CARDIOLOGY

EUROPEAN HOSPITAL

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It's ESC time again!

Kim Fox, President of the European Society of Cardiology

And the focus is *heart failure*

Given the exponential increase in the patients presenting with heart failure in recent years, a total of 53 sessions have been dedicated to the topic of heart failure. The sessions include clinical updates and state-of-the-art lectures, but also the newest on diagnosis and therapy will be presented. In their welcoming address, Kim Fox and Jeroen Bax highlight some of the lures of this important and notable event for cardiologists worldwide

Jeroen Bax, Chairman of the Congress Programme Committee

1–5 September and the Vienna venue for the annual Congress of the European Society of Cardiology (ESC) will engross about 22,000 people, arriving from all over the world to attend Europe's biggest cardiology meeting. 351 sessions are planned to take place in 28 rooms, and there will be many presentations of original scientific work.

Four named lectures – four presenters

- *The William Harvey Lecture* on Basic Science will be presented by Professor P Carmeliet
- *The Geoffrey Rose Lecture on Population Science* by Professor P Puska
- *The Rene Laennec Lecture on Clinical Cardiology* by Professor W McKenna
- *The Andreas Gruentzig Lecture on Interventional Cardiology* by Professor T Luescher.

The Focus sessions

These consist of live transmissions from European locations – Katowice, Berlin, Bad Nauheim, Bern and Vienna – to demonstrate practical skills in imaging and intervention. Clinical Practice sessions will encourage interactive discussions between an expert panel and audience. Two of the session will focus on mild heart failure (HF) and end-stage HF.

Joint sessions

The American Heart Association and the American College of Cardiology, as well as societies representing subspecialties such as hypertension, atherosclerosis and diabetes, etc. will present joint sessions.

12 main sessions

These will be packed with important clinical topics, e.g. the relation between anaemia and heart failure, or the role of BNP in heart failure.

The safety of drug-eluting stents will be another hotly discussed subject, as will the increasing role of non-invasive imaging using different modalities, and the development of percutaneous valve therapy.

New ESC guidelines

Five new ESC guidelines are to be released on acute coronary syndromes without ST elevation, valve disease, cardiac pacing, hypertension and prevention of cardiovascular disease. In addition, the new Universal Definition of Myocardial Infarction (endorsed by the AHA, ACC and ESC) will be presented.

The EHSP

Lessons from the Euro Heart Survey Programme – an extensive questionnaire involving many hospitals in ESC countries across Europe – will be the focus of four other sessions.

Annual meetings

The five ESC Associations will report on their annual meetings or present their news in 90-minute sessions organised in the Association Corner. The five include subspecialisations – echocardiography, heart rhythm, prevention, percutaneous coronary intervention, and heart failure.

Working lunch

Participants can also fill their lunch periods with attendance at nine practical sessions under the banners *Meet the Expert; Read with the Expert*, and *How to*.

Three Hotlines - Two Clinical Trial Updates

Late-breaking trials and the most recent updates on published trials will be presented. These sessions frequently include large, randomised clinical trials that have major impact on patient management.

Basic Science

The Council for Basic Cardiovascular Science will present sessions in a bench-to-bedside format, focusing on the translational aspect of basic science, but also highly specific basic science research will be presented.

Abstracts and posters

Submitted abstracts: almost 10,000. Reviewers to grade abstracts: Acceptance rate: 37%.

New for 2007: the State-of-the-Art and Featured Research Track. Sessions will include a keynote lecture by an expert, combined with four oral presentations of the highest ranked abstracts on a specific top.

MRI and the diagnosis of arteriosclerosis and plaque imaging

The spatial-anatomic visualisation offered by MRI already provides immense diagnostic possibilities for cardiology. However, as yet, the potential of this imaging modality is far from exploited, according to Professor Bernd Hamm (right), of the Radiology Department at the Charité Hospital, Berlin. Daniela Zimmermann of European Hospital, asked him why

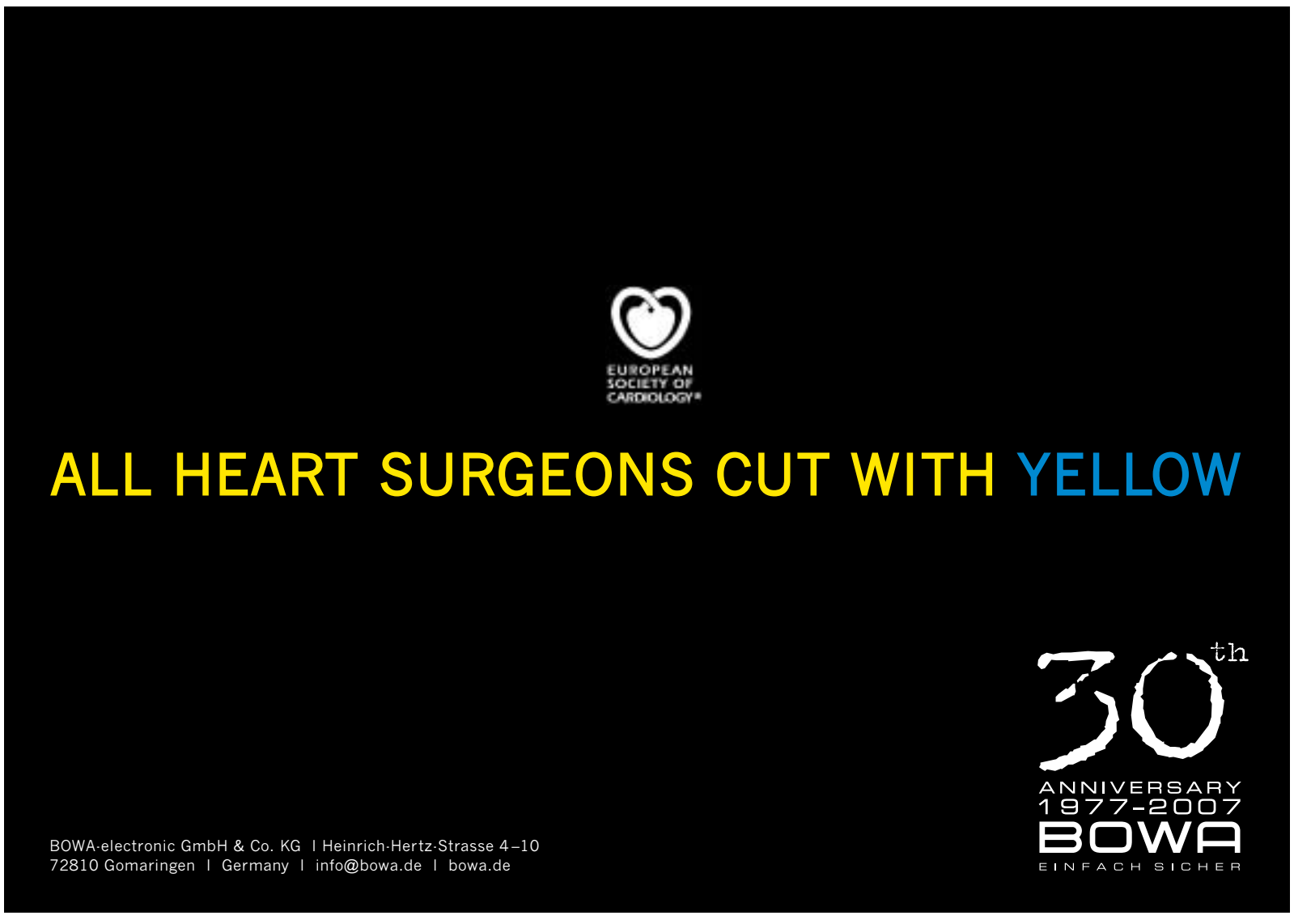
Professor Hamm: 'As far as the visualisation of vessels and vessel periphery is concerned, MRI has made other imaging modalities all but obsolete. Whole-body angiography, which is state-of-the-art MRI technology, for the first time offers the possibility to visualise all vessels non-invasively. Patients who suffer from a stenosis – which in most cases is accompanied by arteriosclerosis – will particularly benefit from this new technology. Arteriosclerosis is a systemic condition, which quite often means you will find stenoses in different regions of the body that have not yet become clinically relevant. In such cases, whole-body angiography can significantly influence therapy management: Imagine a patient who is diagnosed with a stenosis in the pelvic region but the whole-body angio shows a second stenosis, for example in the carotid artery. Obviously, to prevent future intra-operative complications, we will treat the latter first. This non-invasive method has many advantages – both for the physician and patient.'

What role does molecular imaging currently play in cardiology?

'In molecular imaging we – just like everyone else – are in the very early stages. We do basic research, so to speak. Research into the visualisation and differentiation of stable and vulnerable plaque is very important for us. Vulnerable - that is inflamed - plaque can rupture at any moment and cause thromboses, which are often fatal. At this point we do not have a method do distinguish vulnerable from stable plaque. This is where molecular medicine comes in: The macrophages (cells that play a crucial role in the inflammation process of the plaque) bind well with magnetic nano particles. In the Nano for Life Working Group, a research co-operation between Siemens and here at the Charité in Berlin, we work with ultra small iron particles that can make vulnerable plaque visible in MRI. Even more: we can determine the status of the inflammation, because the higher the inflammation activity the better the uptake of the iron markers. Based on the number and distribution of the markers in the body, we can then provide a very precise risk analysis for the patient. MRI is the most sensitive procedure to visualise these markers.

'There are also CT research projects that are important for cardiology – the non-invasive visualisation of the coronary vessels, for example. We are working with a 64-slice CT which is able to visualise the coronary vessels very reliably.

'In summary we expect immense progress in cardiological imaging in the near future – progress which will enable us to diagnose diseases earlier and more precisely.'



A next-generation diagnostic tool for cardiovascular disease, using a nanoscale iron particle, is now under development at a unique industry-government-university named Nano AG. A report from Siemens describes the research and progress at the centre

Hot Spots: NANOSCALE CONTRAST AGENT FOR IMAGING CORONARY ARTERIES

'The tiny particles under investigation are less than seven nanometres across, with an iron core that is highly responsive to the intense magnetism of an MR system. Most MR imaging of coronary arteries already employs contrast agents to improve image quality. Coronary arteries are small and due to the movement of the heart during the cardiac cycle, there is very little net imaging time, so you need a contrast agent to get a sufficient signal-to-noise ratio. The super paramagnetic iron oxide particles under development have an optimal signal-enhancing effect far above that of existing contrast agents. An on going phase II trial is measuring blood flow through coronary arteries. The goal is to compare images made with the nanocontrast agent to those made with traditional X-ray angiography.

A second application for the highly responsive nanoscale particles is more speculative, but could prove more valuable. With assistance from Siemens, the consortium leader of Nano AG, Prof. Taupitz and colleagues at other luminary academic sites are trying to attach the tiny particles to peptides that bind to specific structures in the body, which could turn the nanoparticles into disease–hunters inside the body.

To detect arterial plaque, the nanoscale iron oxide particles could be attached to a factor that would, in turn, attach to compounds involved in apoptosis. Programmed cell death in the artery wall is one sign of vulnerable plaque. A second tactic could link to compounds associated with angiogenesis, which often occurs in unstable plaque. In either case, the tiny particles will enrich within the pathologic vessel walls and generate hot spots on a MR image.

