EUROPEAN HOSPITAL

WWW.EUROPEAN-HOSPITAL.COM

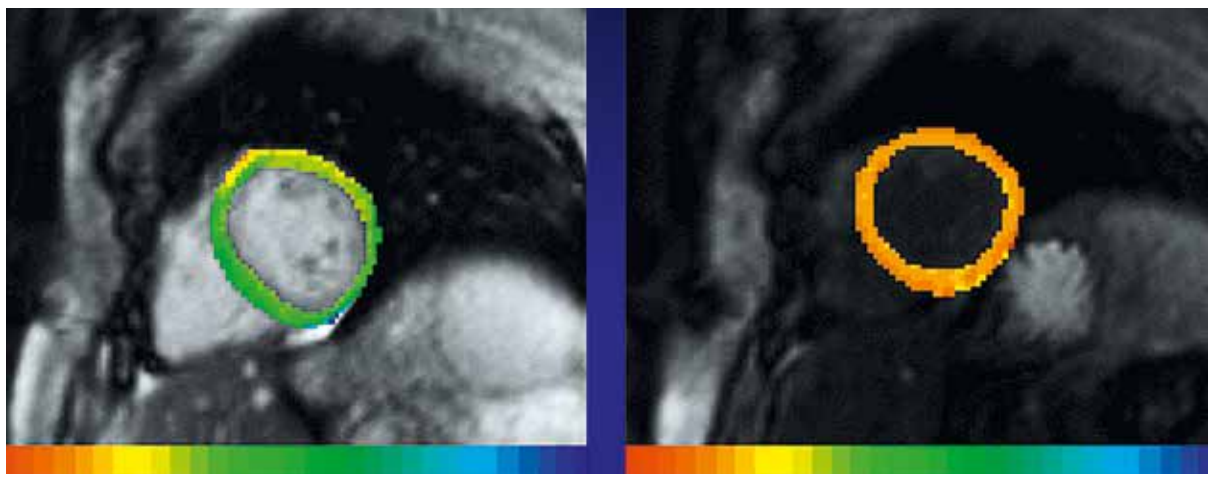
CARDIOLOGY 2014

NEWS AND TECHNOLOGY UPDATES FOR CARDIAC CARE

BARCELONA • SPAIN 30 AUG - 03 SEP 2014

# Fusing PET-MRI – a winning combination

## A comprehensive view of multiple cardiovascular disorders may set a new gold standard, John Brosky reports



Pre- (left) and post-contrast image set showing, by parametric imaging the drop in T1 time (red = shortest, blue = longest

**Someone once described** the fusion of positron emission tomography (PET) and magnetic resonance imaging (MRI) as a great technology looking for an application.

There is some disappointment in other medical fields, acknowledged Thomas Schindler MD, Director of Cardiovascular Nuclear Medicine at Johns Hopkins University Medical School in Baltimore. Initial PET-MRI failed to show superiority against PET fused with computed tomography (CT), the standard in that field to detect some cancer and associated metastatic disease.

Yet, PET-MRI may be a winning combination and gold standard for evaluating various heart diseases and disorders, including ischaemic and hypertrophic obstructive cardiomyopathy, cardiac sarcoid involvement, myocarditis, and so on. 'The indications to apply both modalities are well established. The question now is determining if there are additional clinical benefits among HF patients where we apply a fusion of MRI-PET to acquire more clinical information, a comprehensive overview of structure and function. Now we need to show the added diagnostic and clinical benefit of doing so.'

At this year's congress of the European Society of Cardiology (ESC), on 2 September Prof. Schindler will focus on the potential role of PET-MRI in the assessment of myocardial viability in ischaemic heart failure patients during a Spotlight Symposium on multimodality imaging. 'In the cardiovascular domain, we are now able to vision both anatomy and function,' he said, adding that both types of information are needed to make a decision as to whether it is worth doing the revascularisation, or whether it is better to pursue conservative medical treatment.

The targeted patient population is characterised by severe heart failure with a left-ventricular ejection fraction of less than 35%, regional wall motion abnormality, such as akinesis or dyskinesis subtended to an occluded or highly stenosed vessels. This is commonly the case when a patient with acute myocardial infarction missed the six-hour window for revascularisation by percutaneous coronary intervention (PCI), or because the diagnosis was missed, or because a patient experienced a silent infarction.

'The question for the interventional cardiologists becomes whether it is worthwhile to re-open the chronically occluded vessel in view, to restore coronary flow to potential viable or "hibernating" myocardium, which may then recover contractile function translating into an improvement in symptoms, physical capacity and prognostic outcome. PET/CT with the radiotracer FDG is highly sensitive in the detection of residual myocardial viability in areas of infarction, while MRI with delayed-imaging of gadolinium trapping in the myocardium can reliably detect old scar tissue and/or fibrosis with specific T1-weighted sequences. In this respect, cardiac MRI provides more specific information on potential recovery of heart function after coronary revascularisation.

There are heart centres using primarily PET, and centres that use MRI, he said, and each modality comes with a certain bias.

Continued on page 2

**Professor Thomas Hellmut Schindler MD** is Director of Cardiovascular Nuclear Medicine and Associate Professor PER at Johns Hopkins University Medical School, Baltimore, USA. He has an international reputation in the field of Cardiovascular Imaging with focus on PET. His authorship of over 71 peer review publications shows an impact factor exceeding 287. Professional memberships include the ESC (European Society of Cardiology), and on the cardiovascular committee of the European and American Society of Nuclear Medicine and Molecular Imaging.

# Clinical tests to confirm coronary heart disease

## Hybrid imaging is of little clinical value, reports Axel Viola

**PET-MRI, according to** many experts, is the best clinical procedure to confirm coronary heart disease (CHD). Prof. Markus Schwaiger begs to differ: 'We can learn a lot from this type of set-up,' says the Director of the Clinic of Nuclear Medicine at Klinikum rechts der Isar in Munich, Germany, who nevertheless is convinced that hybrid imaging in the shape of positron emission tomography (PET) and magnetic resonance imaging (MRI) 'will not become the gold standard in cardiology.'

Overall, the professor agrees that cardiac imaging has developed extremely quickly over the past few years. While clinicians continue to struggle with the diagnosis of many diseases today, they 'can choose among a whole slew of procedures to diagnose CHD early and to track the course of the disease.'

However, the wide range of available diagnostic imaging techniques and modalities has a downside: it has become difficult to develop recommendations for an integrated diagnostic work-up. Part of the problem is the fact that experts are divided into different camps as Prof. Schwaiger explains: 'There are those who are convinced that a fast CT scan is ideal, others consider perfusion imaging more important.'

Schaigersupports a different approach: The imaging procedure should be selected depending on the probability of a coronary heart disease. 'If CHD needs to be excluded, fast CT or CT-Angio are the methods with the highest negative predictive value. For patients with confirmed calcifications, however, the combination with a perfusion marker makes sense,' he explains, since the marker shows the area that is compromised under physical or pharmacological stress – the so-called ischaemic burden can be evaluated. Today, the relevant guidelines demand a pre-interventional ischaemia test. 'The literature on single photon emission tomography, also called SPECT, indicates that an intervention is useful when more than ten percent of the left ventricular myocardium is ischemic,' Schwaiger underlines.

Modalities such as PET, SPECT and MRI are well suited to evaluate myocardial perfusion. 'PET allows rather precise quantitative perfusion measurement,' he points out adding that in this context the so-called coronary flow reserve is not only of diagnostic but also of prognostic value: 'Limited coronary flow reserve is associated with poor survival rates, or with a high risk of cardiovascular complications.'

Although quantitative measurements with PET and increasingly with MRI might present an alternative to the invasive measurement of the fractional flow reserve (FFR), they cannot entirely replace it due to their complex and thus expensive material requirements.'

The clinical value of hybrid imaging is, according to Schwaiger, rather low: 'I consider PET-MRI a research tool rather than a method to be used everywhere for coronary diagnostic purposes – it is much too expensive. The Formula 1 of imaging so to speak.'

PET-MRI is useful for validation

Continued on page 2

**Professor Markus Schwaiger** has directed the Department of Nuclear Medicine at Klinikum Rechts der Isar, at Munich's Technical University in Germany since 1993. He is also a Professor at the University of Michigan in Ann Arbor/ USA, where he headed the Department of Cardiovascular Nuclear Medicine from 1987-'93. The professor's main area of research is biomedical imaging using MRI-PET, PET/CT und SPECT/CT.

# Looking for the perfect modality

## Today there is no method available to detect vulnerable plaque

**Report: Axel Viola**

**What's the ideal solution** for vulnerable plaque imaging? 'A non-invasive imaging procedure with high spatial and temporal resolution, and without radiation exposure, and which provides information on coronary plaque composition precisely and in series.' Quite a tall order, as Prof. Grigorios Korosoglou is well aware. Whilst this perfect method is not – yet – available 'it would enable us to determine whether and where vulnerable plaques have accumulated, meaning plaques that are at risk of rupture and which will most likely cause a myocardial infarction within the next few years.'

Today, there is no method available to detect vulnerable plaque, not even at the department of cardiovascular imaging at Heidelberg's University Hospital, which is headed by Prof. Korosoglou. 'Coronary angiography shows stenoses and is the current gold standard in the diagnosis of coronary heart disease. But there is no modality that can tell us which plaque is unstable and thus a potential source of a future cardiac event such as a myocardial infarction.'

Currently, interventional or surgical therapy for patients with coronary heart disease (CHD) is geared towards obstructive lesions: only those lesions are treated which significantly narrow the coronary artery lumen. 'But today we know that a myocardial infarction is not necessarily caused by these lesions,' Prof. Korosoglou explains, 'but by those which were not considered significant in angiography.'

While certain diagnostic procedures can identify potentially dangerous plaque based on plaque morphology, most of these techniques are 'not clinically established', Prof. Korosoglou underlines, 'such as intravascular ultrasound, known as IVUS. This invasive procedure is based on virtual histology to identify plaque with a large necrotic core and spotty calcifications. Studies have indicated that a large necrotic core correlates with plaque at risk of rupture.'

Cardiac CT is used routinely to classify patients with suspected CHD and is considered by the European Society of Cardiology to be a modality that will play an increasingly significant role. Cardiac CT is particularly useful because it not only visualises stenosis but also allows the characterisation of the coronary artery walls and the composition of atherosclerotic plaque. Recent CT studies have indicated that patients with a high number of non-calcified so-called low attenuation plaques have a significantly higher risk for future cardiac events, such as a myocardial infarction or sudden cardiac death.

