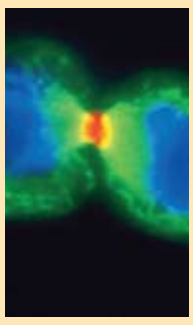
EUROPEAN HOSPITAL

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



VOL 19 ISSUE 4/10 AUGUST/SEPTEMBER 2010

War on NHS reform

United Kingdom - A Government White Paper on healthcare reform has caused Unison, Britain's biggest public sector trade union (over 1.3 million members), to launch legal action against the Government 'as a matter of urgency'. The reason? The day after the paper was presented in July, NHS CEOs were instructed by NHS CEO Sir David Nicholson to implement the proposals 'immediately' -- without being given time to comment on the reforms. This instruction, said Unison, was unlawful.

The Government also failed to consult the public over plans to change the NHS radically.

Among the changes presented by Health Secretary Andrew Lansley are the abolition of Primary Care Trusts and Strategic Health Authorities, and giving more power to general practitioners to control where funds are spent.

Andy Burnham, Shadow Health Secretary and Labour leadership candidate, backed Unison: 'There is no democratic mandate for the break-up of the NHS', he said, adding that, as the Coalition Government's agreement explicitly ruled out a top-down NHS reorganisation 'these dangerous plans represent one of the biggest and quickest u-turns in political history.' The reforms, he said, could cost billions of pounds at a time when cuts to frontline services are increasing. 'GPs are unprepared for it, NHS staff don't want it and patients never asked for it.'

Governments urge hospital staff to do more but at the same price

Facing billion-euro deficits, European healthcare systems are putting hospital operations under the microscope to find areas where costs can be slashed dramatically. Under these circumstances, GE's new Performance Solutions unit is quickly gathering ground in helping hospitals to meet those challenges, *John Brosky* reports

The crisis in European healthcare has moved beyond a political solution as national health services face more immediate financial pressures with rapidly expanding budget deficits.

Millions of patients are lining up every day for medical care valued in billions of euros from hospitals that are challenged for the staff and equipment to meet these ever-growing demands.

In the face of this urgent and life-threatening condition, governments have now turned sharply towards the hospital, desperately demanding doctors and nurses do more with the same. 'The good news here is that there are value pools that can be unlocked by improving quality of care, efficiency and access,' says healthcare specialist Laurent Amiel.

Recently the GE Healthcare Performance Solutions unit for Europe, the Middle East and Africa was created to support process improvement in hospitals through programmes sponsored by several European countries. As head of this new unit, Laurent Amiel told *European Hospital* that, until recently healthcare has been focused on improving clinical outcomes and has delivered 'outstanding results'. We are all living longer, he added, gaining as much as five hours of life expectancy each day.

There is still, he believes, 'significant room for improvement in terms of performance, which would improve quality of care, increase access -- and decrease costs. Unless we can improve performance on the frontline of care, we will not meet the challenge posed by our communities that expect a continuing high quality of care but today are unable or unwilling to pay for that care.'

Laurent Amiel: *'The staff knows where the waste is. It is they who propose the most radical solutions'*

The answer, he said, lies in the vast 'value pools', which is how he views the opportunities that can help reduce deficits accumulating in healthcare systems.

More than €130 billion in savings could be realised annually among European systems, he suggested, by unlocking the value in deficit spending and converting it into savings for struggling health services.

The key to unlocking the value is focusing on how a clinical team delivers services while improving the quality of that care. 'Waste in healthcare systems is expensive,' he pointed out, ' quality healthcare is not. For example, there's a large variability in clinical decision-making where patients with similar conditions receive different care. Working with physicians and nurses to create a more consistent care plan results in consistent clinical quality while delivering operational savings.'

Improving performance proved to be 'cash-releasing,' according to James Barbour, Chief Executive of the National Health Services (NHS) Lothian Hospital in Edinburgh.

In 2007 Barbour brought in experts from GE Healthcare to implement a LEAN approach to processes, an experience that he said was genuinely empowering for frontline staff who were asked to identify unnecessary steps. 'The staff knows where the waste is,' he said. ' It is they who propose the most radical solutions.'

A dramatic example was a reduction in waiting times for colorectal referrals from 29 weeks to just two weeks -- with no change in staffing and no additional equipment. In another department, CT scanning waiting times were reduced from 21 weeks to six weeks with reports generated in 12 hours instead of three days.

' Using techniques for process improvement the staff at Lothian were able to provide a higher quality of care, more quickly,

continued on page 2

The European Health Forum Gastein

6- 9 October 2010 Bad Hofgastein, Austria

More than 600 distinguished guests from 40 countries are expected at this year's European Health Forum Gastein (EHFG). 'Since its foundation in 1998, the EHFG has developed into an international meeting point for the highest-ranking healthcare politicians, managers and scientists from all over the world,' said EHFG President **Professor Günther Leiner**. 'When the issue is health-political discussion and exchange of experiences on the highest level, then the EHFG is probably unique in Europe today.'

Guests include around 20 ministers and secretaries of state for healthcare, high-ranking representatives of the EC, World Bank, WHO and others from healthcare and services industries.

Key speakers at the Plenary Sessions include Minister of Health Alois Stöger diplomat, EU Commissioner John Dalli and WHO Director Zsuszana Jakab.

Financial crisis endangers aging with dignity

One of the key themes, *Demographic change and the future of health*, poses the question how regions worldwide can learn from one another. Prof. Leiner stressed that European healthcare systems must prepare for future demographic challenges because the proportion of those aged over 60 years will increase from the current 20% to 35-38% in 2035. For Austria this means that the 75-85-years group, currently around 465,000, will increase to over 700,000 and the 85-years group will increase from currently 104,000 to 280,000. In 2035, between 2.7 million and three million people in Austria will be over 60 (Source: Statistik Austria). 'The world will look very different in the future and policies must be prepared,' Prof. Leiner reflected.

Forum EU action and local partnerships for health

For the first time, in 2008 the majority of the world's populations lived

continued on page 2

contents

EUROPEAN HOSPITAL
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EH 4/10

Global E-Health Forum®
Hamburg 2010

Strategies, Solutions and Services for Sustainable Healthcare Delivery

Ljubisav Matejevic, Founder and Director of the Global E-Health Forum:
"E-health, meaning the application of information and communication technologies across the whole range of functions that affect the health sector, can make an important contribution to ensure a high-quality healthcare service for all citizens now and in the future."


Ljubisav Matejevic

The Global E-Health Forum, which will take place on October 25 + 26, 2010 in Hamburg, Germany, will address the main challenges healthcare systems all over the world are facing: demographic shifts, the impact of globalization and an increased burden of chronic diseases and expensive treatments. Due to limited budgets and increasing demand for high-quality healthcare services, new cost-efficient, reliable and interconnected systems need to be developed. E-health can make a significant contribution to ensure high-quality, sustainable healthcare systems.

The first conference day at the Hamburg Chamber of Commerce will feature strategy and best practice presentations of speakers from Asia, Europe, New Zealand and the U.S.A. The conference program also includes workshops and discussion forums as well as an accompanying exhibition of solution providers. An evening reception for the attendees will be held at the U.S. Consulate General.

The second day will take place in two hospitals of Asklepios, recognized as one of the most innovative leading hospital groups. There, conference attendees may expect hands-on presentations and workshops as well as guided tours. A panel discussion entitled "Connecting Competence for E-Health Services – What Customers Expect, What Healthcare Has to Deliver" completes the program. The primary aim of the organizers of the Global E-Health Forum, the Hamburg Chamber of Commerce, IBM and the European Health Telematics Association (EHTEL), is to provide a cross-sector forum for representatives from hospitals and clinics (CEOs, CFOs, CIOs), governments, health insurance organizations, service providers and the media. Policymakers, users, suppliers and implementation managers will have the opportunity to learn from each other and to develop collaborative working relationships.

For further information on the English-language conference and registration, please see *www.global-ehealth-forum.com.*

COMPETITION

For your chance to win this special prize, enter today! Simply go to our homepage at www.european-hospital.com

Just 0.5 inches thick and weighing only 1.5 lbs – both less than any laptop or netbook -- the iPad is the latest big winner from Apple

Your chance to win an Apple iPad!

'iPad,' said Steve Jobs, Apple's CEO, 'is our most advanced technology in a magical and revolutionary device at an unbelievable price. It creates and defines an entirely new category of devices that will connect users with their apps and content in a much more intimate, intuitive and fun way than ever before.'

iPad's responsive high-resolution Multi-Touch display lets users physically interact with applications and content. Using it, you'll be able to browse the web, read and send e-mails, import photographs from a Mac, PC or digital camera to organise into albums, watch videos, TV shows or YouTube, listen to music, play games, download e-books from Apple's new iBookstore, and so much more – all you'll need is lots of spare time to enjoy this exciting personal communications device.

iPad's brilliant 9.7-inch, LED-backlit display features IPS technology that produces sharp, clear images and consistent colour with an ultra-wide 178-degree viewing angle. Manoeuvring when playing games or scrolling through web pages is smooth and accurate due to the highly responsive Multi-Touch display.

'iPad features 12 next-generation Multi-Touch applications,' the manufacturer reports. 'Every application works in both portrait and landscape, automatically animating between views as the user rotates iPad in any direction. The precise Multi-Touch interface makes surfing the web on iPad an entirely new experience, dramatically more interactive and intimate than on a computer. Reading and sending email is fun and easy on iPad's large screen and almost full-size "soft" keyboard.'

HOW TO ENTER

Simply fill in the Readers Survey form (left) or go to our website: www.european-hospital.com

PLEASE NOTE:

- **The closing date for entries to the EH 4/10 competition: 1 October 2010 .**
- **Entries received after that date cannot be entered in the draw.**
- **The winning entry will be drawn from the correct answers.**
- **Only the winner will be contacted directly.**
- **The winner's name and location will be published in a future issue of European Hospital.**
- **NB: The prize is not exchangeable for cash.**
- **The usual competition rules apply.**

Why enter?

It's so easy – and, since we launched our competitions some years ago, winning medical and healthcare workers throughout Europe have been delighted to receive the fine prizes featured in *European Hospital*.

So, don't delay, enter our competition today (why not right now!). Simply go to the EH website.

Good luck!

The winner of the Krups ice cream maker featured in our competition in EH issue 3/10 and on our website, is: Milan Obradovic, specialist paedodontist at the House of Health, in Ljig, Serbia

The European Health Forum

continued from page 1

in cities; the highest European urbanisation growth was seen in the new accession countries. In many West European countries 80% of the population live in cities. Inequalities in health outcomes within a city, and between cities, can be compared to the differences between the developed and developing world. Therefore, for Europe to be ready for the future it is vital to focus on health and social environment in cities, i.e. urban health and well-being, which relies on multi-disciplinary, multi-agency, vertical and horizontal policy-making approaches, building on partnerships involving civil society, industry, health/social care professionals, governments (local, regional and national) and non-governmental organisation, including the voluntary sector. The EU has many actions for partnerships/stakeholders in the field of improving health for city populations, from empowering citizens, to research projects and programmes. The parallel forum will aim to demonstrate how local and regional partnerships integrate to achieve a healthy environment within the context of both EU policy and research mechanisms.

European Health Award 2010

The 13th EHFG has announced the €10,000 European Health Award for cross-border healthcare initiatives in Europe that have significant potential for quality improvements and increases in efficiency. The shortlist includes, amongst others:

Chronic Diseases Alliance: a united prevention approach

Chronic, non-contagious diseases are responsible for 80% of all deaths within the WHO Europe region. They are linked to four major problems: tobacco, bad diet, alcohol and lack of exercise. Although not always curable they are largely treatable. The project *European Heart Network* unites ten non-profit European healthcare organisations, representing over 100,000 healthcare workers. The objective is to develop evidence-based recommendations for interventions on a broad scale and facilitate united political initiatives for the effective prevention of these diseases across Europe.

Life with Parkinson's Awareness Campaign

The campaign to create greater awareness of life with Parkinson's disease, initiated by the European Parkinson's Disease Association (EPDA), unites France, Germany, Greece, Hungary, Ireland, Italy Norway, Romania, Spain, Slovenia, Slovakia, Turkey and the UK. The objective is to ensure that all Parkinson's sufferers and their families can access the correct disease management and treatment. This is to be achieved through the development, distribution and translation of printed and digital information for further use by member organisations and in national campaigns. Consistent media work on all levels also aims to inform these patients in the best possible way, to improve disease management and manage the high social and economic burden efficiently.

EUnetHTA Joint Action: European Network for Health Technology Assessment

Health Technology Assessment, the assessment of the effects of medical-technological and pharmaceutical innovations and the control of efficiency and cost effectiveness, is a central task required to optimise the use of limited resources in healthcare systems and make the distribution of resources transparent. EUnetHTA is a project started by the *National Board of Health Copenhagen* financed by the EU, to run for several years. Participants: 23 member states, as well as Norway, Switzerland and Croatia. The objective is to achieve sustained, permanent cooperation in Health Technology Assessment in Europe; streamlining individual activities to reduce redundancies; development and application of processes for the efficient exchange of information about new technologies, and coordination between all decision makers with regards to efficiency and follow-on costs of medical-technological innovations.

Report: Hans Christian Pruszinsky

Predicting future admissions

Health organisations across the UK are using mathematical modelling to try to predict future hospital admissions. *Mark Nicholls* reports

The aim of the predictive modelling systems being trialled in the UK are to identify which people in a given population are the most likely to be admitted to hospital in the next 12 months and then focus preventive measures on them to try to avoid hospital admission.

Primary Care Trusts (PCTs), which commission hospital services in the UK, are favouring the model as they try to cut costs during a period of increasing NHS financial constraints.

Dr Geraint Lewis of the Nuffield Trust – an independent health policy charitable trust aiming to promote analysis and informed debate on UK healthcare policy -- an expert in the concept of predictive modelling, explained: 'Predictive models use relationships in routine electronic data for the whole population to make predictions at the individual level. Modellers typically use data from years one and two to make predictions in year three. The outcome of interest is typically an unplanned hospital admission. A predictive model allows analysts to assign a 'risk score' to every person in the population, reflecting their individual risk of unplanned hospital admission in the next year. Those people at high risk can be offered extra support to try to reduce their risk.'

Various models are used and include detail such as age, gender, patterns of hospital admissions and diagnostic codes of an individual, plus some area-based variables from the Census, including deprivation. The Combined Predictive Model adds to this data information about A&E attendances, out-patient visits, and variables taken from the GP electronic medical record, including lab tests, blood pressure readings and prescriptions.

The idea of devising predictive risk models first developed in the USA in the 1990s from 'risk adjustment' techniques used by insurers and has since been adapted for use in the UK health system.

Dr Lewis added: 'We know that a small number of people in the population account for a large proportion of emergency hospital admissions. Unplanned hospital admissions are very costly so, in theory, if these high-risk people could be offered preventive care aimed at reducing hospital admissions, this could lead to large net savings.'

Predictive models are specifically 'tuned' to identify people at risk of unplanned hospital admission in the next 12 months, rather than those currently at high risk. This is important, said Dr Lewis, because of a phenomenon called ' regression to the mean' , which states that patients who are currently at high risk will in future have fewer hospital admissions on average, even without intervention.

'In the UK it tends to be PCTs rather than the hospital that uses predictive models, since commissioners can benefit financially from a reduction in hospital activity,' said Dr Lewis.

Many PCTs have started using these models, though it is acknowledged that the interventions based on their predictions have been insufficiently evaluated so far.'

The Nuffield Trust is currently evaluating a range of interventions aimed at reducing emergency admissions, including the Partnerships for Older People Pilots (POPP), and Virtual Wards in Croydon, Devon, and Wandsworth, London.

But the potential benefits from predictive modelling - of patients not having the experience of an unplanned hospital admission; and a potential saving for health commissioners and providers by avoiding these admissions, need to be demonstrated in practice. 'A crucial next step,' said Dr Lewis, 'will be to evaluate interventions based on predictive models, to find out whether net savings can be made in reality.'

Meanwhile, in Canada a group of Toronto hospitals are using the LACE predictive model to identify patients at risk of readmission in the next 30 days, where those patients at high predicted risk are offered a 30-day ' admission' to a virtual ward when discharged. 'The virtual ward operates in the same way as a hospital ward - a multidisciplinary team, daily ward rounds, a single set of notes - except that the patient stays at home,' Dr Lewis explained.


Geraint Lewis

The outcomes of the Toronto trial are likely to be closely monitored by UK hospitals following the recent announcement by the UK coalition government that hospitals will not be reimbursed for readmissions occurring within 30 days.

Governments urge hospital...

continued from page 1

which resulted in greater patient satisfaction and cost savings,' said Laurent Amiel. 'The staff designed the new processes, and they are happy with the change, as they spend more time with patients and not doing paperwork. We know how to help because we use these same methodologies every day to improve processes at GE Healthcare.'

