

# EUROPEAN HOSPITAL@ ESC2008



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## HOT TOPIC cardiovascular imaging

Every summer the European Society of Cardiology (ESC) holds Europe's biggest annual meeting of specialists in cardiovascular medicine, inviting and drawing in top international medical professionals. *Karoline Laarmann* asked **Professor Kim Fox**, President of the European Society of Cardiology and Consultant Cardiologist at the Royal Brompton Hospital, and professor of clinical cardiology at Imperial College, London, UK, about the most relevant issues and highlights planned for this year's programme.

**Last year's key focus was on heart failure. What will be this year's hot topic?**

**KF:** 'This year we decided to go for cardiovascular imaging because any cardiovascular condition that will be discussed during our congress always involves imaging in some form. Imaging is the cornerstone not only for diagnosing a condition but also to assess prognosis and tailoring individual treatment, too. By imaging we are talking about procedures from the simplest form such as the electrocardiogram to the most complicated non-invasive imaging techniques – MRI, nuclear imaging, echocardiography and, more recently, car-

diac CT scanning, and of course not forgetting to mention all the invasive techniques: cardio-angiography and cardiac catheterisation.'

**Which of the current imaging modalities is making the strongest progress?**

'The gold standard is multimodality imaging, because although a single tool may be sufficient, patient evaluation is often best when used in conjunction with other techniques. Every imaging technique has its individual strengths and weaknesses; they all give a different piece of information, so it depends on what you intend to measure.

Therefore one of the hot ESC topics will be to discuss which are the right imaging tools to use for a special problem. Of course we have considerable hopes in molecular imaging. It may be the tool to identify different forms of heart muscle diseases that may respond to different therapies and, in particular, may respond to stem cells. If it were to be shown that stem cells were to be beneficial, then to deliver the stem cells will require sophisticated imaging. The second hope we nourish in molecular imaging is to identify vulnerable plaques. We've just started to get some imaging information by using intravascular ultrasound of the coronary artery.'

**What form does work sharing take between cardiology and radiology imaging?**

Nowadays the management of a patient is multidisciplinary, to achieve the best quality of healthcare. As a cardiologist I think that radiology is extremely important in particular cases where physics is involved – radiation in particular. Radiologists need to be involved in ensuring that proper safety is taken into account. However, when it comes to actually deciding which imaging tool should be used for a patient, the cardiologist must be the person to make the decision. The most controversial issue here

is: Who should execute the procedure? The demarcation lines for that are changing currently and they differ from country to country. In the UK, for example, the radiologist will lead on cardiac CT, most of the others by cardiologists but with special expertise in imaging. I assume that coronary CT will probably remain the area of radiologists just now.

**What will be the biggest challenges for cardiology in the future?**

'Heart transplantation is a fantastic technique but we clearly need to think about some form of alternative technique, which may be stem cells or a form of artificial heart. Better still, of course, would be better implementation of prevention. We probably could deal with most of the cases of heart failure if prevention would be better, which brings me to obesity, which causes an increasing number of heart diseases. Last year, at the ESC opening ceremony, I emphasised my dislike of smoking. Now I see child obesity as a major issue to take care of. But it is much tougher to handle because you cannot legislate what people eat. The trouble is that fast food is much cheaper than a healthy diet. It will take huge educational programmes to accomplish a change of thinking.

'Finally, it would be very helpful to identify the 20–30% of patients benefiting from treatment with drugs, because this would lead to enormous cost savings and allow access to medicinal treatment for people who truly need it. What we are doing now is treating the whole population with a drug or procedure from which only a few profit. But the most important thing to do in cardiology is prevent ischaemic heart disease. We have to identify the people who show an aggravated risk to optimise our strategies of prevention and treatment based on the individual.'

### euHeart

#### Aiming to personalise CVD diagnosis and treatment

Royal Philips Electronics is to lead 'euHeart', the new European Union (EU) funded research project that aims to improve CVD diagnosis, therapy planning and treatment.

By targeting the diagnosis and treatment phases of the care cycles for heart conditions such as heart failure, coronary artery disease, heart rhythm disorders and congenital heart defects, the euHeart project complements the recently announced *HeartCycle* project (also led by Philips) which focuses on the long term management of chronic

heart disease patients.

The newly created 'euHeart' consortium aims to improve the diagnosis, therapy planning and treatment of CVD by developing computer models that simulate the normal and disease-related behaviour of each individual patient's heart and aorta.

Supplied with information about how specific CVDs affect heart function at molecular, cellular, tissue and organ level, these computer models have the potential to allow doctors to

*continued on page 2*

Professor Henning Sass (left) and Guy Peeters MD (right), chairmen of the Boards of Management of the Aachen and Maastricht university medical centres, respectively, with Dr Henk van Houten (centre), head of the Healthcare Research Programme at Philips Research, together for the signing of a letter of intent for a joint cross-border medical research programme for CVDs



#### euHeart Consortium membership (alphabetical order)

Academic Medical Centre Amsterdam (Netherlands); Berlin Heart (Germany); Deutsches Krebsforschungszentrum (Germany); HemoLab (Netherlands); Hospital Clínico San Carlos de Madrid Insalud (Spain); Institut National de la Santé et de la Recherche Médicale (France); Institut National de Recherche en Informatique et en Automatique (France); King's College London (United Kingdom); Philips Healthcare (Netherlands, Spain); Philips Research (Germany); PolyDimensions (Germany); Universitat Pompeu Fabra (Spain); University of Karlsruhe (Germany); University of Oxford (United Kingdom); University of Sheffield (United Kingdom); Volcano Europe SA/NV (Belgium).

Professor Kim Fox is the acknowledged European expert in the understanding, investigation and treatment of angina. His major roles in many significant international clinical trials include EUROPA, HPS, and ASCOT etc, which have revolutionised the treatment of this condition. He also chairs the task force producing the European Angina Guidelines as well as the committee responsible for the audit for the management of these patients in Europe.



Prof Fox has published over 400 papers in leading scientific journals, lectured to national societies worldwide, and has given the Finlayson Lecture to the Royal College of Surgeons in Glasgow, the St Cyres Lecture to the British Cardiac Society and the Andrea Cissalpino Lecture to the Italian Society of Cardiology.

For his services to cardiology he is an elected honorary member of the French Cardiac Society and the Japanese Circulation Society.

# Hypertension worldwide

## Social and cultural differences affect risk factors for cardiovascular diseases

Countries vary widely in their capacity to manage hypertension, but globally the majority of diagnosed hypertensives is inadequately controlled. Not treated it can cause cardiovascular disease (CVD), myocardial infarction and stroke. According to the WHO, hypertension is estimated to cause 4.5% of the current global disease burden and is as prevalent in many developing countries as in the developed world. Here, three experts from three continents comment on risk factors and hypertension management in their countries.

**Dr Fiona Turnbull, George Institute for International Health, University of Sydney, Australia**



Blood pressure-related disease is a major global health problem and is responsible for nearly eight million deaths annually. About half of all stroke and coronary heart disease is attributable to non-optimal blood pressure (BP). Furthermore, about 50% of these major cardiovascular events occur in people who are so-called 'normotensive'. Therefore major health gains can be achieved by lowering BP, even in people who are not hypertensive according to traditional threshold values. Obviously obesity and nutritional factors, especially salt consumption, play a major role in blood pressure. With the rapid epidemiological transition occurring in low-middle incomes, such as China and India, CVD attributable to BP is becoming increasingly prevalent in developing as well as developed countries.

Although lifestyle factors are important, drug therapy remains the mainstay of blood pressure control and, given the millions of people increasingly prescribed therapy, it is critical to be able to discern even small differences in the benefits of different drug classes. A major component of my activities has been the leadership since 2003 of the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC). This is an international collaboration of the principal investigators of major trials of blood pressure-lowering regimens. The collaboration seeks to provide clinicians, patients and policy-makers with the most reliable information about BP drugs and their effects on major cardiovascular events, such as stroke and coronary heart disease, by conducting meta-analyses (pooled analyses) of these trials.

The work of the Collaboration is conducted at the George Institute for International Health in Sydney, Australia. This international initiative is based on information from more than 30 trials collectively including nearly 200,000 patients from the UK, Europe, US, China, Japan and Australasia. The collaboration brings together not only the data from the largest BP trials but also the expertise and experience of the principal investigators of these trials, who are leaders in their respective fields. To date, the Collaboration has provided important information about the effects of newer compared with older classes of BP-lowering drugs and about their effects on stroke, coronary heart disease in patients of different age, sex, and disease status. These findings have informed major international BP guidelines as well as clinical practice. A major challenge to this research is to ensure continually that the research is translated into practice. Huge gaps between evidence and practice exist and large proportions of the global population at risk of blood pressure-related disease continue to remain untreated. Part of the problem is that doctors persist in using outdated models of treatment based on managing individual risk factors rather than consideration of the patient's 'absolute risk' of experiencing a major cardiovascular event.

As new drug classes and new indications for treatment evolve, the work of the BPLTTC will continue to be a valuable source of reliable information about the effects of these important drugs.

