers are written manually.

Transfer of the worklist to modalities - There is no consistent transfer of the electronic work list from RIS to the modalities (they are older models). All relevant data must be entered manually particularly for the older modalities, which is a potential source for errors.

Diagnostic findings - The diagnostic process (dictation, writing, proof-reading, corrections and revision) and particularly the interaction between doctors and the typing-pool, is clearly a source for errors and there's a potential for time optimisation.

Since PACS arrived, what are the most important disadvantages and advantages?

Disadvantages

- MTRA was not integrated into selection and purchasing process
- Selection, purchasing and implementation took too long, so when the system effectively went into operation, it was already too small
- When pictures are printed from PACS (e.g. CT) and the person involved does not ensure the printer is at the right level, all pictures may be printed twice (expensive)
- When there is a problem within the IT system, the complete PACS system goes down
- Under certain circumstances, images that are sent to the PACS are not saved in the right place; in which case the IT specialist must reprocess
- Retrieval of master images from the main storage can take up to hours; the IT specialist must be contacted
- Data must be entered absolutely correctly when an examination takes place in rooms where a patient's data cannot be transferred into the examination computer, otherwise the images cannot be found in the PACS; the technician must reprocess in these cases
- High service and maintenance costs
- Display is monitor-dependent

Advantages

- Waiting times for the patients have reduced significantly
- Examinations can start more promptly
- Increased patient frequency is possible
- There is reduced film development and thus fewer toxic developing substances
- Lower film costs
- Better quality, as images can be saved digitally without losing data
- Better availability for diagnostic findings, visits or interdisciplinary consultations.

Overview - At present the PACS has stored about 8,897,000 images (files) with some 5,308 GB (raw) total data volume.

Computed tomography

- 25,450 CT exams
- average 238 images per picture
- approx. 6 million data files

Magnetic resonance

- 10,494 MR exams annually
- average 247 images per picture
- approx. 2.5 million data files

Additional modalities

- 248,400 data files from gastro, bones, etc.

continued on page 18

continued from page 17

In view of these volumes, the short-term archive (magneto-optical disc) will be filled within two years. Consequently, the oldest storage media must be removed from the library at regular intervals and replaced by blank ones.

Suggestions for improvement

Our wish list:

- The permanent employment, in the hospital, of a contact for doctors and IT people, who is capable of developing the most important IT strategies for the individual IT and medical-technical projects (such as PACS, RIS, KIS). This will ensure realisation of the intended synergies, consolidation and conformity for the systems.
- The nomination of a project manager from within the department/hospital, for a large and complex project such as PACs, the implementation of which takes several years and possibly longer. This person should be the connection between the hospital (professors, doctors, RTAs), and IT and manufacturer, and should be accepted as such by all those involved.
- The nomination of someone from the department/hospital, to take care of various IT-specific tasks. Experience in other hospitals clearly prove that this position is a prerequisite: It should not directly include the implementation of IT projects, but aspects such as:
  - cooperation with IT, manufacturer, medical technology and doctors
  - Training involving the IT user systems, such as RIS and PACS
  - First contact person regarding IT-relevant questions for doctors and RTAs
  - Constant training for new doctors as well as RTAs, for various IT systems, so that these are actually used consistently.

... and thus I would like to end our PACS story, but it's nowhere near finished.

Finally, I would like to express my gratitude to: Mr Weigl MA, and his team at Consulting AIMC, whose help enables us to accomplish the impossible.

Personalised medicine

Dr Burkhard Ziebolz, of Roche Diagnostics

On average, some 30% of patients do not experience any sustained alleviation of their symptoms from their prescribed medicines - a disastrous figure for healthcare costs. One of the reasons for these less than ideal effects is that a single drug is used to treat a large number of genetically different individuals who present with a common clinical picture at the phenotypical level. It is hardly surprising that a drug does not produce the same effect in all the recipients. Moreover, many individuals suffer specific side effects, so they must switch to a less effective type of treatment. What is needed is a more targeted treatment that produces the specifically desired effect in the patient.

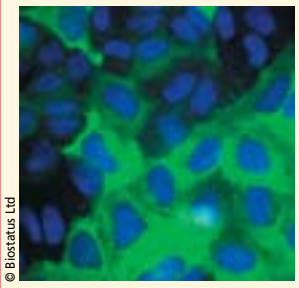
'Personalised medicine' is based on a molecular understanding of the causes of disease in an individual and it opens up the possibility of more effective treatment for illnesses. The type of metabolism possessed by the respective patient is an important aspect in this adapted drug treatment. People metabolise active substances in different ways. Therefore, a treatment and selection of drugs tailored to the individual is crucial to a successful outcome. It avoids the situation where patients receive inappropriate drug treatments and incorrect dosages - which in turn can lead to serious adverse drug reactions (ADR).

Highly specific diagnostic methods are needed to provide doctors and patients with practically useful information for customised treatment. The so-called AmpliChip CYP450 from Roche Diagnostics is currently the only diagnostic tool capable of helping to avoid inappropriate drug reactions or serious ADRs. Based on DNA-chip technology developed by Affymetrix, the test enables a comprehensive analysis of the two genes belonging to the gene cluster known as cytochrome P 450 in the genomic DNA of patients' blood samples. These genes play a prominent role in the metabolism of many commonly prescribed drugs. The chip can be used to identify the specific type of metabolic group to which a patient belongs. The results enable the physician to be more effective in making the right choice and dosage of drugs for the treatment of various common illnesses, such as heart disease, pain, cancer and mental disorders.

Roche Amplichip

The chip analysis is currently implemented in specially designed service centres that receive the patient samples from the relevant medical specialist. On completion of the analysis - which takes just eight hours - the specialist receives a report with a reference to the patient's metabolic type.

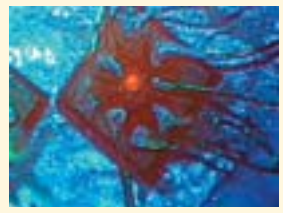
Microscopes the size of human cell



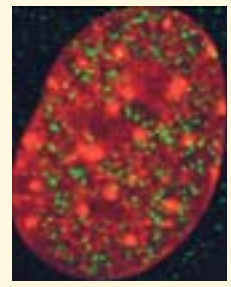
© Biostatus Ltd

Fluorescent living cells trapped in a thermoreversible gel, developed by BioStatus Ltd for on chip analyses

© UK Optical Biochip Consortium



Laser Chip - A red light emitting laser chip - the core of the optical biochip



© Cardiff University

Nuclear Label - A single cell nucleus emitting light from red and green fluorescent probes used to detect cellular abnormalities

Optical biochips that are no larger than a single cell and could lead to a quicker creation of new drugs and medical tests, have been developed by an interdisciplinary research team funded by the Biotechnology and Biological Science Research Council (BBSRC), and the *Engineering and Physical Sciences Research Council* (EPSRC).