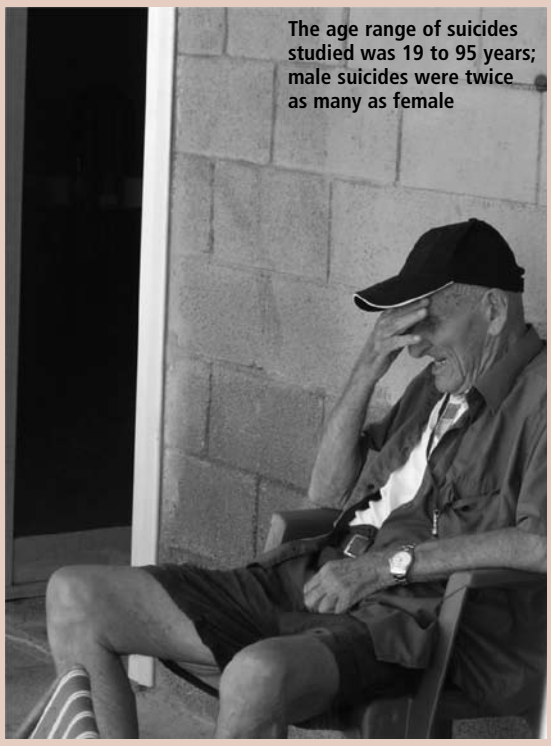
General Electric is widely considered one of the best-run companies in the world.

In addition to its work with the NHS, the Performance Solutions group recently won a series of contract awards in France from ANAP (Agence nationale d'appui à la performance des établissements de santé et médico-sociaux), the national agency created to introduce change management and process improvement for a first wave of 50 public hospitals.

Elsewhere in Europe the group has worked with hospitals in Spain, Italy and Germany.

WARNING Staff may fail to spot suicide risk

Around 5,000 people kill themselves in England and Wales each year


The age range of suicides studied was 19 to 95 years; male suicides were twice as many as female

Previous research has indicated that the emergency department might be well-placed to pick up patients vulnerable to suicide. However, according to a small, new study carried out by researchers at Manchester University, although people who frequently present themselves at hospital emergency departments may be at high risk of suicide, emergency care staff may fail to spot their vulnerability.

The suicides were identified from information submitted to the National Confidential Inquiry into Suicide and Homicide by People with Mental Illness at The University of Manchester.

The researchers reviewed emergency department hospital records from 38 hospitals for 286 people who committed suicide between 2003 and 2005 -- and who had been in contact with mental health services within 12 months of their death.

There were twice as many men as women, and the average age of the suicides was 47 (ranging from 19 to 95 years).

Analysis showed that more than four in 10 (43%; 124) of all the 286 suicides had sought treatment at emergency care departments at least once in the year leading up to their death. Importantly, among these 35 (28%) had visited emergency care facilities more than three times in the last year of their lives. These 'frequent attenders' died by suicide significantly soon after their last visit to emergency care than those who attended less often.

Over half (55%) of those who took their own lives were unemployed or on long term sick leave at the time of their death.

One in five cases had a primary diagnosis of schizophrenia and other delusional disorders; almost half (48%) had affective disorders, such as bipolar disorder or depression. Around one in 10 (9%) were dependent on alcohol and 3% were drug dependent.

The frequent attenders were significantly more likely to have a history of self harm and alcohol misuse. They were also more likely to be unemployed and to have sought help for psychological reasons, including self harm.

Best practice guidance but…

Best practice guidance recommends that self-harming patients who seek emergency care should be given a psychosocial assessment, but the researchers found little documented evidence to suggest this was happening. 'Although psychiatric services clearly have a prominent role in preventing suicide in mental health patients, emergency care departments may represent an important additional setting for suicide prevention,' said Research Assistant Damian Da Cruz. 'Frequent attenders may represent a high-risk group, and this should be recognised by emergency services. Closer liaison with general practitioners and mental-health services to ensure appropriate and consistent management of these often complex cases may be of benefit.'

Source: Emergency department contact prior to suicide in mental health patients. Online First Emergency Med J 2010; doi 10.1136/wmj.2009.081869

Health insurers' data is inadequate for healthcare research

Computer stored data from German health insurers are still inadequate for health services research, according to a study* led by Professor Wolfgang Greiner, Head of the Healthcare Management department at Bielefeld University, working with his research team in cooperation with the health insurance fund Techniker Krankenkasse. The professor concluded that this data source should only be used very cautiously and with reasonable diligence.

'Health services research is in vogue in Germany,' he said, when presenting the study at this year's German Capital Congress. However, this research area is still in the early stages in this country. The first annual Congress of Health Services Research was held in Cologne in 2002 The German network of health services research was founded in 2006.

Unlike clinical randomised controlled trials, health services research focuses on scientific analyses of the daily routine of treatment and medication, using a trial design specially suited to the everyday work of physicians and all their patients, without knockout criteria, as in conventional clinical trials, it also factors in a cost-benefit calculation.

That's why one problem for this country's health services research is encountered in the data acquisition. The data has to figure out effectively followed medical care in everyday life, not in a special clinical setting, and the group to be evaluated statistically is a good deal larger than in clinical trials. Consequently the costs for these specially designed health services studies, including extra data acquisition, are very high (primary studies). Also, there is still a lack of interest in that kind of research here and a reserved attitude due to the high costs, Prof. Greiner pointed out.

Therefore the routine data of health insurance funds can be regarded as a valued asset for health services research. Improved technical requirements and a change in the mindset within the management of the health insurance funds now allow the use the funds' data for health services research (secondary studies). The patients can be made anonymous and assigned to treatments and medications over years. 'As a by-product of administrative billing and reimbursement, the health insurance funds data reflect the direct treatment and prescription process and therefore they can be seen as most comprehensive data base in general healthcare,' Prof. Greiner said.


Wolfgang Greiner

In 2009, Prof. Greiner closed the study* that analysed whether health insurance funds routine data are suitable for research. In cooperation with the German health insurance fund Techniker Krankenkasse and supported by the pharmaceutical company Bayer-Schering, he and his team examined the follow-up therapy of 14,001 patients after their first implantation of hip or knee joint endoprosthesis. The retrospective study surveyed the follow-up therapy for three months after surgery, using data from 2006 and 2007. The result of the study is astonishing: Two in three patients did not receive a common thrombosis prophylaxis. 'This result does not reflect reality or, in other words, it is very unrealistic. But it points out the constraints of the data,' said Prof. Greiner.

The research team revealed that many patients received thrombosis prophylaxis in the post-operative phase of their hospital stay and it is continued within the often following rehabilitation in a rehabilitation centre.

Indeed, the German health insurance funds only collect data from outpatient care (ambulatory treatment). Prof. Greiner concluded: 'The analysis of routine data of health insurers requires high caution and diligence. We need an increased set up of theory and methodology to balance the lack of a scientific purpose of data and to offset their limitations,'

In July, Prof. Greiner was appointed to the German Advisory Council on the Assessment of Developments in the Healthcare System. In this position, he will possibly provide political decision-makers with more understanding of the situation and what is needed for health services research in Germany.

Report: Bettina Döbereiner

** Study to be published in Gesundheitsökonomie + Qualitätsmanagement (Thieme-Verlag).*

17th Congress of Medical Biochemistry and Laboratory Medicine

Making lab automation work

5-9 October 2010

Belgrade, Serbia

Organised by the Society of Medical Biochemists of Serbia and the Institute of Medical Biochemistry of the Clinical Centre of Serbia, the 17th Congress of Medical Biochemistry and Laboratory Medicine will also include the 6th EFCC Symposium for Balkan Region (7 Oct), with a focus on *Implementing Laboratory Automation, Quality and Efficiency*. This event promises introductions by eminent foreign and local experts to ways of achieving full automation and laboratory consolidation, with the goal of adhering to the philosophy of *Lean and Six Sigma* laboratory efficiency.

Svetlana Ignjatovic

Karoline Laarmann asked **Professor Svetlana Ignjatovic**, of the Institute of Medical Biochemistry, Clinical Centre of Serbia and University School of Pharmacy, Belgrade, Serbia, who coordinated one of the EFCC symposiums, about the current and possible future forms of automation

No medical field has expanded more rapidly in technology than laboratory medicine, Prof. Ignjatovic pointed out, 'particularly in the area of instrument automation. The applications of laboratory instrumentation broaden as the rate of technology development accelerates. The field of laboratory automation and robotics has its roots in the early 1980s, when the Japanese were learning from Dr Sasaki that clinical laboratories could become more efficient if they adopted some of the technology already popular in manufacturing. Components of an automated lab include the mechanisms for sample preparation, transport, analysis and storage, and the control and information system.

'The three most important forms of clinical automation are total lab automation, integrated modular lab automation and point-of care testing lab automation. Fully integrated total lab automation systems include sample sorting, routing, centrifugation, aliquot preparation, analysis and sometimes post-analytical storage and retrieval. Modular systems of lab automation allow more flexible use of space or positioning of functions in existing facilities. The trend in automation has moved to a modular approach for a number of reasons: large investment, inflexibility and long implementation time of total lab automation. Other automation models include decentralisation through the use of automated point-of care (POC) testing. The target test platforms of lab automation are in four areas coinciding with traditional lab divisions: chemistry, immunochemistry, routine haematology and coagulation.'

Workflow improvements

Lab automation uses mechanical and computer technologies to perform a scheduled series of tasks that increase the, accuracy, reliability and throughput of lab tests, Prof. Ignjatovic pointed out. 'The automation of workflow eliminates most of the manual processes, decreases human exposure to hazardous material and decreases the need to find and train skilled technicians. Consequently, patients get more valuable, reliable results because of greater availability and efficiency of lab results. The lab benefits from increased productivity and capacity, improved result turnaround time, improved staff safety and utilisation and improved information management/data handling. Injuries and other risks are minimised with automated processes because human error is eliminated, or at least significantly reduced. The most significant cost savings of automation implementation are from the reduction in personnel (their salaries, benefits, and taxes).

Overcoming hurdles

'The necessary questions before the implementation of lab automation are what to automate and to what extent?' said Prof Ignjatovic. The optimal degree of automation depends on the laboratory setting and cost, throughput and flexibility considerations, as well as the time needed to complete installation, available space, proportion of tests that are routine, availability of skilled technicians, safety, and reliability. Staff training plays an important role in the successful implementation of lab automation, she added. The implementation requires specialised services (electricity, plumbing, communications, ventilation), which can be problematic if updating older buildings. 'Another important issue is how to manage, access, and manipulate the large amounts of data generated by automated systems.'

Measuring success

'Activity in a clinical lab typically involves the quantitative or qualitative determination of an analyte or a cell in a patient sample. Instrumentation may include tests for haematology, coagulation chemistry, immunoassay, drug screening, and others. The lab provides as much as 80% of the information used by doctors to make important medical decisions. Laboratories must provide doctors with fast, accurate test results and decrease variability in test turnaround time to help lower patient length of stay.'

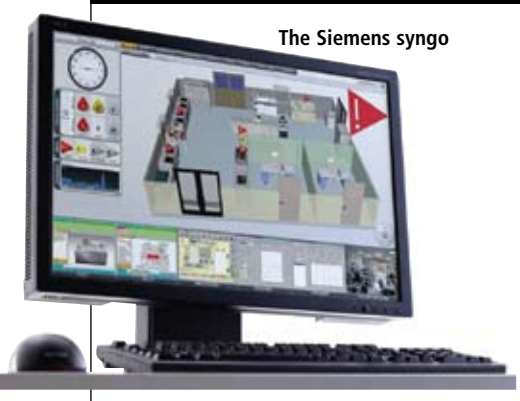
Implementation steps include modernisation of the analyser ('primary tube sampling', 'full menu random access' systems, electronic programming by the lab information system, improving the flow of information from place of request to place of releasing report, physical reorganisation of the laboratory, establishment of a central lab ('Core Lab configuration').

'The optimal degree of lab automation depends on the lab setting and considerations of cost, throughput, and flexibility. Other considerations include the time required to complete the installation, available space, proportion of routine tests, availability of skilled technicians, safety and reliability. Integration of a lab automation system with the lab information system (LIS) is essential to efficient test requisition, sample testing and result reporting and is vital to implementation success.'

Lab automation in Europe

According to data from the Web the installation of total lab automation systems and/or modular systems grew dramatically in the 1990s, particularly in the USA, Japan, and Europe. Today, there are 170 laboratories in Japan, 35 in North America

continued on page 7



The Siemens syngo

AACC 2010

California, USA: 20,000 visitors and 700 manufacturers showing products in almost 2000 booths at the American Association for Clinical Chemistry (AACC) annual meeting underlined the importance of this, the world's largest gathering of clinical laboratory professionals

During the opening of the AACC Plenary Sessions, Dr John Q Trojanowski credited biomarkers for recent advances in the diagnosis of Alzheimer's disease, thus kicking off key addresses that focused on policies relating to health reform; embryonic stem cells derived from non-human primates; cardiovascular disease prevention, and included an address by pioneering biomedical scientist Leroy Hood MD PhD, of the Institute for Systems Biology, who has proposed that genome and DNA sequencing be the basis of a new healthcare system centred on the four Ps: Predictive, Preventive, Personalised and Participatory.

International experts in science, medicine and technology also discussed cardiac and tumour markers, molecular pathology, point of care (POC) testing, infectious diseases, lab automation and management.

Beckman Coulter showed its expanded chemistry and automation portfolio that offers total lab solutions from a single vendor with a global presence. These included the compact AU480 and AU680 chemistry systems, the fastest AU Analyser ever designed, the AU5840. The company also reported that its new automation systems for sample processing -- AutoMate 1200 and AutoMate 2550 will optimise and streamline pre- and post-analytical work by eliminating many of the manual steps that occur between sample collection and analysis.

Among new products, Siemens Healthcare Diagnostics showed the syngo Lab Process Manager, software that simplifies workflow with an integrated technology platform that consolidates and visualises critical information at one central location. Automation solutions included the Advia Automation Centrifuge Module that processes up to 300 tubes/hour and can be customised, and a refrigeration module for StreamLAB storing up to 15,000 multiple tube types and sizes. The Advia LabCell and WorkCell automation systems can now be connected to the Dimension Vista 1500 Intelligent Laboratory System, thus combining the benefit of an integrated chemistry and immunoassay system with the productivity and capacity of a high-volume automation system.

The AU 680 from Beckman Coulter

Advia Centrifuge shown by Siemens

Also from Siemens, a new POC instrument -- Clinitek Status Connect System -- in conjunction with the Multistix family of urinalysis test strips, provides flexible connectivity, data integration and operational control to reduce risk in POC testing environments. New assays include the fully automated MPO assay on the Dimension System, which predicts a patient's risk of major adverse cardiac events; new hepatitis assays; and a new fully automated chemi-luminescent immunoassay, which is now available on the ADVIA Centaur CP System.

The Versette Automated Liquid Handler shown by Thermo Scientific

Abbott showcased novel tests and new upgrades to testing platforms: The Architect HIV Antigen/Antibody Combo Assay, a first-of-its-kind test that detects HIV infection earlier than ever before; a molecular assay for identification of Chlamydia and Gonorrhoea; an enhanced integrated analyser, the Architect Plus, which offers significant workflow improvements.

Thermo Fisher Scientific announced the European launch of the QMS Everolimus Immunoassay Reagent kit as the newest product among immunosuppressant drug monitoring products. This kit enables quantitative determination of Everolimus in whole blood, an active ingredient in Certican, on automated clinical chemistry analysers. Thermo Fisher's other innovations included the new Versette automated liquid handling platform, the Direct TIBC Reagent (dTIBC), reported to increase the accuracy of results by as much as 20%; the Jewett refrigerator and freezer, specifically designed to store high-value, critical samples, reagents, vaccines, blood and plasma, and a Parathyroid Hormone (PTH) Control, the newest product in its immunoassay quality control portfolio.

AACC 2011: 24-28 July, Atlanta, Georgia. Details: www.aacc.org.

Thermo Scientific's Jewett Lab Refrigerators and Freezers

Beckman Coulter's AutoMate 2550

At a meeting hosted by Siemens Healthcare Diagnostics at AACC 2010, an expert panel shared perspectives on information technology (IT) in the clinical laboratory. Representatives from Henry Ford Hospital (Detroit, MI), Alegent Health (Omaha, NE) and Johns Hopkins Bayview Medical Centre (Baltimore, MD) spoke about the increasing importance of IT in helping today's laboratory to meet the challenges of cost containment, quality of care, increasing workload, and staff recruitment as well as retention

Eric Olson MA, Vice-president of Informatics & eBusiness at Siemens Healthcare Diagnostics, reviewed results from a recent survey of US clinical laboratories that point to the labs' needs for real-time alerts of testing and operational status; centralised access to instruments, data management and LIS from one screen, and lab productivity reports. These needs are paralleled by statistics that showed a continuing and dramatic decline in lab training programmes and the number of graduates in clinical laboratory science and medical technology. Eric Olson proposed two ways of meeting today's challenges: giving labs access to the same kinds of process management technologies used to manage complex operations in other industries, and a new approach to training, whereby labs could provide standardised, yet personalised, training plans for each employee, on an ongoing basis, with an aim towards a more holistic approach that embraces skills beyond operations and technical competency.

In lively discussion with the media, the panellists expanded on diagnostic IT needs and conveyed a bold vision of patient-centric clinical diagnostics in which the clinical lab plays a more significant role in patient care, delineating the tools and infrastructure needed to realise that vision.