**Dr Yackoob Kassim Seedat, Nelson R Mandela School of Medicine, Faculty of Health Sciences, University of KwaZulu-Natal, Durban, S. Africa**



Sub-Saharan Africa (SSA) contains a diversity of ethnic groups, cultures and countries (54 in all) of vastly different socio-economic status. Data from many parts of sub-Saharan Africa are poorly explored because of financial constraints. South Africa is one of the few countries where data are reasonably accurate. Available data focusing on black groups indicate that hypertension seems more common with increasing acculturation, with a group of truly rural dwellers still being relatively protected. However, it is not known what proportion of the African population lives in truly rural conditions, relatively immune to the advances of civilisation versus those succumbing to urbanisation either rapidly or gradually.

The prevalence of hypertension according to rural studies undertaken in the 1970s, 1980s and 1990s has generally been low: 4.1% in Ghana, 5.9% in Nigeria, 7% in Lesotho and 9.4% in the rural Zulu. The migration of people to urban settings led to an immense increase of BP due to change in diet of new arrivals in the cities and higher pulse rates due to psychosocial stress and hard work.

Salt intake and lack of potassium due to inadequate fruit and vegetable consumption are also main causes for hypertension here. Other factors are obesity, particularly observed in black females, whereas alcohol excess is a problem particularly in black males.

Because SSA is the world's poorest continent, only low cost hypertension programmes can be afforded. The healthcare expenditure in many SSA countries is around US\$10 per person annually in contrast to between US\$2,000 and \$5,000 in industrialised Western countries. The major health challenge is still HIV/AIDS which takes a large portion of healthcare resources. There is a lack of adequate financing for research, but a comprehensive CVD programme is absolutely necessary. Furthermore, there is inadequate financing for researchers who need to be trained in excellent research centres so that they can learn techniques in research methodology. It would be helpful if researchers from the developed world could provide expertise and engage in collaborative work. We need administrators and politicians in sub-Saharan Africa to be convinced of the value of research on risk factors in CVDs. Inadequate funds, inexperience and lack of infrastructure remain important barriers to hypertension diagnosis and therapy.

To sum it up: The effects of urbanisation which influence the prevalence of hypertension and CVDs in SSA are decreased physical activity, increased energy and fat consumption and increased psychosocial stress. This leads to obesity, dyslipidaemia, diabetes and an increase in blood pressure. The future approach to CVD prevention should be a population focus on societal change and not only individual focus on high risk factors. This should include primordial prevention, salt restriction and physical exercise.

**Dr Tomasz Zdrojewski, Dept. of Hypertension and Diabetology at the Medical University of Gdansk, Poland**



Generally we can say that, with the political transformation in Poland over the last 15 years, the risk factors for CVDs have dramatically changed, some of them significantly decreased (e.g. smoking) and some increased (e.g. psychosocial factors). With regard to hypertension the consumption of too much salt is our main national problem. The recommended daily allowance is 7g but every Pole eats 10–15g, in

poor families it is even 15–20g. The government began to take action last year with an information campaign on Polish TV and radio. Additionally, there are attempts to convince industry to replace sodium by potassium.

Education is the crucial factor in prevention and control of arterial hypertension. One step to increase public awareness was to make primary physicians measure BP during every patient visit.

The place of residence is also a major indicator for prevalence and a starting point for the control of hypertension. One can say that Poland, especially during the early and very rapid phase of political and economic transformation, has been separated into two sections: large cities and small cities (county boroughs) and villages. People in large cities have had much better access to the best medical treatment, so we have many more cases of severe heart failure in the countryside, for example. Consequently, the hospitalisation rate of the rural population has been much higher in the last 15 years.

However, we have made significant progress in recent years, due to huge investments and the long term and complex health policy project – National Cardiovascular Diseases Prevention and Treatment Programme (POLKARD 2003-2008). For example, Poland now has a tight nationwide network of interventional cardiology and cardiac surgery centres. Access to these procedures dramatically improved and large inequalities significantly decreased. For example, in 2002, 2,300 coronary angiographies were performed per million people, and almost 900 percutaneous coronary revascularisation interventions (PCI), the respective numbers in 2007 were 3,850 coronary angiographies and 2185 PCI.

I hope this improvement in access to best procedures, changes in population awareness, healthier diet and less smoking are the most important factors responsible for a 30% reduction in CVD premature mortality in our country. This year we want to check this hypothesis and calculate the importance of each factor using the IMPACT model elaborated and published in most prestigious medical journals by Prof Simon Capewell from the University of Liverpool.

One side effect of the transition to a market economy was that we lost our national industry and the drugs to treat arterial hypertension became more expensive. Furthermore, primary care was privatised which, in the beginning of this process, especially in small cities and villages, made access to basic medical care more difficult. However, over the last five years we have observed an opposite trend and social and medical awareness of arterial hypertension is increasing again. At the moment about 66% of the population who have arterial hypertension know about it.

Another important problem is the very poor control of people who already had a stroke or myocardial infarction. I am the coordinator of an international study for Poland, Ukraine and Russia. This shows that very few patients receive adequate post-myocardial infarction or post-stroke treatment. My most recent project is the 400 Cities Programme, a very large-scale educational and prevention project to fight CVDs. We focus on the smaller cities, where the epidemiological situation is worse than in large cities and, for example, offer special classes in primary schools or special training for the nurses, doctors and administrative staff responsible for healthcare in their cities.

*continued from page 1*

investigate the effects of different therapy choices on a virtual model of the patient's heart and aorta, before going ahead with the option that offers the best clinical outcome. The availability of clinical decision support tools that utilise these personalised heart models could therefore improve the outcome for patients with life-threatening conditions such as heart failure, coronary artery disease, heart rhythm disorders and congenital heart defects.

However, as Henk van Houten, senior vice president of Philips Research and head of the Healthcare Research programme, said: 'The development of computer models that integrate structural and functional information of the heart and then personalise it to individual patients is a mammoth task that will require the multi-disciplinary effort of researchers with strong know-how in biophysical

modelling and image processing, clinical experts, and engineers in the device and imaging industries.' But, he adds: 'In the euHeart project we are confident that we have brought together the necessary expertise,' which could, he says, make a real contribution to improving cardiac treatments.

### From molecules to organs

A characteristic of biological complexity is the intrinsic interaction of physiological behaviours across a range of time scales and anatomical levels. The computer models developed in the euHeart project will therefore relate what happens at cellular and microvascular levels to what happens at tissue level, and what happens at tissue level to what happens at organ level. This will require the integration and interconnection of existing and future models from many different areas of biological research, including molecular biology, biochemistry, bio-

physics, anatomy and physiology – a task that will be facilitated by the use of standardised mark-up languages such as CellML and FieldML to describe them.

### Patient-specific

Most importantly, the resultant comprehensive model will be adaptable to reflect the condition of a specific patient's heart, using anatomical and functional information obtained via diagnostic techniques such as medical imaging (CT, MRI, ultrasound, etc.), blood flow and blood pressure measurements or electrocardiograms. At the intra-cellular level, the model could even take into account specific gene defects in individual patients.

By having an accurate personalised model of the patient's heart to work with, doctors may be able to gain a deeper understanding of the patient's disease. This could allow them to make more accurate diagnoses, predict the likely effectiveness of different

treatment therapies and improve therapy planning. In addition, the models could lead to improvements in the development and programming of implantable devices such as pacemakers, left ventricular assist devices, and endografts.

### Therapy planning

Because of the need to build the model over time, particularly in relation to incorporating molecular-level to organ-level disease pathologies for diagnostic purposes, the first applications are likely to be in therapy planning for pre-diagnosed conditions, e.g. heart arrhythmias, sometimes treated by radio-frequency (RF) ablation. During this procedure, the cardiologist relies on experience to decide which areas of tissue to destroy, a task complicated by the fact that each heart's electrical activity is subtly different. Aided by a computerised model that reflects the patient's unique heart structure and function, the cardiolo-

gist may be able to test the results of destroying different tissue areas before actually operating on the patient.

In addition to RF ablation therapy for arrhythmias, other clinical focuses for the euHeart project include heart failure (cardiac resynchronisation therapy and congenital cardiac surgery and left ventricular assist devices), coronary artery disease, and diseases/defects in the heart valves and aorta.

### Work packages

The euHeart project is broken up into a number of work-packages that include database management/validation for individual (sub-) models and their coupling together into larger structural/functional models; the development of appropriate mark-up languages and communication infrastructures for model description/exchange; the personalisation of anatomical models from image data;

Recent studies have shown that overweight and obesity during childhood and adolescence have a negative impact on the functioning of the internal walls of the arteries (vascular endothelium), paving the way to the development of an arteriosclerotic disease from an increasingly early age. They also prove that, regardless of age, race and sex, child and adolescent obesity affects the vascular endothelial functions. 'The evidence that the risk factors of cardiovascular diseases that reveal themselves in adulthood begin in childhood or adolescence makes it imperative that prevention strategies be planned from a very early age,' said **Dr Héctor Trunfelliti**, President of the Paediatric Cardiology Committee of the Argentine Federation of Cardiology (FAC), speaking this May at the World congress of Cardiology, held in Buenos Aires. 'These risk factors, such as overweight and obesity, as well as a sedentary lifestyle, nicotine addiction, dyslipidemias, hypertension and type 2 diabetes, share a common element that cannot be denied: the adoption of poor health-related habits characteristic of western societies.'