Biological samples are placed on optical biochips then fluorescent chemicals are used, together with tiny light emitting lasers, to enable analysis of cells or targets within them, to study cellular conditions for certain diseases or to develop new treatments by studying the way cells react to a drug.

Biochips also present the possibility of a micro-laboratory, the size of a credit card, which could perform medical diagnoses, and reduce the number of hospital visits for tests.

The initial research has led to the creation of a spin-off firm, BioStatus Ltd, supported by a BBSRC Small Business Research Initiative grant. BioStatus has developed the research to refine fluorescent probe technology and advance the analysis of biological samples.

Lead researcher, Professor Paul Smith, said: 'Our research and the outcomes from the spin-off firm, could help to revolutionise how we examine biological samples. Our next step will be to develop simple, small diagnostic devices. Future generations may be able to use these as the basis for hand-held systems that can perform diagnostic functions that currently need a laboratory test.'

The research, carried out at the University of Wales College of Medicine, involves researchers at Cardiff University, the University of Bangor, the Gray Cancer Institute, London, and in collaboration with the University of Warwick and laboratories in the USA.

*** The Biotechnology and Biological Sciences Research Council (BBSRC) is the UK funding agency for research in the life sciences. Sponsored by Government, BBSRC annually invests around £300 million in a wide range of research that makes a significant contribution to the quality of life for UK citizens and supports a number of important industrial stakeholders including the agriculture, food, chemical, healthcare and pharmaceutical sectors.**

Links: BBSRC http://www.bbsrc.ac.uk. Professor Paul Smith: smithpj2@cf.ac.uk. This research is featured in *Business* (4/05), the Biotechnology and Biological Sciences Research Council journal.

Management: a new paradigm for clinical laboratory scientists

By **Dr Bernard Gouget**, Advisory Board member of the SFBC-FESCC (Société Française de Biologie Clinique - Forum of the European Societies of Clinical Chemistry and Laboratory Medicine)

Dr Bernard Gouget

Clinical chemistry raises a strategic health issue. Clinical laboratory scientists must adapt to technological challenges by keeping pace with changing analytical methods, as well as to economic challenges through innovative management and networking, to be able to incorporate within their practice all the emerging disciplines of laboratory medicine, whilst committing themselves to the priorities of quality and safety. The environment in which medicine laboratory is practiced has undergone a paradigm shift in the midst of the medical, legislative, regulatory, technological, sociological and economic upheavals that have forever changed the practice of medicine. In addition to clinical laboratory sciences, laboratory managers need to possess broad knowledge of clinical medicine, the science basics of medicine together with administrative knowledge and experience. Their managerial responsibilities involve the directing of quality testing for patient care with concomitant high levels of expertise in finance and personnel management meeting the increasing need for new qualifications. They must play a leadership role in enhancing the image and increasing the visibility of laboratory medicine.

Laboratory managers are therefore faced with new responsibilities. Leadership and managerial skills are essential, mainly due to the areas covered by the advance in biological and medical science: the variety and volume of testing, exponential growth of sophisticated tests, new instrumentation, automated data processing and information management systems. Economics and governments are accelerating these changes in a predatory environment. Competition, mechanisms for consolidation alliances between laboratories and service agreements have won new frontiers for laboratories. Often regarded as a threat, these mechanisms are also seen as an opportunity by those who are willing to think creatively. At the same time, public expectations have never been higher and, paradoxically, funding has never been under such pressure. The task facing laboratory managers is therefore an extensive one, encompassing technology, science, human resources and finance with the specificity that these include a patient care component.

The monograph *Managing changes in the clinical laboratory*, produced by the International federation of clinical chemistry and laboratory medicine (IFCC) Education and Management Division, aims at preparing the clinical laboratory scientist for the changes affecting laboratory management. It draws attention to opportunities for new missions, methods of practice, professions, coordinated structures and new responsibilities. It is a practical tool that makes an essential contribution towards the quality and future of laboratory medicine.

Links : www.ifcc.org http://www.fescc.org/fescc/2ndStratPlan.htm

MRSA 'breakthrough'

UK - A researcher working on the development of a new antibiotic that could treat patients infected with methicillin-resistant Staphylococcus aureus (MRSA), has been granted £280,000 towards developing a series of lactonamycin-like substances, by the Engineering and Physical Sciences Research Council. Philip Parsons, professor of organic chemistry at the University of Sussex, said: 'We know lactonamycin, a naturally occurring antibiotic, can kill MRSA. But it is has not been available as a drug therapy, partly due to its novelty and complexity. We are looking at a simple way to synthesise the antibiotic and its compounds, which could also be highly effective in the fight against infection.'

Research has shown that lactonamycin, an extract of the bacteria *Streptomyces rishiriensis*, is active against MRSA. The Professor, who has discovered a 'one-pot' method - a cascade reaction - during which several reactions take place at once, said: 'This will be important not just for producing lactonamycin, but for making other compounds, natural products and drug substances more efficiently.'

Philip Parsons with John Board, DPhil student and model of the antiobiotic lactonamycin

European Hospital at the ECR

Daniela Zimmermann reports on the 2nd Hospital Administrator Forum

ECR President Antonio Chiesa

Maximilian Reiser (left) and Jörg Debatin

From right: Peter Bogner, Helmut Ringl, Henio Sobiszewski, Volker Hüsken and Kim Egger

Eberhard Kamper (left) Managing Director, bsbb, and Hans-Peter Bursig, Managing Director of Forum Deutsche Medizintechnik & ZVEI, at the European Hospital booth, ECR 2005

Apart from MEDICA, held in Dusseldorf, the annual European Congress of Radiology (ECR), in Vienna, is the most important event of the year for our European Hospital team. This year, there was an added reason to look forward to the biggest European imaging convention: in joint cooperation with the ECR and bsbb, the congress and event management company, we held the *2nd Hospital Administrator Forum*. Whilst the magazine has focused, for several years, on one of the most exciting and innovative developments for hospitals today: the combination of radiological diagnostics with IT and networking, the Forum presented an opportunity to promote, communication between radiologists and hospital administrators, not only through our pages, but during a live event.

About 110 radiologists, hospital doctors, IT managers and industry representatives from 27 countries - hailing from Australia to Switzerland - assembled to discuss subjects such as '*Successful Hospital Management - Facing the Challenges of Hi-tech and Financability*'.