A journey towards full automation

St Jude Medical Center, in Fullerton, California, has always taken pride in its reputation as one of Southern California's most respected and technologically advanced hospitals. With 384 licensed beds and over 700 physicians the centre offers a comprehensive array of services and programmes, including cardiac, stroke care, a breast and cancer centres, full maternity services, orthopaedic services and rehabilitation centres.

The laboratory's leadership is well aware that to stay at the forefront of quality patient healthcare, continual improvement is necessary, which is why a few years ago it set out to developed an innovative strategy to improve the centre's performance by reducing turnaround times (TAT), establish a paperless environment and produce error-free results.

To accomplish those goals, St Jude Medical Center partnered with Beckman Coulter, Inc. to guide the laboratory through the necessary steps to establish a fully automated laboratory. This collaboration would result in achieving full automation in three phases:

Phase I: Improved pre-analytical processes to reduce errors

- Reduction of unnecessary steps through LEAN Six Sigma
- Introduced automated sample collection with bar-code labelling done in the patient's room.
- Consolidated workstations for chemistry, haematology and immunoassay

Phase II: Going paperless

- Application of laboratory software: Interfacing instruments to host LIS
- Standardisation of workflow
- Verification by exception

Phase III: Automation

- Institution of a full automation line
- Refrigerated storage stockyard
- Beckman Coulter Data Manager and Command Central Software

St. Jude began its journey with the implementation of LEAN Six Sigma step reduction. This effort streamlined sample processing by eliminating unnecessary or no-value added steps – nearly two thirds of the steps used at that time in chemistry and immunoassay processing.

'The LEAN step reduction process set us on a path that would take us to the next level in patient care,' said Ard Roshan, Director of the St Jude Medical Center Laboratory.

The lab then instituted an automated pre-analytical sample collection system that outfits phlebotomists with handheld devices to scan a patient's wrist band and generates a bar-coded label, which is then placed on the collected sample. During this process the phlebotomist assesses the patient to verify that the information that appears on the device corresponds correctly with the patient profile – e.g. whether the patient's gender and age are correct. The phlebotomist may quiz the patient, if appropriate, to verify the patient's name as well.

Once the sample is collected and presented to the laboratory, the bar-coded tube is read and placed in the queue for analysis. Ard Roshan's laboratory is supported by a full automation line, the Beckman Coulter Power Processor, which includes an automated inlet. The inlet sorts and directs samples around the line for analysis. It also includes a refrigerated storage unit, from which a sample can be automatically recalled for further analysis or repeat analysis as determined necessary by the patient's physician.

Consolidating analytical workstations for chemistry, immunoassay testing and haematology testing provide measurable initial workflow efficiencies and set the stage for fully automated workflow practices.

Once workstation consolidation was complete, Ard Roshan initiated a drive toward a paperless lab. A critical component of this phase was the Beckman Coulter data management system. The Beckman Coulter data manager created the ability to practice autoverification and verification by exception, which freed laboratorians to focus on troubled samples and other aspects of the laboratory.

The third and final phase of the laboratory's innovation strategy involved the implementation of Beckman Coulter's Power Processor with a refrigerated stockyard and the addition of Beckman Coutler's Command Central Software. Samples are process automatically beginning on the Power Processor inlet, which sorts and directs samples around the line for analysis, including centrifugation, chemistry and immunoassay testing. It also includes a refrigerated

storage unit for up to 3,000 tubes, from which a sample can be automatically recalled for further analysis or repeat analysis as determined necessary by the patient's physician.

Tangible Results from Full Automation

By investing in automation that addresses all aspects of sample handling, from pre-analytical sorting and sample prep to post-analytical sorting and storing, St Jude went beyond the essential goal of improving turnaround times and producing quality results to find staff efficiencies, increased capacity and clear monetary savings.

The efficiencies found through the automation of this laboratory facilitated the reduction in time spent per billable procedure – chemistry, special chemistry and immunochemistry – from 0.13 minutes to 0.09. This reduction equates to an overall recurring cost savings of $114,000 per month. These savings made it possible for the laboratory to recoup its investment in 18 months (six months earlier than estimated).

In addition, St Jude has achieved a 99.9% error-free rate, a 99.5% physician satisfaction rate, placing it among the top 4% of hospitals in the USA and is in the 90th percentile in employee satisfaction.

The impact of diagnostic IT

What more do we need?

Managing exceptions

Even as diagnostic IT systems reduce the amount of data needing review by flagging exceptions, labs are beginning to look for more capabilities to guide the technologist in triaging situations, such as quality control (QC) failure. Veronica Luzzi PhD, Associate Director of Chemistry, Henry Ford Hospital, suggested that IT should provide guidance, perhaps in the form of 'more advanced QC algorithms.' Sheryl Wilson BS, Senior Executive at Laboratory Services, Alegent Health, concurred and noted that standardised guidelines will further help technologists respond appropriately to real-time alerts in a high-pressure environment. More flexibility in rule development is also desired, whereby labs can fill in gaps based on specific lab needs.

Process management

IT can help manage scarce human resources through process management and having centralised visibility and control of all facets of lab operations. Veronica Luzzi gave patient specimens tracking as one example. Being notified that a specimen is waiting, or one needed for a critical test ordered by a clinician has not yet arrived, is very important to the lab and could avert difficult situations, e.g. losing a specimen. All three panellists embraced the notion of central control, as in an air traffic control room, where all facets of lab operations can be viewed and real-time updates keep the lab abreast of upcoming requirements and ongoing progress. This central control cuts across disciplines (e.g., haematology, chemistry) and has no geographic boundaries, expanding beyond individual hospitals to entire networks, in a future where telemedicine is integrated into lab operations.

Rethink training

Sheryl Wilson pointed out that technologists are sometimes hesitant to cede control to technology. She spoke of her lab's experience in posting policies and procedures online to help lab personnel be less dependent on printed information. All agreed that simpler, easier-to-use operator interfaces will make IT less intimidating. Above all, personalised training makes sense, as does a more holistic approach to training, which embraces not only techniques but also other skill sets, such as management. Reticent in the past, lab personnel now see the productivity gains in quality and effectiveness and beginning to embrace technology as key to their success and improving the quality of their jobs.

The whole patient

Importantly, the panel members spoke of the need for clinical diagnostics to become engaged in the 'whole picture of the patient, not just in the lab,' she said. 'Rather than numbers, we want to see patients.' This means putting patient results in the context of the patient's medical history, current status, results from other diagnostic modalities, such as imaging, current treatment and, ultimately, available genomic/proteomic profiles. The goal is to allow the lab to deploy clinical science in supporting clinicians with actionable diagnostic information that goes beyond numbers or levels. This will not only help clinicians make sense of test results, it will help labs determine when patient results should be brought to the attention of the caregivers.

Sherrie Hoffman, BS, MT (ASCP), Technical Specialist at LAB/LIS, Johns Hopkins Bayview Medical Centre, noted that labs want to have a valid reason to 'pull clinicians away from something they are doing'. Achieving this goal will place several demands on IT -- not just diagnostics IT in the lab, but the HIS, LIS and EMR. It means an integrated, seamless system that enables appropriate access to needed patient information -- connecting the dots between the many sources of patient data. 'The next challenge is to integrate all this technology into one IT system that simplifies everything. How many hospitals can use that? I think we all can,' Sheryl Wilson concluded.


Veronica Luzzi


Sheryl Wilson


Sherrie Hoffman

Into the future

Real-time, centralised control and the deployment of IT in enhancing productivity and quality; a view towards a more important role for clinical diagnostics in patient care supported by a standardised, integrated healthcare IT system, and a new paradigm for designing and implementing training were recurring themes during the invigorating dialogue between the clinical lab, media and Siemens Diagnostics Healthcare.

continued from page 5

and several in Europe with total automation systems installed or in progress, and many more laboratories with various forms of modular automation or work cells.

What about Serbia? Today's clinical laboratories prefer the modular approach to automation, with total labautomation and POC testing planned for the future, the professor said. 'The Centre for Medical Biochemistry, as part of the medical services within the Clinical Centre of Serbia, has its own organisational and technological principle that ensures the undisturbed and efficient flow of human biological material and information. At the Centre the analytical process is highly automated to ensure all operations are performed uniformly, in a repeatable manner and proper order. This, she said, achieves higher productivity, reduces analysis cost, variability of results and error analysis. 'Also, we began with the automation application in the pre-analytical and post-analytical phase in emergency and polyclinic laboratories where they implemented LIS ('middleware'). The middleware technology enabled us to implement autoverification for all haematology and some chemistry and immunochemistry testing. The LIS application and bar-code technology has enabled a special improvement in lab quality through the automatic sample identification, automatic analytical data collection, results monitoring and the determination and generation of consolidated reports of the lab examination. The combination of processes consolidation and integration, and organisation through the transition of technology to the organisation process of the Centre is achieved through ongoing reorganisation of clinical laboratories to increase efficiency, quality and lowering healthcare costs.'

All laboratories at the Centre for Medical Biochemistry, Clinical Centre of Serbia, he added, are accredited in accordance with the demands and standards SRPS 17025:2006 and SRPS 15189:2008

The accuracy and reliability of medical laboratory examination results are vital part in healthcare delivery, and these plus the effective operation of laboratories are the main goals of laboratory managers. To ensure a high quality operation, medical laboratories have quality management systems and, through laboratory accreditation, show their competence.

Quality management systems are based on international laboratory standards ISO/IEC 17025 and ISO 15189 and/or guidance of good practices in different disciplines. Accreditation of medical laboratories began in many European countries about 20-25 years ago, whilst some are still in the process of starting medical laboratory accreditation.

Tuija Sinervo, Lead Assessor at FINAS, the Finnish Accreditation Service, describes current practices and suggests ways to improve existing services


Tuija Sinervo

Managing the medical laboratory

ISO/IEC 17025 is a general standard for all types of laboratories, but ISO 15189 is intended only for medical laboratories and describes how a medical laboratory should operate. In the beginning of accreditation the focus of assessments was on the technical operation of laboratories, but later laboratory management also became increasingly important in assessments. Medical laboratories have exploited (piggyback) their quality management systems and accreditation quite well, by improving operation in many ways. Despite this, there are still some things that can be improved. The task of management is to plan the entire laboratory operation well and monitor the operation and customer service. These are areas where medical laboratories still need to improve.

The management reviews and internal audits are effective tools to monitor the operation of a laboratory and are widely used. However, not all laboratories have the capability to develop these tools to collect information fully about their operation and to find ways to improve that operation.

An important aspect of laboratory operation is the need to maintain good co-operation with their healthcare customers, so a laboratory uses the most suitable examination methods and equipment for patient care. Laboratories have organised this cooperation in different ways, but better management of this co-operation is needed so that it is well planned and the laboratory management gains all necessary information about the customers' needs and feedback. Laboratories follow possible nonconformities in their operation and take corrective actions if necessary. However, the procedures are not always clear enough for personnel to be aware of what those nonconformities are and which should be recorded and notified to the management or a responsible person.

The effective handling of customer feedback also needs clearly documented procedures.

Technical Competence

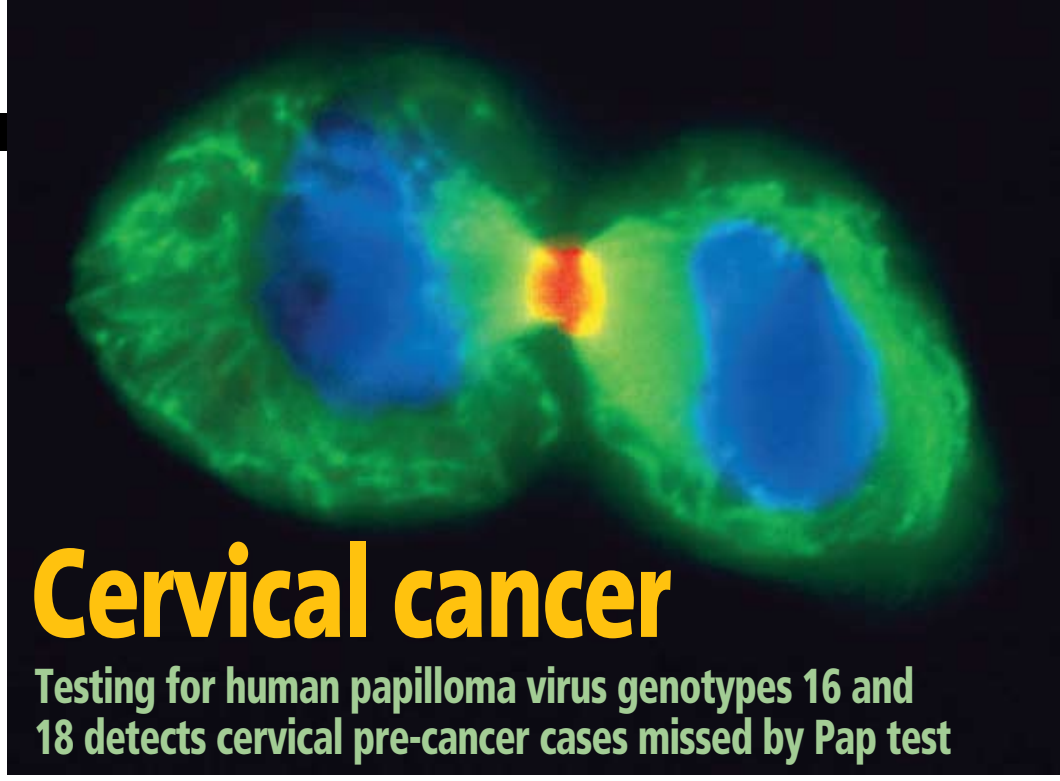
The high quality of a laboratory operation is based on competent personnel. Laboratories train and educate their personnel continuously. However laboratories should pay more attention to the planning and effectiveness of training. A training plan may not cover all personnel, such as new doctors, chemists, physicists and head nurses, and the effectiveness of training is not monitored systematically. Although laboratories ensure the accuracy of patient examination results by using validated/verified examination methods, but there is still need for better planning of validation and better documentation of validation results.

The traceability of examination results is important so that they are comparable and also enable long-term patient monitoring. The understanding of the importance of traceability is increasing all the time, but still there are laboratories that are not very familiar with the concept of traceability. Laboratories follow the accuracy and reliability of patient examination results with internal and external quality assurance programmes, but the objectives for quality assurance can be missing and there are no unambiguous criteria for the acceptance of quality assurance results. Laboratories report their examination results without delay and inform clinicians of critical or urgent results.

Laboratories should document more clearly these reporting procedures, so that personnel could more systematically follow defined procedures. Laboratories give to healthcare units all necessary information to guide patients regarding the right preparation for examination, but one main problem is that patients do not follow these instructions. There is still need for better co-operation in guiding patients about preparation.

In conclusion: What healthcare units expect from medical laboratories are expert consulting to select proper patient examinations and to use proper patient sampling methods; state-of-art examination methods; clearly reported examination results and consultation to interpret results.

Further details: FINAS, Finnish Accreditation Service, Finland: finas@finas.fi



Cervical cancer

Testing for human papilloma virus genotypes 16 and 18 detects cervical pre-cancer cases missed by Pap test

Data from the ATHENA (Addressing THE Need for Advanced HPV Diagnostics) USA registration trial, involving more than 47,000 women, demonstrate that two human papilloma virus genotypes, HPV 16 and HPV 18, can identify those women with cervical pre-cancer missed by cytologic examination with a Papanicolau (Pap) test.

In the trial, 1 in 10 of the women, aged 30-years+, who tested positive for HPV genotypes 16 and/or 18 by the cobas 4800 HPV* test had cervical pre-cancer, although their Pap test had been normal. The data demonstrate the importance of HPV genotyping to increase the accuracy of assessing cervical cancer risk, especially by screening for the two highest risk HPV genotypes (16 and 18), and underscore the limitations of relying upon cytology (Pap) testing alone in identifying women with cervical pre-cancer, Roche points out.

Thomas C Wright Jr MD, of Columbia University, who presented the data at the 26th International Papilloma virus Conference in Montréal, Canada, said: 'The ATHENA data show that women who are positive for HPV 16 and/or 18 should be directly referred for closer examination of the cervix by colposcopy. Screening for high-risk HPV genotypes provides important additive information to Pap testing, and screening for the two highest risk types, HPV 16 and 18, should be included to provide predictive information about a woman's risk for having cervical pre-cancer or cancer.'

Novel findings from the clinical trial, show that women positive for HPV 16 and/or 18 with the cobas 4800 HPV Test who had a normal Pap test were at the same risk of having cervical pre-cancer as women who tested positive for any of the 14 high-risk HPV types with an equivocal Pap test (ASC-US, Atypical Squamous Cells of Undetermined Significance). The latter clinical situation is broadly accepted to carry a risk of pre-cancer that warrants immediate investigation, underscoring the importance of testing for HPV genotypes 16 and 18 in women with normal Pap tests.

'ATHENA is a landmark trial demonstrating how state-of-the-art medical diagnostics can address the limitations of cervical cancer screening with Pap tests alone,' said Daniel O'Day, Chief Operating Officer for Roche Diagnostics. 'If more women were tested for high-risk HPV genotypes, specifically genotypes 16 and 18, more cervical pre-cancer could be found and treated earlier. This would prevent progression to cancer and ultimately save lives.'