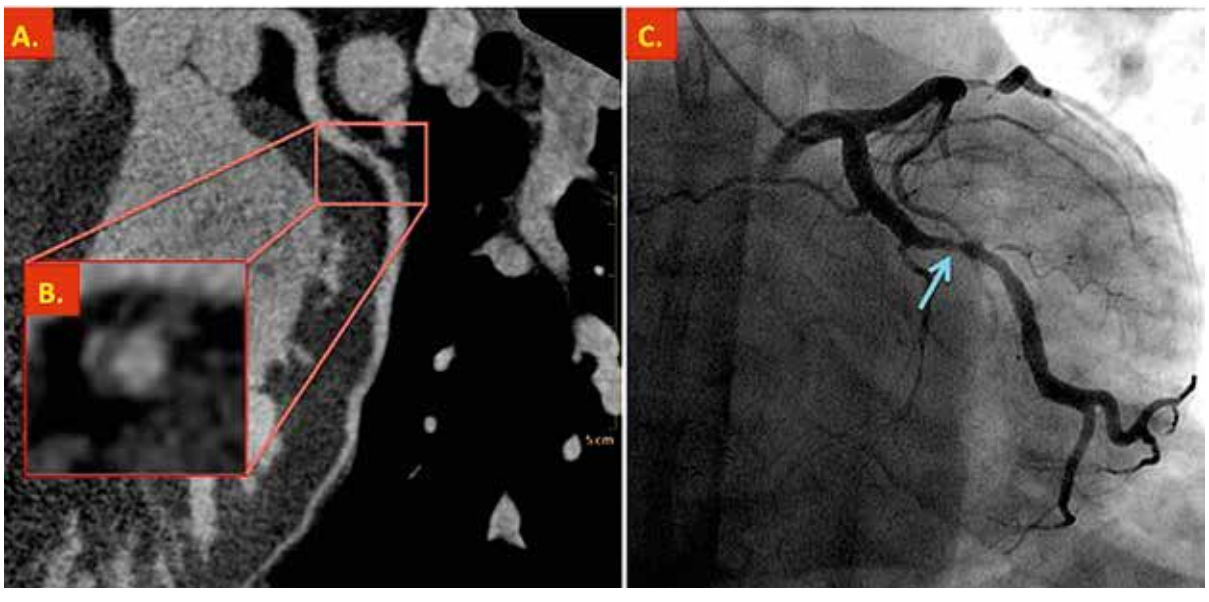
Magnetic resonance imaging (MRI) is another modality which might offer the possibility to identify vulnerable plaque but it also is, as the Heidelberg-based cardiologist explains 'still in the experimental stage. There is for example the attempt to use iron-containing nanoparticles in MRI to visualise inflammation-rich plaques. Plaque macrophages take up the intravenously applied nanoparticles. Thus MRI provides information on the accumulation of macrophages in the plaque which is considered a surrogate parameter for plaque instability and by extension unstable cardiovascular disease.' MRI, however, still has certain technical limitations: the spatial resolution of the MRI scans is not yet sufficient to provide detailed images of the coronary plaques.

There is another high potential among the imaging modalities, as Prof. Korosoglou points out: 'Fluorine-18 positron emission tomography combined with computed tomography, known as PET/CT, might become clinically relevant.' Fluorine-18 is a radiotracer that was previously used to visualise bone formation. Recent clinical studies with acute myocardial infarction patients have shown increased fluorine uptake in ruptured plaques. Moreover increased fluorine uptake was reported in patients with seemingly stable CHD – in exactly those plaques that had been classified as particularly at risk of rupture according to the IVUS scores.

Thus PETC/CT might be a non-invasive modality to detect plaques at risk of rupture or even the early stages of the rupture before the cardiac event – the infarction – happens. Not all plaques, however, take up fluorine-18: particularly patients with a high degree of calcification seem to be metabolically inactive with regard to fluorine-18.

'These very different approaches show that there are many aspects of atherosclerosis which we have not yet understood. We used to think, for example, that the degree of calcification correlates directly with the risk of a future cardiovascular event. Today we know it might be possible that only moderately calcified and metabolically active plaques are those with the high risk of rupture,' he summarises. Conclusion in a nutshell: There is much work to be done in atherosclerosis research.

**Professor Dr Grigorios Korosoglou** has headed Cardiac CT in the Internal Medicine and Cardiology Department at University Hospital Heidelberg since 2010. In 2012 he also became head of Cardiac MRI there and was also appointed Deputy Medical Director of the Department of Cardiology and Angiology at GNR Clinic Eberbach.
Inter alia, Dr Korosoglou's clinical research focuses on capturing myocardial perfusion with 'myocardial blush' in the cardiac cath lab and determining the composition of atherosclerotic coronary plaque with cardiac CT.




**Cardiac CT of a patient with stable CHD. Multi-planar and circumferential reconstructions (A&B) show a non-calcified, so-called low attenuation plaque with moderate (50%) stenosis of the circumflex coronary artery. The patient presented after 13 months with a non-ST-segment elevation myocardial infarction (NSTEMI), most likely due to a plaque rupture at this point of the circumflex coronary artery (blue arrow). Invasive coronary angiography (C).**

### DATE FOR THE DIARY

* 2 September 2014; 2:00 – 3:30 pm, Sarajevo – Village 1
Symposium: Multimodality/hybrid and other imaging
3.00 p.m. Professor Grigorios Korosoglou presentation:
Arterial vulnerable plaque imaging: Which modality to choose?

## Clinical tests

**continued from page 1**

purposes since it shows the extent of the correlation between MRI and PET signals and how the signals of both methods contribute to the overall characterisation of the disease. Thus the professor concludes that PET-MRI is, above all, a research method which, due to the high costs, is currently not suited for routine diagnostics.

Despite the enormous progress of imaging procedures in perfusion measurement Prof. Schwaiger is hesitant to write off conventional diagnostic procedures such as scintigraphy, particularly in view of the techniques that are available worldwide both in- and out-patient settings: 'It may well be that a correctly performed perfusion scintigraphy is not as sexy as the latest innovation; nevertheless, it's still – and will continue to be for some time – the most frequently conducted examination in ischaemia diagnostics.'

### DATE FOR THE DIARY

* 2 September 2014. 8:30-10 a.m. Rome – Village 1
Symposium Positron Emission Tomography (PET)
8.50 a.m. Professor Markus Schwaiger will present 'Advantages of PET/MRI in the assessment of coronary morphology and ischemic heart disease'.

## Fusing PET-MRI – a winning combination

**continued from page 1**

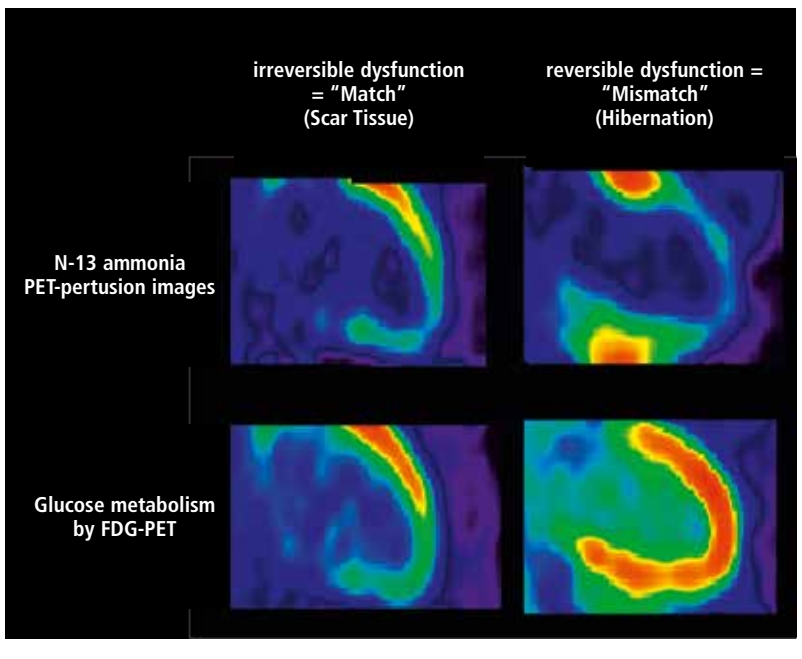
'Combining the two modalities creates the potential for more objective information for the decision-making process and can lead to a more highly individualised therapy decision for interventional and medical treatment options in patients with ischemic cardiomyopathy.'

He hopes his presentation will gather both MRI experts who would like to appreciate the value of PET and, vice versa, PET experts who wish to appreciate the value of MRI as 'these two experts will need each other in the future as the use of the fused modalities becomes established.

Currently there are precious few groups who have started clinical research in this domain, and the only published works remain feasibility studies and do not provide clinical outcome data, that would allow more definite conclusions. Functional and clinical outcome data are underway, but it will take a couple more years before publication,' he explained.

The lack of this clinical evidence means the diagnostic procedure is not yet embraced in society recommendations and guidelines, which creates yet another significant barrier to adoption, which is a resistance to reimbursement among insurers.

When you try to convince insurers to pay for two modalities for one exam, of course they say that there is no outcome data to justify he exam. This is one of the reasons that PET-MRI has been slow to start, because centres with this capability have not been able to apply it in a wider range of applications.




**PET assessment of myocardial viability or hibernation**

Schindler said he had been successful winning agreement for reimbursement on a case-by-case basis by patiently building credibility with insurers, emphasising the potential for an improved outcome for the patient in the event that revascularisation is justified, and emphasising the cost savings of up to €10,000 to €25,000 when interventional or surgical revascularisation procedures are not needed.

'This is not a screening method,' he said, 'and I speak every day with colleagues in cardiology or internal medicine to explain why the examiis justified for some patients but not others, and then with insurers to justify the value of the exam against expense.

'PET-MRI is likely to become the gold standard in determining the potential in recovery of cardiac function in ischaemic jeopardised but viable myocardium in heart failure patients. However, clinical outcome data are needed to prove that image-guided and individualised vascular medicine with PET-MRI technology leads to an improved clinical outcome and prognosis in high risk patients.'

# Cardiac resynchronisation

## Newly implanted defibrillators enable MRI scanning

**This summer the** world's first implantations of Biotronik's new ICD and CRT-D series (implantable cardioverter-defibrillators and cardiac resynchronisation therapy defibrillators) took place at the Spedali Civili Hospital, Brescia, Italy. 'My ICD and heart failure patients are frequently indicated for MRI scans to diagnose potential comorbidities,' said Dr Antonio Curnis. The researcher had implanted the firm's ProMRI Inventra HF-T and Sentus quadripolar lead in a 73-year-old patient with congestive heart failure. 'With the Biotronik devices, I know I can give my patients high-quality therapy and broad access to diagnostics,' Curnis explained.

With Sentus quadripolar leads and the Inventra series, the manufacturer confirms that it is the first and only company to produce cardiac resynchronisation devices and leads for heart failure (HF) patients that are approved for MRI scans. As patients age, they may develop comorbidities, and MRI scans can be critical in diagnosing conditions such as stroke, brain tumours or orthopaedic conditions.