The fact that a comparatively small forum managed to attract participants from 27 nations with very different experiences of healthcare systems underlines the importance of constructive dialogue - an opinion shared by leaders of the ECR, as well as its President, **Professor Antonio Chiesa**. Welcoming the debate on hi-tech and finance he said: '*The time has already come in which hospitals no longer rely solely on doctors - an opinion they also share. Doctors understand that a modern hospital is defined not only by its highly professional medical teams, but also by state-of-the-art equipment, informatics applications, and innovative programmes. Administrators play a key role in this changing world, where progressively reduced resources are met with rising costs. With an increasingly older and more numerous population, these obstacles prove a hefty challenge.*'

In his '*Radiological innovations: between hi-tech and financability*' lecture, **Professor Maximilian F Reiser** MD, Professor and Chairman, University of Munich, Department of Clinical Radiology, at Grosshadern, Germany, and mentor and moderator of the forum, added: '*Radiologists and hospital managers should make every effort to convince financial decision makers that investment in medical technology and an IT infrastructure can improve the quality of healthcare and at the same time reduce costs. The one-sided orientation and support for pharmaceutical research and development has long been proven as an expensive error.*'

An answer from the other side of the fence swiftly followed. **Professor Jörg F Debatin** MD MBA, formerly director of the radiology institute at the University Clinic, Essen, and currently Medical Director and CEO at the University Medical Centre, Eppendorf, Hamburg, responded, in a relaxed though proactive manner: '*Healthcare is rapidly evolving from a totally non-transparent and heavily process-regulated system to a competitive market. To survive in such a market, hospitals will require the conscious development of marketing and sales strategies. These should be based on a product portfolio defined by quality, profitability and unique selling proposals. However, the basis of marketing and sales strategies must lie in providing transparency to the customer - the patient - regarding outcome quality and pricing of healthcare products.*'

Dr Volker Hüsken, CEO at the University Hospital, Cologne, Germany, and **Dr Helmut Ringl**, of the Department of Diagnostic Radiology, University of Vienna General Hospital (AKH), Austria, discussed technology, the implementation of new IT systems and the implications for hospital staff.

Dr Hüsken emphasised that hospital processes should be organised to allow doctors to concentrate on medicine, and that IT departments should do what they are best at: being technical advisors to all departments and for all processes.

Concentrating on the practical aspects of PACS implementation, Dr Ringl advised on the avoidance of mistakes when making decisions on purchasing these systems, which he described as brilliant instruments - when they work properly.

Professor **Peter Bogner** MD PhD, Vice-director of the Institute of Diagnostic Imaging and Radiation Oncology, University of Kaposvár, Hungary, described the hard work involved in setting up an IT project to link nine institutions of different size and competence. With a background of exclusively public funding and the involvement of the Hungarian national medical insurance body, the hospitals decided against a common, central archive accessible by everyone. Hence, he said, they are now looking for a suitable model that allows transparency and transport of data in a secure, protected manner.

Henio Sobiszewski, Regional Manager Central Europe, Toshiba Medical Systems Europe (OD), and **Kim Egger**, Sales Director Healthcare, of the Netherlands-based finance firm De Lage Landen, which specialises in asset financing and vendor finance programmes, introduced a model that enables independence from public funding. This demonstrated how, by establishing a limited company, the complete modernisation of a radiology department in a Polish hospital became possible. The concept had not only liberated employees from enforced models of working hours but also had ensured that capital could be acquired.

Later, in a relaxed atmosphere, complemented by a buffet on the top floor of the Ares Tower, discussions flowed on until quite late. In conclusion, everyone was unanimous: the exchange of knowledge and opinions at the Forum should continue. So, we are looking forward to the *Hospital Administrator Symposium 2006*.

European Hospital advances on Asia

Korea - Holding a leading position as a European healthcare journal is simply not enough! Following the first appearance of *European Hospital* at KIMES in 2004 (below), our magazine has again been distributed in Seoul, this time at the KIMES *21st Korea International Medical & Hospital Equipment Show* in March, where 845 companies from 32 nations presented over 12,000 products, in 28,746 square metres of exhibition space.

KIMES focuses mainly on the development of the medical technology industry in Korea and neighbouring states. The event aims to support and promote international trade in every way. To encourage communication and information exchange on medicine, IT and medical technology, the organisers had arranged 21 conferences and seminars on a wide range of topics.

To our delight, masses of the 50,682 visitors and exhibitors, flocked to the European Hospital stand and our Korean team - C H Park and Kevin Choi - reported that KIMES 2005 was a big success. *European Hospital* issues had been scooped up - down to, and including, the very last copy.

KIMES, Korea's biggest medical show, will be held in Seoul again in 2006. Details: www.kimes.info

CH Park and Kevin Choi manned the European Hospital stand in Korea

Pilot projects

Anja Behringer reports on the 2nd Telemedicine Forum, organised by Tele Medical Systems AG (TMS)

Christa Stewens and Franco Renzo

Germany - Telemonitoring complements, but does not replace traditional, time and staff intensive home visits or regular visits to surgeries. Clearly structured, reproducible communication between doctor and patient, based on modern technology, initially requires the development of appropriate software for different disease-management programmes (DMP). 'This scientific approach then has to be applied,' said Professor Karl Lauterbach MD, director of the Institute for Health Economics and Clinical Epidemiology at the University of Cologne. Franco Renzo, President of TMS (based in Switzerland), described the way in which the firm's system can address and combine subjects such as health passports, DMP and telemedicine: '...as long as the interests of different groups can actually be reduced to a common denominator.'

Indeed, controversy developed from the start, at the Regensberg forum. One bone of contention was electronic patient files: Whereas Roland Sing, head of the board at AOK Baden-Wurttemberg and member of the board at Initiative D 21, stressed the importance of introducing new IT-systems, stating: 'Patients should never look at their files without supervision, because they may find some rather unpleasant things,' whereupon, Karl Lauterbach vehemently demanded: 'They must!'

Christa Stewens, Bavarian Minister for Employment and Social Affairs, Families and Women's Issues, spoke of Ingolstadt, a pilot project in which patients are the 'master of their data' - aimed to reduce mistrust. 'One develops a different approach to one's health,' the minister said, before describing another 24 current projects on the teleconsultation, teleradiology, telemonitoring and teletherapy as well as electronic treatments. Christa Stewens then introduced the model project Donaustauf, which involves telemonitoring for 900 patients.

Professor Michael Pfeifer MD, Medical Director of the Hospital Donaustauf, near Regensburg, described the first practical experiences with telemedicine and telemonitoring for patients with chronic pulmonary disease. This involved 45 patients suffering chronic obstructive pulmonary disease (COPD) and bronchial asthma. It transpired that regular transmission of lung function readings to the treatment centre can be carried out by patients and that they were happy to do this. These first positive experiences led to the model project run by AOK Bayern, which will see telemedical monitoring of 900 patients with COPD and asthma.

The first phase of the project aims to prove that long-term telemedical supervision is possible and is accepted by patients, and to improve and stabilise pulmonary disease, defined by the number of hospital admissions and exacerbations of the disease. The project also aims to support not only patients but also the doctors treating them, who will be regularly informed about test results and clinical data - or who can actively demand these data - with the help of applied telemedical procedures.