Released at the congress were the preliminary results of the Educando (Educating) Plan, a project, developed by the Argentine Federation/Foundation of Cardiology, and launched in 2001. The plan aims to prevent cardiovascular disease from childhood, and is targeted at primary school teachers, to encourage healthier lifestyles by providing information about the disease and prevention. 'Its clear and didactic message can be easily communicated to children,' explained Dr Rodolfo La Greca, co-director of the plan.

Since the programme began in 2001, around 8,000 primary school teachers, in charge of about 100,000 children between four and five years old, have received training. 'We will try to convey the Argentine experience because, due to its characteristics the Educando plan is unique as regards the centralised and unified management of the plan, addressed to teachers and not directly to children, who sometimes do not receive the

and the biophysical (structural and functional) personalisation of the models. The clinical relevance of the project will be ensured by additional application work-packages that will focus on specific model development for each of the clinical focus areas listed above – tailoring the model to specific diseases.

#### Funding

The euHeart consortium comprises public and private partners from 16 research, academic, industrial and medical organisations, from six European countries. Planned to run for four years the budget is around euros 19 million; 14 million of this provided by the EU as part of the EU 7th Framework Programme. The project forms part of the Virtual Physiological Human (VPH) initiative – a collaboration aiming to produce a computer model of the entire human body so that it can be investigated as a single complex system.

# CHILDHOOD OBESITY

## New strategies to prevent obesity and sedentary lifestyles

message properly,' Dr La Greca pointed out, adding that teachers are the proper vectors to convey life quality concepts to children.

The World Heart Federation in Colombia also has a project to promote healthy life habits in childhood and adolescence. 'Healthy Habits For Life', presented through the television show Plaza Sesamo (Sesame Workshop), consists of the

development of audiovisual materials that encourage pre-school children (aged between three and six years) to take regular physical activity and eat a healthy, balanced diet, and to promote the importance of instilling healthy life habits in children among their carers. Along with this the project encourages multi-sector collaboration for the prevention

of cardiovascular disease, said **Dr Shahyar Sheik**, President of the World Heart Federation, who added that it also aims to '...identify those elements of the programme that are cost-effective in order to reproduce them; and to develop an association with Plaza Sesamo that can be spread to other countries.'

This project began in 2006,

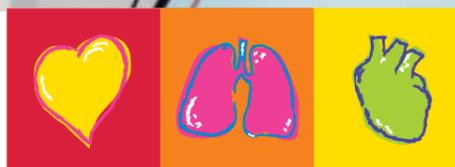
with the development in Colombia of audiovisual content that focuses on healthy life habits, designed to be used by health and education professionals and to enable the later evaluation of their impact on both children's and parents' activities. Six out of the 27 audiovisual materials initially planned have been broadcast in 2007 within the Plaza Sesamo show, which is broadcast virtually all over the American Continent through the cable TV channels Discovery Kids, TeleFutura and Televisa, and others. New episodes are being broadcast during 2008.

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# EuroPrevent 2009

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This year sees the fifth anniversary of EuroPrevent. This international gathering of scientists, clinical cardiologists, health workers and others, provides an opportunity to exchange experiences, upgrade skills and knowledge and propose strategies to provide the best preventive cardiology.

Deadline for abstracts: **19 November 2008**

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The ageing population and growing risk factors have made a significant impact on driving up the number of registered heart failure (HF) cases. Existing pharmacological strategies are improving the survival rates of acute and early-stage HF patients, ironically providing a growing body of patients with progression of the disease to HF.

With no new drug therapies addressing advanced HF and existing pharmacological strategies failing to compensate for a weakening heart, alternative solutions have to be found. In view of long waiting lists for heart transplants and the growing lack of

donor hearts, significant numbers of patients die while waiting for a heart transplant. However, cardiac resynchronisation therapy, mechanical circulatory support devices and other alternative technologies have demonstrated promising results, and the continuing rapid technological developments in this area suggest we may only be a decade away from eliminating the reliance on heart transplants, according to a new report\* by Datamonitor, an independent market analyst that provides online data, analyses and business forecast platforms ([www.datamonitor.com](http://www.datamonitor.com)).

# Heart

## The growing HF population

The number of HF sufferers is expected to climb to epidemic proportions. Worldwide, HF affects nearly 23 million people. In the United States, HF affects approximately 4.7m persons with approximately 550,000 incidences of HF diagnosed annually. Estimates of the prevalence of symptomatic HF in the general European population are similar to those in the United States and range from 0.4 to two percent of the total population. Existing gold-standard pharmacological strategies are able to provide superior compensation of acute and early-stage HF patients, increasing their survival rates without ensuring a full recovery. This results in an increasing long-term shift of such patients into the advanced HF group.

With no new drug therapies addressing advanced HF and existing pharmacological strategies failing to compensate for a weakening heart, alternative, non-pharmacological solutions have to be found, reports Dr Sergey Ishin, Datamonitor's senior cardiovascular analyst. 'Cardiac transplantation continues to be the gold standard for the treatment of end-stage HF. However, the number of potential transplants far exceeds the number of donors. In the US, about 2,500 heart transplants are carried out each year and research has suggested that up to 100,000 patients have advanced heart disease that would benefit from transplantation. This leads to 30% of patients on the waiting list dying annually.'

Cardiac resynchronisation therapy (CRT), through multiple randomised clinical trials, has demonstrated promising results in terms of both safety and efficacy, improving left ventricular efficiency and, subsequently, improving functional class. 'However, one of the greatest limitations of this technology is the fact that existing CRT devices, similarly to pharmacological treatment, can only temporarily improve symptoms and to some degree delay the progression of myocardial deterioration. Unfortunately, neither can prevent, stop nor reverse it. This unfortunate situation eventually brings advanced HF patients back to the heart transplant waiting lists,' Dr Ishin points out.

## Improving survival with alternative solutions

Although advances in surgical techniques and immunosuppressant therapy make it possible to perform successful heart transplantations even in the most critically ill patients, the rapidly growing end-stage HF population creates a tremendous gap in the number of patients waiting for new hearts and the number of organs that actually become available, Dr Ishin adds: 'In view of this, in addition to avoiding the immunosuppression and rejection complications of transplantation, mechanical circulatory support devices work as the only promising option which can help resolve the issue of organ availability and save more patients.'

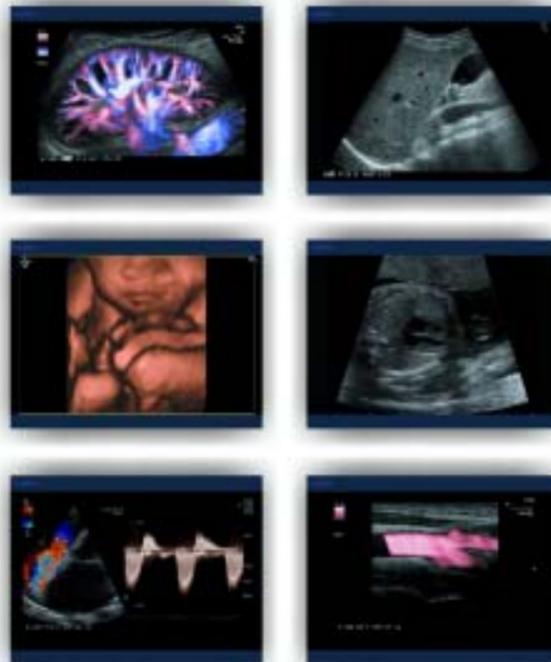
The idea of finding a mechanical alternative to donor transplants is not new, Datamonitor points out. Mechanical circulatory support devices and total artificial hearts have been under development since

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# failure Can technology diminish reliance on heart transplants?

the 1950s, but only recently, with advances in technology, have they started demonstrating some serious potential in completely eliminating the need for heart transplants. With many different design concepts tested throughout the decades the new face of mechanical circulatory support technology started to emerge. Bulky, immobile systems have gradually been replaced with more portable and even fully implantable solutions providing full patient mobility.

Even though scientists initially desired to create a complete artificial heart the lack of technological solutions at the time prevented rapid development in this area. Further research subsequently showed that it is more feasible to create a device that supports only the left ventricle. Presently, Dr Ishin continues, ventricular assist devices are the most well researched and technologically diverse area. 'The biggest advantage of ventricular assist devices over a complete artificial heart is the ability to instantly provide sufficient cardiac output to the patient, possibly for a very long period of time, and at the same time avoid any irreversible surgical modifications and keep an albeit weak, yet still functioning patient's heart working while potentially improving its functionality. Originally most of these devices were designed just to provide the necessary support while a patient is waiting for the donor heart. This is so called bridge-to-transplantation approach. Technological progress, however, made it possible to implant these devices for a significantly longer period of time, creating an opportunity for the so-called destination therapy approach, when the device can be left implanted permanently, eliminating the need for heart transplant.'

Miniaturisation of the components is one of the most important keys in the developmental process. New, totally implantable solutions, such as Jarvik 2000 and BerlinHeart Incor, may not only eliminate the need for the heart transplantation, but also allow full patient mobility and a return to normal life.

## Still far from complete replacement of transplants

In spite of rapid technological developments and successful clinical trials there are still a considerable number of issues associated with this technology Dr Ishin says. 'Among them are material biocompatibility and coagulation control, mechanical reliability of internal components, smaller device size allowing implantation into smaller patients and children, power sources, size of the batteries and device energy consumption, which would allow for fully implantable solutions with better infection control and patient mobility. Even the most advanced devices allow fully independent device operation for no longer than 20 minutes before it has to be connected back to its external batteries, which can be rather bulky and heavy.'