'The quadripolar Sentus lead eases the implantation process by giving physicians access to challenging vessels. With CE approval in early July, Biotronik's new implantable defibrillator series includes the industry's first quadripolar left-ventricular leads to be approved for MRI use.'

In addition to ProMRI technology, the firm's new ICDs and CRT-Ds reduce inappropriate shocks with MorphMatch morphology detection criteria and anti-tachycardia pacing (ATP) optimisation. 'While delivering shocks at the right time can save patients' lives, shocks should be minimised to appropriately control arrhythmias, improve patients' quality of life and increase device longevity,' Biotronik point out.

Dr Werner Jung, at the Schwarzwald-Baar Clinic, Villingen Schwenningen, Germany, successfully implanted a 72-year-old HF patient with a new ProMRI CRT-D from this bio-tech manufacturer.

Speaking of the 'exceptional quality of Biotronik products, the surgeon said: 'Many heart failure patients are very ill and shocks put stress on the body and mind. By choosing a device with unique algorithms that reduce shocks, I can give my patients peace of mind and restore their sense of safety.'

The company has included its Closed Loop Stimulation (CLS) technology in ICDs for the first time. 'CLS helps patients experience the most natural rate adoption possible by utilising their neurological information,' the company explains. 'It's the only system that allows pacemakers, and now ICDs, to react naturally to patients' physical as well as mental activity or stress.'

**The world's first ProMRI quadripolar leads**

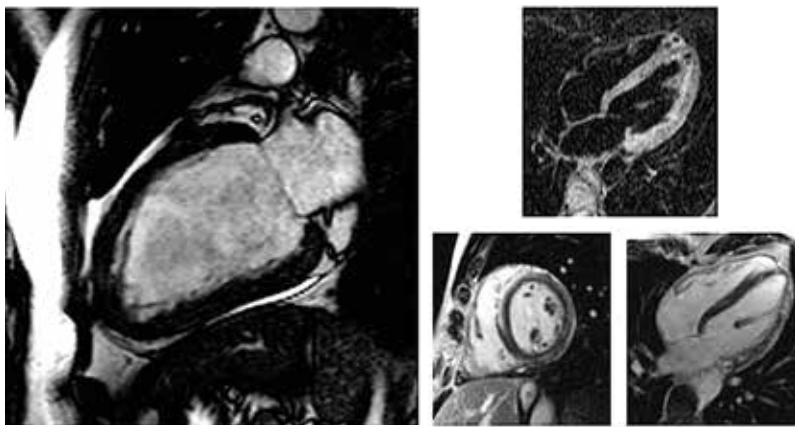
**The CRT-D System**


**FIRST TO IMPLANT THE NEW DEFIBRILLATOR SERIES:**

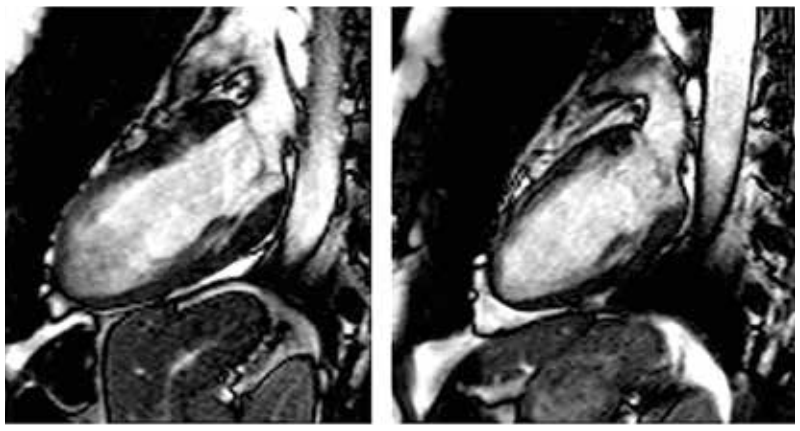
**Antonio Curnis MD**, Spedali Civili Hospital, Brescia, Italy
**Werner Jung MD**, Schwarzwald-Baar Clinic, Villingen Schwenningen, Germany
**Tisiano Moccetti MD** and **Angelo Auricchio MD**, Cardiac Centre Ticino, Lugano, Switzerland
**Anthony Stanley MD**, Sunninghill Netcare Hospital, Johannesburg, South Africa
**Martin Winterhalter MD**, SRH Clinic, Gera, Germany.

# When cardiac catherisation delivers no result...

## radiologists diagnose the causes of nonspecific chest pain using MRI



Example: Myocarditis – 23-year-old male with no abnormalities is seen in pumping function during an echocardiographic and MRI examination. After contrast medium administration, inflamed necrosis in the sub-epicardial myocardium becomes visible in the late enhancement sequence. All the information available, such as normal pumping function, no wall motion abnormalities, oedematous changes and the late enhancement sequence pattern, make a myocarditis diagnosis highly likely



Example: Takotsubo Cardiomyopathy – 45-year-old female, with no abnormalities, seen during the cardiac catheter examination. However, with limited pumping function, the patient's life was in danger. MRI scanning shows left ventricular apical ballooning and a corresponding oedema in the tissue without significant abnormalities seen in the late enhancement sequence – typical for Broken Heart Syndrome. This type of cardiomyopathy can be caused by stress without the presence of a vascular obstruction. After three months the problem had completely disappeared (right)

Dr Tilmann Emrich MD, Clinic for Diagnostic and Interventional Radiology at Mainz University Hospital

**The significant benefits** of cardiac catherisation remain undisputed. However, cross-sectional imaging modalities are serious competitors when it comes to arriving at the right diagnosis.

Recently, during the German Radiological Society Congress, Dr Tilman Emrich presented the results of his study on the diagnostic importance of cardiac MRI (CMR) for patients suffering acute chest pain, elevated levels of cardiac enzymes and a negative coronary angiography.

A 23-year-old male without a known pre-existing illness, and a 45-year-old female who had recently suffered a severe blow, were admitted to A&E at Mainz University Hospital and treated in the specialist chest pain department. The ECG showed no abnormalities but blood tests showed elevated troponin levels. Independent of the patients' age and sex everything pointed towards myocardial infarction. As per the established guidelines for these cases, the patients are therefore taken to the cardiac catheter laboratory. However, the cardiologist could find no evidence of a myocardial infarction.

'In this case, the cardiologist is faced with a dilemma. What should he do – send the patient home or continue treatment without a diagnosis?' asked Dr Tilman Emrich of the Clinic for Diagnostic and Interventional Radiology at Mainz University Hospital. His answer: 'In this situation, a heart MRI can be helpful as it enables an examination of the functionality together with the anatomy and analysis of the tissue. The clinical and laboratory results suggested an undiagnosed heart problem for both patients.'

Studies published to date have documented the field of application for cardiac MRI in these cases, although there is as yet no study on a case where a patient's radiological diagnosis was cross-checked with the cardiologist's final reference diagnosis in the context of clinical proceedings.

Back in 2007, this prompted Emrich, then still in specialist radiology training, to carry out a cardiac MRI in 125 patients whose cardiac catheter examination did not have any indicatory results, and to compare both diagnoses.

His work was overseen by Professor Karl-Friedrich Kreitner and the study was carried out between 2007 and 2010 - with a satisfactory result. 'The MRI scan showed multiple cardiac pathologies and in nine out of ten cases the MRI diagnosis concurred with the cardiologist's final reference diagnosis.

The five most common indications were myocarditis, dilated cardiomyopathy, acute myocardial infarction, Takotsubo cardiomyopathy (Broken-Heart Syndrome) and hypertensive heart disease,' explains Emrich. The MRI scan helped to make the right diagnosis for all cases of myocardial infarction and Takotsubo cardiomyopathy; in the other cases there were only slight variances.

In the case of four patients, the cardiologists were not able to make a final diagnosis at all.

Reprinted from RöKo HEUTE 2014, the official congress publication of the German Radiology Congress

# Complementary cardiac imaging

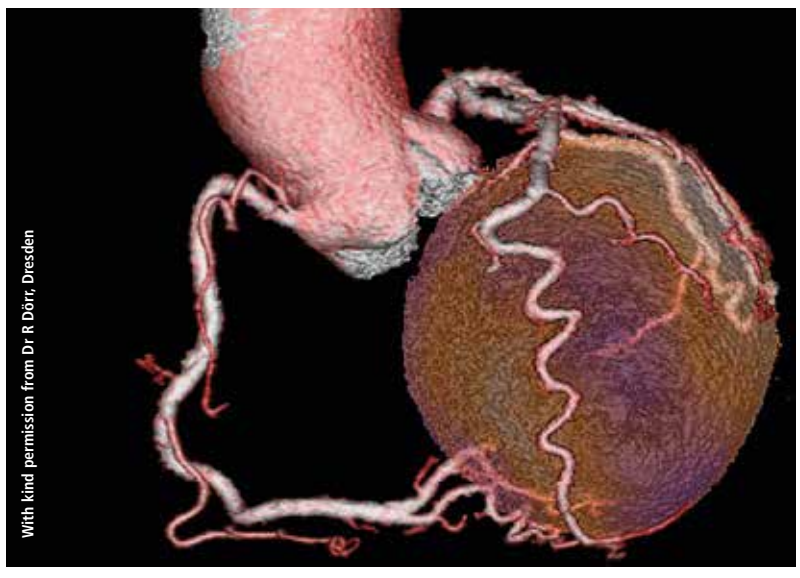
## CT angiography combined with PET perfusion measuring becomes gold standard

**'Positron Emission Tomography** (PET) and Computed Tomography (CT) are highly complementary in cardiac imaging,' explains University Professor Marcus Hacker, Head of the Department of Nuclear Medicine at The University Clinic for Radiology and Nuclear Medicine, Medical University of Vienna. 'The strength of CT lies in coronary diagnostics, the strength of PET in myocardial imaging. Both procedures complement one another in an ideal way.

'In clinical practice we often see coronary pathology without perfusion defects and, vice versa, impaired coronary circulation without any visible damage to the coronary vessels. In these cases the complementary information from the PET/CT hybrid procedure is also very helpful.

'With PET alone the perfusion of the heart muscle can be measured with various radiopharmaceuticals; however, it is also possible to examine the metabolism of the myocardium (glucose, acetate, fatty acids, for instance) or the myocardial innervation. Even infections (endocarditis, cardiac sarcoidosis, amyloidosis) can be diagnosed with the help of PET.'

On the one hand, CT is used to improve the PET information in the sense of an attenuation correction, i.e. a purely technical measure. On the other hand, the CT data can be used to calculate the coronary calcium score. 'The best discipline is the CT angiography, i.e. the visualisation of the contrast medium-filled coronary vessels and the quantification of the grade of stenosis,' Hacker emphasises, and confirms: 'The opinion now tends to be that if you have PET/CT available you should run the entire range of procedures, i.e. CT angiography plus PET perfusion measuring.' Both procedures complement one another and thus deliver benefit.