The Telemedicinecentre (TMZ) is staffed 24/7, so that patients can contact someone at any time with questions about the system or their illnesses. Active telephone contact with the patient, through the TMZ, is initiated if there has been no contact and no transmission of results for over three days, or when results on lung function look critical. Based on the results of the Asthma-Knowledge-Test for asthmatics and the modified Asthma-Knowledge-Test for COPD patients, knowledge has increased among asthmatics about the way they are dealing with their illness and how they cope with emergency situations. During the trial, there has also been a general improvement in knowledge about the illness among patients with COPD. As there has been no specific training for patients, this must be viewed as a concomitant effect of learning.

So far there has been no evaluation of the medical progress of the illnesses, such as exacerbation rate, number of emergency and hospital treatments and use of drugs. The primary objective of the first phase of the model project was to see if it was feasible and acceptable to carry out a care programme based on telemedicine for patients with chronic obstructive pulmonary diseases. In other projects, the efficiency of the programme with regards to clinical parameters such as the reduction of the exacerbation rate and hospital admittance is being examined. These insights should indicate for which patients a monitoring programme based on telemedicine is sensible and effective.

Everybody agrees on the general medical and social progress through telematics. However, detailed, legal points will continue to remain the subject of much discussion. Dr Manfred Zipperer, Head of the Action Forum Telematics in Healthcare, pointed out: 'It is to be seen how the existing projects are to be integrated into the organisational and financial framework.' In view of the pressure put on the system by the law, he stressed the importance of '...at least complying with the basic legal requirements'.

Sana's new flagship

Installing a €70 million network

A 'hospital of short distances' is being built by the Sana-Kliniken-Gesellschaft mbH & Co KGaA, based in North Rhine-Westphalia. The company reports that the aim of the new Sana-Klinikum Remscheid GmbH is to set an example for top medical services, optimum patient care and - despite the ongoing economic restructuring of the German healthcare system - economic success. The new Sana clinic, is to be heavily based on IT innovations, and will have a network to provide telephone conversations and data and images linked through a joint IP-network. The chosen technology supplier is Cisco Systems, which includes 250 WLAN base stations as the backbone of one of the largest wireless Voice-over-IP-networks in Europe.

Sana's total investment will be around €70 million, for what should be '... an absolutely reliable network,' said Michael Willman, Head of IT at the Sana-Klinikum Remscheid.

The clinic has appointed ISIS Multimedia Net GmbH & Co KG as the prime contractor for the design and finishing of the high-performance network. 'To meet the enormous demands of the Sana-Klinikum we are using Cisco System's networking technology,' said Jürgen Übachs of ISIS, who is responsible for the Remscheid project. 'Thanks to the quality of service we can now integrate intelligent services and applications into the network without problems. For example, bandwidth can be scaled in a flexible way with increasing flow of data. And - at least as important - the products are based on Voice-over-IP technology supplied by Cisco Systems. There is only one network for telephone conversations, medical results, digital X-ray or CT images and multimedia contents for the patient-entertainment system.'

Seamless integration of WLAN and Ethernet-Backbone

Voice-over IP, i.e. the ability to transmit telephone conversations according to internet protocols (IP), is not limited to the fixed network: around 250 Cisco Aironet 1200 WLAN base stations cover the comprehensive, wireless radio network. This is seamlessly integrated with the cabled Ethernet-Backbone, which is why all services and quality characteristics, from voice-over IP to multimedia and quality of service, are available in the WLAN, with no restrictions. This makes clinical treatment mobile.

Cost-intensive maintenance - essential with conventional telecommunications technology - is not required for the IP telephones. This is why Michael Willmann quotes voice-over IP as a very instructive example of how technology used in an intelligent way can promote more flexible processes in hospitals, whilst simultaneously lowering administrative costs.

The IT staff at the hospital has been working with Cisco Systems equipment since 1999, so will not require expensive retraining for new technology - another cost advantage.

Overall, said Michael Willmann, 'We estimate savings resulting from increases in productivity of around 20% for 2005.

It is one of the world's biggest investments in IT for healthcare. But what will it really cost? *Report by Peter Howieson*

The NPfIT

UK - The NHS in England* is a complex environment, with over 50 million potential patients, 1.2 million staff, 14 million transactions in a typical week, 10,000 component organisations, and over 60 Royal Colleges and bodies. (*Scotland has a separate organisation).

As reported in previous issues of European Hospital, back in 1998 the NHS unveiled its strategy to modernise its IT Systems to help improve services back, and in 2002 the Government set up the **National Programme for IT** (**NPfIT**) in England, with **£2.3 billion** to be invested over its first three years, which have now ended.

The plan intends to connect over 30,000 general practitioners (GP) to almost 300 hospitals; give patients access to their personal healthcare data, and transform the way the NHS works. Information is expected to move around quicker with healthcare records, appointment details, prescription information, and up-to-date research into illnesses and treatment accessible to patients and health professionals whenever needed. The plan also intends to support individual choices, enabling first hospital outpatient appointments to be made at a time, date and place to suit the patient. As planned, the NPfIT was to be rolled out in four phases over a period of eight years: April 2002 to December 2010.

When the National Programme has run it course, it should have delivered:

- An Information and Communication Technology (ICT) structure to provide secure and high-speed communications between users, as well as supporting the necessary infrastructure to provide telemedicine services.
- A National Booking Service for online booking for all patient appointments.
- A National Prescription Service for electronic prescriptions with full clinical and patient support.
- An NHS Care Records Service (NHS CRS) which would also manage both the National Booking Service and the National Prescription Service

In May 2004 the Government earmarked £2.3 billion for the next three-year period, to include the cost of buying new systems and the training and education needed to help staff to adapt to new ways of working. Funding for future years will be handled as part of the Government's annual spending review. The total value of contracts awarded (covering 7-10 years) is over £6 billion. Further central funding will be needed to cover supplier contracts for their 10-year lifetime. However, central funding will not cover all aspects of the NPfIT's delivery, but it is not yet clear what proportion of funding will need to be found locally. Currently the NHS spends around £850m annually, primarily locally, on IT systems and their support. On top of this, funding for the NPfIT will require

£370m in 2003/4
£730m in 2004/5
£1.2 billion in 2005/6

The new systems will be implemented by groups of commercial suppliers - known as **National Application Service Providers** (**NASPs**) and **Local Service Providers** (**LSPs**) - which will work together (see figures 1 & 2).

The new National Network, which replaces the private NHS communications network NHSnet, will be of higher capacity and will provide fast, broadband networking services to the NHS making it possible to deliver the reforms and new services including electronic transmission of prescriptions, and picture archiving and communication systems (PACS).