Currently, physicians must rely on indirect methods to specifically image diseased arteries. It is a change in paradigm for vascular diagnosis. We may have to look not so much at flow-limiting stenosis, or narrowing, but at the composition of the plaques and the change in the vessel walls. Using a specific contrast medium means to get functional information and then to make a prediction of the risk of plaque rupture in the artery.'

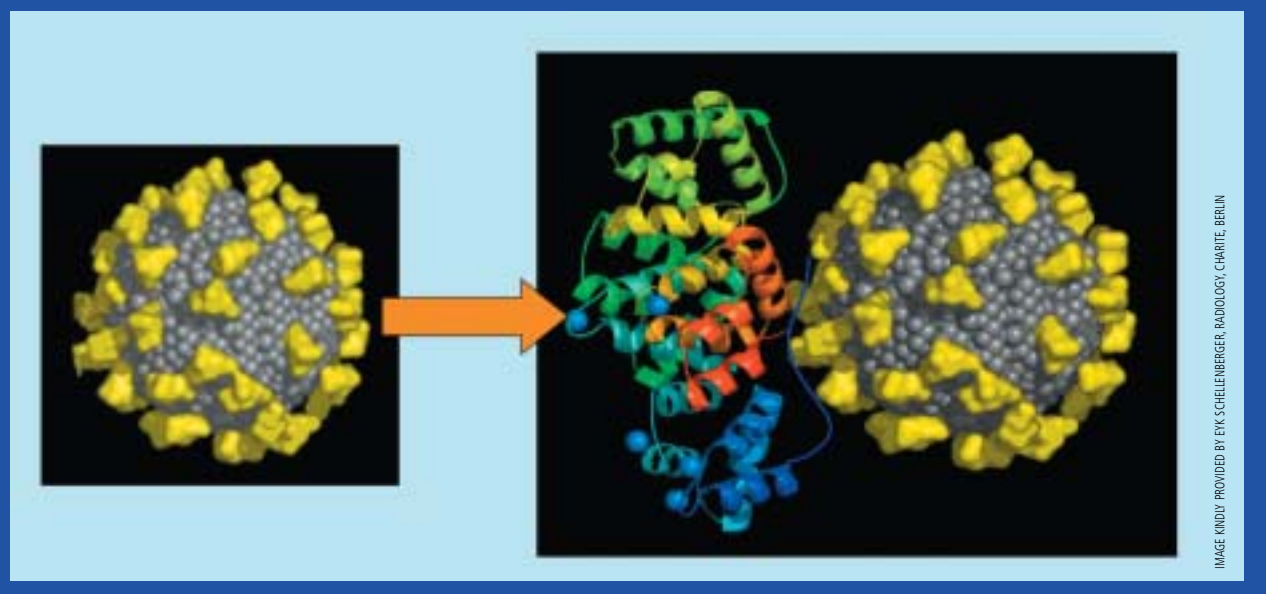


IMAGE KINDLY PROVIDED BY EYK SCHELLENBERGER, RADIOLOGY, CHARITE, BERLIN

VSOP particle with yellow molecules indicating the citrate bound to the iron oxide surface (grey). Functionalisation of the particle by specific peptides e.g. Annexin V

For and against

Absorbable metal stents

Dr Dirk Boese, West German Heart Centre, Essen

By **Dirk Boese MD**, with **S Sack MD** and **R Erbel MD**, of the West German Heart Centre in Essen, and Cardiology Department at the University of Duisburg-Essen, Germany, have summarises

Coronary stents provide wall wrapping of dissection, prevent elastic recoil, and reduce restenosis after percutaneous transluminal coronary angioplasty. In addition, drug eluting stents loaded with antiproliferative agents inhibit intimal hyperplasia and offer a further reduction of restenosis. But stents are foreign bodies ('metal jackets') that transform elastic vessels into rigid tubes, impair vasomotion, and, due to the potential risk of even late thrombosis, require long term antiplatelet treatment.

To overcome limitations of current stent technology, a magnesium-based absorbable metal stent (AMS-stent) was developed in Berlin, by Biotronik GmbH & Co, and successfully tested in animals and below the knee interventions. The magnesium stent provides vessel scaffolding within the first weeks after implantation and is completely absorbed within eight weeks before long term complications may occur.

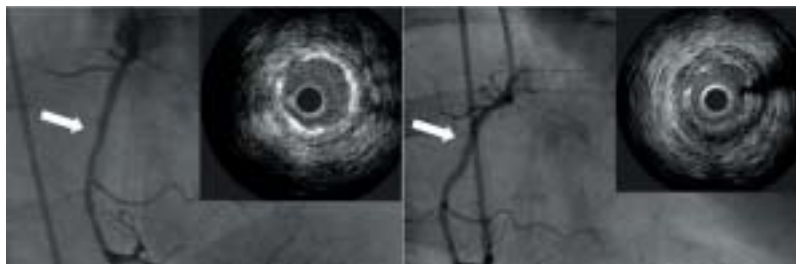
The efficiency of absorbable metal stents in the treatment of coronary artery stenosis was determined in the PROGRESS-AMS (Clinical Performance and Angiographic Results of Coronary Stenting with Absorbable Metal Stents) clinical trial. Seventy-one stents (3.0 - 3.5mm in diameter) were successfully implanted in severe coronary stenosis of 63 patients (mean age 61.3 ± 9.5 years). Procedural success could be achieved in all patients and the diameter stenosis could be reduced from 61.5% (±13.1%) to 12.6% (± 5.6%). During implantation, the stent characteristics were comparable to stainless steal stents (elastic recoil ~ 7%) and no MACE (Major Adverse Cardiac Events) were observed during hospital stay. After four months, the ischemic driven revascularisation rate was 23.8% and therefore comparable to conventional stainless steal stents. Intravascular ultrasound (IVUS) examination during four months follow-up demonstrated an advanced absorption process with only small 'stent remnants'. In the 12 month clinical follow-up period no stent thrombosis was observed.

This study is the proof of concept that biodegradable magnesium stents can achieve an immediate result similar to the result of other metal stents and be safely degraded after four months. Nevertheless, the restenosis rate remains high and modifications of the stent characteristics, i.e. prolonged degradation and/or drug elution are objects of further development addressing the problems of excessive recoil and proliferation.

Due to reduced radiolucency of the used magnesium alloy, the AMS-stent cannot be visualized by X-ray and induces no metallic artifacts during assessment with computed tomography and magnetic resonance. This characteristic allows the non-invasive assessment, even of the stented segment, after implantation of an AMS-stent and gives new opportunities in the follow-up examinations after coronary artery interventions.

Contact for references and further details: Dr Boese. +49-201-7234888 e-mail: dirk.boese@uk-essen.de

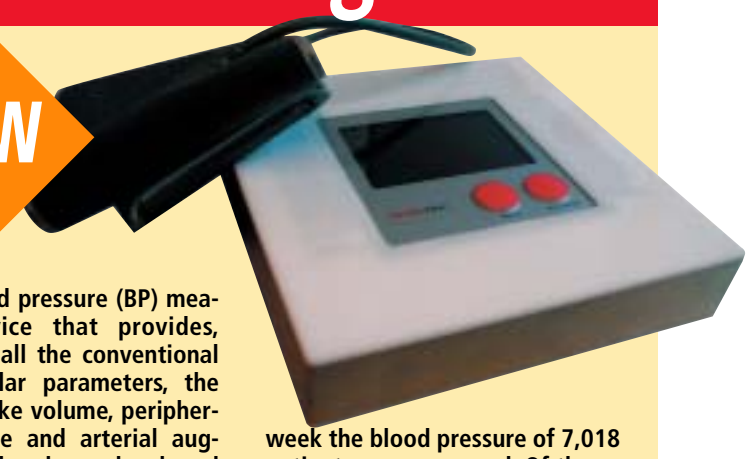
Absorbable metal stent (from Biotronik) after expansion (left panel) and in electron microscopy magnification (right panel)



Final angiographic result after implantation of a 3.0x15 mm AMS-stent in a proximal right coronary artery. Arrow indicates stented segment. Intravascular ultrasound examination indicated a good stent expansion with complete stent apposition (Panel A). After four months, angiography revealed a good long term result, without significant restenosis. IVUS- control proved a nearly complete absorption of the AMS-stent with only stent remnants (Panel B).

BP measuring device

NEW



A new blood pressure (BP) measuring device that provides, along with all the conventional cardiovascular parameters, the cardiac stroke volume, peripheral resistance and arterial augmentation, has been developed at the Austrian Research Centre (ARC), Vienna-Seibersdorf, have been working to develop a new, more powerful method to measure blood pressure. The result of seven years' work by researchers, the device, named CardioMon, is now ready for sale.

The ARC refers to one study in particular to underline the need for their advanced measuring system. Conducted during a *Vienna Cardiovascular Events* programme in 2005, within one week the blood pressure of 7,018 patients was measured. Of those, 1,109 people were receiving treatments. However, only 175 were being correctly regulated, mainly because conventional blood pressure measuring methods could only indicate symptoms, but not the cause of problems. For those, invasive methods, such as catheterisation, have been necessary. The ARC reports that its CardioMon will make such a difference to this, that it will have supplanted all conventional blood pressure measuring tools in just a few years.

Cardiac resynchronisation therapy

Worldwide clinical trial gets underway

Switzerland – A clinical trial of cardiac resynchronisation therapy (CRT) in patients with advanced heart failure and a narrow QRS complex <120 ms, has been initiated by Zurich University.

The clinical benefits of CRT, as an adjunct to drug therapies, in patients with NYHA class III/IV heart failure (HF) have been shown repeatedly in randomised trials and clinical practice. *The Miracle ICD trials* [Young JB, Abraham WT, Smith AL, et al,. Combined cardiac resynchronisation and implantable cardioversion defibrillation in advanced chronic heart failure: The MIRACLE ICD Trial. *JAMA*. 2003;289:2685-2694], *and Companion trials* [Bristow MR, Saxon LA, Boehmer J *et al*. Cardiac-resynchronisation therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;350:2140-50] suggested that CRT, which paces the left as well as right ventricles simultaneously, used in conjunction with an implantable cardioverter defibrillator (ICD) improved the quality of life, functional capacity and exercise test performance in patients with HF with a wide QRS (⩾120 ms) interval. Indeed current guidelines for the selection of suitable patients for CRT based on the published evidence advise that optimal candidates to benefit from CRT have QRS >120 ms. [Strickberger SA, Conti J, Daoud EG et al. Patient selection for cardiac resynchronization therapy: from the Council on Clinical Cardiology Subcommittee on Electrocardiography and Arrhythmias and the Quality of Care and Outcomes Research Interdisciplinary Working Group, in collaboration with the Heart Rhythm Society. Circulation 2005;111:2146-50.]

This means that until now, the majority of HF patients, those with a narrow QRS complex, have been excluded from CRT, although suffering from dyssynchrony. The *Echocardiography guided Cardiac Resynchronisation Therapy* (EchoCRT) study aims to provide the necessary evidence base to expand therapeutic options for this population.

EchoCRT is the first prospective, randomised clinical trial to evaluate the impact of cardiac resynchronisation therapy in HF patients (NYHA Class III) who show mechanical dyssynchrony as assessed directly by echocardiography. Echocardiogram (ultrasound of the heart) will provide a direct measure of ventricular dyssynchrony, which is not apparent on indirect assessment by ECG because of the narrow QRS. More than 1,000 patients with advanced HF (NYHA Class III) will be randomised into treatment groups with CRT or no CRT. Both groups will receive an ICD to protect against sudden cardiac death, but in only half of the patients will the CRT capacity be switched on.