With kind permission from Dr R Dörr, Dresden

3D image fusion of SPECT-Perfusion and CT-coronary anatomy

Although PET perfusion measuring – with specificity and sensitivity of more than 90% – achieves a very high accuracy on its own compared to the more invasive coronary angiography, a simultaneous CT angiography additionally facilitates the attribution of any perfusion defects detected to the respective coronary stenosis that actually cause them. With PET alone, this can only be achieved in around 30% of cases. 'This makes it possible to plan revascularisation measures,' Hacker explains. Furthermore, first studies show that CT angiography also has an additional benefit regarding individual risk stratification of patients through the detection of coronary stenosis and non-calcified plaque deposits.

Computed Tomography angiography on its own is increasingly chosen as the first line examination to exclude coronary heart disease in patients with low to medium prior test probability for coronary heart disease. However, when the result of the CT angiography is not completely without pathological findings PET has significant additional benefits. 'The positive predictive value of CT angiography to assess existing perfusion defects is very limited at around 30-40%.

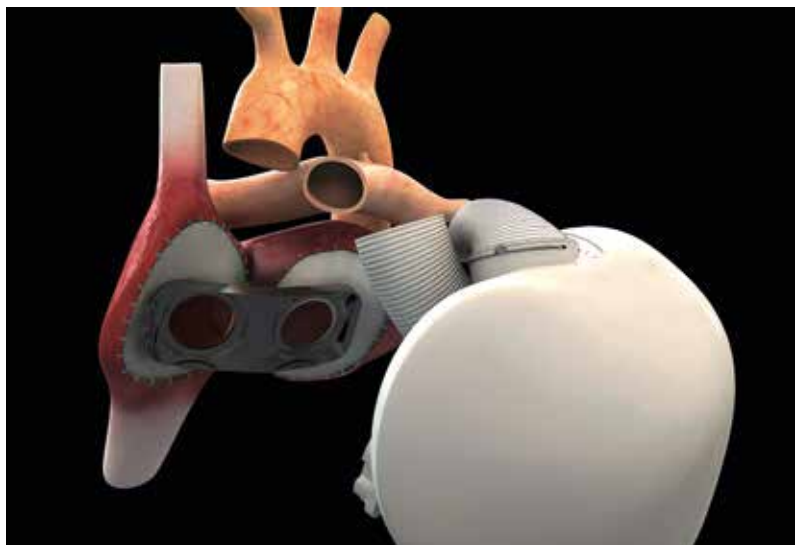
When pathological changes in the coronary arteries can be seen, then CT angiography cannot predict whether these changes will lead to perfusion defects in the myocardium or not,' Prof. Hacker explains. PET perfusion measuring is therefore the decisive criterion for treatment planning and risk stratification.

'CT angiography with PET perfusion measuring facilitates complete, non-invasive, combined coronary-pathological and function cardiac diagnosis,' he summarises, and predicts a great future for this hybrid procedure that has long moved on from its explorative stage. Unlike PET/MRI scanners, PET/CT scanners can be found in many facilities because of the oncological applications. Prof. Hacker: 'PET scanners without CT are no longer even being manufactured.'

Bavarian-born **Professor Marcus Hacker** has led the Clinical Department for Nuclear Medicine at the Medical University of Vienna since July 2013. Before this role the nuclear medicine expert was Head of Pre-clinical Imaging at the Clinic and Polyclinic for Nuclear Medicine, Ludwig Maximilian University in Munich.
His aim is to increase the implementation of personalised diagnosis and treatment concepts and accelerate translational research projects.
Since 2012 he has been head of the research group for Cardiovascular Nuclear Medicine of the German Society of Nuclear Medicine (DGN).

* Reprinted from RöKo HEUTE 2014, the official congress publication of the German Radiology Congress

# Three artificial hearts to be implanted



The 'self-regulating' artificial heart refers to the ability to speed up or slow down its flow rate – if the patient is performing a vigorous physical activity, for instance, the heart will respond by beating faster. This is made possible via 'multiple miniature embedded sensors' and proprietary algorithms running on the integrated microprocessor.

Report: John Brosky

**French authorities have given the green light for continuing the clinical trial for the first fully implantable mechanical heart after a four-month review of the device and the causes of death of the first patient to receive the prosthesis**

**The manufacturer, Carmat, can** now continue its recruitment of three other patients authorised for this first trial to test device safety and feasibility. All implantations will be performed in France.

Congratulating participants on the quality of their work in collecting and analising the data from this first implantation, Carmat CEO Marcello Conviti said in a company announcement that 'complementary measures' have been put in place to continue the trial in order to assure the best conditions for safety.

In an e-mail response to *European Hospital*, the company said the measures 'concern notably manufacturing processes or protocols which the company does not wish to discuss.'

The company also said that it will not communicate any further information until the full trial for safety has been completed.

## The first artificial heart that was implanted

The first patient to receive a totally implantable artificial heart died 75 days after the procedure. The cause of death on 2 March 2014 was not disclosed in a short announcement made by the Hôpital Georges-Pompidou in Paris.

Christian Latremouille MD, at the Hôpital Georges-Pompidou, noted that a survival of 74 days for the first patient with end-stage heart failure widely exceeded the 30-day endpoint for the safety study.

The 76-year-old patient was 'fully aware of the risks and by his confidence, his courage and his willingness has made a remarkable contribution to the efforts undertaken to combat a rapidly progressing disease,' the medical team stated.

The heart was implanted on 18 December 2013, by the surgical team led by Dr Latremouille with the participation and guidance of the inventor of the device, Alain Carpentier MD.

## The artificial heart adapts blood supply

This was the first time an artificial heart requiring no external pumps had been implanted. Only two wires exited the body at the abdomen, one to supply power and a second to monitor device performance.

This is also the first artificial heart capable of adapting the blood supply according to a patient's activity, varying from three to nine litres per minute, rather than keeping to a constant supply.

In an interview with the French weekly, *Journal du Dimanche*, Carpentier said the first patient's death 'is not linked to a complication of the patient, nor to the fundamental principles of this prosthesis.' He said the risk of thrombosis was limited, that the patient did not demonstrate any cerebral deficiency, and that an autopsy confirmed there was not the least bit of clotting in the device nor in the circulatory system.

'In this sense, the trial was a success,' he concluded.

# Listen to your heart 24 hours a day

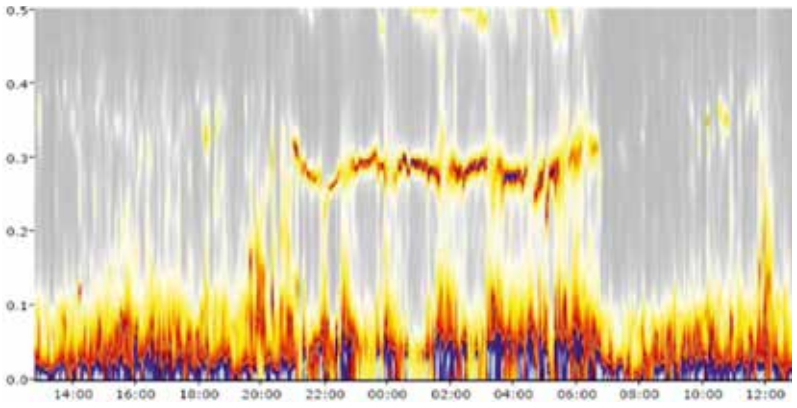
**The 'Fire of Life' developed by Schiller is an intuitive visual presentation of frequency-domain heart rate variability (HRV) that makes the assessment of 24-hour results fast and simple. In discussion with European Hospital, Dr René Hefti, senior consultant and medical director at Klinik SGM Langenthal spoke of his experiences with this unique system**

**HRV analysis is important –** Functional disturbances of the autonomic nervous system are always accompanied by reduced heart rate variability (HRV). With the heart being a central target organ of autonomic regulation, heart rate is a crucial regulation parameter for many processes in the body and offers a wealth of information on the functional status of the human organism.

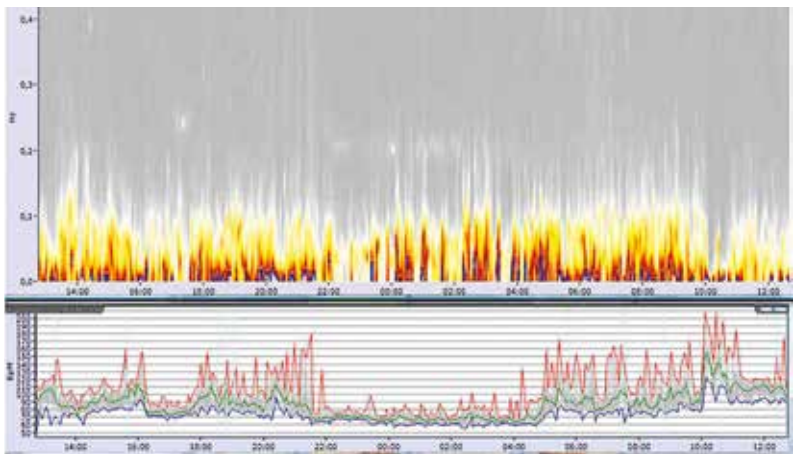
Usually, heart rate is analysed statically, for example with spectral analysis, in order to filter relevant information. Conventional ECG devices compress the data and much information is lost.

'However, the functional status of a highly complex system, such as our autonomic nervous system, cannot be described by a few parameters. The complete information can only be culled from the 120,000 RR intervals in 24 hours.

Schiller reports: 'Fire of Life can present these data, which map the regulation processes of the autonomic nervous system, in a non-compressed way and in high resolution. This allows the integration of HRV analysis in many clinical specialities, such as internal medicine, cardiology, occupational medicine, psychiatry, psychosomatic medicine or sleep medicine.'




**24h HRV assessment with spectral analysis: spectral image of a 27-year-old female patient with stress-related arterial hypertension. Good and age-conforming regulation capability (SDNN 220 ms) with slight parasympathetic dominance (RMSSD 52, Log LF/HF 0.38), retained sleep structure with rhythmic deep sleep phases, pronounced REM (rapid eye movement). No signs of sustained autonomic dysfunction.**



**24h HRV assessment with spectral analysis and HR trending: spectral image of a 58-year-old male patient with arterial hypertension and CHD. The total regulation capability (Total Power 1192, SDNN 84 ms) is reduced and not age-conforming. Significantly reduced parasympathetic activity (RMSSD 9ms) is accompanied by a relative sympathetic dominance (Log LF/HF 0.87). Sleep structure is to a large extent retained, but heart rate (HR) drops below 60 bpm during the night.**

## HRV in cardiology

'In cardiology HRV is above all a risk marker: the lower the HRV, the higher the risk of cardiac events or cardiac death,' says Dr René Hefti, senior consultant and medical director at Klinik SGM Langenthal, in Switzerland. He uses HRV analysis to record autonomic dysregulation in hypertensive patients, for example: 'Some hypertensive patients are difficult to assess due to a number of stress factors, such as psychosocial stress, poor sleep quality, lack of physical exercise, etcetera. Thus hypertension ought not to be looked at as an isolated phenomenon. HRV allows us to gain a comprehensive picture of the regulation processes.'