** As demonstrated in the ATHENA trial, the Roche cobas 4800 HPV Test (launched with CE Mark in 2009) is the only HPV test under investigation in the USA that simultaneously detects 12 high-risk HPV types (HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) as a pooled result, as well as HPV genotypes 16 and 18 individually.*

A bright future for biobanks

The relationship between histology, morphology and molecular biology within tissue samples presents opportunities to solve important medical scientific questions to disease mechanisms


Peter Riegman

Ten years ago, molecular biologist Dr Peter H J Riegman set up a unique bio-bank for medical research at the pathology department of Erasmus Medical Centre, Rotterdam, The Netherlands. The Erasmus MC Tissue Bank now holds 30,000 samples from about 15,000 patients. However, when Dr Riegman discusses his bio-bank with international colleagues they do not immediately associate it with a clinic or (academic) hospital using existing diagnostic and treatment paths.

Such a collection can only grow with the cooperation of clinicians and the hospital's support of the infrastructure. Consequently, the clinicians and scientists need to be viewed as essential in any decision to release samples from the bio-bank.

Unlike in other European countries, in the Netherlands hospital-obtained residual tissue can be stored for research without a signed patient consent -- the patient is informed and can object by filling out and signing a form. Thus, whilst most biobanks operate on a prospective basis with volunteer probands, the Erasmus MC Tissue Bank can collect biological samples from all interesting cases and use these in a 'trial zero situation' without assurance that it might become useful for future medical scientific experiments. However, the chances are very high because if material is stored, over time information about the disease development increases (follow-up data), making the sample all the more valuable for scientific experiments.

Cancer is the focus because 85- 90 % of the tissue samples arriving in the pathology department are 'leftovers' from tumour resections. 'In cancer disease particularly there is a classification of different molecular subtypes. While normally it can take years to collect an adequate number of samples from a certain subgroup, a tissue bank can promptly deliver edited study resources. But, over the years, scientists become more interested in the material and it happens that more and more of our retrospective samples turn out to be prospective ,' Dr Riegman explained during a discussion with *European Hospital*. 'Of course, all collected health data and biological materials are anonymous and carry only a code number. Erasmus MC scientists can also search the collection online and request tissue samples over the Erasmus MC intranet.'

Another advantage of a clinic-based bio-bank is that the medical wards, pathology department and tissue bank work together as an integrated supply chain to guarantee high-quality samples through good collection and handling techniques. For various reasons, obtaining appropriate samples is difficult, Dr Riegman explained, '…primarily, because there is no standard pathology guidance about how to store human tissue, so normally you find all different kinds of fixation times and lag times out there. In addition, there can be considerable variation in many other pre-analytical parameters that cannot be influenced, such as treatment anaesthetics, the time of day surgery takes place, concomitant disease treatment, etc. Only if the samples are snap-frozen within half-an-hour, according to studies in the literature and accepted standards, are there minimal distinctions for future research analysis. This means that, first our surgical site staff sends in the material fresh from an operation instead of already fixed in formalin and after the procedure. Secondly, there has to be a pathologist on call who decides immediately what can be stored in the bio-bank and what is needed for diagnostic purposes. Of course, we are only allowed to store material that does not disturb the diagnostic process. In addition, only if the specimen is large enough is it divided in two: One part will be snap frozen for research the other will be formalin-fixed and paraffin embedded for quality control of the bio-bank. In a third step, the bio-bank personnel take care of snap-frozen sample and store it in liquid nitrogen and finalise the administration in the bio-bank database.'

Besides the clinic-based bio-bank, Erasmus Medical Centre also drives a population-based bio-bank. 'Even though we know each other very well, our departments work quite separately,' he explained. 'The population-based bio-bank discovers the biomarkers that indicate predisposition, while the clinic-based bio-bank is needed to search for how such markers behave in disease, identify drug targets and realise personalised medicine. Nevertheless, it's a plan for the future that all our disciplines work together in a biological research centre as a kind of healthcare research pipeline, where all the samples – population, environment and clinic-based data – converge.'

Institutional collaboration is not the only essential in the work of bio-bankers: Because no bank can cover the large number of samples of a certain tissue type, the formation of large networks of systematic tissue banks have been created in Europe. Peter Riegman heads not only the Erasmus MC Tissue Bank but also coordinates the European Human Frozen Tumour Tissue Bank [OECI-TuBaFrost]) with other European Institutes and in collaboration with the Cancer Research organisations EORTC (European Organisation for Research and Treatment of Cancer [www.eortc.be]) and OECI (Organisation of European Cancer Institute [www.oeci.eu]). OECI-TuBaFrost is mainly an exchange platform offering insight in which bio-bank certain tumour material is available and who to contact to request these materials. Standardisation efforts therefore play a key role in the work of OECI-TuBaFrost.

The OECI-TuBaFrost (www.tubafrost.org) infrastructure has been adapted and will be introduced shortly to the OECI members. It now combines the experiences of three European bio-banking projects: EuroBoNeT, BBMRI and OECI-TuBaFrost. This allowed the development of the new concept of tackling elaborate translation and upload procedures of sample data and it avoids the protective attitude of the investment made in the collection as much as possible. This facilitates a relatively open catalogue of biobanks consisting of a database filled with a questionnaire and offering closed project environments to those wanting to begin a new cooperation in a multicentre study based on sample exchange.

'I believe that biobanks have a bright future,' observed Dr Riegman 'The relation between histology, morphology and molecular biology within tissue samples give us the opportunity to solve important medical scientific questions to disease mechanisms.'

Report: Karoline Laarmann

The automated volume breast scanner

Ultrasound catches up with slice imaging

Innovative technologies such as elastography, shearwave and 3-D have been cause for euphoria in today's ultrasound world. The most recent development in breast imaging also has the potential to revolutionise this field, because the Automated Volume Breast Scanner (ABVS) is allowing user-independent and reproducible image acquisition for the first time. Thus, ultrasound has finally caught up with other diagnostic imaging modalities and can be integrated with modern multi-modality concepts used in breast diagnostics.

Dr Frank Stöblen, diagnostic radiology specialist and co-owner of Diavero, a diagnostic imaging centre in Essen, Germany, has worked with the Siemens Automated Breast Volume Scanner Acuson S2000 ABVS for over a year. As the first European user to have performed more than 2,000 examinations with this new technology, he described his experiences and observations in an interview with *Daniela Zimmermann* of European Hospital

ABVS solves many problems of ultrasound technology in general, said Dr Stöblen. 'First, the technology is automated, which means the transducer, user-independently, always generates images of the same quality. While ultrasound is one of the most frequently used imaging technologies, it is often done incorrectly and the technology itself, as well as its application, is subject to very few quality assurance checks. Thus, hand held ultrasound is an extremely subjective procedure with results entirely dependent on the knowledge and experience of the physician.

'ABVS, however, scans the entire breast automatically without user intervention. Moreover, integrated 3-D technology provides coronal views that were impossible to generate with conventional ultrasound equipment. The physician no longer has to be present during ABVS procedures. The examination can be performed by assistants. Ultrasound has always been a very haptic technology and therefore I'm sure it will take some time before radiologists get used to the new concept. Working with ABVS is a bit like driving a remote-controlled car.

'The second advantage is the reproducibility of full-field volume images. ABVS generates a complete data set that can be called up on a workstation – wherever and whenever needed. Sure, in the past ultrasound images were integrated into the PACS, but these were always a few isolated images. Now we can store up to 1,800 images per examination and scroll through them like we scroll through a video – just the way it's done in multislice CT. This has diagnostic potential, because we can now detect architectural deformations that we couldn't see before. Furthermore, a second opinion can now be based on the exact same images as the primary opinion.

'And, last but not least, research and training will benefit from the volume data sets as they allow a complete retrospective analysis and can be used as teaching files.'

When do you use ABVS?

'In early detection ultrasound improves tumor detection above all in women with dense breast tissue. We were able to show in some smaller studies that ABVS can find all solid lesions. In a cancer prevention study with 300 previously examined women, with an average age of 30 years, ABVS detected two carcinomas.

'As far as benign lesions are concerned, 3-D ultrasound is even slightly better than mammography. It can help to clarify ambiguous findings in dense tissue, such as cysts. However, ultrasound is not suited to detect microcalcifications.

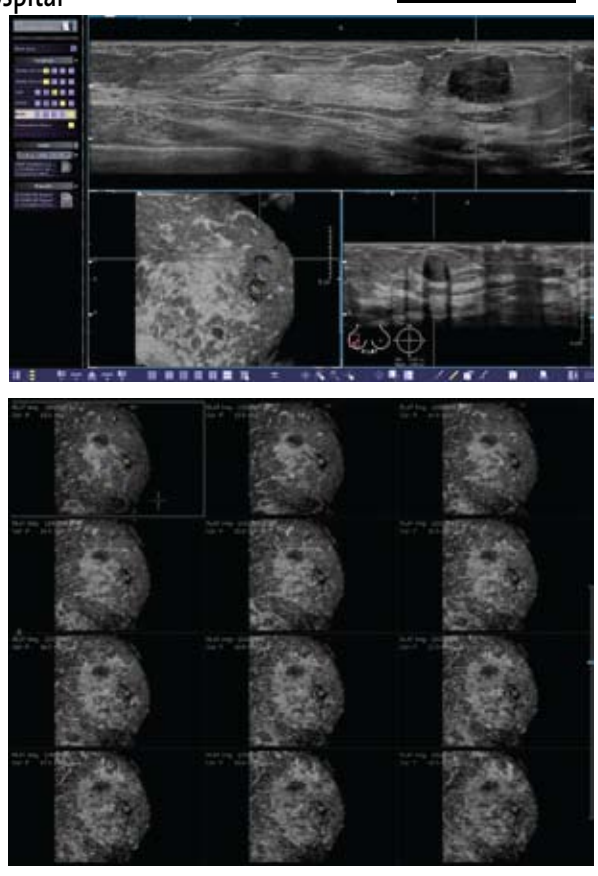
Will there be additional applications beyond breast imaging?

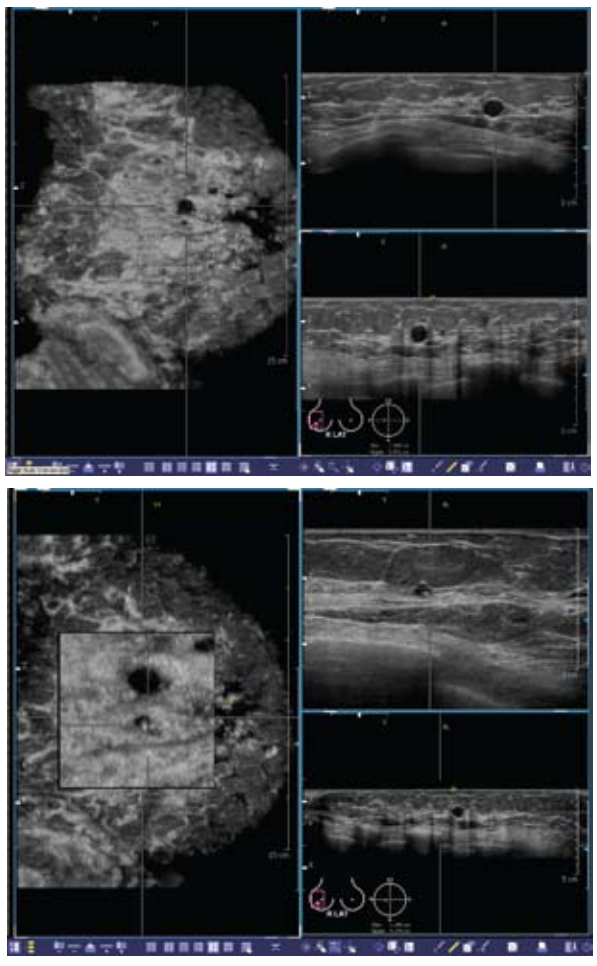
'Definitely. I am sure there will be applications for other organs, such as liver, vessels and the thyroid gland, very soon. Mamma diagnostics was just the beginning. It allowed us to gather know-how since the breast is a surface organ and easily accessible. Moreover, mamma diagnostics is moving towards multi-modality. You do need all three modalities – mammography, ultrasound and MRI – in order to perform a differential diagnosis. Consequently, there are more and more multi-modality workstations in which the ultrasound images can now be integrated – thanks to the volume scanner.

Frank Stöblen

What technological enhancements do you expect for ABVS?

'The next step will be the integration of elastography into the 3-D system. Most likely shearwave will be the best technology, but at this point it cannot be realized since during tissue measurement with elastography the region of interest must not move -- a tricky technological problem but not impossible to solve.'





Making the best out of digital mammography with contrast-enhancement

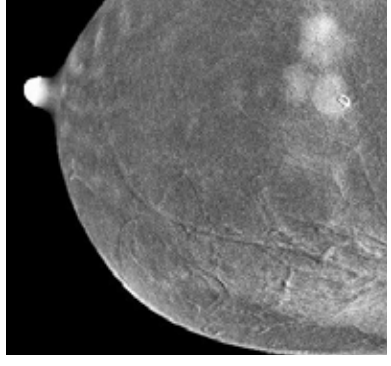
Standard mammography is the most relevant diagnostic tool to address breast cancer: It shows excellent image quality, a smooth workflow, high connectivity and a very good clinical outcome in terms of sensitivity and specificity. However, there are certain shortcomings to it, especially in dense breast tissue.

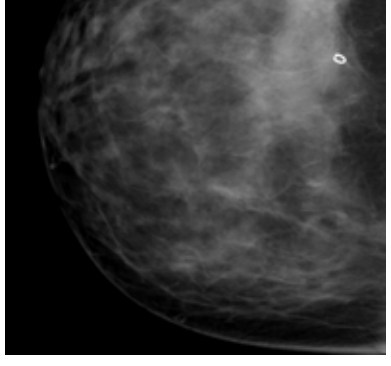
Report: Karoline Laarmann

Over the last 12 years, technical and clinical research is done with contrast-enhanced spectral mammography (CESM) in several scientific centres in Europe and North America to reduce ambiguity in the diagnosis of breast carcinoma with the help of contrast agents. Leading this role – like in mammography technique at all – is France with the Institut de Cancérologie Gustave Roussy (IGR) in Villejuif. The French government invested into two big R&D projects for CESM from 2002 until 2005. The development of CESM was developed in close cooperation between science institutes, hospitals, and industry. Former IGR Medical Director Prof. Robert Sigal and his team conducted the first study using CESM in 1998. (NB : Shouldn't we not mention here the subsequent IGR studies of 120 women with known lesions, publications?)Today, Prof. Robert Sigal is President of GE Healthcare in France, the company which launched the first commercially available CESM-technology on a mammography system this summer. In an interview with EUROPEAN HOSPITAL Prof. Sigal explained how the technique works: "We utilize the fact that tumor evolution affiliates with abnormal vessel growth. The sprouting angiogenesis can be made visible by the contrast agent. For that, firstly contrast agent s injected intravenously, then, two image acquisitions are performed with two different energy levels: one of the tissue and one of the contrast enhancement. The exam only takes 5-10 minutes. The two acquisitions are automatically processed to provide a standard view plus a second image which highlights the region where the contrast agent is present. The two images are viewed together at the workstation The whole secret lays in the fast switching of energy level algorithms and a patented data recombination algorithm to extract the iodine information: It allows for visualization of the blood vessel information together with the usual breast tissue structure images side by side." But what about inflammatory areas? "It is true that these iodine contrast agents are non-specific. However, pre-treated breast carcinoma in most cases shows no forms of inflammation. And keep in mind that this is angiotechnique with a highly negative predicitive value: If there is no contrast enhancement at all, cancer in most cases can be excluded."

Robert Sigal

In the first clinical trials, it showed that CESM significantly improves the accuracy of breast exam in sensitivity (for every 100 cancers potentially find 13 more) as well as in specificity (6 more benign lesions out of 100 can be correctly classified). Now is the time for CESM to prove its value in long-term clinical routine and find its position in a row with the established image modalities. Because CESM might be so beneficial in dense breast it is directly competing with ultrasound as an additional tool to standard mammography in suspicious cases. "It can be performed after ultrasound to increase diagnostic confidence, or even before ultrasound, because it is possible to carry out the exam almost immediately after a standard mammography exam on the same device. CESM can be implemented as a technical upgrade to GE's digital mammography equipment." Nevertheless CESM in comparison to ultrasound means dose exposure, but at least the overall increase of dose is less than 20 %.





There are other applications for CESM which are currently being evaluated, reveals Prof. Sigal, for instance in follow-up of patients: "One of the questions here is in how far it can compete with MR after breast cancer treatment, especially in view of MR being less available and more expensive. In addition, the reading of MR images requires a lot of training and experience. CESM is a very straight-forward technique which makes breast lesions visible even for non-professionals. But study results in this field are not available yet."