In 2007 the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)

reported device malfunction in 9% of all reported implantation cases. Factors that affect the probability of device malfunction are directly related to the number of individual components and moving parts in the system. Hence, simplification of design and reduction in the number of components and moving parts should improve long-lasting performance and durability of devices.

In addition to device malfunction, device-related infections are

one of the most frequent complications of ventricular assist device placement. Infections are reported to occur in no less than 13% of cases, Dr Ishin points out. 'Although device-related infections can involve any aspect of the device: the surgical site, the driveline, the device pocket, or the pump itself, and more than half of all device-related infections include multiple sites, the existence of external components, such as drivelines and batteries, leads to a sig-

nificant increase in the chance of an infection, leading back to the problem of external power supply and longer lasting batteries.

'Although at present we can not completely eliminate the need for heart transplantation, rapid technological developments indicate that we are not that far away from sorting mechanical issues, coagulation control and device-related infections with serious breakthroughs expected within next five to 10 years,' Dr Ishin concludes.

*\* Datamonitor's report Stakeholder Opinions: Heart Failure; When drugs do not work: Treatment of advanced heart failure with medical device therapies (Report author: Dr Sergey Ishin) provides in-depth analysis of the current status and future potential of treatment opportunities in advanced stages of HF. It includes an overview of existing and emerging technologies including cardiac resynchronisation therapy and mechanical circulatory support devices.*

*Details: [www.datamonitor.com](http://www.datamonitor.com)*



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For the fourth article in his series of articles for *European Hospital*, **Professor Stefan Schönberg** of the Institute of Clinical Radiology and Nuclear Medicine (IKRN), University Hospital Mannheim, Medical Faculty of Mannheim, University of Heidelberg, invited his colleague from Mannheim, Henrik J Michaely, and experts from the David Geffen School of Medicine at UCLA for a round-table discussion on:



## Advances of vascular MRI at higher field strengths

**Stefan G Ruehm, Kambiz Nael, Derek Lohan and Henrik J Michaely\*** describe impressive images that benefit patient treatment

Contrast-enhanced MR angiography (CEMRA) has evolved as an increasingly competitive diagnostic modality challenging both catheter angiography and CT angiography (CTA) for imaging of nearly all vascular territories. Over the recent years, improvements in gradient technology, pulse sequences, and postprocessing algorithms, combined with dramatic improvements in radiofrequency (RF) technology, have enabled the current status of CEMRA applications at 1.5T. Lately, whole-body 3T MRI systems have been introduced, with the promise of greatly improved signal-to-noise ratio (SNR) compared to 1.5T. With 3T imaging it appears feasible to obtain almost double the available SNR compared to 1.5T.

However, the move from 1.5T to 3T involves more than just increasing SNR: For some pulse sequences, many of which are now routine for imaging at 1.5T, there are substantial trade-offs at 3T such as so-called dielectric resonance effect, which can result in bands of signal loss on the MR image, particularly when RF intensive techniques (e.g. steady state free precession sequences) are employed.

High field imaging at 3T has proven to be particularly beneficial

in combination with parallel imaging techniques. This technique allows for a reduction of MRI measurement times by using spatial information from multiple surface coil elements at the same time to substitute for the overall number of phase-encoding steps which determine the scan length. With the appropriate coil arrangement and receiver chain, it is possible to accelerate an acquisition manifold. In this context, a specific number called 'acceleration factor' characterises the increase in data collection speed. However, the penalty for the increased speed of parallel acquisition is a drop in SNR. Since there is more SNR available at 3T, it is possible to use higher acceleration factors at SNR values still adequate for diagnostic image quality. Therefore with identical acquisition times, images can be collected with higher spatial resolution or greater anatomical coverage compared to 1.5T.

Contrast-enhanced MRA is based on the use of T1-weighted fast spoiled 3-D gradient recalled-echo sequence in combination with the T1-shortening effect of gadolinium-based contrast agents. As an attractive feature of contrast-enhanced MRA at 3T the sensitivity to injected

gadolinium agents is increased. This is based on an increase of the longitudinal relaxation time (T1) of background tissues with higher field strengths, which allows the use of smaller volumes of paramagnetic contrast agents.

With recent advances in scanner gradient performance, fast data acquisition times for isotropic three-dimensional (3-D) data sets for 576 matrix acquisitions have become possible enabling high spatial-resolution 3-D imaging during a comfortable breath-holding period.

An additional feature of MRI is the capability to generate temporal-

ly resolved 3-D images that display the first-pass transit of contrast through the vascular system. Time-resolved MRA can provide additional functional information and requires only very small doses of contrast. For many applications, in-plane resolution can be preserved while through-plane resolution is commonly traded for rapid temporal sampling.

### Clinical Applications

In many institutions 3-D CEMRA has found its role as the method of choice for the evaluation of the craniocervical vasculature. Indications include a variety of conditions such as atherosclerotic disease, aneurysms, and arteriovenous malformations, presurgical assessment of tumours as well as post-treatment surveillance. The ability to time-resolved contrast-enhanced 3-D MRA with high spatial resolution is particularly valuable for the characterisation of arteriovenous malformations and allows the differentiation between high versus slow flow lesions. This may play an



Stefan G Ruehm



Derek Lohan



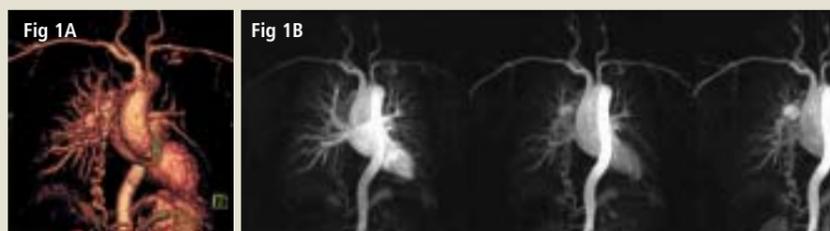
Henrik J Michaely



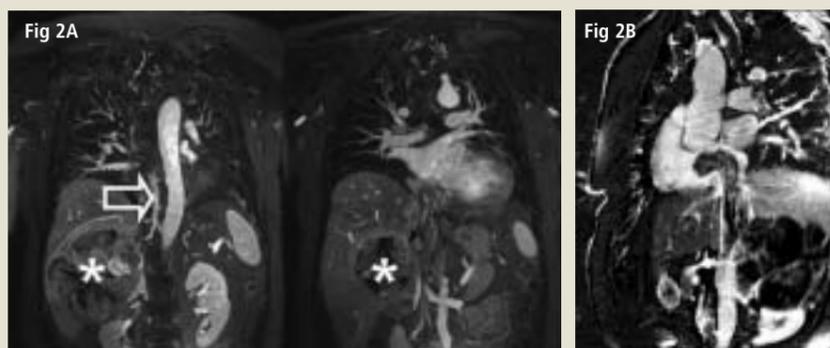
Kambiz Nael

**Table: Benefits of 3 Tesla CEMRA for improved therapeutic strategies**

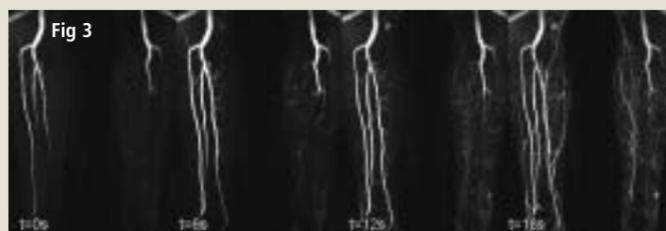
Technique	Problem	Solution
High-resolution MRA	Stenosis quantification	Improved accuracy for determination of significant stenoses
	Fibromuscular dysplasia	Better detection of distal renal artery involvement by string-of-beads changes
Time-resolved MRA	Occlusion	Detection of collateral flow
	High-grade stenosis	Improved visualisation of altered haemodynamics
T1 morphologic imaging	Activity of vasculitis	Improved detection of subtle vessel wall enhancement



**Fig. 1:** 1.5T high resolution MRA (A) and time-resolved echo-shared MRA (B) of a patient with pulmonary AVM. With both techniques an aberrant feeding vessel originating from the abdominal aorta can be appreciated. The time-resolved technique additionally demonstrates the dynamics of the blood flow.



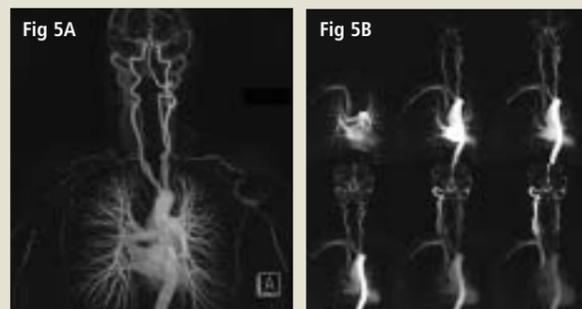
**Fig. 2:** 20mm thin MIP of the 3T-MRA (A) and 3T-phase-sensitive inversion recovery (PSIR) images of a patient with giant adrenal carcinoma. The carcinoma can be well depicted on the coronal MRA images (star, A) which was acquired after the administration of 15ml of Gd-BOPTA (Multihance). There is also tumour growth into the inferior vena cava and reactive dilatation of the azygos system (arrow). In the cardiac exam the extension of the thrombus into the right atrium is well demonstrated. As the MRI demonstrated that the thrombus was not attached to the atrial wall a surgical resection of the tumour was performed.