The co-principal investigators in Zurich are Dr Frank Ruschitzka and Dr Johannes Holzmeister.

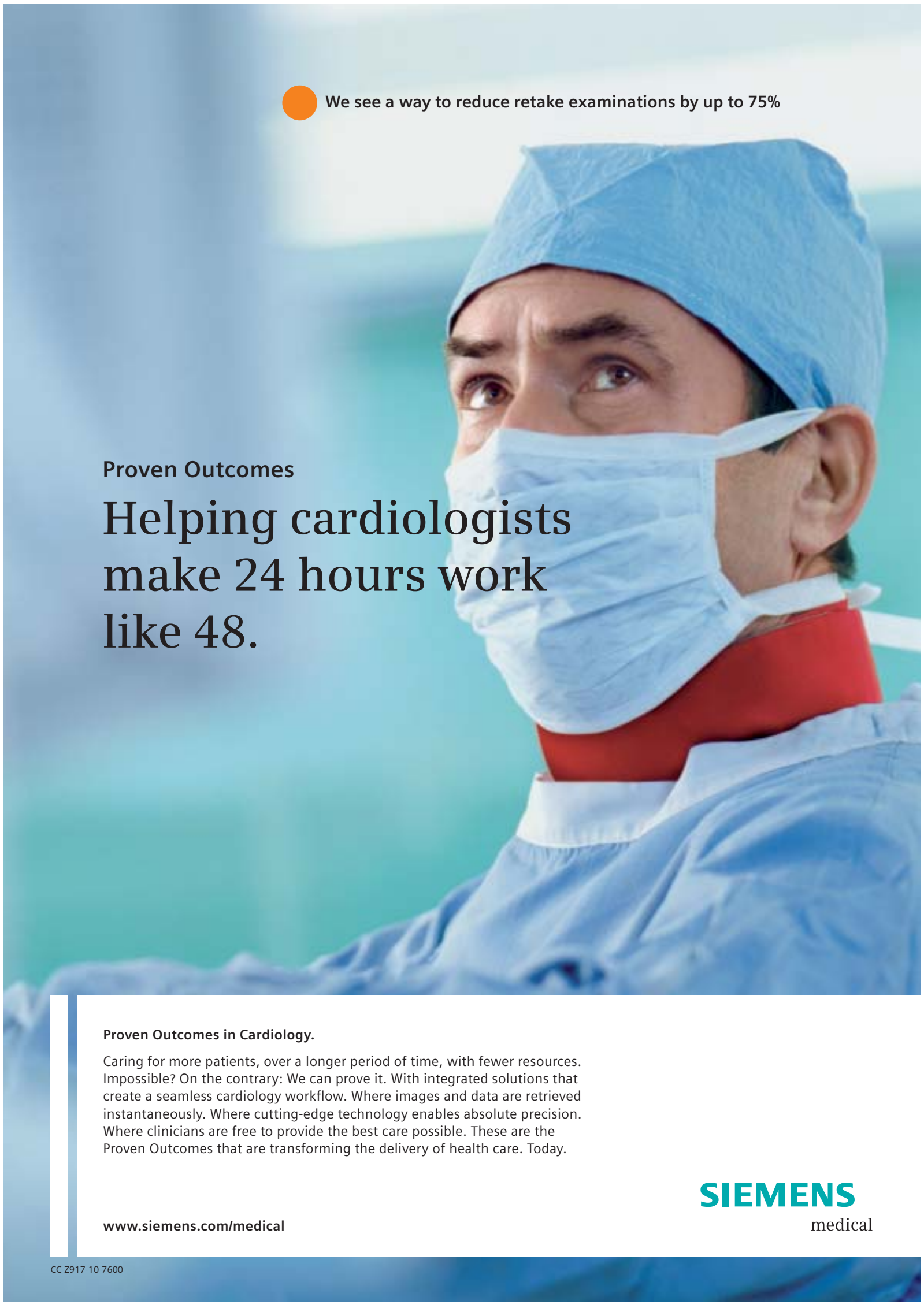
In an interview with Dr Ruschitzka, we asked why Zurich has become the international centre for this study and what the rationale is behind the EchoCRT trial.

'This is a very large clinical trial of a medical device and will involve 120 different centres worldwide, but it's led by Zurich because of our wealth of experience in clinical cardiology trials.' The trial is sponsored by Biotronik, which manufactures the implanted devices but, Dr Ruschitzka pointed out, 'EchoCRT is an independent, investigator led trial overseen by an international executive committee.'

'Many cardiologists feel, as I do, that we are not treating many HF patients who would benefit from CRT simply because there are no scientifically evidence-based guidelines telling us to. I have used CRT successfully in patients with narrow QSR, and so have many others. The medical literature supporting this belief is increasing with observational studies and anecdotal cases of success in several thousands of these patients.

'The ESC recently conducted a poll asking its members if they thought patients with a narrow QSR would benefit from CRT. The time is now right for a large-scale, international trial to provide the definitive answer. Recruiting will begin in the first quarter of 2008 and will probably last for up to two years. The trial itself will probably run for a further two or three years after recruiting is complete depending on when we reach the numbers required statistically of primary end-point. It would be stopped immediately if it became obvious that the benefits of CRT therapy were statistically superior. The results are due in 2011.

'I'm very confident that CRT is the way to go with HF patients with narrow QRS. These are very sick patients with a high morbidity and mortality. I am convinced that it is unwise to withhold CRT from this population and that EchoCRT will provide the necessary evidence to support this treatment change.'



Progenitor cell transfer for cardiac repair after myocardial infarction

By **Stefan P Janssens**, Professor of Medicine at the Cardiology Department, Gasthuisberg University Hospital, KU-Leuven, Belgium

Progenitor cell transfer to repair the damaged heart has emerged as an innovative and promising recent development in cardiovascular medicine. Since the first reports that adult bone marrow-derived stem cells were capable of transdifferentiating into a cardiomyocyte phenotype, research in regenerative medicine has advanced in an explosive manner.

A variety of progenitor cell types that reside in bone marrow, or circulate in the blood, are capable of improving function of the infarcted heart in pre-clinical models, but underlying mechanisms remain incompletely understood. Consequently, the traditional view of the heart as a terminally differentiated organ has been challenged by several groups, who have reported the isolation of cardiac stem or progenitor cells - characterised by the absence of traditional cardiomyocyte, endothelial, or smooth muscle markers, and that have a slow turn-over rate, and might constitute an endogenous reservoir for cell-based repair.

However, massive cell loss of cardiomyocytes and these progenitors alike, such as after acute myocardial infarction, precludes sufficient repair capacity of these endogenous progenitors in the infarcted territory. Therefore, cell-based repair requires inventive strategies to mobilise or deliver significant numbers of progenitor cells to sites of injury and secure their survival, or to stimulate neighbouring cardiac precursor cells to multiply, integrate, and couple with spared myocardium and enhance myocardial function.

While those strategies are very appealing, a major question is whether we have the knowledge and tools to implement them at this stage in clinical practice, at an equitable cost-benefit?

Initial trials of autologous bone marrow cells focused understandably on safety and feasibility both in patients with acute myocardial infarction (AMI) and chronic ischemia and reported enhanced recuperation of LV function. However, by virtue of their design, these studies were not randomised, or lacked a proper control population undergoing the exact same interventions as patients receiving cell transfer. Subsequent double-blind, placebo-controlled randomised trials of autologous bone marrow cell transfer in myocardial infarction patients have shown augmented recovery of global LV function after cell transfer of variable magnitude (absolute increase ranging from 1.2 to 2.5%). The latter was associated with a favourable effect on myocardial perfusion (evaluated as coronary flow reserve), infarct remodelling with a greater reduction in infarct size and greater recovery of regional LV function. Although we are still in a preliminary phase of clinical development, meta-analysis of published randomised controlled trials and cohort studies of bone marrow cell transfer (including 999 patients) confirmed an overall benefit, above and beyond state-of-the-art therapy.

While the absolute increase in global function recuperation may seem modest at first glance, it represents an incremental improvement of almost equal magnitude as the initial therapeutic effects of primary coronary revascularisation. Moreover, we now have convincing data from the largest randomised double blind study that a delayed strategy of cell transfer offers the greatest benefit and that it is almost exclusively observed in patients with a significant reduction in myocardial function at baseline.

These insights will help to facilitate strategies whereby cell-based treatment algorithms are reserved for patients suffering the largest infarcts and where cell transfer can be established according to the highest scientific standards. Indeed, quality assurance of all stem/progenitor cell isolates requires significant haematological expertise, and has been shown to have a major impact on clinical results in early exploratory trials.

At this stage, while safety has been uniformly reassuring, proof of clinical efficacy (improved survival and reduction of heart failure) awaits larger multi-centre outcome trials that are presently being designed. To implement standardised, SOP-based cell isolation, and characterisation protocols, haematological and cell culture expertise from experienced institutions, including central blood bank or Red Cross laboratories or bone marrow transplant centres, will be indispensable.

Finally, enabling such treatment at an affordable cost will require intense collaboration between translational scientists, physicians, healthcare administrators, and private and public health insurance companies.

The therapeutic potential of adult stem cells in CVDs

By Professor **Bodo-Eckehard Strauer MD**, Head of the Department of Cardiology, Pneumology and Angiology at Dusseldorf University Hospital

Cardiac infarction is characterised by tissue ischaemia with loss of contractile heart muscle. The consequence is cardiac insufficiency and disturbance to cardiac rhythm. About two thirds of all patients have no symptoms before an infarction; about two thirds of all patients do not survive their cardiac infarction. About a third of surviving infarction patients experience increasingly worsening heart function in the first year after the infarction (remodelling).

The aim of therapy is to re-open the infarcted vessel using acute procedures (balloon dilatation and stent implantation), though this is merely the tip of the iceberg and the destroyed heart muscle usually remains useless. This is where treatment with stem cells comes in as causal therapy, striving to regenerate heart muscle by injecting stem cells into it.