The Fire of Life application measures HRV over a 24-hour period thus providing information on the autonomic overall balance, sleep quality, the linkage between respiration and heart rate and similar indicators to support management of the hypertensive patient. 'The application's spectral images show the quality of the regulation processes while the frequency values offer quantitative data,' the cardiologist explains. 'I don't need HRV to diagnose hypertension, but I do need it to understand whether and to which extent hypertension is accompanied by autonomic dysfunction.'

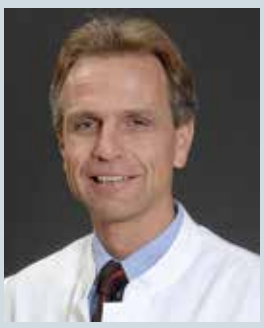
## Individualised therapy

The results of the HRV analysis provide crucial information for an individualised therapy of the hypertensive patient. 'If we see pronounced sympathetic dominance, which continues through the night and is accompanied by reduced vagal activity, we not only need drugs that decrease sympathetic tone but also immediate measures to increase vagal activity, such as regular physical exercise or deep relaxation techniques, for example based on HRV bio-feedback. At the same time, risk factors and psychosocial stress need to be reduced,' he explains.

Long-term HRV measurements allow the physician to monitor the quantitative efficacy of therapeutic measures. If the sympathetic tone decreases and vagal tone increases, which indicates a better balance of the autonomic nerve system, therapeutic measures are effective.

In addition, the easy-to-understand spectral images play an important long-term role in guiding and motivating the patient.

24-hour HRV monitoring can be used in the same way to manage other cardiovascular diseases such as coronary heart disease.



**Dr René Hefti** is senior consultant and medical director at Klinik SGM Langenthal, Switzerland, and teaches psychosocial medicine at the University of Berne. He attended medical school at the University of Zurich and following his graduation in 1987 he gained experience in internal medicine and cardiology at different hospitals in Switzerland and Austria. In 1998 he participated in a research project on cardiac insufficiency and beta blockers at Kuwait University Hospital in Sanaa, Jemen. Dr Hefti focuses on stress physiology, autonomic regulation, heart rate variability (HRV) and psychosocial components of cardiovascular disease.



## UNCOMPRESSED AND VISUAL PRESENTATION OF HRV WITH SCHILLER'S FIRE OF LIFE

- Analysis of the autonomic balance: the relationship between sympathetic and parasympathetic activity over a 24-hour period
- Analysis of the structure and quality of sleep and respiratory events
- Visualisation of baroreceptor data and blood pressure regulation analysis
- Stress and recovery management (burnout prophylaxis)
- Quantification of autonomic dysfunctions, such as diabetes mellitus

# TAVI r in the

**Report: Mark Nicholls**

**A hospital with** a reputation for trailblazing heart surgery has taken transcatheter aortic valve implantation (TAVI) onto the next step in the UK.

Led by Head of Cardiology Dr Jan Kovac, the team at Leicester's Glenfield Hospital repaired a dysfunctional heart valve by using the Lotus Valve System to treat aortic stenosis in an 84-year-old patient who did not require general anaesthesia and was fully conscious throughout the operation.

The Lotus Valve System, an implant measuring 23mm, offered the surgeons improved control of the valve throughout the procedure, enabling increased precision and the ability to reposition or retrieve the valve, even after insertion if necessary.

Developed and produced by medical solutions company, Boston Scientific, the Lotus Valve System also employs an Adaptive Seal feature, designed to minimise the Paravalvular Leakage (PVL), a complication associated with implantation of a prosthetic heart valve and one of the main causes of death in heart valve replacement procedures.

Dr Kovac said: 'This new generation of keyhole surgery further expands options for future patients. Until recently, there were very limited options to help people with this life-limiting condition who were considered inoperable or too high risk for cardiac surgery.

'Features of this current Lotus release make it a potential step forward in precision and elimination of regurgitation, potentially enabling more patients to be treated under local anaesthesia.'

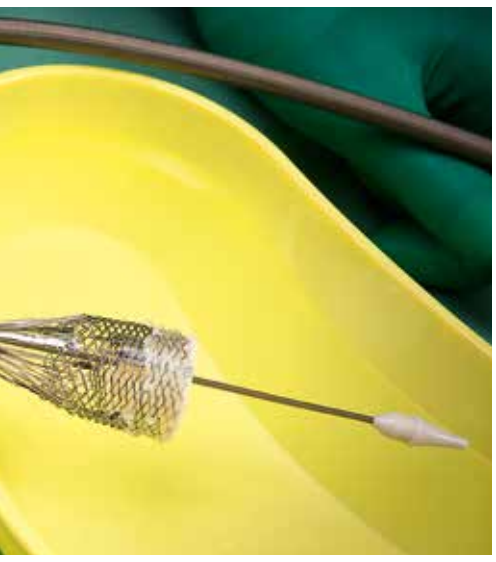
Aortic stenosis, in which thickening and stiffening in a heart valve prevents it from opening and closing properly, affects around 3% of the population over the age of 65 and 5% of people older than 75 years.

The procedure was carried out by percutaneous transfemoral access to place an 18 stent, using a 6F catheter and temporary pacing wire with balloon aortic valvuloplasty, followed by a TAVI implant.

Dr Kovac added: 'This is further recognition of the work done by the pioneering cardiac team at

*Transcatheter aortic valve implantation*

# ises another step United Kingdom



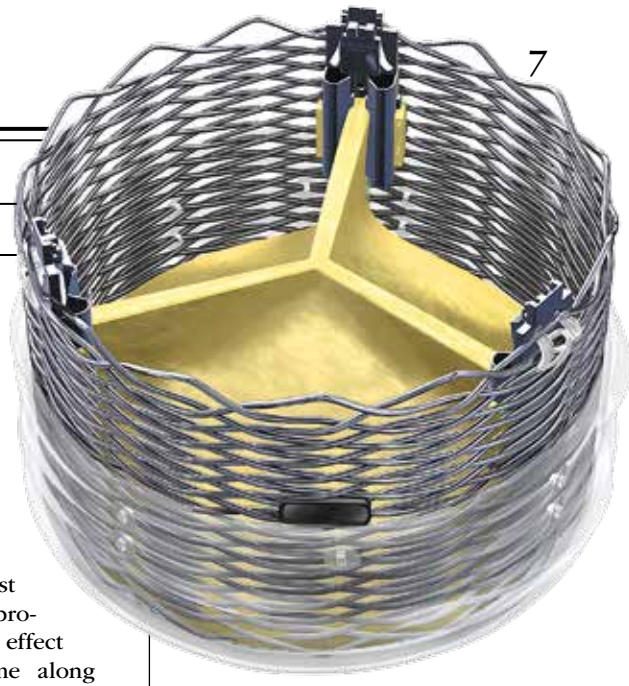
**The Lotus Valve System is a differentiated second-generation TAVI technology that consists of a pre-loaded, stent-mounted tissue valve prosthesis and catheter delivery system for guidance and percutaneous placement of the valve**

Glenfield Hospital. We are now into our eighth year of the TAVI programme and the first UK TAVI patient is still fine, seven years after implant, which itself is remarkable.'

The Leicester programme is constantly evolving as Dr Kovac's team endeavour to tailor treatment to individual patients with as many as possible having the least invasive procedures. 'We are constantly looking for newer designs coming to mainstream,' he said. 'The Lotus release was chosen with these in mind as initial data suggested very good sealing, non-disruption of cardiac output during implant and the option of repetitive repositioning.'

Jane Healy, vice president of Medical Affairs at Boston Scientific, added: 'The Lotus Valve System offers a unique and effective new treatment alternative for patients with severe aortic stenosis at high risk with surgical valve replacement. This is the first commercial implant of the valve in the UK, following our CE mark approval in October 2013.'

The repair of a dysfunctional heart valve by using the Lotus Valve System to treat aortic stenosis sits among a line of surgical 'firsts' for the Glenfield unit, which treats local patients as well as those from much-further afield. Others have included the congenital interventional team performing the first closure of septal defects in 1996, the EP team pioneering robotic AF ablation, and Dr Kovac's first TAVI in the UK in 2007, the first of several hundreds providing better functional effect and long-term outcome along with shorter hospital stays.









**Dr Jan Kovac** is Head of Cardiology at Glenfield Hospital in Leicester. He arrived in the United Kingdom 20 years ago to pursue a career in innovative medicine and subsequently gained a reputation for conducting 'UK firsts'.

He was named the NHS Innovator of the Year in 2009 for his role in bringing TAVI into NHS/UK and being one of the worldwide pioneers in the field.

Dr Kovac's unit is involved in generic trials to compare moderate risk patient outcomes between surgical replacement and TAVI – now an integral part of Glenfield's cardiac service – in an initiative simply named UKTAVI.

*Flaws in the current line of transcatheter valves open the field to a next-generation design*

# Bringing surgical quality to TAVR valves

**Report: John Brosky**

**A cardiac surgeon,** Wolfgang Goetz MD once stitched together custom aortic valves in the operating room. Today he is CEO of Transcatheter Technologies in Regensburg, Germany, a firm bringing to market a novel design for a next-generation aortic valve that he believes solves key issues challenging the current models for transcatheter aortic valve replacement (TAVR), specifically paravalvular leakage, improper positioning, durability of leaflets, and a high rate of pacemaker implantation.

In July 2014, ahead of print, the journal EuroIntervention published results from the first-in-human implantation of the TRINITY heart valve from Transcatheter Technologies, emphasising the unique ability to both reposition, and where necessary, retrieve the device.

The lack of these capabilities in first- and second-generation TAVR devices leads to suboptimal positioning of valves in many cases, the abstract text notes, which 'may result in paravalvular regurgitation, AV conduction delay, or compromise of coronary perfusion'. In the highlighted case, repositioning was required during the procedure and 'repositioning of the Trinity resulted in optimal position without paravalvular leakage and with perfect function,' according to the EuroIntervention abstract.

'The reposition-ability for the Trinityvalve that we provide is not meant to be used all the time,' explained Goetz, noting that in about 30% of the cases of TAVR implants, the cardiologist is not satisfied with the valve positioning.

When there is a positioning problem, this feature on Trinity, he said, 'allows an operator to go back and solve the problem without surgery, and without risking the life of the patient. It has been compared to having an airbag in your car. You don't drive the car expecting to have a crash, but if it happens, you really want to have that security feature.'