**Fig. 3:** Time-resolved MRA in a patient with left-sided foot ulcer and PAOD. In the dynamic time-resolved-echo shared MRA at 3.0T (TREAT, 1.5 x 1.4 x 1.5 mm spatial resolution, 3s temporal resolution) after administration of 7 ml of gadofosveset (Vasovist) a regular run-off of the right lower extremity can be appreciated while on the affected left side no patent arterial vessel can be seen. There are only small collateral branches excluding interventional revascularisation.



**Fig. 4 (a+b):** Conventional renal angiogram (a) and corresponding 3-D high-resolution contrast-enhanced MR angiographic oblique maximum intensity projection (MIP) (b) from a female patient with fibromuscular dysplasia of the right renal artery. This is evidenced by beading and irregularity of the distal third of this vessel on both imaging techniques. While of inferior spatial resolution to conventional radiographic techniques, CE-MRA at 3 Tesla maintains high diagnostic accuracy, while precluding the requirement for arterial puncture and ionising radiation exposure.



**Fig. 5 (a+b):** High-resolution 3-D contrast-enhanced MRA full-thickness MIP (a) obtained at 3 Tesla with injection of 12cc of Magnevist (gadopentetate) in a patient with Giant Cell Arteritis. An aberrant right subclavian and conventional left subclavian artery are occluded, with resultant arterial collateralisation. Dynamic time-resolved images acquired with a TWIST sequence using a relatively diminutive dose of 5cc Magnevist, confirms delayed bilateral upper extremity perfusion due to the attenuated size of these collateral vessels.

important role for determining adequate treatment strategies which include conservative treatment, embolisation therapy or surgery.

With a critical stenosis level of 70% as determined by the NASCET study to be the threshold for treatment of patients with thrombendarterectomy, improved spatial resolution for accurate stenosis grading of carotid arteries appears mandatory. Similarly, high spatial resolution imaging for improved characterisation of vascular wall invasion can play an important role to determine resectability of neck tumours. Cranio-cervical contrast-enhanced MRA can be used to evaluate patients following treatment for vascular disease, for example to assess re-stenosis after endovascular treatment following stent placement or for follow-up of patients with vessel dissection in order to detect possible progression of stenosis or occlusion which may mandate invasive therapy such as surgery or stenting to prevent ischemic cerebral complications.

Applications in the pulmonary circulation include evaluation of pulmonary embolism, pulmonary hypertension, and congenital heart disease. Pulmonary venous MRA plays an increasing role for accurate planning and follow up of radiofrequency ablation therapy in patients with cardiac arrhythmia.

For the abdominal vasculature, clinical applications include the assessment of atherosclerotic arterial disease, aneurysms, and dissections, as well as the preoperative

assessment of tumour extent. In addition, MR venography is a rapidly growing application in chest, abdomen, pelvis and lower extremity which benefits from high spatial resolution and the potential reduction of contrast volumes.

Indications for renal MRA include the diagnosis of atherosclerotic renal artery stenosis, fibromuscular dysplasia (FMD), renal aneurysms, dissections, as well as the evaluation of patients pre- and post renal transplantation. In combination with functional imaging techniques such as ultrasound, nuclear medicine imaging, phase-contrast MRA

or perfusion MRI, the accurate characterisation and quantification of the severity of stenotic renal artery disease plays an important role for planning revascularisation strategies. High-resolution MRA at 3T may help to limit the over-estimation of the degree of stenotic disease and may therefore avoid unnecessary renal revascularisation procedures which may further increase the risk of patients with borderline renal function.

FMD represents the second most common cause of renal artery disease. It tends to affect younger patients. Patients benefit from

early diagnosis since there is a good response to balloon angioplasty. FMD usually affects the mid and distal artery segments. These segments may be missed on conventional MRA at 1.5T due to limited spatial resolution. It is expected that CEMRA at 3T increases sensitivity and specificity for the early detection of FMD.

Similarly to single station MRA, multistation peripheral or whole-body imaging can be performed at 3T yielding high spatial-resolution data sets with isotropic submillimeter voxel size. With the combination of parallel imaging, an appropriate

contrast-injection protocol, and flexible table movement, venous contamination can be minimised or avoided. The procedure is feasible and holds promise for screening applications.

In summary, a wide spectrum of vascular diseases may benefit from imaging at 3T. Our experience suggests that CEMRA at 3T is robust and besides providing spectacular images holds promise to improve patient care by improved diagnostic accuracy which may positively affect therapeutic strategies.

*\*Henrik J Michaely is a consultant to BayerHealthCare*

## Atrial and ventricular contraction is differentially regulated

**Beta-3-adrenergic receptor activation increases human atrial tissue contractility and stimulates the L-type Ca<sup>2+</sup> current**

**France** – The contraction of the atria and ventricles is differentially regulated, according to a study by **Rodolphe Fischmeister** and colleagues, at INSERM UMR-S 769 in Châtenay-Malabry. The contraction phase of the heart beat is controlled by several pathways, including one initiated by stimulation of cell surface proteins known as beta-adrenergic receptors. At the molecular level, the flow of Ca<sup>2+</sup> through protein channels known as L-type Ca<sup>2+</sup> channels has a central role in the regulation of the contraction of the heart by beta-adrenergic receptors.

Previous data have indicated that stimulation of beta-3-adrenergic receptor (beta-3-AR) decreases the contractility of tissue from human ventricles and decreases the activity of ventricle L-type Ca<sup>2+</sup> channels in various animal models. In contrast, Dr Fischmeister and team have found that beta-3-AR stimulation increases the activity of L-type Ca<sup>2+</sup> channels in heart cells isolated from human atria and increases the contractility of the atrial tissue.

The finding that beta-3-AR stimulation has opposing effects on human atrial and ventricular tissue could lead to the development of therapies that target beta-adrenergic receptors to treat CVDs.

Details: [www.inserm.fr](http://www.inserm.fr)

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# HIFU surgical ablation products gain CE Mark **NEW**

St. Jude Medical, Inc. has received European CE Mark approval and US Food and Drug Administration (FDA) clearance for its *Epicor LP* cardiac ablation system, a second generation technology that uses HIFU (high intensity focused ultrasound) for surgical ablation of cardiac tissue to disrupt abnormal cardiac electrical impulses.

The first patient to undergo treatment with the Epicor LP System was a 73-year-old male with coronary artery disease and atrial fibrillation (AF). The procedure was performed by cardiac surgeon **Malcolm Dalrymple-Hay FRCS PhD FECTS**, at Derriford Hospital in Plymouth, UK. The patient, who has suffered persistent AF for over three years, had a normal heart rhythm upon completion of the ablation procedure.

'An increasing volume of published literature is demonstrating the benefits of treating pre-existing AF in patients who are undergoing valvular or coronary artery bypass surgery,' explained Dr Dalrymple-Hay. 'The Epicor LP System provides a technology that is flexible enough to treat AF patients during either standard open chest procedures or minimally invasive surgical procedures.'

'In surgical ablation performed with a HIFU energy source, energy is focused from outside a beating heart. This treatment has been designed to create precise and complete lines of cardiac tissue ablation to block chaotic electrical impulses. The patient does not need to be placed on a heart-lung bypass machine nor is the heart stopped. Because HIFU energy is directed from outside the heart inward (instead of from the inside out as is sometimes the case in ablations performed with other energy sources), the risk of unintended peripheral damage is minimised,' St. Jude Medical explains.

'In contrast, the traditional surgical approach requires that patients be placed on a heart-lung bypass machine with their hearts stopped while a cardiac surgeon cuts maze-like patterns in the atrial tissues and then sews the incisions to encourage the formation of lesions, or tiny scars. Surgeons may also use alternative energy sources, such as radiofrequency or cryotherapy, to create lesions in heart tissue. The lesions disrupt the abnormal electrical impulses that cause AF.'

'The Epicor LP system has a lower profile (smaller relative to the first generation technology) as well as other features designed to facilitate easier device introduction and placement around and on patients' hearts,' St. Jude Medical continues, adding: 'The Epicor LP System is equally suited for use in both closed-chest procedures performed through a single incision, and in open-chest procedures.'

In the December 2007 edition of *The Annals of Thoracic Surgery*, the results of an independent investigator clinical trial led by **Mark Groh MD**, showed that AF is effectively treated using the Epicor Cardiac



Ablation System when used concomitantly to corrective heart surgery. The investigators reported that more than 83% of all patients, followed for at least six months after surgery, were free from AF. In addition, 86% of the patients followed for at least 18 months remained free from AF. The investigators reported that there were no device or ablative procedure-related adverse events and specifically noted an absence of oesophageal, coronary or phrenic nerve damage.

The 2007 results confirmed the findings of an earlier European multi-centre trial published in the September 2005 *Journal of Thoracic and Cardiovascular Surgery*. The investigators in the European clinical trial reported an 85% freedom-from-AF rate at six months post-procedure - the study's primary efficacy end point - in patients concomitantly treated for AF with the Epicor cardiac ablation system.