In January 2004, a NHS-wide agreement - the first of a series that the NPfIT is negotiating with IT suppliers - was made with the Oracle Corp for the NHS to consolidate and standardise on a single, secure, resilient database infrastructure. Already a key IT supplier to the NHS, Oracle's involvement has now increased as a result of the recent NHS Care Record contract awards, in which the firm is a sub-contractor to a number of the LSPs. They are supplying the infrastructure that will underpin the NHS Care Records Service, which will provide all over 50 million patients with an individual electronic NHS Care Record detailing key treatments and care within either the NHS or social care. It is estimated that, from 2008, this infrastructure will deal with up to five billion transactions annually.

Connections to the new '**N3**' network began in April 2004 and, in 2007, it is expected that the 18,000 sites that deliver healthcare in England will be linked electronically for the first time. This will include the migration of 10,000 sites with current NHSnet connections over to N3. Priorities for this migration will be based on a variety of factors including LSP needs; when current connection contracts expire, and potential savings that can be made in each location. Formal procurement began in January 2003. As well as the prime contractor, the role of sub-contractors will be key, with a number of subcontractors involved in more than one service.

As reported in European Hospital, in May 2004 Eastman Kodak Company's Health Imaging Group was selected as one of the digital solutions suppliers for the NHS NPfIT. Kodak is part of an alliance led by Computer Sciences Corporation (Capital Care Alliance). The system will feature:

- Computed Radiography (CR) machines that enable physicians to capture x-ray images digitally
- A PACS to store and distribute radiology images
- A Radiology Information System (RIS) to manage all information stored in the PACS.

As seen in figure 2, Accenture won the (December 2005) two LSP contracts for the North East and Eastern regional clusters, with a combined value of c. £2 billion. In February this year, Accenture signed up four new IT suppliers, to assist with the IT infrastructure in those clusters:

Cognos will supply ReportNet, a web services-based reporting tool, to assess disease trends, bed availability and waiting lists.

EMC Documentum will supply a platform of content management services, to provide quick/easy access to a wide range of content and documents including X-rays, doctors' notes and research material.

First DataBank Europe will provide software to warn of potential adverse effects of drugs at the point of care (POC).

Informatica software will be used to enable faster/easier access to various legacy systems that track patient data for the electronic care records system.

However, sounding a negative note in February this year, Mike McGrath, chief financial officer of Accenture, said the scale of problems with its NHS government contract had now reached a magnitude where they had to be revealed to the market. There had been delays in deployment of a new assessment care system, he said, and talks were now taking place with the NHS on different deployment plans. Losses of $110m to $150m were expected on the contract in the current fiscal year and losses would continue at a lesser level in 2006. However, be added that the contract was expected to turn the corner and start to become profitable in 2007.

Fig. 1 National Application Service Providers (NASP's) are responsible for buying and integrating IT systems to be used nationally, such as the NHS Care Records Service

Service Contract	*Contractor*	*Value*	*Period*
NHS Care Records Service	**BT**	**£620m**	10 years
Choose and Book (E-booking)	**Atos Origin** (formerly SchlumbergerSema	**£65m**	5 years
N3 (the New National Network)	**BT** will act as a system integrator to buy connections from a constantly updated set of approved national and local telecoms companies **BT Syntegra** for new software to manage information and payments under the Quality and Outcomes Framework		
Broadband Network +	**BT**	**£530m**	7 years

Fig 2. Local Service Providers (LSPs) are based around five regions, formed from 'clusters' of strategic health authorities. The five regional clusters are: London, North East, Southern, Eastern and North West & West Midlands. LSPs are responsible for delivering IT systems and services to be used locally. Local Service Provider (LSP) contracts have been awarded to:

Service Contract	*Contractor*	*Value*	*Period*
LSP, London	**Capital Care Alliance**, led by **BT**	**£996m**	10 years
LSP, East of England	**Accenture**	**£934m**	10 years
LSP, North East + LSP North West	**Accenture**	**£1099m**	10 years
LSP, West Midlands	**The CSC Alliance**	**£973m**	10 years
LSP, South	**The Fujitsu Alliance**	**£896m**	10 years

Bio-hazard!

Bacteria flourish in warm, damp laundry rooms

The barrier washer: built into a wall separating soiled from clean laundry

Hospital acquired infections (HAI) adversely affect thousands of patients - and poor laundering procedures can be among the causes. The warm, damp environment of a laundry room makes an excellent breeding ground for bacteria introduced in contaminated clothing, where the constant circulation of inadequately laundered sheets, gowns, uniforms, towels, etc. means contamination is quickly spread. During the SARS outbreak in Taiwan, for example, a hospital laundry worker was thought to have been a significant source of the infection because the hospital lacked hygienic laundry equipment and appropriate laundering procedures had not been followed.

Laundry is front-loaded but, after processing, is removed from the back or side

Whilst the need to scrupulously separate of clean and dirty materials is good old-fashioned common sense, certain aspects of good hygiene require greater technical knowledge, such as how to keep a soiled linen area at a lower air pressure than a clean linen area (negative air pressure).

Electrolux Laundry Systems, which produces washer extractors, dryers and finishing equipment, and which tailors laundry solutions to the specific needs of businesses and healthcare institutions, reports that its approach is based on the *Risk Analysis and Bio-contamination Control System* (RABC), a *European Standard* (EN 14065) for controlling the microbiological quality of laundered textiles.

The model is focused around:

- **Audit**: Understanding the laundry process in its entirety, so that the right processes can be identified for the demands of a specific environment.
- **Equipment**: Reviewing whether the right equipment is in place, from specialist barrier washers for decontaminating infected materials that are used in sensitive patient environments, to straightforward tools, such as closed trolleys for transporting clean linen.
- **Control**: Constant reviews of the microbiological quality of the linen, levels of decontamination, etc. (Electrolux works with specialist laboratories, such as the Pasteur Institute, to verify hygiene standards).

Barrier washers - in one way, out the other

Electrolux also reports that its barrier washers, designed for laundries with stringent hygiene demands, provide a reliable defence against the spread of germs, bacteria and dust particles in the laundry process. 'The barrier washer is built into a wall, physically separating soiled from clean laundry. Laundry to be processed is loaded into the front of the machine and unloaded from the back or side. As a result, the Electrolux barrier washer is the ideal solution for fighting nosocomial infections in health care institutions. When it comes to hospital laundry hygiene, there's no room for compromise!' the firm emphasises.

- *Electrolux Laundry Systems is a part of the Electrolux Group, which employs over 70,000 people to produce and distribute powered appliances for kitchen, cleaning and outdoor use (e.g. refrigerators, washing machines, cookers, vacuum cleaners, lawn mowers, etc). The company sells over 55 million products annually, in over 150 countries.*

Further details:
www.electrolux.com/laundrysystems

Antimicrobial film protection

Autotex AM, a new hard-coated polyester film used as a covering for hygiene critical surfaces, such as membrane keyboards, fascia panels, walls, shelf and bench tops, was recently launched by Autotype International. The firm reports that this is the first material of its kind to incorporate built-in 'Microban Antimicrobial' protection, shown in tests to inhibit growth of a wide range of bacteria, fungi and moulds, including MRSA, Salmonella Enteritidis, Escherichia Coli and Listeria Monocytogenes. When micro-organisms come in contact with the substrate surface of the film the antimicrobial elements penetrate the cell walls and disrupt cell functions, which prevents growth or reproduction.