'We have learned from the clinical experiences of the big players, problems with paravalvular leakage because valves do not seal properly, problems with valves interfering with the heart's electrical conduction system. When I look at the valves that are now on the market, the big players have not solved these problems,' he said, adding that the problems persist even with the newest line of improved valves.

'There are ways to solve this,' said Goetz. 'We have a conforming skirt that provides small flaps that will lay over any leakage. As for the pacemaker problem, our plan has been for a valve that we can implant with a unique anchoring system so high in the aortic root that we don't touch the conductive tissue in the left ventricle, a few millimetres below the annulus plane.

'We've done two first-in-human implants now reaching one-year follow-up, which show that the Trinity will work as designed. With these patients we were able to demonstrate a step-wise procedure with a precise positioning at a location where we do not compress the conductive system. None of the patients had paravalvular leakage, none had pacemakers implants,' he reports. 'It's not a study that gives us statistical power, but it showed our hypothesis worked.'

If Goetz is proud of the success achieved in addressing these well-known challenges, he reserves his real passion for the little-discussed issue of durability of valve leaflets in current generation TAVR devices.

'What about durability?' he asks. 'I am not talking about the durability you need to receive CE mark approval, which is 200 million cycles mechanical testing. You won't get to the market unless you have this. Trinity has now reached 600 million cycles. The mechanical durability of our leaflets is incomparable.

'Our objective is to demonstrate the same durability performance as a surgical valve. 'The big problem with TAVR devices is the crimping. No matter if you have a self-expanding or a balloon-expandable model, you have to crush the valve leaflets,' Goetz explains. 'As a cardiac surgeon my first question was to ask what they are doing to these leaflets. The leading valve producers can show you how they produce surgical heart valves with very special technologies to ensure they never crush the valve leaflets, to prevent any damage to the integrity of the material. They avoid damage to the surface of this very fragile material they are using for leaflets.

'As a surgeon you are told to be very gentle and be careful to never to touch the leaflet, because where you have touched or damaged the integrity of the material, it will start to deteriorate faster.'

'Now TAVR comes along and they are crushing these leaflets to squeeze them into the catheters and, for sure, they are damaging the leaflets. You break collagen fibres, and you cause disruption of leaflet surface, which was already shown in several studies. It is very well known that this is going to lead to early deterioration of the leaflets. The proof will only come once TAVI is performed in patients with a longer life expectancy' he said.

'What we do is offer a valve that is pre-mounted on a detachable tip,' he explained. 'The expanded valve and leaflets are packaged in a liquid. Before implantation, the valve prosthesis is folded and the leaflets are stored in a 'garage' in which the leaflets are not crushed. Once the valve is in position, a sleeve slides back and then the valved stent is expanded. Now you can release the valve or you can stepwise fold the valve again if you need to reposition. We have quality control with a pre-mounted valve and we save time in the operating room because assembly is faster, that will

**The Trinity valve is pre-mounted on a detachable tip. The expanded valve and leaflets are packaged in a liquid. Before implantation, the valve prosthesis is folded and the leaflets are stored in a 'garage' in which the leaflets are not crushed.**
**Once the valve is in position, a sleeve slides back and then the valved stent is expanded.**
**Now the valve can be released or folded again if repositioning is needed. The leaflets are only folded but not crushed, the sheath is protecting the prosthesis but does NOT fold the valve**



*Remote monitoring of undiagnosed cardiac conditions*

# The 12-lead mobil

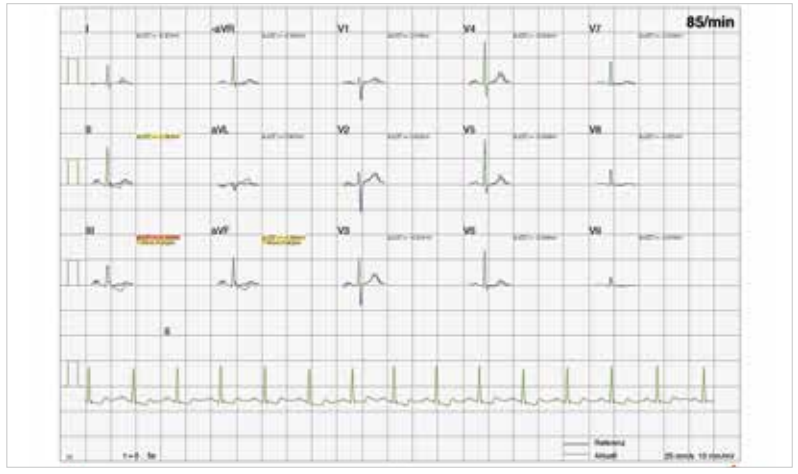
**CardioSecur, a personalised** mobile 12-lead ECG system with four electrodes for iPhone and iPad, enables patients to monitor their symptoms and transmit the data to their physicians in less than a minute. The system is reported to be ideal for patients with intermittent, difficult to diagnose cardiac symptoms and those who are still symptomatic post-intervention. This also could be use as a tool to monitor drug safety, the manufacturer points out.

'The patient records a reference ECG reading while sitting calmly with no symptoms. When symptoms occur, the patient takes a control ECG reading for 10 seconds, which is compared to the reference reading. An instant assessment of rhythm, heart rate and perfusion status is performed, see image 2.

The ECG data is uploaded to a database accessible by the patient's physician immediately, so that viewing the 12-lead ECG data is at the exact moment of the cardiac event (image 1).

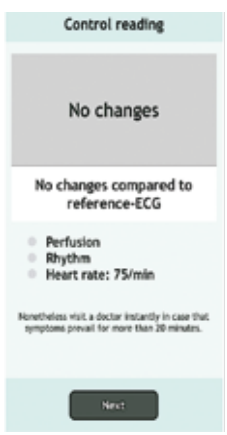
In the REDUCE-Trial (Revealing timely ECG changes Decreases the likelihood of Undesirable Cardiac Events-Trial) by ZNA Middelheim, Belgium, 51 patients were given the mobile 12-lead ECG system for a period of three months to record their ECG weekly and when they experienced symptoms. Medical conditions included: recurrent palpitations of unknown origin (41.2%), atypical chest pain (33,3%), angina pectoris (13.7%) and tachycardias of unknown origin (11.8%).

1,237 ECG readings were recorded and CardioSecur diagnosed a new or undiagnosed condition in 10% of the patients. Four were diagnosed with arrhythmias: two with atrial fibrillation; one with monofocal ventricular premature beats with bi- and trigeminia; one with AV nodal re-entry tachycardia.




**Using the system, the attending physician is able to access the patient's uploaded 12-lead ECG data at the exact moment of the cardiac event and take action**

**Depending on the discrepancy between the two readings, the patient receives an instant message based on a traffic light system: no change to baseline (white); make doctor's appointment (yellow) and contact a doctor immediately (red)**



# To pulse or not to pulse

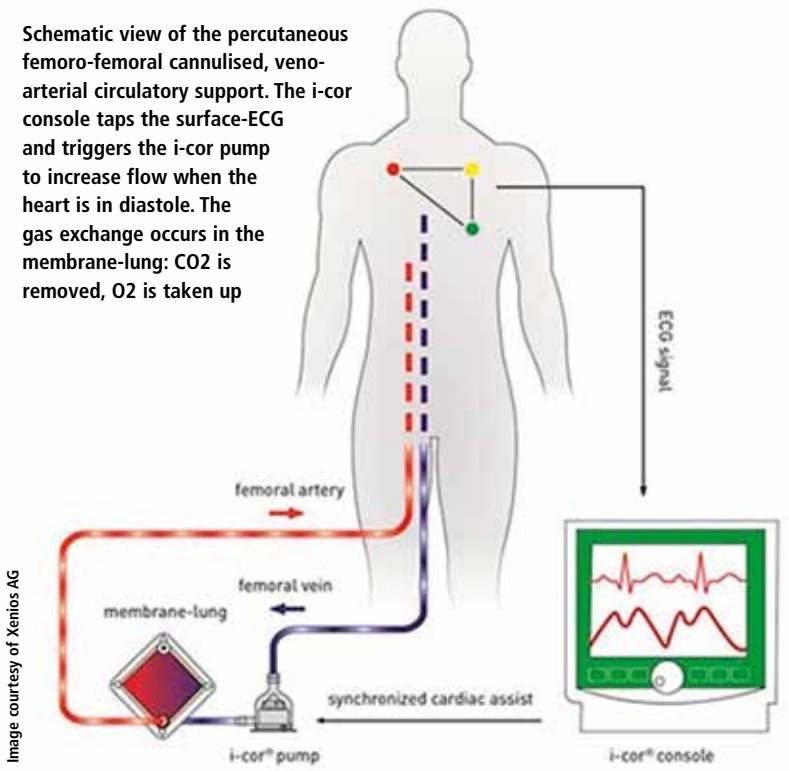
**Whether mechanical, temporary cardiac assist systems should pulsate in the same way as a biological heart is a discussion topic, which raises the pulse rates amongst all those involved within the industry and in hospitals. The latest developments confirm this, reports *Holger Zorn***

**Wolfgang Goetz MD** gave up a successful career as a cardiac surgeon to start Transcatheter Technologies (Regensburg, Germany). After practicing for years at the University Hospital in Regensburg, Dr Goetz went to Singapore to lead a research project for developing an autologous heart valve prosthesis. Practicing again at the German Heart Centre Munich, his experience with clinical trials revealed to him the advantages and disadvantages of TAVR valves and inspired the start of his own company.

**It happened in Orlando**, Florida on 14 November 2011: Dr Timothy J. Gardner, Medical Director of Christiana Care's Centres for Heart and Vascular Health and Past President of the American Heart Association, reignited the debate surrounding pulsing after around two decades of relative calm on this topic. Gardner talked about the development of a synchronised cardiac assist device.

This would be as small as an ICD and was to detect the patient's ECG signal. Connected to the subclavian artery, it was going to generate a stroke volume of 30 cc – in the counter-pulsation known from the IABP. That was predicted to take the strain off the heart, improve coronary circulation and improve the supply of the peripheral organs.

One weak point was the limited frequency: The device only pulses to 100 bpm; above that it would pulse continuously and the physiological advantage would be gone. However, Gardner encouraged everyone to trial the device and amongst 'plenty of good reasons' included the 'current need for an activity-friendly IABP'. At the end of January 2012, again in Florida – but now in Fort Lauderdale – Dr Renzo Cecere, Director of the Mechanical Assist Programme at McGill University Health Centre in Montreal, Quebec, reported on his first two implantations of the new assist devices in humans. He was pleased with the recovery potential, which the new product from Abiomed called Symphony offered for 28 days up to the point of its scheduled explantation, and expressed hope that the comparatively simple intervention would soon make it possible to not only treat patients with congestive heart failure with a conventional LVAD at the therapy-refractory terminal stage when they no longer respond to medication, but to slow down the progress of the disease at a relatively early point, thus significantly increasing quality of life.