St. Jude Medical acquired Epicor Medical in 2004 and worked closely with Dr James Cox to develop the Epicor Medical HIFU ablation system and its related surgical procedure. 'Dr Cox is the developer of the Cox-Maze surgical procedure for the treatment of AF and is acknowledged by his peers as a pioneer in the field. Since the acquisition, St. Jude Medical has been committed to improving the manufacturability and performance of the HIFU surgical ablation technology,' the company adds. The company is continuing its pursuit to expand clinical data, as well as additional tools to facilitate minimally invasive procedures, for the technology.

The first generation Epicor System gained regulatory approval for the treatment of AF in Europe in 2006. In the US, the first generation Epicor System and the Epicor LP System received clearance from the FDA for the surgical ablation of cardiac tissue but have not been indicated by the FDA specifically for the treatment of AF.

St. Jude Medical has over 12,500 employees worldwide and is headquartered in St Paul, Minnesota. The firm focuses on developing systems for cardiac rhythm management, atrial fibrillation, cardiac surgery, cardiology and neuromodulation.

# Echocardiography acquires instantaneous, non-stitched full-volume images in a single cardiac beat **NEW**



Acuson SC2000

The Acuson SC2000 volume imaging ultrasound system - reported to be the first system in the world to acquire non-stitched real-time full-volume 3-D images of the heart in one single heart cycle - will be launched by Siemens Healthcare at the European Society of Cardiology (ESC) meeting in Munich. Referred to as 'Echo in a Heartbeat,' this new technology marks the greatest paradigm shift in ultrasound since the introduction of 2-D imaging in the late '70s, Siemens explains. 'Instantaneous, non-stitched, full-volume imaging comes 55 years after echocardiography pioneers Inge Edler und Hellmuth Hertz acquired the world's first cardiac ultrasound recording using Siemens technology in 1953.'

Klaus Hambuechen, CEO of Ultrasound, Siemens Medical Solutions USA Inc. added: 'The system has unparalleled capabilities in information rate processing that allow us to acquire a full volume of the entire heart with 90 degree pyramids. With a high-volume acquisition rate like this - in one second, every second - acquisition time is dramatically reduced, improving the overall workflow in the echocardiography suite.'

## Next generation system architecture and transducer technology

The Acuson SC2000 cardiology platform is expected to change the way echocardiography is currently practiced. 'Its advanced architec-

ture delivers vastly more information than today's conventional systems and is strengthened by Siemens patented Coherent Volume Formation technology. Coupled with the system's high-volume acquisition rate, Coherent Volume Formation moves away from serial line-by-line acquisition towards simultaneous, multiple beams, delivering excellent image resolution,' Siemens reports.

'The proprietary 4Z1c transducer features revolutionary, patented active cooling technology, enabling full output power within regulatory limits. This results in improved penetration, reduced noise and high-volume acquisition rates when compared to conventional 3-D transducers. The 4Z1c is a single transducer solution for adult echo applications that provides all the modes needed: volume imaging, 2-D, M-mode, colour Doppler, and spectral Doppler. This breakthrough technology showcases Siemens acoustic mastery and delivers on the long-awaited promise of true volume imaging for every patient.'

## Better outcomes through workflow-driven examination sequences

The Acuson SC2000 system is designed to support advanced cardiovascular applications. The knowledge-based workflow software uses learned pattern recognition technology and an expert database of real clinical cases. This enables the system to recognise anatomical patterns and landmarks, as well as to perform automatic measurements streamlining clinical workflow.

'The system automatically derives reference plane images from the full-volume cardiac capture dataset and offers automated full-volume contouring for fast qualitative and quantitative analysis. Customisable, programmable, and protocol-driven workflow sequences deliver repeatability for better outcomes: greater efficiency, accuracy, consistency, and care - from data acquisition to diagnosis,' Siemens adds. 'To further enhance efficiency, the offline workstation enables reporting as well as complete review and processing of the acquired volumes.'

The company has also addressed the ergonomics of the system to meet and exceed today's recommended ergonomic guidelines to reduce work-related stress injuries and to accommodate the varied work environment of sonographers. The new system is expected to become available in Europe this autumn.

## Beijing Olympics research finds enlarged hearts can be good hearts



Cardiologist **Dr Malissa Wood**, of the Massachusetts General Hospital, Boston, USA, has reported that a study of Olympic athletes, using GE Healthcare's Vivid I cardiac compact ultrasound technology, has allowed the medical research team in Beijing to identify healthy patterns of heart enlargement that can differentiate it from hypertrophic cardiomyopathy.

Previously, it was believed that heart size is indicative of risk of Sudden Cardiac Death (SCD); however, Dr Wood's research with the USA Weightlifting and US Men's Rowing teams has shown that it is the health of the systolic or blood-pumping action - not the heart size - that is the distinguishing factor of a healthy heart. 'As a result of these findings, we are in the process of developing a cardiac fitness index to be released later this year that will help trainers and coaches understand how cardiac conditions impact performance of high-endurance athletes,' Dr Wood said. 'Our work also will provide healthcare professionals with insight into new, more effective ways of assessing and treating heart disease for the general public.'

Based on Dr Wood's findings, **Dr Patrick Schamasch**, Medical and Scientific Director of the International Olympic Committee (IOC), has recommended routine cardiac monitoring of Olympic athletes. 'I fully support the action to have preparticipation cardiovascular screening mandatory for elite athletes. This will evaluate athletes before participating in sports for the purpose of identifying (or raising suspicion of) abnormalities that could provoke disease progression or sudden cardiac death. Ensuring the well-being of all athletes is the IOC's priority, and we feel that the identification of the relevant diseases will allow clinicians to make decisions earlier on, of whether a player can stay in the game or not, but above all tailor their training programs to best meet their needs and ensure athlete safety.'

## CVD specialists meet footballers

### World's first symposium on sudden death syndrome among European athletes

**Spain** - The world's first symposium on the molecular analysis of sudden death syndrome (SDS) among athletes drew in leading cardiovascular researchers and several top Spanish footballers. Sponsored by Applied Biosystems, and held in the Madrid's Hospital Clinico San Carlos, the I Symposium de Prevención en el Fútbol aims to initiate the development of new tests to identify sports players at SDS risk.

This syndrome, most common in men under 40, generally causes immediate cardiac arrest during strenuous exercise. Reports of unexpected deaths of young men participating in marathons, cycling races and football matches are not unusual. Sudden death can be caused by a variety of diseases or genetic factors. Genetic causes usually have no symptoms, so professional athletes at risk of the syndrome can appear to be in peak physical condition during routine medical and fitness checks. Currently available CVD tests are usually insufficient to detect an individual at risk of SDS - only a genetic test will provide the required accuracy and reliability.

A roundtable discussion ensued on methods to identify specific molecular or genetic changes in people at risk. Applied Biosystems points out that these biomarkers could be used to develop a test panel for screening football players or other sportsmen to identify their risk of sudden death. There are several known genetic causes of sudden adult death, including abnormalities of the heart muscles, and malfunctioning of ion channels - vital cellular structures through which ions (e.g. calcium, potassium or sodium) pass in or out during a heart's normal functioning. Malfunctions of these channels can result in cardiac arrest. Several ion channel abnormalities have been identified that are known to increase the risk of sudden cardiac arrest, including long QT syndrome and Brugada syndrome.

## Rolling out ScanCath

**USA** - With the recent opening of its new headquarters in Newark, California, NovaRay Inc's CEO and President, Jack Price announced that the firm will now 'scale-up and roll-out with the development of our first clinical product, the ScanCath cardiac catheterisation system.'

NovaRay, which develops digital cardiac X-ray imaging technology, explains that the ScanCath cardiac catheterisation system provides advanced imaging capabilities coupled with reductions in radiation.

# Economic recession: a cause of later CVD?

**Germany** – Bad economic conditions, e.g. a recession, at the time of birth may lead to a higher risk of cardiovascular mortality much later in life, according to a recent study published by researchers at the Institute for the Study of Labour (IZA) in Bonn.

The study showed that individuals born in a recession on average live 15 months less than those born under better conditions and that this difference can be mostly attributed to cardiovascular health risks. 'What is surprising is that such effects may pop up 70 or 80 years after birth,' said **Gerard van den Berg**, Economics Professor at VU University Amsterdam and Programme Director at IZA, who co-authored the study with **Gabriele Doblhammer-Reiter** and **Kaare Christensen**. In the intervening years no extraordinary health events may occur, until suddenly the fatal cardiovascular problems arrive. The authors report that they do not find such long-run effects on cancer in general, although certain types of cancer have been linked to low birth weight, another marker of early-life conditions.

The team used data on individuals born around 1900, as well as that of twins in Denmark, whose mortality causes have been systematically gathered for many years. The latter made it possible to check whether a twin pair's health outcomes are more similar later in life if they were born under adverse conditions than if they were born under good conditions. The finding was that they are more similar later in life if the starting position was bad. Conversely, if an individual is born under better conditions, then individual-specific factors dominate more.

Why might a recession, for example, cause later damage to the cardiovascular system? Dr Van den Berg said analyses carried out by the team for specific parts of Denmark suggest that long-run effects are particularly triggered by the combination of suboptimal nutrition and a suboptimal health infrastructure early in life. Low household income is less harmful for the baby's future if the environment has good healthcare and hygiene facilities. In addition, stress is possibly a major factor. Parents who are economically stressed may produce offspring with features that make them more susceptible to CVDs at advanced ages.