Oncologists gather for 'white nights' in St Petersburg

White nights in St Petersburg draw in not only romantics, but June in this beautiful city also sees thousands of delegates arrive to attend the many scientific conferences and congresses. Among oncologists, the 'white nights' period means another annual scientific conference organised by the NN Petrov Research Institute of Oncology. For its continuing focus on breast cancer, the halls are packed


Vladimir Semiglazov

European Hospital discussed this important event in the oncology calendar with the Chairman of the Scientific Organising Committee, **Vladimir Semiglazov MD**, who is also head of surgery at NN Petrov Research Institute of Oncology, in St Petersburg, Chairman of the Society of Oncologists of St Petersburg and the Leningrad region, and corresponding member of RAMS

Asked why breast cancer is an annual focus, Vladimir Semiglazov explained that oncologists come from almost all of Russia, as well as other countries, because diagnoses and treatments are developing rapidly and doctors need to keep abreast of new data. 'Not all of them can read foreign publications and Russian journals don't have the latest data and are only published six times a year. Practitioners should be aware of trends in breast cancer diagnosis and treatment, the successes and failures.' Similar conferences are held in other cities, he pointed out, '…but our lecturers are always top people in their countries -- and doctors know that.'

Breast cancer diagnosis and treatment is slow in development, he pointed out. 'There are a million new cases of breast cancer in the world annually. In the USA the proliferation of this form of cancer has reached epidemic proportions, affecting one in every seven American women, and the US invests seriously in fundamental research. Russia has spent almost nothing on science. Although we have too high a morbidity: more than 50,000 new cases are registered and 24,000 women die annually.'

Within scientific hypotheses regarding the causes of breast cancer, one this is clear, Dr Semiglazov said, 'Tumours are hormone-dependent and it's believed the main "culprit" is oestrogen, which is produced in the ovaries. Hence, prevention and treatment associated with anti-oestrogens.'

Referring to a large study conducted in the USA and Britain and involving 30,000 at risk women (persistent recurrence of the disease in direct relatives, long-term benign processes, lack of birth, etc), he said: 'Half of the women are simply observed and had a mammogram, while another group took anti-oestrogenic drugs. Over the years it became clear that, among the treated women, the incidence of cancer was reduced by 50%. It would seem a huge success! However, reduction in the frequency of relatively favourable tumours, which are so well treated, did not determine mortality. But hormone-independent difficult-to-treat cancers are not amenable to prevention. Moreover, such chemoprophylaxis increased the incidence of cancer of the uterine endometrium. Although the reduction of breast cancer was higher than the growth of endometrial cancer, but individually it is difficult to predict the possible prognosis. Therefore, this approach to prevention was not recommended.'

The second route, now being researched in Britain and at the NN Petrov Research Institute of Oncology, is the use of aromatase inhibitors -- drugs that reduce oestrogen levels. 'About 4,000 women have already been included in this study; recruitment of 8,000 more is necessary.'

Screening, but…

'Russia has declared that the country's screening programme is running and there are 1,500 mammography centres. I've lectured in almost all the cities where, according to officials, a screening programme has begun - Tomsk, Kemerovo, Nizhny Novgorod, and Barnaul. I've been shown a huge number of mammographs, but seen mainly enormous tumours -- doctors only confirm the diagnosis that a woman came to them with herself.

'However, for screening to detect tumours -- when neither doctor nor woman can see anything, when the tumour is not palpable, when the surgeon doesn't see it and needs to be shown the image for exact tumour size and location – we need special equipment, stereotactic biopsy machines. However, apart from Moscow and St Petersburg, not one region with a screening programme has this technology.

'Only if all the screening conditions in the programme can be met -- more than 60% of appointments kept, monthly monitoring by each physician etc. as well as quality control in the X-ray, laboratory, radiology (whether radiologists read the information correctly), pathomorphology (whether the pathomorphologists understand the disease), surgery (monitoring the surgeon's work) – could we talk of a decline in mortality after seven years. And that's providing that, with the detection of small tumours, we simultaneously have all the features of adequate treatment.

'Incidentally, the first stages of financial investments in screening programmes are costs for tumour treatments, and only seven years later is it possible to record a four-fold reduction in costs: in the first stage of a cancer only minimally invasive surgery is needed.'

So, is it a fallacy to open a screening centre in 2010 and claim that mortality will fall in 2012?

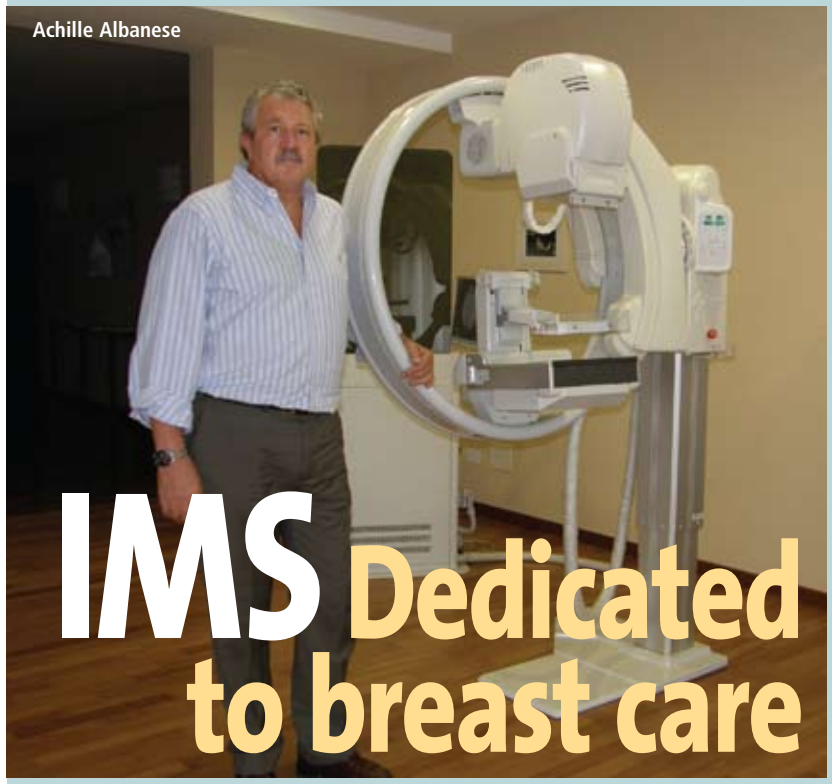
'Certainly. We could wait for results in 2017, but I think that's unlikely. I can hardly imagine it will be easy to get even at-risk Russian women (say, over 50 years) to come regularly for a mammogram. Special programmes should be developed to work with the public. Finland, for example, has developed special computer software that calculates the time of a woman's next visit for a mammogram and then she and her relatives are posted a reminder and asked to explain any reason for not attending.

'It's a very important "nuance" and officials who develop a programme simply do not know it and should consult with experts. Also, the number of mammographs is not so important. According to the International Agency for Cancer calculations, our country would be very well-equipped 500 mammography centres – not 1500! Problem number one: Proper organisation.

When I speak to radiologists about screening I face a storm of indignation: '*We aren't going to work for nothing*!' They see 100,000 surveys to identify 200 cases of early stage breast cancer. Yes, 99,800 images will be "clean", but that's the idea of screening: to study and tell the woman she is healthy and need have no concern for two more years.

'Oncologists need this information very much -- when I went to the regions I lectured from early morning to evening that they need modern drugs in the right quantities and radiologists' assistance. In many Russian areas the first and second are big problems, and sometimes the only route they can take is to send patients for treatment in Moscow or to us. That's why it's so important to prevent breast cancer.'

COMPANY PROFILE


Achille Albanese

IMS Dedicated to breast care

The Italian firm Internazionale Medico Scientifica (IMS) produces highly innovative mammography units under the brand name *Giotto*. More than 3,500 Giotto systems are now in use in 38 countries, mostly in Europe, America, China and the Far East. Reason enough for *European Hospital* to visit IMS in Pontecchio Marconi, Bologna

Legend has it that the 13th century Florentine artist Cimabue noticed a 12-year-old boy drawing a sheep on a rock and promptly made Giotto di Bondone his apprentice. Years later, when Pope Boniface VIII sent a messenger for proof of Giotto's skills, with one stroke of his brush the artist drew a perfect circle for despatch. His abilities in painting, sculpture and architecture thus placed Giotto among the world's greatest artists. 'He became patron saint of the Giotto mammo system not only because he was a real master of his trade,' explained Achille Albanese, Marketing Director at IMS, 'but because the ID card of the Giotto is the ring-shaped gantry that makes perfect 3-D visualisation possible.'

Back in 1965, Bruno Toniolo founded a company to sell X-ray accessories, conventional radiography and fluoroscopy units to Europe, the Middle East and North Africa. Having gained invaluable export experience as well as an understanding of the technology and needs of users, by 1980 Toniolo was manufacturing and selling his own range of automatic film processors and X-ray units under the company name IMS,

Ever entrepreneurial, when a US radiologist hinted that a more effective breast examination could be achieved if the radiographer stood face-to-face instead of to the side of a patient, Toniolo perfected the idea by adding a tilting feature to the rotating gantry. This slight-inclination positioning helps the patient to relax her pectorals, enabling the radiographer to pull more breast tissue into the bucky – in a large breast making a difference of up to 2 cm! Thus Giotto, a unique mammography unit, was born.

Launched in Europe and the USA in 1989, to this day three commercially available Giotto units provide both face-to-face and conventional 3-D positioning, with the tilting feature also enabling stereotactic biopsies in upright as well as prone position. 'In some countries, such as France, prone breast biopsy receives higher reimbursement than conventional upright breast biopsy, because it's clinical proven that it's more accurate in breast tissue diagnosis,' explained Achille Albanese.

Entering the white single storey headquarters of IMS headquarters in Bologna confirms the IMS transition from simple vendor to manufacturer. The building houses both factory and an important R&D centre. It was here, for example, that the first amorphous selenium (a-Se) detector was tested under mammography conditions. The first ever clinical trial of the a-Se detector followed in the Breast Department at Maggiore Hospital, a public institution and close science partner of IMS.

In 1998, IMS and Canadian manufacturer Anrad (at that time named Noranda) launched the first selenium-based panel in a mammo unit. In Giotto, a-Se detector technology directly converts X-ray into digital signals to be processed in seconds into high quality images. 'The reading time is a little bit less than one image per second, but Anrad is developing an even faster detector for us, to provide three images per second,' Achille Albanese disclosed.

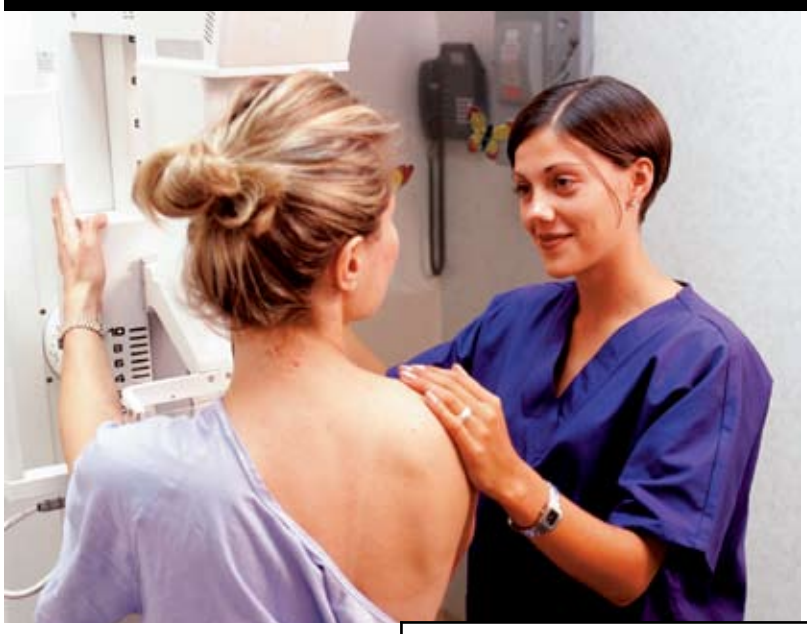
In 2003, the IMS Giotto IMAGE SD pioneered Full Field Digital Mammography (FFDM) in Europe. The technique has improved sensitivity, particularly in the dense breast. A year later, IMS became the first manufacturer worldwide to use FFDM for stereotactic biopsy examinations. Additionally, IMS has always concentrated efforts on dose reduction: the introduction of a combination of Tungsten anode tube with first rhodium and now silver filter, significantly decreases radiation dose up to 50%.

Which market might prove the greatest for the IMS FFDM systems? 'Definitely the USA, because it represents more than 50% of the world's digital radiology market,' Achille Albanese affirmed. 'CR systems are not approved by the FDA, with the exception of a Japanese manufacturer. So, while the FFDM market in Europe and the rest of the world has been shared in the last five years between digital and analogue mammography, CR in mammo is practically unknown in the States. China is another growing market for us – we're already the number two seller in DR systems there.'

The Giotto FFDM must need FDA approval? 'Yes, this is a difficult situation,' he assented. 'So far, there are only two competitors, GE and Hologic, which have received the FDA mark (Siemens has not received approval for its latest FFDM system). But there's a major change. Since digital mammography became an established technology, clinical trials are no longer necessary, which is why the FDA announced a change from stringent pre-market notification to the 510 (k) clearance process later that year. So, we are optimistic.'

New digital technologies are also in the works at the IMS, including two R&D projects on dual energy and contrast enhanced digital mammography. The company's focus definitely remains on digital breast tomosynthesis: 'The starting shot for our first multicentre European clinical trial on tomosynthesis will be this autumn,' said Achille Albanese. 'Again, you can count on it that our tomosynthesis technology will be optimised especially for breast care.'

In the next EH issue (5/10): IMS Giotto breast tomosynthesis



Early detection of breast cancer

Three-country comparison reveals that every year almost 1,000 more lives could be saved in England alone


Henrik Møller

A study looking at breast cancer patients in England compared to those in Norway and Sweden has highlighted the importance of early detection.

The researchers, led by Professor Henrik Møller from King's College London, chose to compare England's survival rates with those of Norway and Sweden because in these countries data is collected on every cancer patient, whereas in other European countries national data are often not routinely collected.

The study looked at all survival rates from all cases of breast cancer diagnosed between 1996 and 2004.

The research, presented to the National Cancer Intelligence Network (NCIN) conference, showed that if England matched Norway and Sweden's survival rates for breast cancer, 957 deaths could be prevented annually in women whose cancer is diagnosed so late that they usually die within two years of diagnosis

When breast cancer is caught early, treatment is often milder and more effective. Survival rates soon after diagnosis can be used as an indicator of whether the disease is being caught early or late, the researchers reported.

Professor Møller said the study had important implications for women in England. 'We could prevent nearly a thousand deaths from breast cancer each year by getting the disease diagnosed earlier, particularly in older women. These figures show how important it is for women, and GPs, to know the symptoms of breast cancer and to act on them without delay. Going for screening when invited will also help to catch the disease at the earliest stage. Although women over 70 aren't routinely invited for screening, they can ask their GP for a mammogram.'

Every year, in England, there are 1,183 excess deaths from breast cancer within five years of diagnosis. Of these avoidable deaths, 260 occur within a month of diagnosis, 557 between a month and a year after diagnosis and 140 deaths happen after a year but before two years since diagnosis.

Crucially, 81% of these deaths occur within two years of diagnosis and mainly in older women over 80. This amounts to 957 deaths that should not have happened, the King's College team pointed out.

In England, over 38,000 cases of breast cancer are diagnosed each year and overall eight out of ten women survive the disease beyond five years with breast cancer survival improving and death rates having fallen in recent decades.

The NCIN was established in June 2008 with a remit to coordinate the collection, analysis and publication of comparative national statistics on diagnosis, treatment and outcomes for all types of cancer.

Chris Carrigan, head of the NCIN, said it was already known that many cancers are being diagnosed too late in England and that the King's College study was important in highlighting the scale of the challenge for breast cancer in particular. 'More women are surviving breast cancer than ever before and we know that significant improvements in breast cancer treatment are being made. But we still have work to do to emphasise the benefits of early detection.'

Professor Sir Mike Richards, National Cancer Director at the Department of Health said: 'This is an important new study. It highlights the importance of early diagnosis in achieving the best possible survival rates for women with breast cancer. Survival rates have improved in this country over the past decade, but there is more to be done. Over the coming months we shall be looking at what needs to be done to achieve earlier diagnosis.'

Report: Mark Nicholls

Novel diagnostic strategies and

Karoline Laarmann reports on the 8th Düsseldorf Breast Cancer Conference, at which world renowned surgeon and oncologist **Professor Veronesi** presented the Honorary Lecture and leading experts evaluated new imaging methods

With a medical career spanning 50 years, 85-year-old Italian surgeon and oncologist **Professor Umberto Veronesi**, Founder (in 1994) and Scientific Director of the European Institute of Oncology in Milan and former National Health Minister (2000 – 2001), is internationally recognised for his contributions to breast cancer prevention (e.g. studies on tamoxifen and retinoids) and treatment; breast-conserving surgery having invented quadrantectomy; improvement to sentinel lymph node biopsy, and making the avoidance of axillary dissection possible in breast cancer with clinically negative lymph nodes.