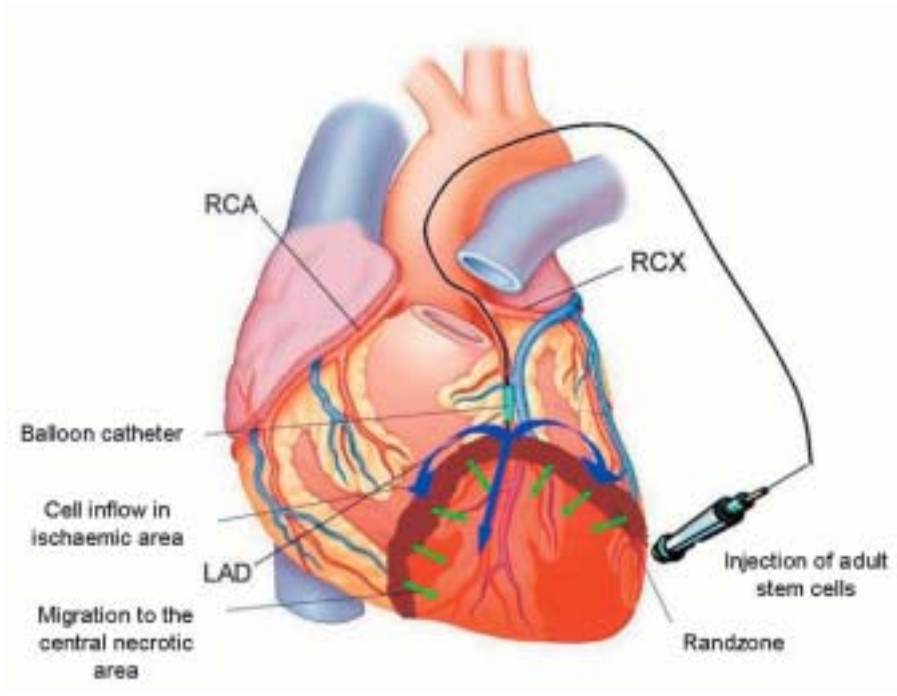


Fig. 1: Method for intracoronary stem cell transplantation: Site of the primary vascular occlusion caused by infarction is dilated with a balloon catheter and bone marrow stem cells are simultaneously and repeatedly injected into the ischaemic area or infarct. This is undertaken in the acute infarction stage (2–8 days after infarction) and in the chronic stage (up to 8 years subsequently). Injection total: 100 to 200 million bone marrow stem cells. Four to six pressure insufflations. Length of PTCA time: approx. 3–4 minutes

	Before cell therapy	After cell therapy	P
n = 50Pat.			
LV-Ejection fraction, %	55±10	63±11	<0.01
Stroke volume inex ml/m^2	48±18	53±17	0.05
EDV, ml	173±55	160±48	n.s.
EDV Index, ml/m^2	87±30	85±25	n.s.
ESV, ml	80±34	61±29	<0.005
ESV Index, ml/m^2	40±17	32±15	<0.005

Fig. 2: Test results from 50 patients with acute myocardial infarction – controlled studies. Before cell therapy i.e. on the 8–9th day after infarction, and three months after cell therapy

Ejection fraction

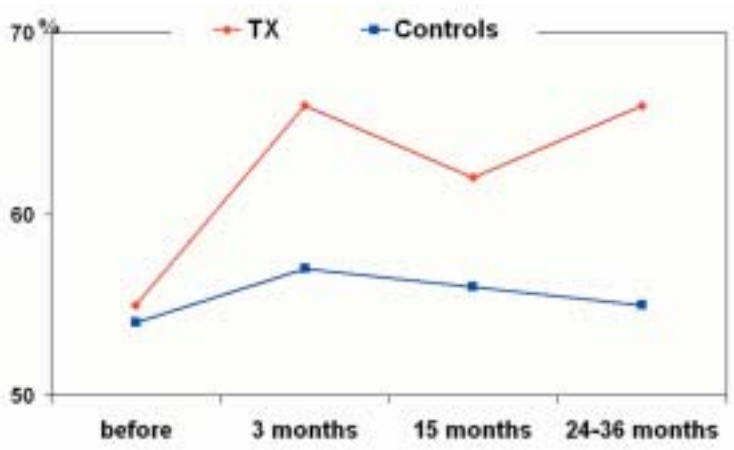


Fig. 3: Ejection fraction over a period up to three years after stem cell transplantation. Maintained improvement can be seen in patients who received stem cell treatment (TX)

Stem cell application

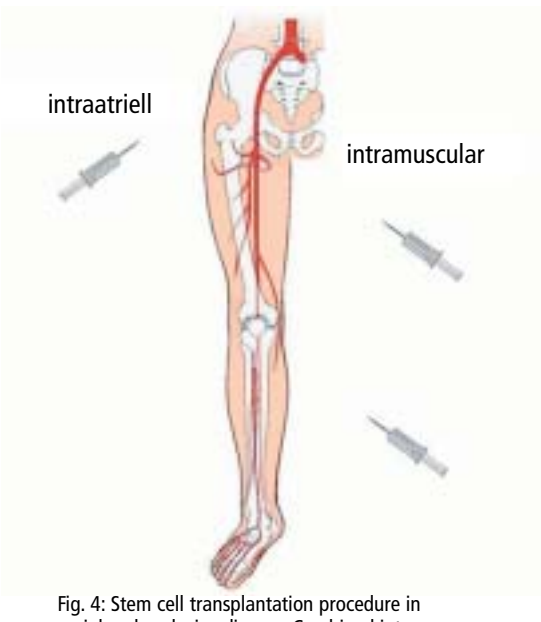


Fig. 4: Stem cell transplantation procedure in peripheral occlusive disease. Combined intra-arterial and intramuscular injection. For better migration, stem cells are injected after repeated compression using a cuff and ergometry loading

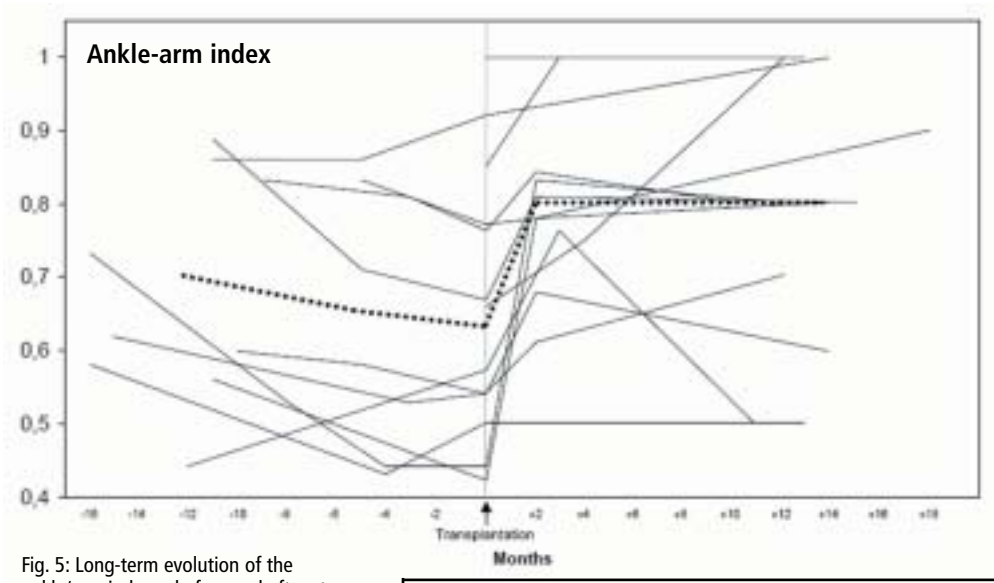


Fig. 5: Long-term evolution of the ankle/arm indexes before and after stem cell therapy. Improvement after six months averages up to 30%

The body itself contains naturally occurring, adult autologous stem cells, e.g. in the bone marrow. They are an ethical resource of cells that is completely safe. The idea was therefore to regenerate heart muscle clinically, by transplanting naturally occurring bone marrow stem cells into the infarcted region. This process was developed in Dusseldorf.

Bone marrow was removed and the cells prepared, then, after re-opening the infarcted vessel by balloon dilatation, they were injected into it under low pressure, using a balloon technique. The vessel was kept open with a catheter (a procedure lasting about 30 minutes), during which time two to three ml of a suspension of stem cells were injected into the infarcted region, a process repeated with four to six insufflations. The intervention was carried out on conscious patients with local anaesthesia, and at most produced mild pain at the site of injection.

Follow-up controls for three years and longer after the infarction show that long-lasting improvement in cardiac function has been achieved, with an average increase in cardiac function of 50% and a reduction in the size of the infarct of about 20%. At the same time, blood supply to the cardiac muscle has been considerably improved, as has metabolism, and physical strength has increased. As yet, no side effects have been reported, so the procedure should be considered an ethically safe treatment of muscle loss after infarction, and causal therapy that is really beneficial to the patient.

The Dusseldorf results have since been confirmed worldwide. Work groups in Frankfurt, Hanover and Rostock have been able to show, even in larger studies, that regeneration of infarcted cardiac muscle can be achieved by transplanting autologous bone marrow stem cells. What is important is that this myocardial regeneration, which, depending on study design, is between 4–16%, is of an order of magnitude that is at least as great as the sum of all therapeutic improvements in ventricular function achieved with balloon dilatation or stent implantation for cardiac infarction. Consequently, added improvement in patients' ventricular function can thus be achieved, on top of surgical intervention and drug treatment.

No complications from the stem cell treatment have been reported so far. There is no malignant degeneration as the cells used occur naturally in the body. No signs of inflammation have been observed, nor have disturbances to cardiac rhythm, angina pectoris or respiratory distress. Complications arising from the procedure itself are much the same as those that might occur in ordinary heart catheterisation procedures, and are insignificant.

It should be mentioned that a similar procedure is also effective in treating peripheral arterial disease. In this case, treatment involves intra-arterial and intramuscular injection of autologous bone marrow stem cells into the limbs affected, the therapy first practised by Bartsch et al. Ischaemic preconditioning, such as by compression induced with a cuff, or even ergometry, greatly promotes migration of stem cells into the muscles.

After three months there was marked improvement in the length of stride, the ankle/arm indexes, oxygen saturation and even venous occlusion plethysmography parameters. Consequently, autologous stem cell therapy can also be classed as a successful procedure for peripheral arterial occlusive disease, where symptoms are refractory to treatment, and in advanced stages of vascular disease.

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Ready for action: The 17.5

The world's first portable, plug-and-play system to provide hours of emergency cardiopulmonary support is now on sale in Europe. *EH correspondent* ***Holger Zorn*** *reports*

The *Lifebridge B_2T* (bridge-to-transport) is the first, fully portable emergency life support system for patients suffering cardiogenic shock, or those showing signs of imminent cardiogenic shock. The machine ensures circulation and sufficient blood oxygenation can be restored in just minutes, thus preventing multi-organ failure leading to death. Whether in hospital or an ambulance, a patient can be connected to the Lifebridge to replace external cardiopulmonary reanimation.

First introduced in 2005 (see EH 3/2005), this equipment recently received a CE mark allowing sales across Europe. Its small size (61 x 45 x 37 cm), low weight (17.5 kg) and power supply via integrated battery make it ideal for ambulant use. The partly guided, partly automated set-up means that in five minutes it is ready for use by emergency doctors or paramedics – without needing a specialised technician.

To avoid air embolisms, seven security steps guarantee maximum patient protection. Access to the patient is either by percutaneous puncture and insertion of cannulae in vessels in the groin or, after thoracotomy, via insertion of central cannulae into the right atrium and rising aorta. Depending on the access, blood circulation of six litres per minute can be achieved, a volume that ensures adequate gas exchange and sufficient perfusion of all important organs.

The German Heart Institute in Berlin tested the Lifebridge during elective routine procedures in bypass surgery. The objective of those trials was to demonstrate the quality of the new, portable system compared with a traditional heart-lung-machine. The Lifebridge ran for up to 103 minutes (average: 82 minutes). Under conditions typically found in this kind of heart surgery, with complete cardiac arrest and no ventilation, the machine facilitated sufficient blood circulation to the organs and adequate gas exchange. Therefore, the Lifebridge also can be used pre-emptively during risky cardiac surgery (e.g. high-risk PCI).