One may wonder whether the results are of significance for present-day birth conditions. Of course, we need another 80 years to know for sure. But there are signs that long-run effects are as important as ever. For example, birth weight studies among recent cohorts show effects on health and adult height that are as strong as ever. And with the advent of the fast food society, nutritional habits among segments of society may not be as good as they used to be.

From this point of view, it may be worthwhile to screen young individuals born under adverse conditions for



CV markers and predictors, and to expose those who have unfavourable test values to preventive interventions. Moreover, the results support investments in nutritional quality and health infrastructure in countries with a high degree of deprivation, as a means to reduce the cardiovascular mortality rate in future years.

As recession looms in various countries, so the effects of economic stress on families may be passed on to the children born during such times, causing a higher risk of them developing fatal cardiovascular diseases in later life

## HeartVue 6S seeks USA marketing

Pegasus/Heartview LLC has announced that clinical studies of its HeartVue 6S Heart Screening System – which obtained CE Mark Approval in Europe almost two years ago – have been completed according to FDA guidelines, as a pre-marketing condition for release in the USA.

The HeartVue 6S Screening System, use as a screening tool, provides a quick, accurate assessment of patients with suspected coronary artery disease in 1–2 minutes.

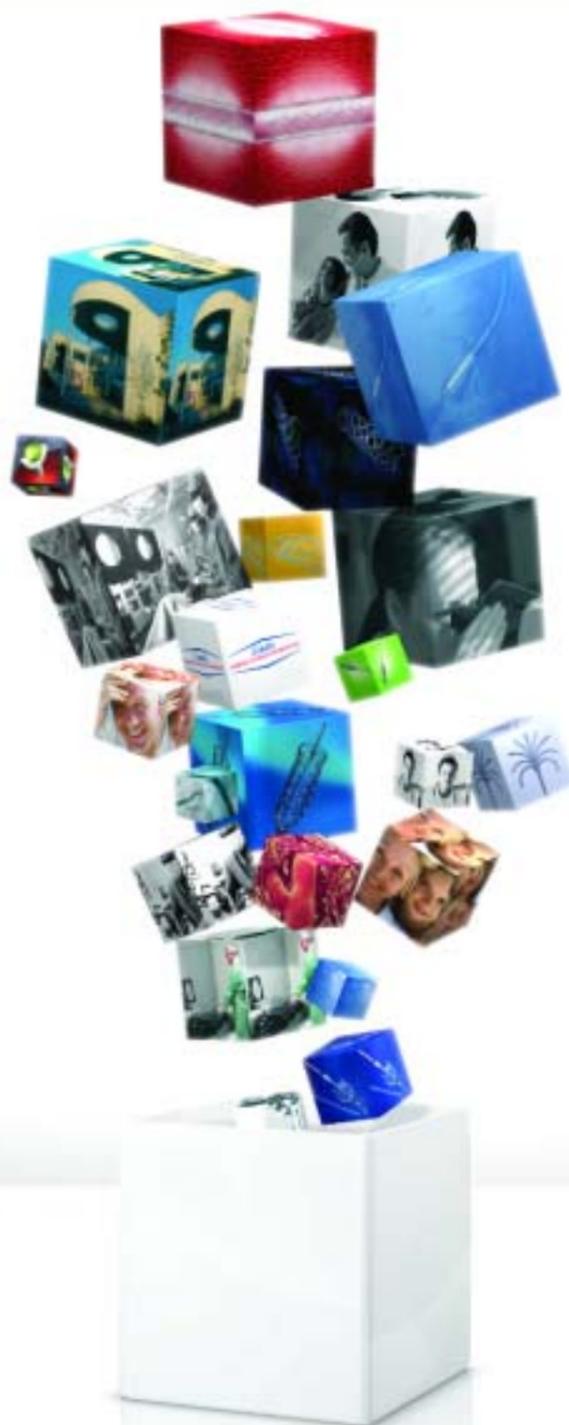
The clinical studies included testing 170 patients of various ages, genders, races, weights and health conditions. The results will now be analysed, interpreted and presented to the FDA in the form of a 510K Filing.

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Source: Gerard J. van den Berg, Gabriele Doblhammer-Reiter, Kaare Christensen: *Being Born Under Adverse Economic Conditions Leads to a Higher Cardiovascular Mortality Rate Later in Life: Evidence Based on Individuals Born at Different Stages of the Business Cycle IZA Discussion Paper No. 3635, Bonn: August 2008.*  
<http://ftp.iza.org/dp3635.pdf>

The diagnostic work-up of syncope patients often raises the question of how much diagnosis is necessary and what examination methods are really needed. To save time, specialists recommend focusing on determining whether the syncope may be caused by a cardiac problem – a question answered quite easily in many cases.

According to Professor Andreas Schuchert, a basic diagnostic work-up for every syncope case consists of three steps: the first a thorough anamnesis, followed by a brief physical examination and an ECG. 'Further measures are only necessary either if no specific type of syncope can be determined or if there are indications of their being caused by a cardiac problem.' Only

### Heart sounds

The basic diagnostic physical work-up often only requires a few steps. 'The first is auscultation of the heart, during which pathological sounds of any kind must be assessed as warnings of cardiac syncope,' Prof Schuchert emphasises. The neck vessels should also be auscultated for stenosis of the carotid artery. The physician should also listen very carefully for an irregular heartbeat or a heart rate below 50 or above 100 beats a minute, which may indicate AV block or atrial fibrillation as the cause of syncope. 'The most important alarm signals are evidence of cardiac insufficiency – for example, the legs are oedematous or there are rattling sounds from the lungs or a

**Karl Eberius MD**, European Hospital's new correspondent, discussed advice for physicians with **Professor Andreas Schuchert**, principal author of the German Society of Cardiology's official statement on syncope



Counter pressure

# SYNCOPE Diagnosis and therapy

cardiac syncope shows a clearly raised death rate (18-33% annually) depending on the study, he adds

### What is relevant in medical history?

Syncope caused by cardiac disorders can often be identified during the anamnesis by asking just a few questions, importantly whether the syncope occurred during physical effort, which, the professor points out, is primarily an indication of aortic stenosis or hypertrophic obstructive cardiomyopathy. Another question: whether there was chest pain before or after the syncope, which may indicate coronary ischaemia, the professor explains. The physician should also check for previous arrhythmia or other cardiac disease. 'If, for example, there has been a heart attack in the past, cardiac syncope should be assumed until there is evidence to the contrary,' says Prof Schuchert, who also considers the family's medical history an important indicator. For example, the sudden death of a young relative from cardiac causes may indicate hereditary heart disease, e.g. Brugada syndrome – rare but it should be considered.

congested liver is detectable more than two finger widths below the rib cage,' he reminds us. 'The combination of cardiac insufficiency and syncope indicates a critically raised risk of mortality and therefore needs to be immediately diagnosed.'

### Vasovagal events

If that basic procedure indicates no cardiac cause, the physician can focus on determining the actual type of syncope – often possible by looking at the medical history. 'A **vasovagal attack**, the most frequent kind of syncope, must always be assumed, for example, when typical symptoms preceded the fainting attack: nausea, sweating, dizziness, drowsiness, weakness, abdominal discomfort or blurred vision,' he explains. 'Similarly when fainting followed a long period of standing tensely or the attack followed pain, emotional stress, anxiety or procedures like having blood taken.'

### Fainting during defecation

**Situational syncope** must be assumed if loss of consciousness occurs while urinating, defecating, coughing or vomiting. 'Unlike the vasovagal attack, the trigger in

these cases is not a diffuse sensation, like anxiety or pain, but a clearly defined situation. Furthermore situational syncope typically occurs more suddenly and without any warning.'

**Orthostatic syncope** occurs when standing up from lying down or sitting. Unlike a vasovagal attack, an orthostatic syncope typically does not occur after standing for a long period but immediately after the change in position.

A **drug-induced syncope** should be considered if the blood pressure (BP) has been too drastically modified in hypertensive patients. On the other hand, if fainting occurs when turning the head, for example while shaving or looking over one's shoulder in a car, carotid sinus syndrome should be considered.

### Additional examinations

Depending on the results from the basic diagnosis, various other investigations may be recommended to clarify the type of syncope. If the medical history indicates an orthostatic syncope, for example, diagnosis can be confirmed by the Schellong test, in which the BP taken after five minutes in the lying position is compared to that taken after subsequently standing up. The diagnosis is confirmed when the systolic value after standing up falls below 90 mmHg or is more than 20 mmHg below the measurement taken when lying down. Prof Schuchert points out that, if the previously ascertained medical history indicates vasovagal syncope, carotid sinus syndrome or situational syncope, the Schellong test is unnecessary. Moreover, tilt tests may be useful, for example when vasovagal syncope is suspected but the medical history does not unambiguously indicate this. However, the predictive value of tilt tests is increasingly challenged.

### Laboratory tests of doubtful benefit

The professor believes laboratory tests are almost always unnecessary for clarifying syncope – particularly true for the determination of Hb levels, a test frequently performed due to a lack of other ideas, but which is actually only necessary if anaemia

is clinically indicated. 'In 99% of syncope diagnoses no laboratory tests are required.'

The same applies to carotid Doppler examinations, which are only indicated when sounds of stenosis can actually be heard on auscultation of the vessels of the neck. 'Otherwise the probability of syncope caused by carotid disorders should be ignored.'