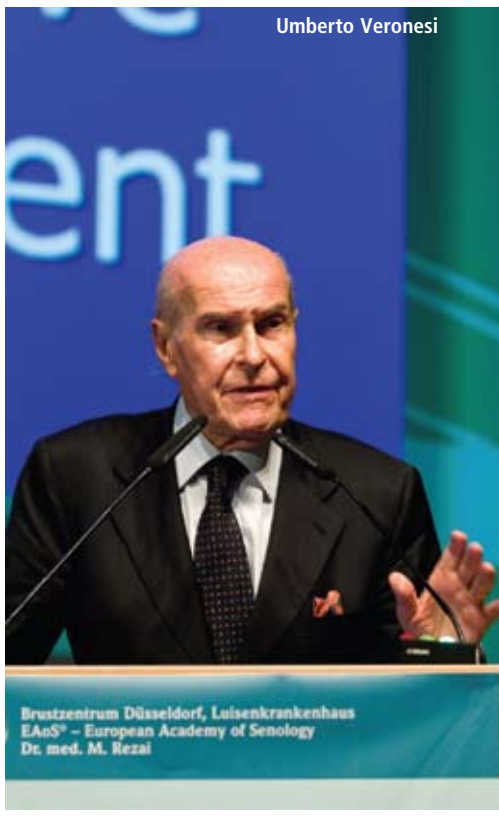
During his Honorary Lecture at the 8th Düsseldorf Breast Cancer Conference in Germany Prof. Veronesi reflected: 'Surgery of breast cancer, more than in other tumours, has gone through a number of revolutions in the last forty years, which did not so much manifest in techniques but in concepts: The rethinking from anatomical concept of cancer spread to biological concept, as well as the paradigm shift from maximum tolerable treatment to minimum effective treatment, are two milestones to mention.'

Invited by Dr Mahdi Rezai (above), medical director of the breast centre at Luisen Hospital in Düsseldorf and founder of the European Academy of Senology, some 1,400 international specialists attended the event in Düsseldorf this June

Both more patient-friendly concepts were essentially initiated by the professor himself in his Milan Trials I – IV. He was the first to prove in a clinical trial published in 1981 that patients with small-size breast tumours undergoing a quadrantectomy (quadrant resection flanked by radiotherapy and axillary dissection) have the same recovery chances as patients undergoing radical mastectomy. The results also revealed that breast cancer is a systemic disease, instead of a local disease as believed in earlier doctrine, which means that metastases spread from early on in the periphery. Consequently local recurrence is not an instigator of new metastases and the survival rate of lumpectomy + radiotherapy and quadrantectomy + radiotherapy is the same.

A discussion raised by the introduction of conservative breast surgery was the evaluation of margins of resection as a possible predictor of recurrence. 'Our Milan trials have shown that patients with negative or positive margins have the same rate of recurrence', Prof. Veronesi. 'The evaluation of the margins is limited, first because the peritumoural spread of cancer cells is often discontinuous and, second, the biopsies on the margins of the specimen are "at random". After surgery, we believe that some cancer cells remain in the breast and therefore radiotherapy must be given to all patients following conservative surgery.'

In the '90s, the professor began to perform sentinel node biopsy as a method for screening the axillary nodes for metastasis in order to spare healthy axillary nodes. The sentinel node is the first that receives lymph from the tumour area, so only if the sentinel node is afflicted by cancerous cells, should all lymph nodes be removed, he said. Another powerful prognostic indicator is the internal mammary node. 'Mammary internal nodes are generally ignored by surgeons, but my clinical experience shows me that if axillary nodes and internal mammary nodes are both negative, survival is good; if they are both positive, survival is bad, and if only one of the two is positive the prognostic power is identical. In other words, the identification of the internal mammary node has the same prognostic value as the identification of the axillary node.



Umberto Veronesi

Hence, patients with positive internal mammary nodes should receive radiotherapy to the internal mammary chain and more intense systemic treatment.'

The further step to improve breast conservation was the development by Prof. Veronesi of ELIOT (Full Dose Intra-operative Radiotherapy with Electrons). ELIOT is a focalised therapy technique to treat a more limited volume of tissue surrounding the tumour bed. A mobile linear

Session: Breast cancer diagnosis and tumour

Presenting an overview of new imaging methods, radiologist **Professor Ingrid Schreer** (Mammazentrum Kiel), said the results of a multicentre prospective study on sonoelastography '… clearly show malignant lesions to have a significantly higher elasticity score than benign lesions. The best cut-off to differentiate benign from malignant lesions is a Uelo score of between three and four; one on the Uelo scale describes soft tissue and five stiff tissue. We arrived at a sensitivity of 96.9% and a specificity of 76.9%, which translates into diagnostic reliability of 82.9%.'

Shear wave technology builds on elastography with an added benefit: tissue stiffness can be evaluated not only qualitatively but also quantitatively. Currently, shear wave elastography is under study in 17 international centres. For BI-RADS 4 lesions the increased diagnostic specificity offered by shear wave is desirable, she pointed out.

Due to gamma camera advances, scintigraphy is experiencing a slight comeback in radiodiagnostics, although only reliable for detection of lesions larger than 11 mm. Specificity is about 60%.

High radiation exposure remains the major limitation of nuclear medical imaging. Positron emission tomography (PET) and single photon emission tomography (SPECT) visualise metabolic process in cells. Fusion imaging, a combination of PET and computed tomography (CT), further increases spatial resolution. However, Prof. Schreer pointed out that the spatial resolution offered by fusion imaging is still insufficient for primary tumour staging.

As a 'by-product' of tumour detection, visualisation of increased metabolic activity in cells also detects inflammatory processes. Currently, the visualisation of receptors on cells via molecular imaging technology is being explored. Using neoangionesis non-invasively in screenings would be an interesting development, the professor noted.

Pathologist **Professor Giuseppe Viale** (European Institute of Oncology, Milan, Italy) spoke of the limitations and perspectives in genetic profiling and proteases.

Although very optimistic about gene expression profiling, current molecular assays present some problems: These tools are prognostic, but not predictive – yet they are often handled as if the latter. Currently, two prospective clinical trials are testing the predictive value of molecular assays: MINDACT in Europe and TailoRx in the USA. Meanwhile, the list of the commercially available molecular assays grows. 'I'm afraid there's a certain pressure to use these assays in daily practice,' he said. 'First because we want to overcome the current uncertainties in the choice of therapy options; then because we like them – they're sophisticated and fascinating – and third, biotech companies are pushing hard to use these tests.' As a take home message Prof. Viale reminded the audience that the identification of patient subgroups that could benefit from expression profiles still depends upon the accurate assessment of clinical-pathological and biological parameters. This assessment will reduce the level of uncertainty in the choice of the systemic treatment. Only then, the added benefit of expression profiles can eventually be ascertained.


Ingrid Schreer


Giuseppe Viale


Tanja Fehm

Gynaecologist **Professor Tanja Fehm** (Women's Hospital at Tübingen University Hospital) explored the possible significance of circulating tumour cells (CTC) as a criterion in therapy selection. Since these cells' survival time in the bloodstream is short, their presence indicates an active source such as metastases or relapse. 'While the prognostic significance of CTC in adjuvant therapy is not clearly proven yet, current studies show promising results,' Prof. Fehm pointed out. Patients who test positive on CTCs show a markedly increased relapse rate. However, this result cannot be replicated after chemotherapy. In therapy monitoring CTCs might act as an indicator for secondary adjuvancy and thus help to optimise adjuvant therapy strategies.

'When metastases are present,' she continued, 'CTCs are already being used as prognostic markers. After the first chemotherapy cycle CTCs already show whether the body responds positively to the therapy. 'We might want to explore whether CTCs can, if necessary, be used after a month to indicate whether a change of therapy is advisable rather than waiting for three therapy cycles to be completed and then use imaging for therapy monitoring purposes,' he suggested, adding that, in therapy monitoring, CTC might fill a gap in real-time biopsy since the phenotype of the CTCs corresponds to the phenotype of the metastases. This means that the CTCs can be characterised in

the future of breast cancer care

accelerator is utilised to deliver a single dose of radiation (50 Gy in three minutes) with multi-energy electrons immediately after the removal of the primary carcinoma. 'The concept behind ELIOT is that local recurrences occur in 90 % of cases in the quadrant harbouring the primary breast carcinoma. So with ELIOT, we are able to pin-point the irradiation on the operative field. A dedicated disk of lead and aluminium is used as a protective device. Therefore, ELIOT reduces radiation exposure to the normal tissue as well as to deep organs like the lung.' Because the radiation course is shortened from 5-6 weeks to only one session, the problem of access to radiotherapy centres, especially in rural areas, is also solved.

Summing up, Prof. Veronesi presented his list of the most important, novel, targeted minimally invasive treatments:

- High-Intensity Focused Ultrasound (HIFU). This uses high frequency sound waves to heat up small accurately-targeted amounts of tissue to a temperature of 80-90ºC. The main advantage of ultrasound in radiotherapy is the real-time guidance without the need of surgical exposure or insertion of instruments into the lesion.
- Proton Beam Therapy (PBT). The energy that protons deliver to the tumour mass is much higher than the usual electron photon beams. While the latter go through the whole body, the irradiation with protons can be controlled to stop, when it has reached the target tissue and to unfold its complete power in the tumour volume first.
- Intra-operative Avidination for Radionuclide Therapy (IART). This is a complex, two-step procedure consists. First the exogenous molecule Avidin is injected in to and around the tumour bed during surgery. Next, the day after, radioactive biotin is intravenously injected into the tumour area. Because Biotin shows a high affinity to Avidin, the intra-operative treatment with Avidin allows for a fast and stable uptake of the radionuclides into the tumour cells.
- Endocrine and biomolecular treatments, like drugs targeting the HER2 receptor, which follow a 'target and control' instead of a 'search and destroy' strategy in cancer. These tumour-biological therapies enable increasingly tailor-made, individualised treatment for the patient.
- The concept of cancer stem cells as the 'root' of a tumour: 'Recent finding suggest that at the heart of every tumour lie a handful of malignant stem cells able to maintain the malignant tissue. In vitro and animal models have demonstrated that breast cancer stem cells are relatively resistant to both radiation and chemotherapy. We need to change our policy of treatment and try to identify markers and membrane receptors of these cancer stem cells as targets for new drugs. For surgeons, knowledge about the presence or absence of cancer stem cells in a sentinel node biopsy could be of great help in decision-making if dissection of sentinel node is needed or not.'

biology

a blood sample and thus give an indication of the phenotype of the metastasis. Comprehensive clinical studies are still required on this issue.

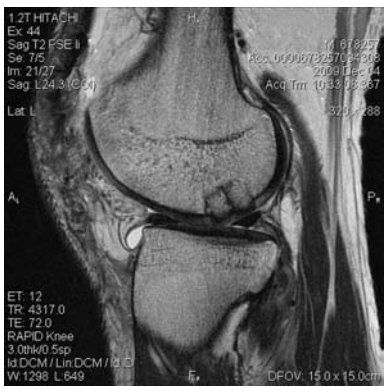
In his closing presentation, Surgeon **Dr Peter Schmid** (Charing Cross Hospital and Hammersmith Hospital, Imperial College London, UK) introduced epigenetics. Epigenetic factors are changes 'imposed' on the DNA sequence that controls gene expression; they are the switches that turn genes on and off. One of the most important epigenetic regulation mechanism is DNA methylation, which marks active and inactive DNA areas. Epigenetics, and above all methylation, are clinically significant because they deactivate tumour- suppressant genes. Thus Methylation can be used to influence the sensitivity of therapies. Epigenetic profiles undergo dynamic processes that can be recognised after only a few weeks, or even days. Moreover, epigenetic markers might have prognostic or predictive relevance. However, this has not yet been sufficiently validated. Dr Schmid expects epigenetic profiles of plasma DNA to become particularly important. 'Further research is required to determine the place of epigenetics next to molecular pathology and gene expression profiling,' he concluded.

Investigating sports injuries

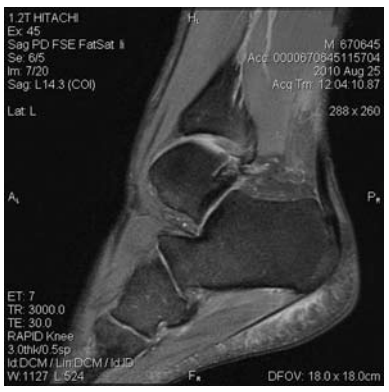
Radiologist **Dr Karl-Friedrich Schünemann** works in a group* practice in the small German city of Paderborn. Focusing on sports injuries and using MRI, CT and X-ray, the specialist medical team provides services such as neuroradiology, orthopaedics and CT-guided pain therapy. 'From the very beginning we focused on specialised radiology,' he explained. 'Today we offer a renowned out-patient spine service and perform many mammographies. We don't want to do assembly-line medicine; we want to provide excellent diagnostics,' he said. 'The fact that we count a number of professional athletes among our clients also attracts many amateur athletes who present with interesting sports-related issues.'

'When a player is injured and an examination unclear, the team physician calls me, explains the situation from his point of view, and asks me to perform an in-depth examination,' said Dr Schünemann. 'So, when the athlete arrives I already have quite a lot of information and rather targeted questions that need to be answered with MRI. Therefore we can tailor the actual MRI examination to the individual athlete's situation.'

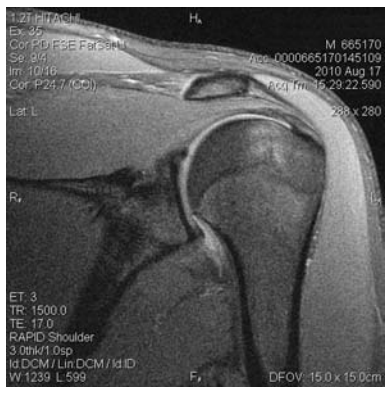
The basics are the same for a professional athlete as every other patient. 'No matter what kind of information was provided by the referring physician, we do a comprehensive and in-depth clinical assessment and anamnesis with any patient – whether a professional athlete, an amateur or anyone else. Based on the information we collect and the guidance received from the physician we can formulate a very precise question – which allows us to offer a precise answer. It is a distinct advantage to be able to discuss the case with the team physician prior to the MRI exam. The direct exchange ensures that no information is lost. And certainly, we also discuss the findings of the MRI scan as well as possible next steps, therapy options and a follow-up plan. All in all, the process is highly efficient and fast. After all, an athlete is expected to get back on the playing field as soon as possible and we are expected to help him do just that.'



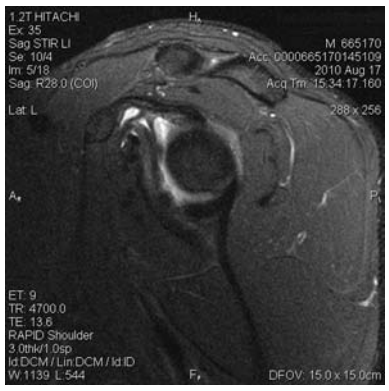
26-year-old basketball player (centre): Situation after post-traumatic cartilage flake fracture and after surgery (cartilage transplant)



Soccer Player (defence): Post-traumatic haematoma under the plantar aponeurosis



22-year-old handball player (amateur): Situation after second traumatic shoulder luxation, fractional inferior glenohumeral ligament



For radiologists, what is special about sports-related injuries?

'In sports medicine, MRI is the modality of choice for unclear joint issues. Beyond the thorough clinical assessment and anamnesis for every individual athlete, it's of utmost importance to gather information on the different training methods and the physical stress exerted during training sessions for the individual sports disciplines. You have to be familiar with the different sports, the techniques used and certainly the typical injuries.

'Since our team is specialised in the treatment of spinal conditions, such as slipped discs, if necessary, straight after MRI the professional athletes can undergo an interventional procedure, performed with ECLOS, the 16-slice CT from Hitachi.

' There's one peculiarity regarding the treatment of professional athletes -- we physicians have to comply with the anti-doping rules. Some athletes with spinal injuries receive cortisone, which means I have to report any cortisone medication to the national anti-doping agency NADA. We fill out a form that we submit to NADA and the athlete receives a copy, which he can present when he is asked to undergo a doping test.

Common injuries

'Every sport has its own typical injuries and injury patterns because very specific body parts and joints are put under extreme stress. With basketball players, as with players of any other "overhead" sport, such as tennis, we see many shoulder problems. 80-90% of the injuries we see in soccer players concern the knees and ankles.

Use of the Hitachi Oasis

'The Hitachi Oasis is an open MRI ,which means that the patient is no longer forced into a tunnel-like tube. From the sports medicine point of view the open architecture of the system offers more space and better access. Take basketball players: they are often very tall – over two metres. In addition, they have a strong, muscular build. With other MRI systems we frequently had space problems, not necessarily with all types of examination but, for example, with shoulder and spine examinations – and precisely those kinds of examinations are often needed for athletes.

'For athletes, and other patients, the advantage is the fact that the joint to be examined can be placed and examined in the centre of the magnetic field. We achieve excellent image quality, which is absolutely comparable to that of a premium-class 1.5 Tesla system.

The open system also facilitates scanning children, because parents can be close to their children, touch them and comfort them. We can examine children from about 4 years of age. It's not easy to examine a four-year-old, but with the open MRI we've been more successful than with the conventional machine – without medication!

'But the major advantage of the open architecture of the Hitachi Oasis is important to any medical discipline. We found that many more patients than we thought suffer severe anxiety or claustrophobia. Most patients who are frightened of confinement in the machine never even show up for an MRI. But with the open MRI many patients agree to a scan because they don't consider the machine as scary as conventional MRI.'

How many patients suffer such anxiety?