'Using Autotex AM with Microban will not eliminate the need for general cleanliness and hygiene, but it will provide an overwhelming reassurance in terms of a constant protection against bacterial contamination,' said Emma Scowen, Industrial Product Manager for Autotype International

Marketing beyond future challenges

Maquet Critical Care (MCC) has been awarded the 2005 Frost & Sullivan (F&S) Leadership Award in its '*Global Ventilators*' category. 'The Global Ventilator market is a highly fragmented industry with over 80 manufacturers fighting for a piece of the pie,' explained the international business consultancy F&S. 'Though the top four players corner almost 80% of the global market, the times to come will be much more challenging, when Brazilian and Chinese makes (which imitate higher technology offerings) flood the market. These top four players are similar in terms of presence across segments, price points and countries. However, the nature of presence and differences in business strategy yield the divergence in performance.'

Maquet, which produces medical equipment and systems for the operating theatre, critical care, cardiopulmonary and extended care facilities, is a division of Getinge AB, which has some 6,600 employees worldwide and reported sales of $1.5 billion+ in 2004.

In its *Strategic Analysis of World Mechanical Ventilators Market* F&S concluded that, having overcome many hurdles, MCC had 'edged out' competitors to firmly rise to the position of leadership in its industry, and continues to invest in numerous parameters relevant to its customers. 'The recipient has displayed excellence in all areas of the market leadership process, including the identification of market challenges, drivers and restraints, as well as strategy development and methods of addressing these market dynamics,' said F&S. 'Furthermore, the Award recipient has continually demonstrated solutions for monitoring market changes and for implementing superior market engineering strategies.' Furthermore, F&S pointed out that the firm's strategy used the same brand, *Servo*, '... to cater across price points and care areas, unlike most other Tier I vendors who use multiple brands. This has helped it bolster the brand name and provide commonality of parts, training & servicing to users/buyers. This is an enviable position to be in, in the era where customers demand user-friendly and modular systems.'

Nils Rosén, Vice President Marketing, and Christian Keller, President of Maquet Critical Care with the F&S award

Worldwide, the firm has installed almost a hundred thousand units.

SEEKING INSIGHT INTO PULMONARY HYPERTENSION

Biotechnologist Dr Soni Pullamsetti (29), of the University of Giessen Lung Centre, has won the Rene-Baumgart Foundation Research Award for her work on Pulmonary Hypertension (PH), for her paper focusing on '*Increased levels and reduced catabolism of asymmetric and symmetric dimethylarginines in pulmonary hypertension*', which provides new insight into the molecular mechanisms of PH, and may serve as a basis for novel therapeutic options.

Soni Pullamsetti received the €5,000 award at the 46th Annual Meeting of the German Society of Pulmonary Medicine

Dr Pullamsetti, from Hyderabad, India, is one of the first graduates of the University's International Graduate Programme 'Molecular Biology and Medicine of the Lung', which she joined in 2002. In a pilot study, under the direction of Dr Ralph Schermuly, Soni Pullamsetti, used observations made in animal models to study patients with pulmonary hypertension and healthy lung donors. 'Many studies have proved the central role of Nitric Oxide (NO) in the blood vessels of the lung. It widens the vessels, improves perfusion and gas exchange. In pulmonary hypertension the activity of NO is reduced. The reasons are not yet clear,' Dr Pullamsetti explained. NO is in a continuous balance with its opponent ADMA (asymmetric dimethyl-arginine), which constricts lung blood vessels. Dr Pullamsetti described the key role of the enzyme DDAH-2 (Dimethyl-arginine-dimethyl-aminohydrolases). DDAH-2 catalyses the degradation of the NO inhibiting ADMA. Her work demonstrated that both in animal models and PH patients the DDAH-2 levels are reduced. Now, DDAH-2 - a relatively 'new' enzyme discovered in 1993 - could play an essential role in the development of novel treatments for PH.

Dr Pullamsetti is the second researcher at the University of Giessen Lung Centre (UGLC) to gain this award (following Ardeschir Ghofrani MD). 'While working on their projects graduate students receive a thorough education by an interdisciplinary faculty in lung medicine - from the molecular mechanisms underlying lung diseases to clinical treatment procedures. For this, we have designed a comprehensive three-year curriculum,' explained Professor Werner Seeger, Head of UGLC. 'All students who decide to prepare their theses in our centre are supported by a full-time fellowship. In return, we expect a lot of dedication to science.'

The training concept was devised by Dr Oliver Eickelberg, who became an assistant professor at the Department of Internal Medicine II, following four years as a researcher at Yale University's Medical School. Dr Eickelberg set up his own laboratory and simultaneously introduced the education concept to Giessen. Today he coordinates and teaches about 60 graduate students from over 12 nations in weekly seminars.

Supported by several funding bodies, which include the German research foundation Deutsche Forschungsgemeinschaft (DFG), and Altana Pharmaceutical Company, Germany, the Graduate Programme has attracted students from all over the world. Dr Christianne Eickelberg, coordinator of the University's International Graduate Programme explained that, although English is the course language, '...conversations echo through the corridors in many languages - among them Chinese, Spanish or Rumanian.' In addition, she pointed out that, in their studies, participants also travel beyond the boundaries of the campus: 'Eager Giessen lung researchers can be found almost anywhere, even on top of Mount Everest, where they have conducted "breathtaking" high altitude studies in search of novel treatment options for pulmonary hypertension.'

T-shirt helps Breast Cancer Communication Award 2005

Germany - A T-shirt bearing slang words for mammaries - such as boobs, knockers, jugs, as well as more sedate terms such as bosoms and breasts - has helped win campaigners the 2005 Breast Cancer Communication Award (value:10,000 euros). The gar-

Ulla Schmidt, Federal Minister for Health and Social Security

From left: Elisabeth Hantke of the Path Foundation, Waltraud Böving of mamazone and Prof. Michael Bamberg, President of the German Cancer Association

ment, designed for *mamazone - Frauen und Forschung gegen Brustkrebs e.V.* and created by advertising agency Unterweger und Partner, will be worn by campaigning breast cancer patients to raise awareness of the consequences of late detection of breast cancer.

The prize, presented at the First Open Cancer Conference by Professor Michael Bamberg, President of the German Cancer Society, was awarded for the T-shirt as well as mamazone's many other activities, including its Info-Mobil (sponsored by the cosmetics firm Avon), and the feature film 'Stages'.