At the launch a panel of experts discussed the merits of portability

In an earlier experimental study at the University of Cologne, cardiac surgery using the Lifebridge was simulated using pigs. The animals' blood gases were kept constant during the entire length of the study. The blood circulation remained constant even when the height difference between the machine and heart was changed. Injection of up to 100ml of venous air also did not reduce blood flow, and even the most disadvantageous conditions did not result in an arterial air embolism (source: Mehlhorn U et al., Ann Thorac Surg 2005; 80: 1887-92).

Gap in supply of technology for the treatment of cardiogenic shock can be filled

Annually, hundreds of thousands of Europeans suffer heart attacks,

STENTING

Platinum chromium alloy enhances design

Boston Scientific Corporation has commenced enrolment of a targeted 1,500 patients for the Taxus Perseus clinical trials, planned to take place in 100 international centres. The aim is to evaluate the firm's third-generation paclitaxel-eluting coronary stent - the *Taxus Element Stent*. This stent features the proprietary Platinum Chromium Alloy (designed specifically for stents) which, combined with a new stent design, is designed to allow thinner struts, increased flexibility, and a lower profile, while improving radial strength, recoil, and radiopacity, Boston Scientific reports, adding that the stent's platform incorporates new balloon technology, intended to improve on the firm's Maverick Balloon Catheter technology.

Dean J Kereiakes MD is principal investigator for the trials and Medical Director at The Christ Hospital Heart and Vascular Centre and The Lindner Research Centre, in Cincinnati. Louis A Cannon MD, of the Cardiac and Vascular Research Centre of Northern Michigan in Petoskey, is co-principal investigator.

Dr Kereiakes predicted: 'This new platform, designed for improved deliverability, should allow us to bring the long-term proven performance of the Taxus Stent to even the most complex and challenging anatomy.'

The first of the two-part study, called Taxus Perseus Workhorse, will evaluate the safety and efficacy of the TAXUS Element Stent compared with Boston Scientific's first generation drug-eluting stent (Taxus Express2). 1,264 patients with 'workhorse' lesions from 2.75 to 4.0 millimetres will be evaluated, with the primary endpoint of target lesion failure (TLF) at 12 months; its secondary endpoint is in-segment percent diameter stenosis at nine months.

The second part, the Taxus Perseus Small Vessel study, will compare the Taxus Element Stent with a historic control (the Taxus V de novo bare-metal Express Coronary Stent System). It will involve 224 patients with lesions from 2.25 up to 2.75 millimetres. The primary endpoint of the small vessel study is in-stent late loss at nine months, and its secondary endpoint is TLF at 12 months. Study success is dependent on both endpoints, Boston Scientific explains.

Hank Kucheman, Senior Vice President and Group President, Interventional Cardiology, said: 'The platinum chromium alloy and new balloon technologies in this system are also being developed in an Everolimus version and is intended to serve as foundational technology in Boston Scientific's dual-drug DES portfolio, including a drug-eluting bifurcation stent and next-generation Everolimus- and Paclitaxel-eluting stents.'

MONITORING

ATRIAL FIBRILLATION MONITORING

FIRST EUROPEAN AF PATIENTS RECEIVE LONG-TERM, CONTINUOUS MONITORING DEVICE

The Netherlands - The first implant of the Reveal XT, an insertable cardiac monitor made by US firm Medtronic, which recently received CE (Conformité Européenne) Mark, was carried out in June by Professor Karl-Heinz Kuck MD, at the Asklepios Klinik St. Georg in Hamburg, Germany.

Medtronic reports that this is the first insertable cardiac monitor to offer long-term and continuous monitoring of atrial fibrillation (AF): 'All other current monitoring tools are either for a limited period or on an intermittent basis. Long-term, continuous monitoring means that a clinician no longer needs to rely only on incomplete data to evaluate how AF may be progressing or treatment effectiveness,' the firm points out.

As is well known, treatment of AF is difficult because episodes often show no symptoms and can go unnoticed by patients. 'Atrial fibrillation is the most frequent cardiac arrhythmia. It is often accompanied by symptoms that are very unpleasant for the patient,' said Prof Kuck. 'Additionally, atrial fibrillation is linked with increased mortality and an increase in the incidence of stroke, by a factor of two- to seven-fold. However, with the new Reveal XT, atrial fibrillation can now be scrutinised over a period of three years with a subcutaneous monitor. This gives us totally new possibilities for monitoring and adjusting the treatment.'

During its three-year activity, the device is reported to monitor AF patients 24 hours a day.

Up till now there has been no method to gather detailed data, over an extended period, on the progression of AF and the effect of treatment. Reveal XT is expected to give new insight into patients' heart rhythms, which might help physicians to evaluate stroke risk and determine appropriate treatment and therapy options for their patients, Medtronic suggests.

Implantation

The Reveal XT is inserted just under the skin, and there is no need for wires or sticky pads to keep it in place. The patient is said to experience no restrictions in daily activities and, because cardiac data is recorded during the patient's normal routines the real-life information obtained could provide important insight to this condition.

The medical devices manufacturer Medtronic, Inc. (www.medtronic.com) is based in Minneapolis; its European office in the Netherlands.

New remote monitoring feature for implantable cardioverter-defibrillators (ICDs)

The company also recently launched a remote monitoring feature for ICDs, which have proved effective (98% of cases reported) in patients suffering recurring ventricular arrhythmias.

These patients have needed to have device check-up's two to four times annually, as well as unscheduled visits in critical situations, Medtronic points out, adding that its new CareLink Network system will enable home-monitoring, with internet-transmission of data from implanted cardiac devices. To do this, the patient holds a small antenna over the device and information on how their heart and ICD are working is transmitted to a secure physician website for a virtual checkup.

'This technology,' said Peter Steinmann, Medtronic's Vice-President for Western Europe, Cardiac Rhythm Disease Management, 'opens up the potential for more efficient chronic disease management and better outcomes.'

kg heart-lung machine

caused by the occlusion of coronary vessels following coronary heart disease. To avoid death or lasting damage a patient ideally needs to receive treatment within 'the golden hour'. However, according to data supplied by MITRA, Germany's heart attack register, in that country alone, the time lapse between heart attacks and start of treatment is on a continuous increase. Between 60,000 and 65,000 patients do not survive their heart attacks (source: Mark B et al., Dts Aerzteblatt 2006; 103: A 1378). Cardiogenic shock kills around 20,000 people. 'Up to 50% of those patients could survive if they received fast mechanical, extracorporeal circulation support,' points out Prof Zerkowski of Basel University, Switzerland.

Ideally, artificial circulatory support should begin during transfer to a specialised hospital, because vital vessels and organs need sufficient blood supply to avoid irreversible damage caused by hypoperfusion. However, mobile emergency systems are not usually used during a transfer, because currently available equipment does not meet requirements for portability and quick, safe use. 'Filling this gap in the supply is of utmost urgency,' said Prof Ruediger Lange, director of the Cardiovascular Surgery Department, German Heart Centre, Munich, during a symposium held during a market launch for Lifebridge. In specialist centres, heart-lung machines used during cardiac surgery must be set up and run by trained perfusionists. Their size and weight make them unsuitable for mobile use. A patient in cardiogenic shock, according to Lange, needs support for cardiovascular function by a lightweight, fast, easy to use machine, which can be used anywhere.

The situation for hospital treatment is similar. Cardiogenic shock develops in 7 – 10% of all infarctions, and it is unpredictable. In such an emergency, currently, doctors mainly use intra-aortic balloon pump counterpulsation (IABP), left-ventricular assist systems along with conventional heart-lung machines (HLM). However, the former can only be used if the heart muscle has remaining functionality. In the case of acute, complete cardiac arrest, the immediate use of a heart-lung machine is necessary.

Even ultra-modern, percutaneous heart-lung machines, which are connected to the patient's circulation via the iliac vessels during external cardiopulmonary reanimation, can only be used after 15–20 minutes. In addition, because they depend on manual operation, user errors and air embolisms cannot be eliminated.

Therefore, a fully-integrated 'click'n'run' heart-lung support system is an urgent requirement, said Prof Zerkowski.

Lifebridge Medizintechnik AG (founded: 1999) has found a market niche with Lifebridge B_2T. With 22 employees, the firm is supported by Bavarian financiers and an investment bank in the United Arab Emirates. It reports that there has already been strong demand from hospitals for this portable heart-lung device, and Manfred Salat, Chairman of the Board, predicts that, as from next year, the Lifebridge should be able to finance further growth internally.

Trial to raise awareness of gender and CVD

More women than men die of cardiovascular disease (CVD) every year, yet females receive only 33% of angioplasties, stents and bypass surgeries; 28% of implantable defibrillators, and 36% of open heart surgeries.

Looking at this situation, Abbott, which produces the Xience V Everolimus Eluting Coronary Stent System, is involved in a clinical trial - in Europe, Asia-Pacific, Canada and Latin America – to study the stent's safety and effectiveness in women patients who have untreated coronary artery lesions.

The first patient to enrol in the trial, called *Xience V Spirit Women*, has been operated on in Argentina, by Liliana Grinfeld MD, at the Italian Hospital in Buenos Aires, Argentina, who reported that the stent system had performed well, and that the patient will be checked for up to five years.

Abbott reports that the trial will focus on '…specific aspects of women's health in relation to coronary artery disease, such as general awareness about the disease, symptoms at time of presentation, referral patterns, and hormonal menopausal status.'

The trial's principal investigator, Marie-Claude Morice MD, at the Jaques Cartier Institute, in Massy, France, commented that it is 'tragic' that women amount to just 25% of participants in all heart-related research studies, and added that the trial had the potential to enhance access to CVD therapy by increasing their and their physicians' awareness.