Schematic view of the percutaneous femoro-femoral cannulised, veno-arterial circulatory support. The i-cor console taps the surface-ECG and triggers the i-cor pump to increase flow when the heart is in diastole. The gas exchange occurs in the membrane-lung: CO2 is removed, O2 is taken up

Image courtesy of Xenios AG

'The concept of a minimally invasive implantable pump for patients in chronic heart failure, coupled with the ability to remodel the heart, is unique and ground-breaking, and we are very pleased with the initial findings of Symphony,' said Cecere.

## From the USA to Germany

Although this study is not yet finished, contrary to the initial plans, another pulsatile cardiac assist device was recently trialled in Germany for the first time. On 25 June, his 56th birthday, Kurt-Josef M. was the first patient worldwide to have the Heartmate III by Thoratec implanted at Hanover Medical School.

One of the innovations of this type of device is an artificial pulse. To achieve this, the revolutions of the pump are slowed down and then sped up again every two seconds. However, this does not work under stress. 'We can't yet do this ECG-triggered,' explains Dr Jan Schmitto, who implanted the device. It is also not yet quite clear what the optimum pulse frequency should be. Whether a pulse beat is even necessary is currently the subject of scientific discussion.

Schmitto cites physiological arguments: 'In older patients in particular we may be able to reduce complications from gastrointestinal bleeding in the long term by generating a little pulsatility.' Moreover, with a lacking pulse there is a danger that the media, the muscular layer of cells in the arteries, atrophies if it is no longer activated – which probably increases the risk of capillary ruptures in the gastrointestinal tract.

Around three months before (25 March 2014), Dr Ulrich Laufs, Professor for Clinical-Experimental Medicine at Saarland University in Homburg, had given a much-regarded lecture. Using the i-cor manufactured by Novalung, the first pulsatile circulatory assist device for interventional cardiology (image) which actively pumps blood, he managed to measure coronary flow, which was around 300% higher than conventional, non-pulsatile perfusion in animal experiments (n=8) with a fibrillating pig heart. As the device also has an ECG trigger, this makes heart-synchronic extracorporeal circulation with diastolic augmentation possible.

It also eliminates the main disadvantage of conventional extracorporeal life support (ECLS): the bloodstream is no longer continuously pumped against the weakened heart. This lowers the cardiac afterload and the need for oxygen. At the same time, coronary perfusion increases and therefore the amount of oxygen available. Last, but not least, the circulation in the end organs improves – as Timothy Gardner put it, 'plenty of good reasons' for the i-cor, which can even pulsate up to a heart frequency of 150 bpm.

reduce the number of personnel required.'Can a small start-up company really expect to find a place in the fast-expanding and fiercely competitive landscape for TAVR devices?

'Definitely,' replies Goetz without hesitation. 'The market is huge, estimated to grow to $4 billion in 2020 worldwide. Analysts have been underestimating the market to this point. Once the Asian markets open up it will be much, much bigger. Even a small share of this market will be big enough for making a viable business.

'As we have seen in cardiac surgery, existing valve prostheses will be replaced by new improved devices with better performance. That is the natural evolution in a market,' Goetz pointed out. 'Products improve, they get better, they will be replaced and there will be a place for a valve that solves the problems of paravalvular leakage, repositioning and pacemaker implantation.'

# e ECG

One ischaemic patient was advised by CardioSecur to make a doctor's appointment during a control reading. The patient was subsequently diagnosed with a stenosis of 90%.

All patients received timely and appropriate treatment due to the availability of precise remote 12-lead ECG data at the time of the event.

The study indicates that CardioSecur is an important tool for diagnosing and managing patients with cardiac diseases such as rhythm disturbances and ischemic episodes, the manufacturer reports, adding that this paper will be presented in Barcelona this August during the 2014 ESC congress.

*Streamlining non-invasive cardiology diagnostics*

# Partnership optimises uniform processes

**By recognition and** early intervention against the most significant risk factors, many heart diseases can be prevented. At the Polikum health centres of Charlottenburg, Fennpfuhl and Friedenau, in Berlin, state-of-the-art medical technology is used for a reliable cardiovascular diagnosis.

A partnership between Henry Schein Medical and the Polikum has restructured the non-invasive cardiology diagnostics area by establishing uniform processes so that doctors can take advantage of synergies and a fluid internal workflow.

At the healthcare centres, CardioSoft from GE Healthcare is fully integrated into the workflow. Combined with Turbomed, this enables reliable data collection – the absolute key to determining the root causes of cardiovascular disease.

The CardioSoft system records the ECG, runs ergometric tests, and measures long-term blood pressure and the long-term ECG. Spirometric data and even data from spiro-ergometry (cardiopulmonary exercise testing) diagnostic tools can be captured, providing high quality results for the physicians. Thanks to the 'Turbomed' billing programme, findings and analyses are placed in the patient's file, allowing access to the data at any time.

In turn, the findings are centrally stored in a single computer system and can be viewed by doctors at the Polikum health centres, depending on activation of access regulations (ensuring patient data protection), even if the patient has been examined at another site or treated by another doctor.

Working with the med-tech network, Dr Marc Oliver Grad, cardiologist and Head of Cardiology at Polikum Berlin, said: 'The benefits of medical diagnosis systems and of incorporating electronically captured data in the patient file are used every day and represent a genuine advancement in quality and functionality.'

He added that, in addition to options in the follow-up survey, he uses one application in particular – 'a stored ECG and pre-ECG can easily be displayed one above the other, channel-by-channel, to reveal minor differences – for example, in the final stages analysis.

'In just a few minutes findings can be made available to external medical colleagues for the entire period during which the patient was in the Polikum, without having to make bothersome requests for files from the archive. Particularly in cardiological emergencies, this lets us pass on valuable information without delay.'

Henry Schein's nationwide network includes 330 technical staff so service and support is very quick, according to Jürgen Hahn, President of the European Medical Group Henry Schein. For medical staff, he pointed out, the automated IT processes are easily learned, and give a clear structure for better work transparency through one procedure followed by all the medics and patient. Finally, he added: 'This is a paperless system that is always up to date.'

His observations are backed up by Sabine Bärwolff, Chief Technology Officer and Manager at the Polikum, who said the need for a fully-integrated system, run with the highest reliability, has been met and added that the partnership with Henry Schein supports the health centres in 'breaking new ground'.

Dr Marc Oliver Grad, Head of Cardiology at the Polikum centre in Berlin

The Polikum health centre in Berlin


Cardiologist Dr Marc Oliver Grad using Vscan, a handheld, pocket-sized ultrasound tool by GE Healthcare

# Too ma stent pr

Report: Mark Nicholls

**In uncomplicated stable angina cases no evidence suggests that angioplasty reduces heart attacks or death risks**

**Heart patients should** be given more information about the purpose of an operation, according to leading UK-based cardiologist Aseem Malhotra MD, who fears that too many cardiac patients are undergoing coronary stent procedures without being told that the operation will not stop future heart attacks.

Every year, about 60,000 people in the United Kingdom receive coronary stent procedures to unblock arteries soon after suffering a heart attack, where it improves their chance of survival.

However, a further 30,000 patients with 'stable heart disease' undergo the surgery each year, despite the fact research shows it will not prevent heart attacks or extend lives in such cases, Dr Malhotra points out.

He believes that too many heart disease patients are undergoing the procedure without being told that angioplasty would not reduce death risk or heart attack and such operations can be being carried out needlessly.

Writing in the *Journal of American Medical Association* (JAMA), Dr Malhotra pointed out that randomised studies have shown there is no clear evidence of stenting benefiting those with stable coronary disease, despite the majority of patients believing that angioplasty would improve their long-term survival rates.

The piece, entitled *'The whole truth about coronary stents: The Elephant in the room'* referred to a

*ECMO's role in a world's first cardiac procedure*

# Correcting Tetralogy of Fallot

Report: Mark Nicholls

**Cardiac specialists** in the UK have performed a world's first operation on a 14-year-old boy suffering a severe heart condition. The patient had a Tetralogy of Fallot - a congenital heart defect with four abnormalities inside the heart – and underwent the procedure at the East Midlands Congenital Heart Centre at Glenfield Hospital, Leicester, earlier this year. the teenager has now made a complete recovery.

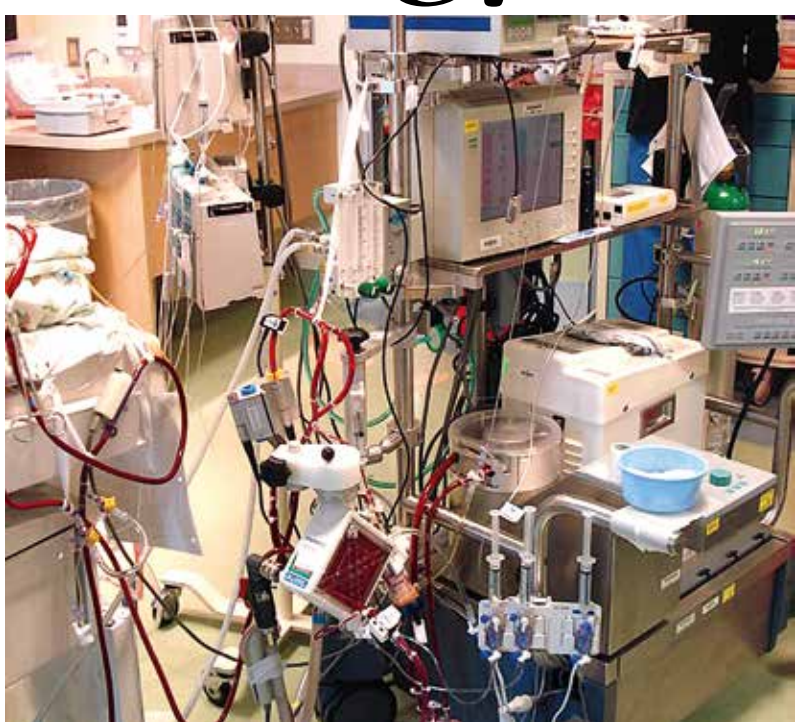
What set this procedure apart as a world first was the way the surgical team worked alongside the ECMO (Extracorporeal membrane oxygenation) unit. That helped ensure that the complex keyhole stent and valve insertion procedure to cure the congenital heart defect was able to go ahead, because of the ECMO unit being on standby to minimise the risk of damaging the patient's heart muscle and provide instant cardiac support if needed.

Consultant congenital cardiologist Dr Frances Bu'Lock, who led the diagnosis and was involved in the planning for the surgery, explained that the patient had a recurrent right ventricular outflow tract obstruction caused by a bar of muscle that contained a branch of the right coronary. It required urgent treatment because narrowing had caused the right side of the heart to swell to twice the size it should be.