Germany is the only EU country that does not provide a mammography screening programme. At the prize giving, Waltraud Böving, chairperson of mamazone, presented Ulla Schmidt, Germany's Minister for Health and Social Security, with a T-shirt, in gratitude for her active promotion of early detection of breast cancer based on EU guidelines.
Details and T-shirt orders: www.mamazone.de

Space travellers and bionic hearing

Hearing aid reflected in an astronaut's helmet. Circled: Buzz Alrin

When medical physicist Valentin Chapero (45) was Managing Director of Siemens Audiologische Technik GmbH (1996-99) turnover trebled, and when, from 2000, he became responsible for Mobile Networks, a division of Siemens AG, its three-year turnover rose by almost 80%. In 2002 he became CEO of the Phonak Group, where he has demonstrated a similar pattern for success, by stimulating the design of innovative products and expanding sales and distribution channels. Certainly he has a flair for publicity. Recently, the firm's new digital hearing aid, Savia, was launched at the Research and Technology Centre (ESTEC) of the European Space Agency (ESA), in the Netherlands. There Dr Chapero spoke, via a live link, with Russian cosmonaut Salizhan Sharipov, at the International Space Station (ISS). Then, onto the stage stepped 75-year-old astronaut Buzz Aldrin, Doctor of Astronautics and member of the first manned lunar landing mission (1969). Why? Dr Aldrin uses a Savia hearing aid: 'When your life has depended on effective communication between earth and the moon, your expectations remain extremely high!' he told the gathering.

Phonak reports that Savia, a group of six in-the-ear (ITE) and three behind-the-ear (BTE) models that can be remote controlled, is the first hearing aid to implement digital bionics that enable users '... to hear as Nature intended, in all situations, including successfully rising to major challenges such as understanding speech in echo-filled environments, or when there are multiple noise sources. Digital bionics also ensure that the most sophisticated features of natural hearing, such as the ability to locate sound sources accurately, are restored automatically by Savia. Localisation is a key element of what is perceived as natural hearing and biologically speaking is the task of a design masterpiece, the human ear.'

SMARTER SAFETY TESTER

An electrical safety tester, made by Rigel Medical, the UK-based biomedical test instrumentation specialist, has been upgraded to include enhanced technical features. The firm reports that the new new portable Rigel 266 Plus '... offers dual functionality in either fully manual or semi automatic mode for medical safety testing requirements in accordance with IEC/EN 60601-1, MDA DB9801, and AS/NZ 3200,' adding: 'Test routines are easily selectable via a large rotary switch and dedicated softpad keys, which allow the user to select individual single fault conditions, quickly and easily.' Additionally, to test medical equipment, leakage measurement sequences can be selected without power-up/down delays. 'The regrouping of single fault conditions in the semi automatic mode reduces the number of required power breaks by up to 80%, saving even more time,' the firm points out. 'A large LCD display also gives a clear indication of test results and single fault conditions, AC or DC measurements and pass/fail limits.'

Free download software for record-keeping is also available.

Universal tips

New P50 Tips for the Biomek 3000, NX and FX and Multimek liquid handlers have been introduced by Beckman Coulter, which reports that the disposable, non-conducive, narrow-length tips enable pipetting from the bottom of deep labware, for maximum retrieval of valuable samples, and are ideal for work in both 96- and 384-well formats, e.g. for compound library profiling and assay development, MALDI-TOF plate spotting, sample pooling, plate replication and hit picking. They pipette a volume of 50 µl with barrier and are certified Rnase/Dnase-free.

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GLOBAL EVENTS

2005

APRIL

2-6 London, England
14th Annual Congress of the International Society for Gynaecological Endoscopy
Hosted by the British Society for Gynaecological Endoscopy.
www.isge2005.org

2-8 Davos, Switzerland
Musculoskeletal Diseases
www.idkd.ch

4-7 Harrogate, England
BES 2005: 24th Joint Meeting of the British Endocrine Societies
www.docguide.com

4 - 8 Edinburgh, Scotland
Molecular Pathogenesis of Virus Infections
www.docguide.com

5-8 Munich, Germany
German Surgical Society 122nd Congress
www. chirurgie2005.de

6-8 Luxembourg, Luxembourg
Int'l Fair for Telemedicine and Telecare
www.medetel.lu

6-9 Bucharest, Romania
RomMedica/pharma/optic
www.rommedica.ro

7-9 Vienna, Austria
Clinical Dermatology 2005
www.docguide.com

8-10 Yokohama, Japan
64th Annual Meeting of the Japan Radiological Society
www.radiology.or.jp

9-12 London, England
Charing Cross International Symposium: Towards Vascular and Endovascular Consensus
www.cxsymposium.com

11-13 York, England
3rd UK Radiation Oncology Conference
www.docguide.com

16-17 Chicago, USA
AOCR - Conference of the American Osteopathic College of Radiology
www.aocr.org

19 - 24 Crete, Greece
10th International Congress on Oral Cancer
www.uicc.org

21- 23 Brussels, Belgium
School of MRI - Advanced MR Imaging of the Abdomen
www.esmrmb.org

28-30 Moscow, Russia
School of MRI - Applied MR Techniques, Basic Course
www.esmrmb.org

MAY

1-5 Lisbon, Portugal
Cistm9 - Conference of the International Society of Travel Medicine
www.cocs.de

4-7 Berlin, Germany
86th German Radiology Congress
www.drg.de

5-7 Budapest, Hungary
8th Congress of the European Society for Paediatric Dermatology
www.docguide.com

5-8 Edinburgh, Scotland
EANO VI - 2nd Quadrennial Meeting of the World Federation of Neuro-oncology
www.fecs.be

7-10 Florence, Italy
1st World Congress of Thoracic Imaging
www.oic.it/thoracicimaging

7-11 Florence, Italy
International World Congress of the Society of Thoracic Radiology
www.docguide.com

7-11 Strasbourg, France
Neurochirurgie 2005 (Neurosurgery)
www.docguide.com

7-13 Miami Beach, USA
13th Scientific Meeting & Exhibition of the Int'l Society for Magnetic Resonance
www.ismrm.org

8-11 Lisbon, Portugal
ICNC 7 - International Conference of Nuclear Cardiology
www.escardio.org

9-11 Stockholm, Sweden
12th European Congress of Clinical Neurophysiology
www.docguide.com

12-13 Bojnice, Slovakia
STAR programme (Schering and Siemens Training in Advanced Radiology)

13-17 Vienna, Austria
10th World Congress of Skin Cancers
www.docguide.com

19-21 Kaunas, Lithuania
5th Congress of Baltic Association for Maxillofacial and Plastic Surgery
www.balticconference.com/bamps2005

21-26 San Antonio, Texas, USA
Aua - Annual Congress of the American Urological Association
www.auanet.org

25-27 Barcelona, Spain
8th International Course Advances in CT & MRI
www.amrct2005.com

26-28 Leuven, Belgium
Interactive course on Head and Neck Cancer Imaging
www.kuleuven.ac.be/radiology