ESC Vienna Booth B-255

prosound

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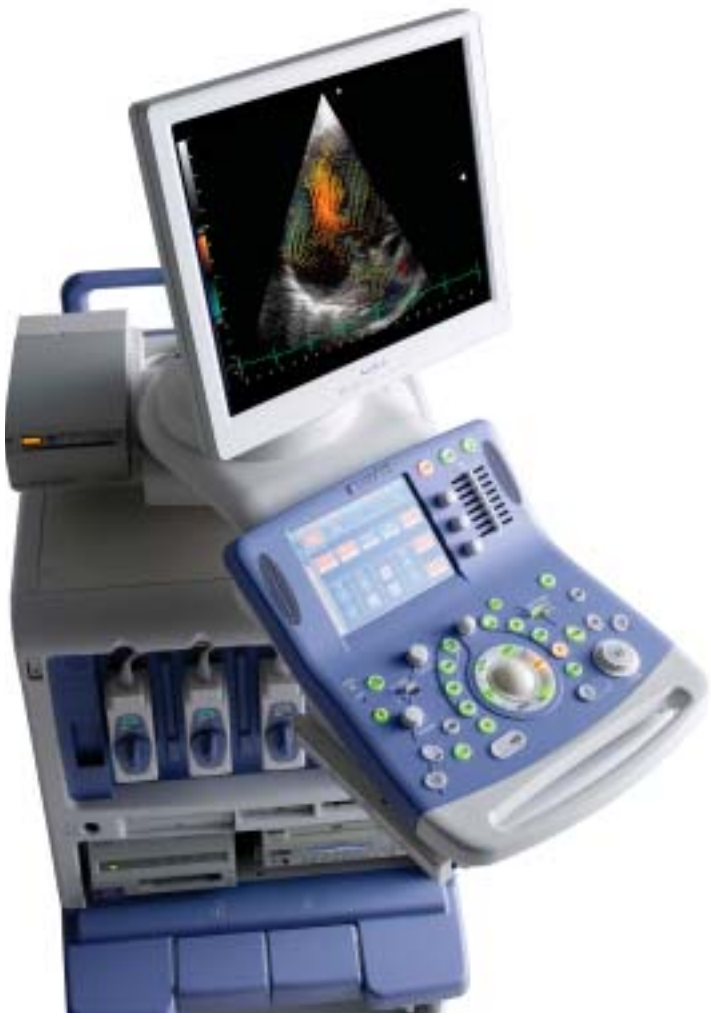
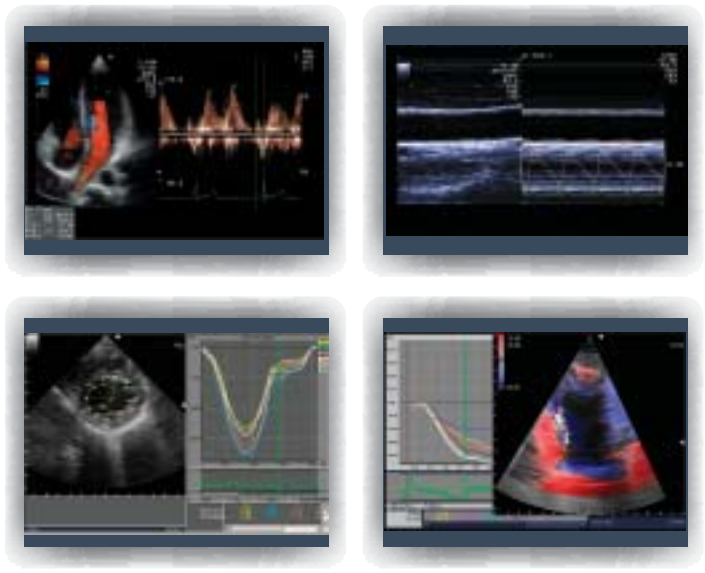
ALOKA technology is the result of a tireless pursuit of quality in imaging, functionality, network management, and analysis. For over half a century, ALOKA has been developing and creating reliable imaging systems for cardiovascular experts, so they can have better insights into healthcare.

The complete ALOKA Prosound CV range is designed to offer high precision and easy to use diagnostic tools to the cardio-vascular specialists; such as ASMA™, 2D tracking™ for asynchrony studies, e-Tracking™ for early atherosclerosis quantification or WI™ for heart/vessel coupling assessments.

ALOKA, the inventor of the first Color Doppler Ultrasound system in 1983, is proud to present its latest innovation at the ESC congress in Vienna: **Vortex Flow Mapping VFM**™, a new proprietary and revolutionizing flow mode opening a new century in the hemodynamic world.





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A non-invasive measurement of arterial wall atherosclerosis

By Thaddeus Chodakauskas BS RDMS and Steve Feinstein MD FACC

Non-invasive ultrasound imaging techniques continue to provide a major role in diagnosis and management of patients with cardiovascular disease. The early presence of atherosclerosis predates major clinical events such as myocardial infarction and stroke. Over the last 17 years, the ultrasound-based measurement of carotid artery intima-media thickness (c-IMT) has become a standard for assessing arteriosclerosis and is recommended by the American Heart Association for the non-invasive assessment of cardiovascular risk.

Carotid intima-media thickness is defined as the distance between the lumen-intima interface and the media-adventitia interface, which corresponds to the inner and outer echogenic lines seen on the B-mode ultrasound image. (Fig.1). Measurement of c-IMT is traditionally performed with the image of the carotid artery in the longitudinal axis, revealing the common carotid artery, the carotid bifurcation, and the internal and external carotid arteries. Although these measurements have been performed for years, significant variability exists when measuring the near wall due to technical and acoustic difficulties encountered when imaging the c-IMT of the near wall.

Due to those technical limitations, clinical measurement of c-IMT using B-mode ultrasound is often applied to the far (posterior) wall of the common carotid artery. With the development of non-invasive imaging technologies, ultrasound methods can be used to reliably measure intima-media thickness (IMT). This measurement serves a non-invasive marker of arterial wall atherosclerotic disease. Studies have found that, on average, based on gender and age, the intima-media thickness will increase 0.01-0.03mm per year. (See tables on historical clinical studies of c-IMT).

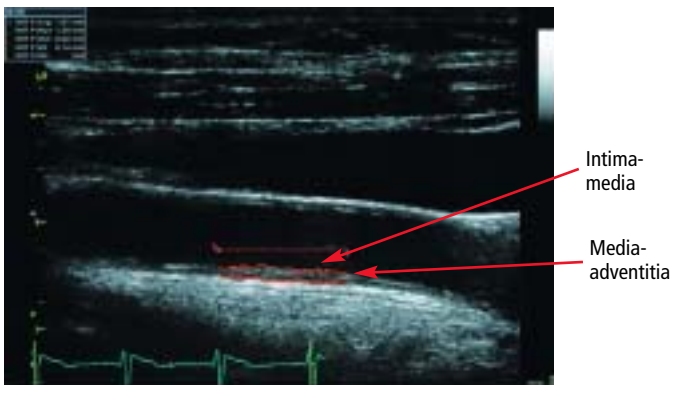


Figure 1: Intima-media wall thickness

Intima-media

To perform these studies, radiographers/clinicians use high frequency (7, 10 or 12) MHz linear array transducers with the Vivid 7 Dimension and the Vivid i to efficiently acquire multiple c-IMT measurements within seconds. The semi-automated measurement for intima-media wall is simple, easy and takes less than four steps. The physician receives immediate results, which consist of these parameters: maximum, mean, average and number of data points examined. Using the software application, the c-IMT measurement can be exported directly to a worksheet and report page and, subsequently, placed in the patient's medical record.

Tips: c-IMT measurements for the Vivid 7 Dimension/Vivid i

Imaging common carotid artery

- Maximise the depth selection and optimise the gain settings to visualise the posterior intima-media wall of the common carotid artery.
- Attempt to capture the common carotid artery with the jugular vein to improve visualisation of the anterior and posterior carotid walls.

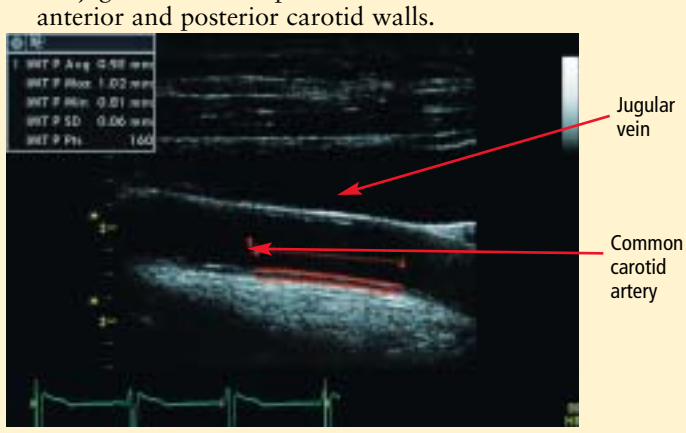


Figure 2: 50-60 data points

Measuring c-IMT

- Identify a single frame during the end-diastolic phase between the P and Q wave off the ECG trace.

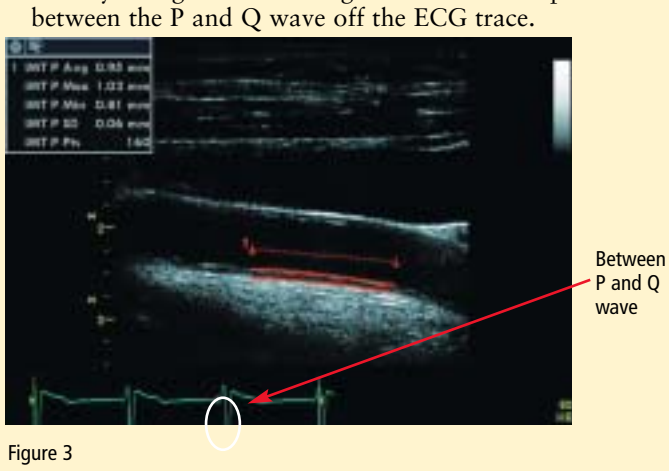


Figure 3

- Approximately 50-60 data points is an adequate sample when used to measure the intima-media thickness.

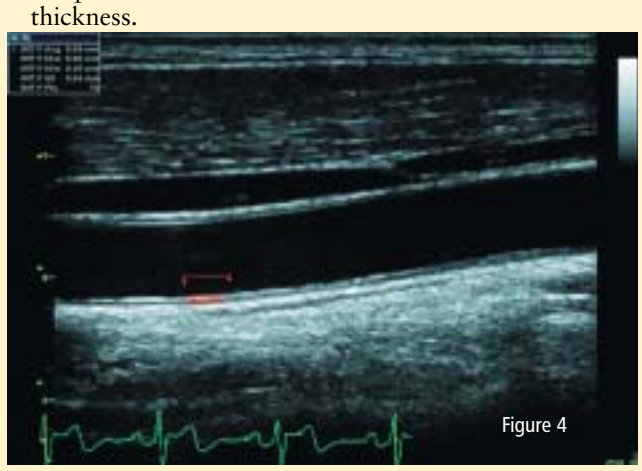


Figure 4

Performing IMT measurement on the Vivid 7 and Vivid i:

- Select Measurement key on the keyboard.
- Select from the measurement menu carotid folder, then CCA IMT, to identify the right or left carotid artery, then CCA IMT Post, for posterior wall.
- Position the IMT cursor above the intimated wall, then press select key to anchor the first cursor. Reposition the second cursor using the trackball then press select key to anchor the second cursor.

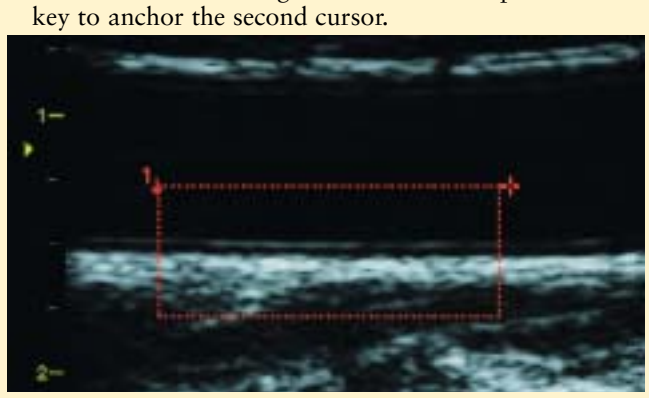


Figure 5

If the IMT measurement result is acceptable, select 'Transfer' in the measurement Carotid folder. The results will be displayed in the worksheet and in the final report.