### Therapy

Vasovagal syncope can often be treated effectively by the simplest methods. Counter pressure manoeuvres are particularly useful in many cases, and in recent years have become a highly popular way to prevent decreasing BP without complications.

Before beginning treatment for vasovagal attacks, specialists recommend sufficient time is given to explain the therapy. 'Patients should know that fainting attacks are not a symptom of a dangerous disease of an organ,' Prof Schuchert emphasises. 'When they know this they can then react more calmly to the fainting, which for many is already a great relief.'

During a consultation the typical trigger factors for syncope should be addressed. 'Someone who tends to have syncope attacks in narrow, overheated spaces should avoid department stores. And a person



Karl Eberius

Andreas Schuchert

who has problems when asked for a blood would be wise to lie down before the procedure,' he advises, deploring the omission of these simple but important recommendations.

Counter pressure manoeuvres are in many cases a very effective aid, widely used in clinical practice to counteract the fall in BP in a vasovagal attack. Counter pressure manoeuvres require a hand size rubber ball, simply carried in a pocket or bag. If a fainting attack approaches, in vasovagal attacks not frequently heralded by typical symptoms, e.g. nausea, dizziness or drowsiness, one squeezes the ball as hard as possible. As a result of muscle contraction, the sympathetic system is evidently activated, producing constriction of the peripheral blood vessels, thus often preventing the fall in BP causing syncope in the preliminary stage.

Alternatively one can perform the manoeuvre shown in the image.

## Treatments

**Orthostatic syncope** – If loss of consciousness occurs directly after standing up from having been lying down or sitting, this indicates orthostatic syncope. The most important recommendation of Prof Schuchert is simply to stand up more slowly so that the cardiovascular system can adapt better to the body being upright. 'Support hose, the sympathomimetic drug etilefrine or the mineral corticosteroid fludrocortisone can also be helpful.'

**Situational syncope** – Mostly occurring during micturation, defecation, coughing or vomiting, in many cases this is not easy to treat and there are no proven evidence-based measures. 'Any therapy that is also used for vasovagal attacks is worth a try,' Prof Schuchert says, adding that many patients are helped by support hose or etilefrine.

### Summation

- Diagnosis is the priority in vasovagal attacks. People affected should be aware that the loss of consciousness does not indicate a dangerous disease of any organ.
- It is important to avoid factors triggering syncope.
- Counter pressure manoeuvres (e.g. squeezing a rubber ball or pulling clasped hands apart) have proved valuable to counteract fall in BP during vasovagal attacks.
- Lifestyle changes can be tried in motivated patients, e.g. increasing physical exercise, fluid and salt intake.
- For vasovagal attacks, midodrine is the first drug of choice (3 x 10 mg/d).
- The benefits of selective serotonin re-uptake inhibitors have not been definitively clarified.
- Support hose, etilefrine and fludrocortisone can be useful for orthostatic syncope.
- There is no evidence-based drug to treat situational syncope.

## EARLY DIAGNOSIS

Hearing future heartbeats at ESC



Simply clasp your hands together with arms at about chest height in front of your body and try to pull your arms apart while not loosening your clasp. In both counter pressure manoeuvres muscles contract for as long as it takes for the signals of the attack to disappear.

#### Medication

Medication can also be useful to treat some vasovagal cases, particularly when other therapies have failed and syncope continues to occur. 'The drug of choice is the alpha antagonist midodrine. At a dose of 3 x 10 mg/d this effectively raises the BP, and in almost all cases the drug avoids recurrence,' the professor says. However, it is not suitable for every patient because it potentially increases the BP. This applies particularly to the elderly, whose BP compared to that of younger people is often already raised. Additionally, since this drug must be taken three times a day, many patients have compliance problems.

If patients suffering vasovagal attacks are already hypertensive, beta-blockers can also be a useful alternative. Although not recommended by the ESC due to unproven benefit in vasovagal attacks, studies in recent years in patients aged 40+ indicate positive effects, so for this age group they are often to be recommended, he points out. Other drug alternatives, including selective serotonin reuptake inhibitors, e.g. paroxetine, are being discussed, but Prof Schuchert recommends their very careful use due to lack of long-term data.

Furthermore, in cases of vasovagal attacks the physician should check whether the patient is taking anti-hypertensive medication, which might cause the syncope and which could be reduced or discontinued.

In some cases a cardiac pacemaker may be an option. 'Such an implant is indicated if, for example, an event or loop recorder, which records the ECG over several months or even years, shows that asystoles are the cause of the fainting attacks,' he points out.

#### Fluids and physical exercise

Often, various lifestyle changes are also recommended to avoid vasovagal attacks: more fluid intake, more salt in the diet and more

physical exercise. However, scientifically, he points out their benefit has not been confirmed, which does not mean such changes are not worth a try in sufficiently motivated patients.

For many specialists, less recommendable is 'tilt training', in which patients stand leaning against a wall, depending on the treatment plan, say for half an hour daily, to train their circulatory systems. Theoretically it produces good results, the professor says, 'But it's time-consuming and thus compliance is very poor.'

## Atrial fibrillation

### Experts gathering to define future research

France – Seeking to set the agenda for urgent atrial fibrillation (AF) research, European and international cardiologists will gather this October at the European Heart House, in Sophia Antipolis, the headquarters of the European Society of Cardiology.

A panel of international AF experts has been invited by The European Heart Rhythm Society (EHRA) and the German Atrial Fibrillation Network (AFNET) to their second joint conference to define new research perspectives and identify

unresolved clinical issues in the diagnosis and treatment of AF.

Among subjects for discussion: anticoagulation in patients at intermediate stroke risk; new concepts for rhythm control drug treatment; what to do if pulmonary vein isolation fails; relevance and intensity of ECG monitoring in clinical practice; relevance of clinically identifiable risk factors for AF progression; what causes the first episode of idiopathic AF, and novel therapeutic goals for AF treatment.

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Under the banner *Hear today the heartbeats of tomorrow*, at this year's ESC meeting GE Healthcare will showcase its latest cardiology technology for the management of cardiovascular disease (CVD) as well as several new products. These include the MAC 1600 electrocardiograph, which is based on Win CE5.0 to provide seamless communication to MUSE and CardioSoft and features automatic sync with a time server. GE points out that the device is scalable, to evolve as a department's needs arise.

\* A GE sponsored satellite symposium will be held on Tuesday, 2 September.

GE at ESC: Booth C520 + D500 in Hall B2.

NEW

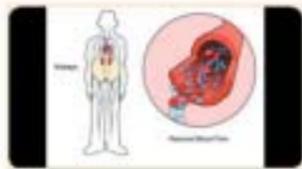
## Website advice for HF patients

A new educational website specifically for heart failure patients, their families and carers, has been set up by the Heart Failure Association of the European Society of Cardiology. On this site, host 'Anna', an animated woman who speaks in a friendly, matter of fact way, guides the visitor through the website advice sections.

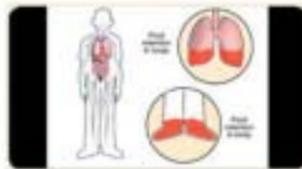
There are also animated explanations covering how the normal heart works, what goes wrong in HF, how the body compensates, and much else (example in illustration).

Cardiologists and physicians who wish to advise patients that they can learn more about their HF condition via their own computers, should pass on this address: [www.heartfailure.org](http://www.heartfailure.org)

Sample of website animated advice:



How heart failure causes fluid accumulation



How diuretics work in heart failure

## Implantable cardiac monitors

Syncope (fainting) is a leading cause of hospital emergency visits. In almost 10% of patients, syncope has a cardiac cause; in 50%, a non-cardiac cause, and in 40% the cause of syncope is unknown. Syncope is difficult to diagnose as syncopal episodes are often too infrequent and unpredictable for detection with conventional monitoring techniques.

Medtronic reports that its new *Reveal DX* and *Reveal XT* can provide diagnostic and monitoring insights into cases of syncope or abnormal heart rhythms,



including ventricular tachyarrhythmias (VT), fast ventricular tachyarrhythmias (FVT), bradyarrhythmias and asystole. 'The Reveal DX continuously monitors the heart's electrical activity to help physicians diagnose whether or not there is a cardiovascular cause for symptoms such as fainting, dizziness and unexplained seizure-like episodes.'

During a simple out-patient procedure, the Reveal DX monitor – weighing just 15g and about the size of a memory stick – is placed subcutaneously in the chest area using local anaesthesia. The monitor then records important cardiac rhythm data, which may help a physician to diagnose the patient and provide appropriate treatment.

Unlike a pacemaker or implantable cardioverter-defibrillator, there are no leads (tiny wires) that extend from the device into the heart's chamber(s). To store an electrocardiogram (ECG) at the time of an episode, a patient places a hand-held, pager-sized activator over the device and presses a button. Later a physician analyses the stored information and determines if the episode was caused by an abnormal heart rhythm.

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### Heart Failure Congress 2009

30 May -  
2 Jun 2009



Among the many aims of the *Heart Failure Association* of the ESC is the establishment of networks for the HF management, education and research. The HFA's next annual meeting will be held next summer in the Palais Acropolis, Nice, France.

[www.escardio.org/congresses/HF2009](http://www.escardio.org/congresses/HF2009)  
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