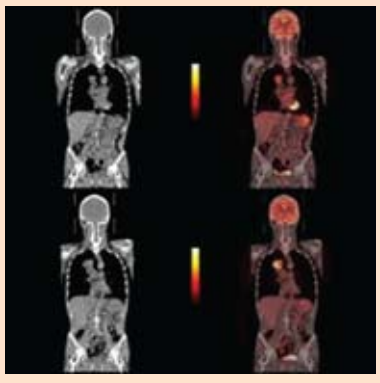
'I'd say at least 20-30%; on some days we even see 40% who refuse to be scanned in a conventional MRI system. That means the acceptance of the MRI procedure increases significantly with open architecture.'

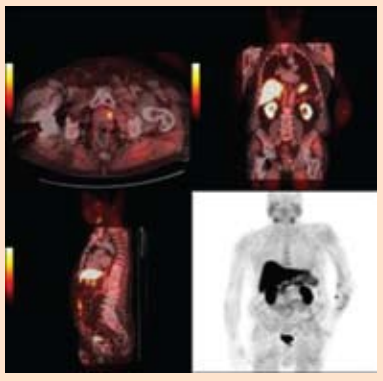
** Group practitioners include Hans-Ulrich Jarck MD, Karl-Friedrich Schünemann MD, Jürgen Wiesmann MD, Carsten Figge MD*
Details: www.roentgen-paderborn.de

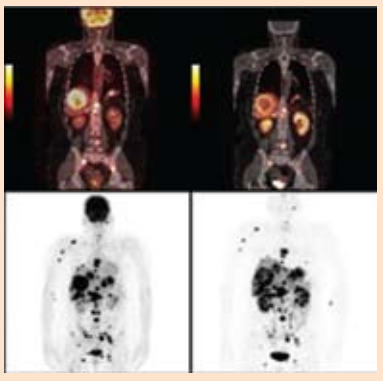
AN IMPROVED VIEW WITH PET/CT

Innsbruck focuses on the Gallium 68DOTA PET/CT

Late in 2009, GE Healthcare's 64 slice Discovery PET/CT 690 began its use in the University Clinic for Nuclear Medicine in Innsbruck, Austria. Apart from routine clinical examinations for treatment control via FDG (fluorodeoxyglucose), the scanner is also employed in clinical research -- particularly for Gallium 68DOTA PET/CT examination. 'We are a worldwide leader in this field,' **Professor Irene Virgolini**, Head of the University Clinic, pointed out. 'We've already supported many institutions in establishing Gallium 68 examinations.'







The procedure is particularly used in cases of neuro-endocrine tumours and radioiodine-negative thyroid carcinoma, where it is mainly used for process monitoring of high-dose treatment. 'We were significantly involved in the development of the generator that generates the Gallium 68, and we produce various compounds, so-called analogues, which are then used for PET/CT diagnostics,' said Prof. Virgolini. 'Currently, for example, we are in the process of developing a specific liver tracer with a Gallium 68 marker, which can then show liver reserve capacity. At the moment this is a market niche, which we hope to fill. We also have a tracer for angiogenesis imaging, which is already undergoing clinical studies. It is aimed at patients who take an angiogenesis inhibitor. We have high hopes that this tracer could have significant savings potential, if it enables us to determine the therapy response.'

A further important field is viability determination in cardiac examinations with unclear results. According to Professor Virgolini, the strength of the PET/CT here lies in the ability to display a clearer image of perfused areas with non-perfused areas due to its better resolution, analogue to the accumulation of FDG. Even though nuclear medicine has always delivered very good results in this field, the combination with a 64-slice CT is advantageous due to the image overlay.

In general, the Innsbruck Clinic has been very pleased with this new technology. 'One of the advantages is that the scanner is a lot faster, and the exposure to radiation is also lower,' Prof. Virgolini observed. 'Our objective for the current year is to carry out 3,500 examinations - clinical examinations as well as research-related ones.'

However, there is one downer, which also affects Austria: Medical insurers continue to refuse reimbursement of the FDG examinations. Prof. Virgolini: 'In the German speaking countries we are significantly behind in this field, even though the latest developments point towards a need for change in reimbursement policies.'

PROFILE

Eizo GmbH

Aiming for split-screen medical monitors

Siemens Automation and Drives (A&D) division developed and supplied monitors exclusively for Siemens Medical until, about 20 years ago, the customer base expanded and A&D ultimately supplied almost all major medical technology firms with monitors for integration into their systems.

In 2007, Siemens decided to focus on its core business and sell off its medical monitors division. At the same time, the long-established Japanese monitor manufacturer Eizo Nanao, which in 2002 had entered the medical imaging market with its RadiForce monitors, wanted to expand its medical monitors division. The company not only wanted to become number one in producing medical-grade monitors but also to establish a stronger presence in Europe. Following the A&D acquisition, Eizo Nanao founded the subsidiary Eizo GmbH Display Technologies, headquartered in Karlsruhe, Germany.

Production

Eizo monitors for surgery and interventional radiology, X-ray, angiography, endoscopy, CT and MRI are being developed in Germany. 'That has always been our strength,' Walter Kupper, Director Product Management & Marketing pointed out. 'Ultrasound, PACS and mammography systems are mainly being developed in Japan because the latter two applications are very similar. Basically a mammography monitor is a PACS monitor specialised in mammography.'

Currently the company is in the process of consolidating many separate monitors into one large-screen monitor. 'In an angiology room, for example, you have six to eight monitors that are now being replaced by one big screen subdivided into six or eight fields,' he explained. 'This isn't merely a front-end issue because you still have to handle the signals originating from the different sources. These different signals are fed into a computer system located upstream from the monitor. Eizo delivers a complete image management system, not just the hardware.

'Apart from the fact that one screen saves space and reduces clutter, the physician can zoom any image up to a very large size and minimise or hide all images that are not interesting for the time being. Certainly, he can adjust the layout to his individual needs.'

Of the system, launched about two years, and in general use for about a year, he agreed that 'It's pretty expensive,' but added, ' While at first glance there's no obvious financial advantage on the purchasing end, there is a very significant advantage in the workflow. That's why physicians love our system and are prepared to pay for it – and they successfully convince their hospital financial management that it's a good investment.

The future

The trend towards large monitors in medical technology he believes will continue. An interventional radiology lab has a patient examination room with monitor and a control room in which there is a monitor that duplicates the examination room monitor's landscape. Up to eight monitors may be connected, with each connected to a work station and each equipped with a keyboard and mouse. 'So far, we have replaced the separate monitors in the examination room with a large-screen monitor. The next logical step is to do the same in the control room.' Thus, in the next-generation control room, monitors will be replaced by one large screen and the entire system will be operated with one keyboard and one mouse. However, the staffing level will not change, he pointed out. 'Most of the time one or two physicians are in the control room, which will not change. But they will no longer receive the information on five or even eight monitors but on one or two large screens.'

COUNTRY ROUNDUPS

UNITED KINGDOM

Concern over insulin drug withdrawal: Loss could add almost €11 million to England's NHS drugs bill

Drug company Novo Nordisk's decision to pull its Mixtard 30 insulin drug from the UK could add almost €11 million to the NHS drugs bill in England alone, according to an editorial in the *Drug and Therapeutics Bulletin* (DTB). This decision could also leave thousands of patients dependent on others to help them take their insulin, said DTB, as it launched its *Don't Drop Mixtard 30* campaign in an attempt to convince Novo Nordisk to change its mind.

Citing commercial reasons, in late June the pharmaceutical firm announced its intention to withdraw its only conventional human biphasic insulin, Mixtard 30, from the UK market by the end of 2010.

The move will affect an estimated 90,000 patients across all age groups with Types 1 and 2 diabetes who need insulin treatment. Guidelines on the care of patients with diabetes, including those issued by the National Institute for Health and Clinical Excellence (NICE), recommend human biphasic insulin as the treatment of choice for these groups.

There are alternative biphasic analogue insulins, but these are all more expensive. 'Assuming a direct swap to Novo Nordisk's analogue biphasic insulin, NovoMix 30, the increased prescribing costs could be over £9 million in England alone,' DTB pointed out. 'This is quite apart from the extra resources needed to review patients, to discuss and decide on alternative treatments, and the disruption and concern such changes may cause for affected individuals.'

The decision also means that biphasic insulin will no longer be available in the ergonomic InnoLet device, which '…could therefore leave many users who have poor eyesight or reduced manual dexterity, dependent on others for their insulin administration,' added DTB.

Published evidence shows that the alternative biphasic analogue insulins are no better than conventional human biphasic insulins in terms of their effectiveness, long term outcomes, or safety.

But Novo Nordisk's biphasic analogue insulin is prescribed 50% more often than Mixtard 30, DTB pointed out, possibly because it comes in a particularly convenient pen format (FlexPen).

'It is possible that the decline in Mixtard 30 sales...could have been prevented if it had also been available in the FlexPen,' commented DTB, adding that the drug is available in this format in Germany, where there do not seem to be any plans to withdraw it.

'My personal experience is that patients prefer the FlexPen for their biphasic insulin. It's very easy to use,' said Dr Wing May Kong, a member of the DTB editorial board and consultant endocrinologist at Imperial College London. 'It makes me wonder to what extent this drift from conventional to analogue insulin is device driven,' she said in an accompanying podcast. German healthcare professionals, she added, had lobbied for conventional insulin to be available in the FlexPen.

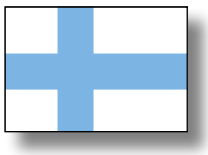
The leading charity Diabetes UK has also remonstrated with Novo Nordisk about the drug's withdrawal in this country.

DTB is running an online petition at www.dtb.bmj.com to protest Novo Nordisk's decision, and said: 'We urge all those with an interest in cost effective prescribing to campaign with us against Novo Nordisk's short-sighted decision.'

** Drug and Therapeutics Bulletin is one of more than 30 specialist titles published by BMJ Group: www.dtb.bmj.com*

FINLAND

Across the country, health initiatives to help reduce the incidence of diabetes are showing signs of success



Finland's national programme for the prevention of Type 2 diabetes (T2D) has already seen a significant sector of the population making meaningful lifestyle changes, while work is also progressing on Type 1 diabetes research in children.

A key figure in this drive to combat diabetes is Professor Jaakko Tuomilehto, at the University of Helsinki's Department of Public Health. He explained that a national programme for the prevention of T2D was launched in Finland with three concurrent strategies for prevention: The population strategy, high-risk strategy, and strategy of early diagnosis and management. With primary and occupational healthcare providers co-ordinating the initiative, the implementation project called FIN-D2D was first conducted in five hospital districts with a population of 1.5 million, from 2003 - 2007.

Its aims were to reduce the incidence and prevalence of T2D and prevalence of cardiovascular risk factor levels; to identify individuals who were unaware of their T2D; to generate regional and local models and programs for the prevention of T2D; to evaluate the effectiveness, feasibility and costs of the programme; to increase the awareness of T2D and its risk factors in the population, and to support the population strategy of the diabetes prevention programme.

Jaakko Tuomilehto

While the long-term impact of the Finnish Diabetes Prevention Study has yet to be realised – with a further follow-up report planned for 2012 – Prof. Tuomilehto said the key activities developed have already become a routine facet of primary care in Finland.

The professor, who has been a pioneer in the fight against diabetes for nearly three decades and as a young clinician was part of the team that helped address the poor rates of cardiovascular health in Finland in the1970s, said: 'This first part of the nationwide programme has concentrated in developing tools and methods for the detection of high-risk individuals and training health personnel. In the areas where FIN-D2D was implemented a significant decrease in the mean level of body-mass index, the strongest risk factor for T2D, has been detected for the first time.'

Longer term, researchers say they will be able to measure the changes in the incidence of drug-treated T2D patients from the national prescription register

T2D is high in Finland, though comparable with other European populations, with obesity the key risk factor, he said. 'We know how to prevent T2D with lifestyle modification and how to identify high-risk individuals with simple risk score tools. We now need to learn how this knowledge can be best translated to the real-life situation. Such research is ongoing in Finland and elsewhere. Thus, I

Seeking the genetic basis of diabetes

Scientists identify 12 new genes associated with Type 2

Mark McCarthy

PHIL SAYER

Researchers have identified 12 new genes associated with Type 2 diabetes (T2D) that look set to improve the understanding of the processes underpinning the condition.

The findings could also offer new biological pathways that can be explored as targets for new therapies to tackle T2D.

The new genes were identified by a consortium of scientists led by Professor Mark McCarthy, of the Wellcome Trust Centre for Human Genetics at Oxford University, in the largest study so far of the connections between differences in people's DNA and their risk of diabetes.

Prof. McCarthy said: 'The signals we have identified provide important clues to the biological basis of T2D. The challenge will be to turn these genetic findings into better ways of treating and preventing the condition.'

The identification of 12 new genes brings the total number of genetic regions known to be associated with T2D to 38. The genes tend to be involved in the working of pancreatic cells that produce the hormone insulin, the control of insulin's action in the body, and in cell-cycle regulation.

Prof. McCarthy said it was a significant theme to the research that several of the genes seemed to be important in controlling the number of pancreatic beta-cells and added: 'This helps settle a long-standing controversy about the role of beta-cell numbers in T2D risk and points to the importance of developing therapies that are able to preserve or restore depleted numbers of beta-cells.'

To arrive at their findings, the researchers (from the UK, Europe, USA and Canada) compared the DNA of over 8,000 people with T2D with almost 40,000 people without the condition at almost 2.5 million locations across the genome. They then checked the genetic variations they found in another group including over 34,000 people with diabetes and almost 60,000 controls.

Although the study found 12 new genetic regions where the presence of a particular variation in DNA sequence leads to an increased susceptibility to T2D, the individual effects are small.

The scientists say that possessing one of these gene variants leads to only a marginal, but clear, increase in the risk of developing the condition.

But the key, say researchers, is that the potential impact of the findings in terms of new biology and possible therapeutic developments could be significant. 'Gradually we are piecing together clues about why some people get diabetes and others don't, with the potential for developing better treatments and preventing the onset of diabetes in the future,' said Prof. McCarthy.

Dr Jim Wilson, Royal Society University Research Fellow at the University of Edinburgh and a member of the research team, said that a 'very interesting finding' of the research was that the diabetes susceptibility genes also contained variants that increased the risk of unrelated diseases, including skin and prostate cancer, coronary heart disease and high cholesterol. 'This implies that different regulation of these genes can lead to many different diseases.'

The researchers now plan to use the availability of new tools for sequencing the whole human genome to explore further sources of DNA sequence variation that have been missed in previous efforts, in an effort to pin down the remaining genetic basis for T2D.

Report: Mark Nicholls

believe that T2D prevention will be successful in the near future across the population.'

Prof. Tuomilehto said it has been satisfying to demonstrate the potential for the prevention of T2D. 'Type 2 diabetes prevention was not discussed at all in the 1980s when I started to advocate it. Today, prevention of T2D has become a reality and is high on the agenda both for research and primary healthcare.'

He also established the first large project focusing on *Childhood Diabetes in Finland* in the 1980s to discover the aetiology of Type 1 diabetes (T1D).

This, he said, appears the main reason for the high incidence of T1D in children in this country is genetic.

Currently, there are several new projects on T1D among children being conducted by other researchers in Finland but, he added, so far no further evidence on environmental/lifestyle risk factors have emerged.

Report: Mark Nicholls

CZECH REPUBLIC

Deadly disease, dismal summary

Recently, the prevalence of diabetes mellitus in the Czech Republic reached 7-8% (783,321 diabetics were treated last year – 419,362 females and 363,959 males) but this figure leaps to 25-30% for diabetes related hospitalisations.

In addition, further on, last year's statistical reports read that less than one fourth of the patients (188,000) were solely on diet, chronic complications were seen in 28 % of these patients, 21,700 people with reported diabetes died (six of them younger than 19 years) and, for 1,967 people the cause of death was stated as 'diabetes'. Interestingly, diabetics under aged 19 years constitute 0.3% of all patients – 1,909 of them were registered. Also, 221,000 diabetic complications were reported – most typical, such as chronic kidney impairment, vision deterioration or loss, atherosclerotic changes, infections and neuropathies.

Healthcare provision was centred on diabetology ambulances (treating 84% of all diabetics) and private practices (treating 16% of all diabetics). All-in-all, over 2.1 million medical examinations and/or treatments were performed in 501 ambulances countrywide.

Public efforts, for free

For example, back in April this year, Czech Diabetic Association, in partnership with Abbott Diabetes Care division, launched the second round of free public assessments of glycaemia and cholesterolaemia. Under the slogan *Diabetes, measure your risks!* the event was quite a success; over and eight-week period, almost three thousand people had their blood glucose and cholesterol levels checked in five Czech towns -- Prague, Brno, Plzen, Liberec and Ceské Budejovice.

Furthermore, blood pressure (BP) checks were offered to all volunteers as an important part of a complete physical examination that potential diabetic patients should have recorded in order to raise awareness of all crucial diagnostic parameters needed to identify cardiovascular disease and diabetes mellitus. The average age of those who wanted their BP and glycaemic/cholesterol levels checked was 56 years; two thirds of these were women. Hyperglycaemia was identified in 20%, hypercholesterolaemia in 32%, and hypertension in 40% of the volunteers – numbers not critical but alarming.