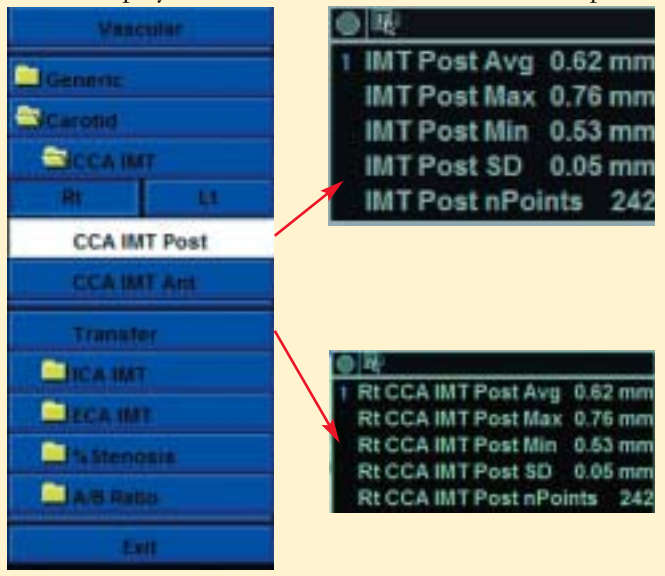


Figure 6

The automated IMT package from Vivid 7/Vivid i: the benefits

- The measurement procedure is not operator dependent and not as time intensive compared with manual IMT measurements.
- The semi-automated technique simplifies the time taken to perform the measurement compared with manual measurement.
- The improved technology enhances c-IMT precision measurements and increases consistency and reliability of the results.
- The methodology is robust, reproducible and builds confidence among radiographers and physicians.

Research Project in Telemedicine

seca Precision for health

PARTNERSHIP FOR HEART

In Germany, approximately 1.5 million people suffer from chronic cardiac insufficiency. Very often, the insidious symptoms are recognised too late, leading to complications and hospitalisation. 'Partnership for the Heart' is a joint project by science, industry and healthcare system led by the Berlin Charité and aiming to develop a telemedical early warning system. The system monitors patients 7/24 at home and a mini-computer records all therapy-relevant vital parameters.

Body weight is an important risk indicator. A sudden increase in body weight for example may indicate beginning water retention in the body. Seca designed scales for this project based on the floor scale seca 867. An integrated RS232 interface and a BlueTooth module allow smooth transmission of the values to the Charité's telemedical centres or the Robert Bosch Hospital in Stuttgart. Blood pressure and ECG are determined in a similar way.

Specialist physicians monitor the values around the clock and initiate appropriate actions when needed – they inform the patient and the family physician or the emergency medical service.

Since the telemedical early warning system is considered a viable alternative to current options it is being supported by the German Ministry of Economics. The government contributes 5 mio. EUR, the same amount is made available by the industry partners.

Further information:
www.partnership-for-the-heart.de

FRED® easyport is a Life-Saver

Cardiac infarction and cardiovascular failure are two of today's most frequent emergencies. SCHILLER's FRED® easyport® pocket is the only pocket defibrillator in the world. It is so small (133 x 126 x 50 mm) and light (490 gr incl. battery) that for many doctors it is already standard equipment in their emergency bag. It is also suitable to accompany risk patients and their relatives around the clock.

This life-saver is always available to give doctors, paramedics and rescue technicians peace of mind in emergency situations.

For example during the World Cup 2006, paramedics on duty at the football stadiums carried out their duties with FRED easyport clipped to a belt around their waist. In Switzerland an entire police department has been equipped with this device to help fight against sudden cardiac death.

Patients at risk can easily carry this small defibrillator with them, after they and their families have been instructed by their doctor. This dramatically reduces the response time to treat ventricular fibrillation and tachycardias, giving the patient a much better chance of survival.

For cardiologists this defibrillator can now also be supplied with a manual shock option, i.e. the doctor can switch off the AED mode and decide the energy level and exact moment of defibrillation.

TWA predicts mortality in patients with normal ejection fraction

Dr Tuomo Nieminen, Tampere University Hospital

Finland - An increased TWA (T-wave alternans) is a significant indicator of all-cause and cardiovascular mortality, as well as of sudden cardiac death in patients with mostly normal ejection fraction, according to a recently published study by researchers led by **Dr Tuomo Nieminen**. Until now, this was only known as an indicator for those patients suffering severe heart diseases predisposing to life-threatening arrhythmias. In an interview with *Meike Lerner*, of *European Hospital*, Dr Nieminen explained the advantages of the TWA measurement, study results and the consequences these have for future research.

'The T-wave represents the electric repolarisation of the heart, Dr Nieminen explained. Thus, alternans in the T-wave is a marker of an alternating repolarisation process, which might indicate cellular disturbances during repolarisation. This is important, since pathological repolarisation phase predisposes to ventricular arrhythmias. In general, the TWA measurement could be used for arrhythmic risk stratification, but it is also one of the diagnostic criteria for long QT interval syndrome, another repolarisation abnormality.

TWA can be measured with a regular electrocardiogram; no extra examinations are necessary. The possibility to measure the T-wave alternans is a special feature within normal ECG software.

There are two methods for TWA assessment: time-domain modified moving average (MMA) and spectral methods. Both methods seem to measure the same phenomenom. For our study, we used the GE Healthcare software embedded with the MMA method, which can be applied in routine exercise test protocol without stabilising the heart rate to any specific level.'

Several studies have proved the effectiveness of measuring TWA for prognoses. What makes this study different?

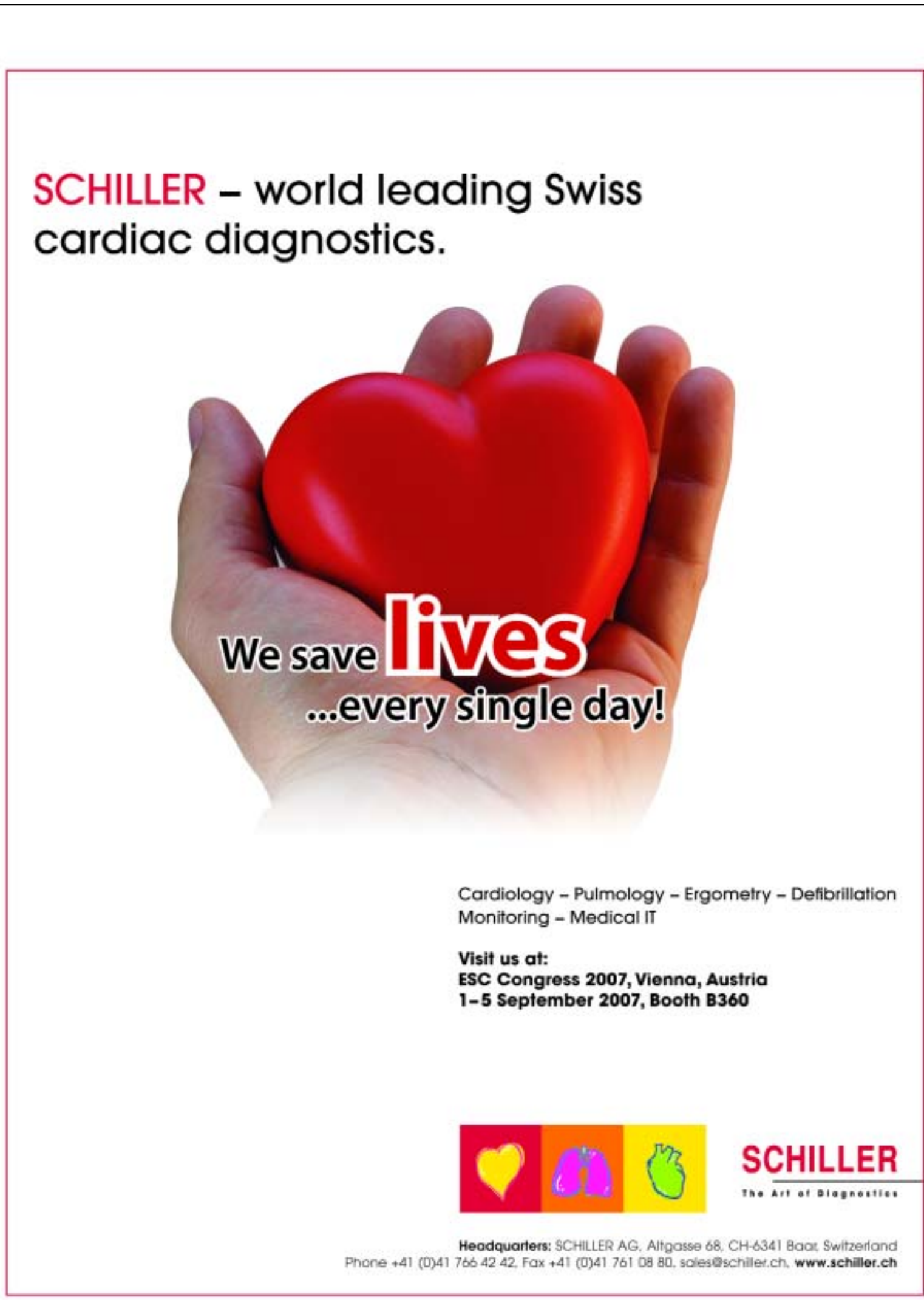
'Essentially all previous studies included patients with an ejection fraction of less than 50 percent, which is called abnormal. But in our population this only refers to 13 percent of the patients.

In 2001, we launched the *Finnish Cardiovascular Study* (FINCAVAS), in which we enrol all volunteering patients performing a clinical exercise test at Tampere University Hospital. We use the standard protocols of the bicycle ergometer test, with an increasing load every minute. This TWA analysis aimed to test whether TWA predicts mortality in our study population. The results of the study show that the TWA measurement provides prognostic value also in patients with a normal ejection fraction.'

What consequences do these findings have for patients' treatment?

'Our results suggest that TWA identifies patients prone to sudden cardiac death at an earlier stage of cardiac disease than supposed before. It is the first but naturally important step to show that a certain marker is associated with mortality. Another equally important step will be to test whether the patients with such a pathological marker will benefit from treatment options, such as anti-arrhythmogenic pharmaceuticals, or an ICD implant. The results of our study did not answer that latter part, which is a big question for the future - studies are being planned and conducted to reach that goal.

We need to bear in mind that estimating the aggregate risk for sudden cardiac death should be based on several parameters. No single marker will suffice, but TWA seems to be a very good candidate to be involved!'



The high risk plaque initiative
THE BASIC STUDY

This will take place in two mobile units, located in a number of large cities in the USA. The design of the study and the protocol development is being formulated in a close collaboration with BG Medicine, which will develop the blood-based biomarkers, and with leaders in vulnerable plaque research from leading Universities in the USA, Denmark and the Netherlands, as well as with partners Merck and Astra Zeneca.

The first patients will be scanned in the autumn of 2007, and the complete bio-imaging study will take about one year. While the compete set of imaging data will be ready in more than a year - the study will take about four years.