28-31 Vienna, Austria
EuroAnaesthesia 2005
www.docguide.com

28-31 Florence, Italy
ESGAR 2005 - 16th Annual Meeting and Postgraduate Course
www.esgar.org

30-3 June Dublin, Ireland
European Society of Paediatric Radiology
www.espr2005.com

30-1 June Madrid, Spain
CNIO Cancer Conference: MAP Kinases and Cancer
www.uicc.org

30-June 3 Dublin, Ireland
ESPR - Congress of the European Society of Paediatric Radiology
www.espr2005.com

JUNE

2-4 Lucerne, Switzerland
School of MRI - Advanced Breast and Pelvis MR Imaging
www.esmrmb.org

2-4 Vienna, Austria
VISAR - 4th Vienna Interdisciplinary Symposium on Aortic Repair
www.visar.at

8-11 Vienna, Austria
EULAR 2005
European Congress of Rheumatology

8-12 Halifax, Canada
4th World Conference on Breast Cancer

8-12 Prague, Czech Republic
10th Symposium European Society for the Study of Purine and Pyrimidine Metabolism in Man

11-14 Taipei, Taiwan
1st International Congress of IASSID-Pacific

19-26 Sweden
European Federation of Audiological Societies

22-25 Berlin, Germany
CARS 2005 - Computer Assisted Radiology and Surgery - 19th International Congress and Exhibition
ISCAS - 9th Annual Conference of the International Society for Computer Aided Surgery
Plus: **CAD** 7th International Workshop on Computer-Aided Diagnosis CMI - 11th Computed Maxillofacial Imaging Congress.
Plus: **EuroPACS** - 23rd International EuroPACS Meeting. www.cars-int.org

22-25 Madrid, Spain
2nd Latin American Congress on Qualitative Health Research

23-25 Cancun, Mexico
1st Latin American Congress in Aging Male

25-27 Kuopio, Finland
School of MRI - Advanced Neuro Imaging - Diffusion, Perfusion, Spectroscopy.
www.esmrmb.org

26-30 Montreal, QC, Canada
International Interdisciplinary Congress on Emergencies

30 - 3 July Aarhus, Denmark
23rd Int. Symp. on Diabetes and Nutrituion
email: annemarie.kruse@ki.au.dk

JULY

2-6 Athens, Greece
IX European Congress of the International Society of Blood Transfusion

3-9 Positano, Italy
Europe/Asia Medical & Legal Conference

16-19 Los Angeles, USA
9th Annual Meeting of the International Association of Medical Science Educators

24-29 San Francisco, USA
Meeting of the International Union of Microbiological Societies (IUMS)

AUGUST

15-19 Sydney, Australia
11th World Congress of Sport Psychology (ISSP)

18-19 Sydney, Australia
Partners in Pain: Patients, Clinicians and Pain Management

26-28 Sydney, Australia
4th Int. Conference on Oro-facial Pain and Temporomandibular Disorders

SEPTEMBER

1-3 Lund, Sweden
School of MRI - Advanced Cardiac MR Imaging
www.esmrmb.org

3-7 Sydney, Australia
International Society of Developmental Biologists 2005

4-7 Lisbon, Portugal
9th International Conference on Methods and Applications of Fluorescence: Spectroscopy, Imaging and Probes

8-11 Ljubljana, Slovenia
ESUR 2005 - 12th European Symposium on Urogenital Radiology
www.esur.org

8-10 Istanbul, Turkey
School of MRI - Applied MR Techniques, Advanced Course
www.esmrmb.org

14-17 San Diego, USA
14th International Congress and Endo Expo 2005

15-17 Prague, Czechoslovakia
11th Prague Dermatology Symposium
Regional Meeting of the International Society of Dermatology
www.praguedermatology.cz

15-21 Rome, Italy
Pan Europe Asia Medical & Legal Conference

18-22 Melbourne, Australia
7th World Congress on Inflammation

18-23 Bethesda, USA
14th International Pigment Cell Conference

18-22 Breckenridge, USA
Tissue-Selective Nuclear Receptors

21-24 Oxford, United Kingdom
18th Annual Scientific Meeting - refresher course
stephen.golding@radiology.ox.ac.uk

22-26 Nashville, USA
27th Annual Meeting of the American Society for Bone and Mineral Research - ASBMR 2005

22-26 New Delhi, India
Interim Meeting of World Federation of Sleep Research Societies

25-18 Basle, Switzerland
ESMRMB 2005
www.esmrmb.org

28-1 Oct Singapore, Malaysia
International Skeletal Society - 32nd refresher course
www.iss2005.com

28-2 Oct San Francisco, USA
American Academy of Family Physicians Annual Meeting

2-7 Rio de Janeiro, Brazil
International Phlebology XVth World Conference

15-18 Berlin, Germany
1st Congress of the World Association of Sleep Medicine (WASM)

OCTOBER

6-7 St Julian's, Malta
ISS Malta
Wendy.Pullicino@rjah.nhs.uk

13-15 Cape Town, S. Africa
School of MRI - MR Imaging of the Abdomen
www.esmrmb.org

14-16 Nice, France
10th Annual Meeting of the European Council for Cardiovascular research (ECCR)

21-22 Zurich, Switzerland
ESCR 2005
www.escr.org

NOVEMBER

2-5 Toronto, Canada
2005 Annual Meeting of the International Society for Traumatic Stress Studies

3-5 Mumbai, India
Hope 2005

10-12 Rotterdam, Netherlands
School of MRI - Advanced MR Imaging of the Vascular System
www.esmrmb.org

10-13 19th San Francisco, USA
Annual Congress of the American College of Phlebology

12-15 Bangkok, Thailand
XIIIth Asia Pacific Congress of the ISBT

17-20 Havana, Cuba
3rd International Meeting on Visual and Neuromuscular Disorders

27-29 Haridwar, India
Psychotherapy, Yoga and Spirituality

2006

JANUARY

3-8 Sydney, Australia
International Congress of Obesity 2006
16-18 Florida, USA
17th Annual International Colorectal Disease Symposium

APRIL

1-5 San Francisco, USA
2006 Annual Meeting of the American Society for Investigative Pathology

23-27 Florida, USA
2006 Annual Meeting of the American Association of Physicists in Medicine

JUNE

19-23 Iraklion, Greece
ESGAR 2006 - 17th Annual Meeting and Postgraduate Course
www.esgar.org

AUGUST

17-22 Brisbane, Queensland, Australia
12th International Congress of Radiation Research

27-1 Sept Prague, Czech Republic
17th International Mass Spectrometry Conference

SEPTEMBER

3-8 Sydney, Australia
International Congress of Obesity 2006

6-9 Boston, USA
15th International Congress and Endo Expo 2006

15-19 Philadelphia, USA
28th Annual Meeting of the American Society for Bone and Mineral