Thousands of patients, hundreds of families

It is estimated that 15 to 20 thousand Czechs suffer monogenic diabetes mellitus. Motol teaching hospital, in cooperation with the paediatrics department of the 2nd Faculty of Medicine in Prague, is vigorously continuing its monogenic diabetes-related activities for children. The scientific project also known also as *Monogenic diabetes – from genetics to treatment* received co-funding from the 'Norway Funds' a year and a half ago, which helped considerably.

The above mentioned medical institutions are the first in the Czech Republic trying to test for monogenic diabetes in children and adolescents with hereditary diabetes, and flexibly adjust their treatment according to the results obtained. Motol deputy manager for EHP/Norway funding, Dr Vladimír Řeha, underscored the importance of scientific research funding secured from abroad, and noted that medical care in EU member countries is equalising. So, a meaningful international cooperation is coming to life, hence project funding reached a not negligible €443,000, and it could boast that this is currently the only granted Czech project of its kind.

Motol teaching hospital teams have been running laboratory diagnostic tests for over two years and have truly succeeded in establishing routine genetic diagnoses of the mutations that put their bearers at risk of this disease. So far, 1,182 children and/or adolescents from 366 registered families and patients from 201 families have had their genetic diagnoses successfully set, and optimal treatment proposed.

Report: Rostislav Kuklik

Sources: The Czech Diabetes Association; Czech Diabetology Society; International Diabetes Federation; FN Motol, Norway Funds, Ústavu zdravotnických informací a statistiky (ÚZIS), and Abbott Diabetes Care division

46th EASD Annual Meeting

StockholmMässan conference centre, Sweden

20-24 SEPTEMBER 2010

Professor Claes-Göran Östenson, chair of the Local Organising Committee of the 46th European Association for the Study of Diabetes annual meeting, will welcome visitors in this the bicentenary year of the renowned Nobel-prize giving Karolinska Institute.

Since its foundation in 1965, the EASD annual meeting has become the world's largest international annual conference on diabetes research, drawing in scientists, physicians, laboratory technicians, nurses and students. At last year's event there were 16,577 participants from 115 countries. Today, EASD has more than 6,300 members.


Claes-Göran Östenson

The EASD encourages major end-point related trials carried out to evaluate diabetes treatments and the organisation provides an outstanding forum to announce those results to the scientific community.

From 2,159 abstracts submitted, the Scientific Programme Committee has selected 1,352 for presentation. Topics include:

- **Auto-antigens in diabetes**
- **Beta-cell imaging**
- **The future of anti-diabetic drug development**
- **Diabetes, obesity and cancer**
- **Diabetes in the context of psychiatric illness**
- **Breaking news from clinical trials**

Made up of six parallel tracks, the programme includes symposia, keynote lectures and debates, covering both basic and clinical science. The scientific programme includes the Claude Bernard Lecture, Minkowski Lecture, Camillo Golgi Lecture and the Albert Renold Prise Lecture. *The Rising Star Symposium* aims to identify promising and innovative young researchers who are developing their research activities in Europe.

Titles of the lectures and symposia are online at www.easd.org. Additionally, soon after the event, webcasts of the major lectures will be accessible via the website.

At the EASD

Diabetes and Risk of Death in Cancer Patients

Does diabetes further increase the risk of death in patients diagnosed with cancer? A team at the Johns Hopkins School of Medicine in Baltimore, Maryland, has discovered something very sobering: Cancer patients are 51% to 85% more likely to die after surgical resection if they had pre-existing diabetes

Hsin-Chieh Jessica Yeh PhD, Dr Yeh, an assistant professor of general internal medicine and epidemiology, was principal investigator of a meta-analysis on this subject. She and a team of professors identified over 8,800 articles published in peer review journals evaluating the effect of diabetes on any prognostic outcome in cancer patients. 20 of these were the most relevant to postoperative mortality, and an analysis of what they reported was published in *Diabetes Care*, the official journal of the American Diabetes Association (April 2010). The studies evaluated the effect of pre-existing diabetes in patients with colon or colorectal cancer, oesophageal, lung, pancreatic, and prostate cancers, and were conducted in Asia, Europe, and the USA. They ranged in size from evaluating 70 patients to more than 32,500 patients. The percentage of patients with diabetes ranged from 1% to 42%.To the surprise of the research team, there was not enough data published on postoperative mortality after surgery for breast cancer and endometrial cancer to analyse the risk of diabetic and non-diabetic women.

Today, an estimated 7% of all adults over age 20 and living in industrialised economies have diabetes. However, an estimated 8%-18% of individuals who are diagnosed with cancer are also diabetic. Dr Yeh explained that individuals with diabetes have a higher risk of developing cancers of the breast, colorectal, endometrium, liver and pancreas. People who are obese and sedentary are at risk of developing type 2 diabetes and cancer.

'Because diabetes can lead to infections, acute cardiovascular events, and metabolic changes, cancer patients may also be at greater risk of dying after they have had surgery. It is well known that elevated blood sugar increases the risk of complications from any type of surgery,' Dr Yeh pointed out.

The researchers speculated several factors relating to the fact that pre-existing diabetes might specifically influence postoperative mortality risk after cancer surgery. One is series infection or sepsis. Peri-operative hyperglycaemia predicts in-hospital infection. Peripheral arterial disease and bladder dysfunction also represent chronic predisposing factors. Myocardial infarction is another. 'Diabetes is a chronic risk factor for atherosclerosis in multiple vascular beds, including coronary arteries. Add the short term effects of hyperglycaemia on platelet function and thrombotic tendency, perioperative renal failure, and chronic kidney disease, all common to diabetic patients, all which may aggravate cardiovascular risk,' Dr Yeh explained.

Her advice: Oncologists, surgeons, and cancer patients should be aware of the excess post-operative mortality risk related to diabetes when considering treatment options. She suggested that more emphasis be placed on peri-operative diabetes care because this treatment might be helpful. However, whether better peri-operative glucose control would reduce the mortality risk is questionable, because intensive insulin therapy has not provided consistent benefits in clinical trials of patients in intensive care units.

Dr Yeh will discuss diabetes and cancer death at the EASD annual meeting.

Report: Dot McSherry, i.t. Communications

Standardised algorithms and protocols for diabetic

Dr Susan S Braithwaite, a visiting clinical professor in endocrinology at the Department of Medicine, University of Illinois, Chicago, specialises in the management of hyperglycaemia among hospitalised patients. Hyperglycaemia, the presence of an abnormally high concentration of glucose in the blood, is a common occurrence in adults who are hospital in-patients, especially among diabetic patients. This condition is associated with many risks, such as surgical infection when undergoing cardiac surgery, and is also a strong predictor of adverse clinical outcomes from conditions such as stroke, congestive heart failure, acute myocardial infarction and community-acquired pneumonia.

With today's pandemic of obesity and escalating levels of type 2 diabetes, hospitals must be proactive to identify patients who do not realise they are diabetic. Staff clinicians are increasingly challenged by the need to control hyperglycaemia without introducing morbidity or mortality that therapeutic misadventures during the treatment of hyperglycaemia can cause. The nature and severity of underlying medical conditions, comorbidities, organ dysfunction and nutritional status all cause insulin resistance to fluctuate. Because medications and carbohydrate exposure frequently change in a hospital environment, the treatment regime patients followed outside the hospital may no longer be appropriate or even safe, Dr Braithwaite emphasises.

'The complexities of institutional care also add constraints that healthcare providers must be cognisant of to work within. Coordination of blood glucose monitoring, nutrition, and administration of medication all are needed for the successful management of diabetic patients. Handoffs by providers, shift changes of nurses, and patient relocations between the emergency department or the pre-admitting office, waiting rooms, the operating room, intensive and critical care units, general wards, and finally, home treatment, all require communication strategies,' Dr Braithwaite adds.

Both individualised patient care and institutional standardisation of procedures to provide excellence in care are needed to maintain the safety of the diabetic patient. To make this goal easier to implement and achieve, Dr Braithwaite is working on the development of algorithms designed to deliver insulin with a certain degree of mathematical consistency for intravenous insulin use, and order sets that integrate the components of monitoring and treatment into an appropriate pattern for patients who receive their insulin by subcutaneous injection.

'Different distinct pathways are needed for patients who are eating and those who are not eating, with choices for the administration of subcutaneous insulin,' Dr Braithwaite said. 'By standardising subcutaneous protocols with a variety of choices representing best practices under various conditions care for diabetic patients will become more uniform in its diversity and reduce the risk of error. My work is to create order sets capable of delivering the individualisation needed by patients, and then to get physicians' prescribing styles to converge under these protocols so that the meaning of their orders will be recognisable by pharmacy and nursing staff and will represent best medical practices.

'The use of protocols also makes patient treatment more efficient. Without protocols in place, every order no longer has to be re-evaluated as a new idea. When on-call physicians are called, because they are not familiar with the patient they often take the action that requires the least re-evaluation, but the decision they make may not be what the patient really needs. With protocols in place, for many contingencies the nurses no longer have to call the ordering physician or the on-call physician with questions and requests for clarification.

'Individualisation can be met with a standardised approach, whether provided on paper or on an electronic medical record much like the format of a computerised order entry system. Diversification is needed with respect to an individual's medical condition and treatment, yet the standardised protocols abolish peculiarities that make it hard for the readers of a physician's order to interpret what was meant. Additional orders for specific situations, such as whether or not to withhold insulin if a patient misses a meal or has an interruption in tube feeding, are readily available.'

Dr Braithwaite also stresses that the use of protocols will reduce errors. 'It is important for a patient's physician who is knowledgeable about and has thought about the patient's case to attach the correct preventive instructions along with insulin orders. But the physician may forget, or the additional orders mis-transcribed, or the orders are misplaced. With protocols defined within distinct pathways, all of the options are there, and can be filled in by checking off a box or filling in a number on a form. The pharmacy has a standard way of handling each item, and this will appear on the medication administration on record as a pre-printed additional direction with the medication.'

But she warns that many of the current computerised order entry systems are quite rudimentary. Orders for prescription medications are placed in isolation, without being seen as part of a pattern of care. Order sets or programmed pathways are needed to integrate the components of diabetes care, such as a matching of point-of-care glucose tests, meals, and medication. Insulin delivered intravenously creates even more complexity.

OBESITY SURGERY ROSE TEN-FOLD IN TEN YEARS

England - The use of bariatric or weight loss surgery has increased ten-fold in National Heatlh Service (NHS) hospitals since 2000, according to a study published in August on **bmj.com**. The researchers suggest that one reason is the increased demand by obese patients now more aware of this treatment option.

Bariatric surgery, which reduces the risk of death, hospital admissions and long term NHS costs, is recommended by the National Institute for Health and Clinical Excellence (NICE) for people with morbid obesity for whom all non-surgical weight loss therapies failed. But little is known about who is actually having bariatric surgery in England.

Thus researchers led by Omar Faiz, Senior Lecturer and Honorary Consultant Gastrointestinal Surgeon at Imperial College, St Mary's Hospital, London, set out to analyse national outcomes after surgery for obesity in the NHS in England. Using the Hospital Episode Statistics database, the team identified all adult patients who had a first elective bariatric procedure (gastric bypass, gastric banding or sleeve gastrectomy) between April 2000 and March 2008.

Mortality rates 30 days and one year after surgery were recorded, with hospital stay duration and unplanned re-admissions. 6,953 bariatric procedures were carried out in the study period. Procedures rose more than ten-fold from 238 in 2000 to 2,543 in 2007

Patients selected for gastric banding had lower post-surgery mortality and readmissions and a shorter length of stay than those selected for gastric bypass. Patients with comorbidities showed poorer post-surgery outcomes than other patients.

The percentage of laparoscopic procedures also increased from 28% in 2000 to 75% in 2007. However, no significant increase in mortality or unplanned re-admission was seen over the study period, suggesting that laparoscopy has been introduced in a safe manner into the NHS, the researchers observed.

Aired at EFORT

Guidelines for Charcot Foot, amputation avoidance, and approaches to fractures

The first subject aired at the EFORT meeting was vascularisation and poor blood supply in diabetics -- and when to amputate, or not

When Swiss orthopaedic surgeon **Dr Marino Delmi**, Past-President of the Swiss Foot & Ankle Society, Member of the Council of the European Foot & Ankle Society, and of the Scientific Foot & Ankle Council of the European Federation of National Associations of Orthopaedics and Traumatology (EFORT), met with other experts in the field, three critical diabetes topics were explored, *Meike Lerner* reports

Marino Delmi

Vascularisation

'We discussed what is necessary to maintain and spare the limb, especially the big toe and so on, and, if we have to amputate, the minimal amount we can carry out to maintain the most of the limb,' said Dr Delmi. 'With current techniques for limb sparing, surgeons amputate less and less. With the vascular status blood supply check we have an increasing number of good techniques and we also have some surgical techniques that can be used as vacuum therapy (VAC) to help heal the scars.'

Diabetic Fractures

The second topic was diabetic fractures -- particularly of the ankle and foot. Problems include the vascular supply, neurological status, neurotrophic skin, nerves and bones, which are often osteoporotic. 'An ankle fracturecan lead to an important foot deformity, which is very tough to treat and could lead to amputation. It is very important to recognise the fact that the diabetic patient is not a normal fracture patient and must be treated with some specific techniques adapted to the patient, with some use of cement and specific screwing, and with more solid implants. We have to brace the patient's foot and keep it immobilised for a longer period of time. All these could lead to a better evolution of the diabetic fracture, with less morbidity, wounding and infection, etc. If a surgeon is not aware of this, he may treat the diabetic patient with fractures in two ways, first as a normal patient with diabetic bones and soft tissues, or like a diabetic patient who is not normal and do no surgery, and so on. We should treat a diabetic patient with fractures as a normal patient, but with the postoperative care of the diabetic. Up to now this was not accepted at all. So, surgeons first have to check what kind of patient they are treating.'

Their meeting and this discussion has lead to guidelines, he said: 'The first one is to recognise that a diabetic with a fracture is not the usual patient, so the bones and joints must be considered as for a normal patient but with specific, more solid implants, more solid devices, which produces better results, avoid breakage of implants, infection or Charcot Foot.'

Charcot Foot

Charcot Foot is a neuropathic foot but with a good vascularisation/ blood supply, Dr Delmi pointed out. 'We don't know why it develops; probably it's due to repetitive micro trauma with added problems linked to neuropathy. We observe the full progress, the deformity or the foot with multiple bones fractures. Multiple dislocations of the joints can lead to deformity, which can be very important in the foot and ankle and lead to challenging skin ulcers. It's not a common problem… but a very tough one. It can be seen in almost 10% of diabetic patients, from 1%-20% depending on the status. 10% is not a few, especially when you know that Charcot Foot can be very disabling if the foot cannot fit into a good shoe or cannot be braced.

'The orthopaedic surgeon, diabetic doctor, or the dermatologist must recognise this entity first -- I mean recognise fractures in a diabetic patient with a neuropathy and first treat the entity conservatively, but with special regard to this illness. And, if you have a deformity you can stabilise or brace it. If this doesn't work you must take surgical measures and consider strong devices and strong implants.

The role of interventional radiology

'MRI is important, particularly to check for the presence of an abscess or osteomyelitis , and SPECT-CT -- a mix of bone scan and CT scan – enables us to see where the inflammation is active; this inflammation is linked with bone deformities or infection. It is very important to be sure that the deformity is active, because you can have a deformity that is inactive, which means you don't have to treat the deformity. However, if it is active, and the pain is coming from there, you'll see that better with a SPECT-CT than a CT scan.'

Interventional radiology

includes a few methods to treat and revascularise diabetic feet. It was previously suggested that this was only the role of the surgeon but has become also to do with radiologists, Dr Delmi pointed out that revascularising the diabetic foot is holistic – it involves the vascular surgeon, orthopaedic surgeon, radiologist etc. 'For example within the amputation process, before amputation, one of the ways to save or to spare the limb is for a vascular surgeon or radiologist -- using the new radiology techniques -- to increase blood supply to the foot.'

in-patients

'Carefully constructed intravenous insulin algorithms that relate the insulin dose to a model of what action is expected to occur have the potential to be safer and more successful than arbitrary rules. Arbitrary rules do not offer the flexibility that is needed to provide safe care for patients receiving intravenous insulin infusion. The algorithms need to be constructed based on underlying concepts that relate the estimates of needed insulin infusion rate to a patient's specific condition, the previous insulin infusion rate, the patient's previous response (rate of change of blood glucose), the current blood glucose, and the distance of the current blood glucose from target.'

Dr Braithwaite's specific recommendations, including algorithm and protocol development, have been published extensively in peer-review medical journals and texts. She will be speaking about this subject at the annual meeting of the European Association for the Study of Diabetes in Stockholm in September.

Report: Dot M. McSherry, i.t. Communications

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Subscriptions
Janka Hoppe, European Hospital, Theodor-Althoff-Str. 39, 45133 Essen, Germany
Subscription rate
6 issues: 42 Euro, Single copy: 7 Euro. Send order and cheque to: European Hospital Subscription Dept

Printed by Frotscher Druck, Darmstadt
Publication frequency bi-monthly
European Hospital ISSN 0942-9085

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