Molecular medicine

A weapon to beat high-risk plaque

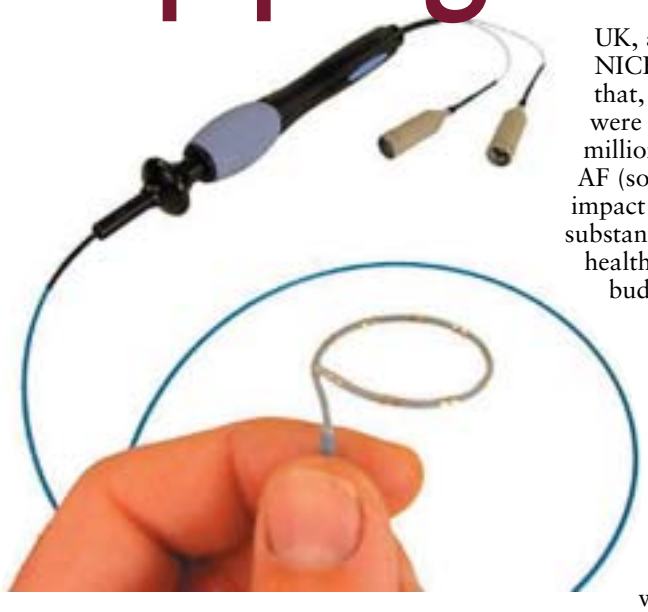

Paul Smit

It has only recently been discovered that very often it is not the size of the plaque in the coronary vessels but its inflammation status that determines the occurrence of a cardiac infarction. This knowledge triggered new research approaches for its early diagnosis and treatment in cardiology – for example the *High-Risk Plaque Initiative* jointly founded by Philips Medizin Systeme, AstraZeneca, Merck & Co, BG Medicine and Humana, which focuses on the possibilities that molecular medicine now offers. The researchers are trying to identify suitable biomarkers that allow the early diagnosis and targeted therapy of inflamed, so-called high-risk, plaque.

In molecular medicine, the High-Risk Plaque Initiative is one of the most important projects of Philips Medizin Systeme, as Paul Smit, in charge of strategy and development in the Dutch company, explained: 'Today, high-risk plaque is recognised as the major cause of cardiac infarction which kills about 50 percent of the patients. This means, in many cases, death is the first symptom of the disease. Furthermore, those patients who survive the event are chronically ill and require medical care for the rest of their lives. This disease is not only dangerous for the patients but also presents an immense financial burden on the healthcare system – a burden that will increase steadily over the next few years. In short, high-risk plaque is one of the most fatal and one of the most expensive diseases.'

In addition, coronary plaque is a highly unpredictable condition because, depending on the degree of inflammation, the plaque suddenly ruptures and causes an embolism, which in turn leads to

Cardiologists meet to sum up progress



Czech Republic – During a meeting of cardiologists in Prague earlier this year to exchange experiences with new methods and treatments to control atrial fibrillation, Dr Josef Kautzner, Head of Cardiology Department at IKEM (Institute of Clinical and Experimental Medicine) pointed out that numbers of patients with AF will more than double during the next 20 years. In the Czech Republic alone, there are about 120 thousand people diagnosed with AF. All these patients have worsened quality of life, twice the mortality due to cardiac failure, and a five times greater risk of cerebral vascular accident (CVA) when compared with the normal population of the same age. AF also causes about a fourth of all CVAs, which means around five thousand people are afflicted by this disease.

The annual treatment of one patient is 40 thousand CZK, i.e. almost 5 billion CZK (178.5 million EUR). Figures for the UK, according to the NICE guidance, indicate that, in July 2006, there were more than 1.4 million UK patients with AF (source: NICE cost impact report) consuming substantial part of healthcare financial budget.

The main goals of AF treatment are widely recognised – to renew normal cardiac rhythm, and to ensure that AF doesn't occur again.

Therapeutic modalities are wide, apart from anti-arrhythmics, modern mini-invasive methods are recently on the rise – cardiostimulators and cardioverters and defibrillators, electric cardioversion and particularly catheter ablation.

In the Czech Republic, the first patient with an implanted cardiostimulator was seen at IKEM back in 1962, and the first digital cardiostimulator was implanted in 2003 in Prague's Na Homolce Hospital. Catheter ablation as an AF treatment has been in use for quite some time.

With new medical technology achievements, three-dimensional imaging has arrived in this scene. New diagnostic approaches allow 3-D views inside of the heart, so cardiologists can combine that imaging technique with a cardiac CT scan, and navigate the catheter through the heart with a full stereometric view.

One of the pioneers in the field of even more advanced medical techniques is London's St. Mary's Hospital (see robot feature on this page).

Report: ***Rostislav Kuklik***

Robot moves steadily in on catheter ablation

Sensei Robotic Catheter System installed in London

The *Sensei Robotic Catheter System*, a first generation robotic platform launched by Hansen Medical at the USA's *Heart Rhythm Society* Scientific Sessions in May this year, is in use in Europe. St Mary's Hospital, in Paddington, central London, became the World's first centre of excellence for training in and development of the system, under the guidance of consultant cardiologist and electrophysiologist **Wyn Davies MD FRCP FHRS**. As of July, over 20 atrial fibrillation patients had been operated on at St Mary's using this robotic surgical aid controlled by the surgeon at a nearby workstation.

The Sensei system and Artisan catheter aim to enable physicians to easily and accurately place mapping catheters in hard-to-reach anatomical locations within the heart with stability, during the diagnostic phase of complex cardiac arrhythmia treatment, Hansen reports.

'The new robotic system allows the operator to perform EP procedures in a more consistent fashion, which I believe will lead to the development of a standard approach for complex diseases,' Wyn Davies observed.

Currently, the majority of clinicians manually guide catheters through the heart to detect and treat a variety of cardiac arrhythmias. This technique requires physicians to perform a series of complex manipulations at one end of the catheter without assurance that the tip of the catheter will respond as desired when inside a patient's heart. Achieving stable contact at anatomic sites within the heart, which is essential for successful mapping procedures, can be difficult, Hansen points out. 'As a result, insufficient contact between the catheter tip and the inside of the heart wall can lead to highly variable and less than optimal procedure results for the patient. Hansen Medical believes its robotic platform overcomes these hurdles and will enable physicians to perform procedures that historically have been too difficult or time consuming to accomplish routinely with existing manual technique.'


Electrophysicist Wyn Davies at the Sensei workstation

St Mary's NHS Trust, which was awarded a 'good' performance in the 2006 NHS performance ratings, has 3,600 staff that provides specialist care for women's health, cardiology, children's services, infection and immunity and robotic surgery. The Trust reports that it has one of the lowest mortality rates in the UK, and a 'rich history of research, development and teaching thriving today through the relationship with internationally renowned university partner, Imperial College London'.

Dr Wyn Davies set up the electrophysics department at St Mary's and also has been praised by the British Medical Association for initiating a 'day return' cardiac treatment service in 2001. With this service, patients receive treatment during a day and return to their local hospital that evening. This has shortened waiting times for beds to become vacant for their potentially life-saving operations. In addition, he pointed out that returning to their local hospitals mean relatives and friends can visit more easily.

The system

The Sensei system is compatible with fluoroscopy, ultrasound, 3-D surface map and patient electrocardiogram data. The two main components that comprise the system are the Artisan control catheter and an ergonomically designed, remotely-placed workstation where the physician sits throughout the procedure. In addition to lessening operator fatigue, the remote workstation creates a virtual shield for physicians against harmful radiation, Hansen added. 'The open architecture provided by the Sensei system, which allows the use of pre-approved catheters from third-party manufacturers, requires a labelling addition from the FDA. The addition is intended to remind physicians that the safety and effectiveness of the system for use with cardiac ablation catheters in the treatment of cardiac arrhythmias, including atrial fibrillation, have not been established. The Sensei system has received CE mark approval in Europe, and the Artisan Control Catheter is currently pending CE mark approval.'

For many patients, a catheter ablation is the most effective way of treating AF; however a shortage of clinicians able to perform these complex procedures contributes to thousands living with the condition and its associated risks. In the UK alone, over 50,000 people develop AF annually, yet fewer than 10% undergo catheter ablation.

St Mary's, which runs one of the UK's busiest cardiac centres, is now one of only four hospitals globally that are using the Sensei robot. Wyn Davies said it has

a cardiac infarction, or a stroke. This sudden rupture of inflamed plaque in a coronary artery explains why 70–75% of cardiac infarctions occur without prior symptoms.

'Hitherto physicians were unable to determine when the plaque has reached a dangerous stage. Today, molecular medicine offers the possibility to identify indicators of the inflammation. The first task of the High-Risk Plaque Initiative is to develop a broad patient screening concept, which we hope will show early indicators in patients with infarcts that are not present in the control group. If we know these early indicators, or biomarkers, which predict an inflammation, thanks to modern imaging methods we will be able to locate the high-risk plaque and determine its volume,' Paul Smit pointed out.

The collected data can be combined with statistical values and thus provide valuable information on the patient's current and future risk. Currently, Philips and the other members of the High-Risk Plaque Initiative are developing a test that will be applied to more than 6,000 patients in coming years.

Early diagnosis of high-risk plaque is no doubt a major step forward. However, it has to lead to targeted therapies for the affected coronary vessels. Today, physicians are rather powerless when it comes to the treatment of plaque, since there are no validated tests to determine the effectiveness of drugs. However, it appears to be proven that regular monitoring and a healthy lifestyle often improve a patient's condition.

Molecular medicine offers promising approaches for other diseases as well - cancer, for example. Currently, methods are being researched that use ultrasound to transport medication through the vessels right to the affected body region. The medication is docked onto micro-bubbles, or a contrast agent, and injected in to the body. With the help of ultrasound signals the physician can trace the bubbles' route to the target region. As soon as the bubbles reach the affected tissue a certain ultrasound frequency causes them to burst and the active agent is released. Because the medication is administered in a very targeted way, a much lower dose than in a systemic therapy is required – which increases the therapeutic success and significantly reduces side effects. The principle has already been tested in pre-clinical trials and is now being developed for clinical use in a joint effort with the pharmaceutical industry. The Philips research team has already gone one step further and is working on finding out whether this innovative method can be used for cardiac diseases.

'We are still in the early stage of research into validated biomarkers and it will take about four more years before we will be able to identify high-risk plaque with the help of biomarkers. However,' Paul Smit concluded optimistically, 'these developments will open entirely new possibilities from which both the patients and the healthcare system will profit: Early diagnosis can significantly reduce treatment and follow-up costs of many diseases.'

Report: Meike Lerner

'enormous potential to help deliver difficult catheter ablation procedures'. Pointing to the shortage of expertise in the UK, which means there are too few centres where highly complex cases can be carried out, he added: 'With further development that we are already embarking on, this robot will enable complex procedures to be carried out almost automatically, increasing the opportunities to treat more patients and ultimately reducing clinical risk. The robot allows accuracy and control of catheter movement which cannot currently be achieved without a skill level that usually takes considerable time to acquire. We are thrilled that St Mary's cardiology unit has been able to pioneer this exciting advance. With the other surgical robotic programmes already established at the hospital, St. Mary's is a world leader in robotic medicine.'

Although capable of use in all forms of ablation procedures, Hansen reports that the robot will predominately be used for complex ablation procedures to treat atrial fibrillation.

The Czech Republic and Germany

Another chosen centre of excellence is the Cleveland Clinic Foundation in Ohio, where the system is being used under the guidance of Andrea Natale MD, who is director for the Centre for Atrial Fibrillation, director of the Electrophysiology Laboratories and head of the Section of Pacing and Electrophysiology there. She had used the Sensei system during clinical evaluation on 25 patients in the Czech Republic and Germany. 'The stability of the Artisan catheter allowed us to perform catheter mapping procedures more efficiently and effectively,' Dr Natale said. 'The incorporation of the Sensei system and catheter did not add time to the procedures, nor did it require increased radiation time, as would normally be expected with new technology. As a result, I'd expect this new system to become the medical standard for performing complex EP procedures, which are currently limited to those individuals with the highest level of skill.'

Report: Brenda Marsh

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