After three previous operations had not resulted in a satisfactory outcome, Dr Bu'Lock said surgeons were running out of options to tackle what had become a 'very severe obstruction'.

Due to the associated risks, the Glenfield team consulted other European cardiologists – there was the possibility the patient may have an acute infarct during the procedure and might become electrically and haemodynamically unstable, or could develop arrhythmias, which would make the procedure impossible to complete.

Their contact led to the decision to use ECMO with a team of more than 20 doctors, nurses and physiologists assembled to perform the procedure, and with the ECMO specialists on hand to support the patient's circulation if he suffered a heart attack during the procedure, with a full life support circuit prepared and ready for use at a moment's notice. 'We did it as a combined procedure,' Dr Bu'Lock explained. 'With the surgeons and the ECMO team in the lab suite, if the patient did go into ventricular fibrillation or cardiac arrest when we inflated the stent and compressed the coronary we would go on to ECMO and complete the procedure.'



Extracorporeal membrane oxygenation (ECMO) system

Deliberately sacrificing the coronary as part of that procedure, with the involvement of the ECMO team, was the first time this type of procedure had been performed this way anywhere in the world. The cardiac and surgical teams at East Midlands Congenital Heart Centre specialise in performing very complicated and unusual procedures with ECMO support; both for people with malformed hearts and also for babies with major heart rhythm problems.

'We are increasingly using ECMO to allow us to do procedures that otherwise we could not safely do – and that other units would not do,' Dr Bu'Lock pointed out with a justifiable note of pride. 'In this case, the patient made a complete recovery – he woke up and said my heart feels different – he's gone back

# ...ny coronary ...rocedures

study in the US involving 144,737 patients in 1,091 hospitals, which suggested that almost half the stenting carried out was unnecessary.

Another study, which found that 88% of patients undergoing a procedure for stable angina believed that angioplasty would prevent myocardial infarction, showed that, given various scenarios, 43% of cardiologists would go ahead with stenting even when they thought it would not be of benefit.

Dr Malhotra suggests that making clear these facts should become a mandatory part of the consenting procedure process. 'We need to address how we can reduce the potential over-use of stenting. One way I'd like to see that happen is to see it included on the consent form as a caveat to the risks and benefits we outline to patients. We need to be saying to patients that, while this may have symptomatic benefits, stenting will not reduce their risk of a heart attack or death and it does not prolong your life. 'It's imperative to provide patients with all the information before subjecting them to a procedure that still carries a 1% risk of heart attack, stroke or death,' he added.

He did point out that the procedure could help those suffering from angina, reducing the amount of chest pain, but said too often patients were given an impression it would achieve far more. 'Of course elective stenting has an important role in the treatment of patients with limiting angina to improve the quality of life when medical therapy is inadequate but few patients are explicitly told that stent won't prevent a heart attack or prolong life,' he believes. Research has also indicated that up to half of stenting procedures carried out in the USA were either 'inappropriate' or of 'uncertain' appropriateness, he points out.

**Dr Aseem Malhotra** is a consultant clinical associate to the Academy of Medical Royal Colleges. He received his interventional cardiology training at Harefield Hospital, the Royal Free Hospital and Croydon University Hospital in London.

'The elephant in the room is that randomised studies have not demonstrated outcomes benefit for stenting stable coronary artery disease in addition to optimal medical therapy despite its widespread use.' His comments have received high-level support from Professor Huon Gray, NHS England's heart disease 'tsar', and Professor Terence Stephenson, chairman of the Academy of Medical Royal Colleges, and have also triggered debate on the subject. Professor Gray: 'There is no evidence that coronary angioplasty reduces risk of heart attack or death in patients with uncomplicated stable angina, and it is important that doctors are clear with their patients about this.' Professor Stephenson: 'This is an example of a legitimate debate of appropriate or inappropriate use of clinical procedures or interventions.'

Oxbridge medical graduate **Dr Frances Bu'Lock** trained in congenital cardiology in Bristol, Birmingham and Liverpool. Joining Glenfield Hospital, Leicester, 11 years ago, today she leads the foetal cardiology service, but also has significant expertise in adult congenital heart disease. Her current major research interest is in the genetics of congenital heart disease, questioning whether gene changes cause congenital heart disease.
Dr Bu'Lock is also the cardiology editor for *Archives of Diseases in Childhood* and the training programme director for Paediatric Cardiology East Midlands.

to full sporting activity.'

Subsequent exercise tests and scans have shown the narrowing has gone and the size and pressure in the right side of the patient's heart has reduced to near normal with the breathlessness having disappeared and energy levels increased.

# Mobile C-arms in hybrid operating theatres

## Valuable for transcatheter valve and aortic interventions and more

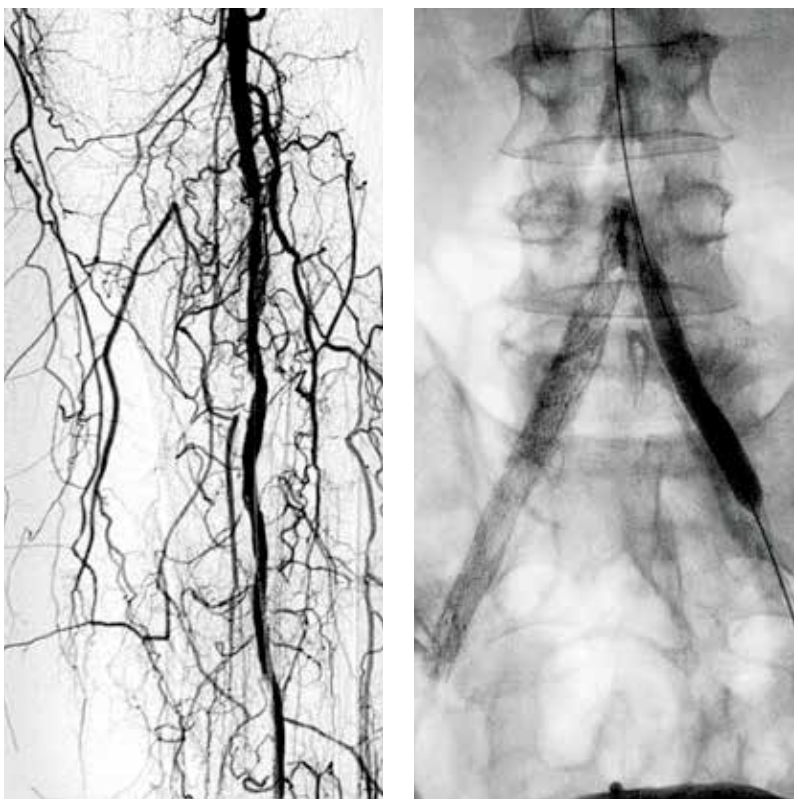
**Hybrid operating theatres** that combine conventional surgical tools with image-guided diagnostic tools, allow cardiologists and cardiac surgeons to perform minimally invasive surgery (MIS). In such surroundings, mobile C-arms offer a flexible, space and cost saving alternative to fixed installations in such surroundings.

In a study of mobile C-arm use, Dr Nikolaos Bonaros MD, at the University Hospital of Cardiac Surgery, Innsbruck Medical University, found that periprocedural new generation mobile C-arm imaging is very useful for transcatheter valve and aortic interventions as well as coronary artery graft evaluation and allows bail-out procedures without time delay (A Bridging Solution for Hybrid Operating Suites: Periprocedral New Generation C-arm Imaging During Cardiac Interventional Procedures, Journal of the American College of Cardiology, 2012).

### High quality MIS imaging

Dr Bonaros uses the Ziehm Vision RFD for cardiac surgery and valve implantation. He experienced the first C-arm motorised in four axes storing up to three positions. This allows the operator to select/restore a position again at any time to access the desired viewing angles and anatomic visualisations without having to constantly reposition the system around the operating table.

'Ziehm Vision RFD Hybrid Edition is the only mobile C-arm to offer an active liquid cooling system in the standard version,' the system's manufacturer reports. 'Advanced Active Cooling ensures reliable imaging without interruption even during lengthy procedures. With its rotating anode and 25 kW power, the mobile C-arm is one of the most powerful C-arms in the market and delivers crystal-clear images even of moving objects such as a beating heart.'



**Mobile X-ray imaging is used for various interventions such as heart valve implantation, vascular procedures for extremities (left image) or triple A procedures (right image)**

**DATE FOR THE DIARY**

Innsbruck, Austria: 14-17 September; FOCUS: Valve 2014, the 6th Training Course for Minimally Invasive Valve Surgery. The course aims to provide educative input on the latest techniques and new technology. Dr Bonaros will present 'The latest generation C-arm fluoroscopy'.
* Ziehm Imaging will present its Vision RFD Hybrid Edition in the industry exhibition.

# 3D targeting of th

## Rapidly advancing cardiac imaging capabilities aid precise planning and intervention guidance

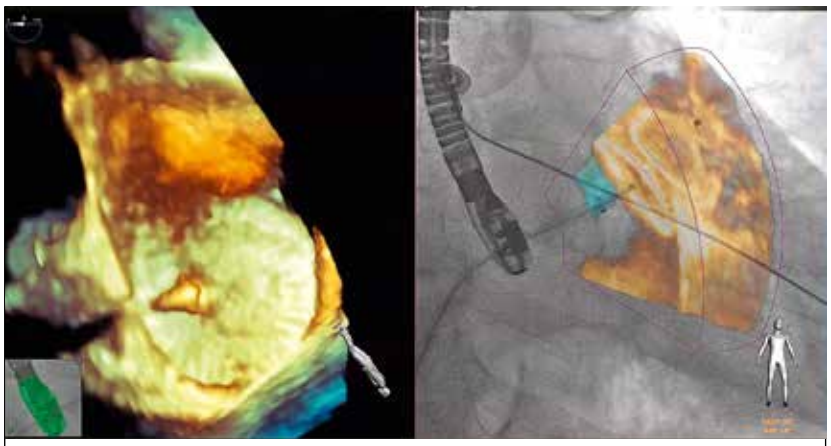
**Report: John Brosky**

**The heart is** a structure in three dimensions and today we see it in three dimensions,' Jose Luis Zamorano Gomez MD declared with satisfaction. 'Even more, the heart is a volume in motion, contracting and relaxing, and the most significant development in cardiac imaging is that we can now study this motion in real time.'

'In the past we needed to seek out experts in imaging technologies to quantify or measure accurately the morphology. Today, the imaging systems do this for us automatically, immediately capturing the volume, calculating the ejection fraction, quantifying the area of an annulus, measuring distances between structures and arteries.'

These quantification tools, he added, tremendously advance the reproducibility of results by greatly reducing inter- and intra-observer variability.

Prof. 'Pepe' Zamorano is currently leading the update for the European Society of Cardiology's (ESC) recommendations for imaging inside the catheter laboratory with the European Association of Cardiovascular Imaging (EACVI). The working group is moving beyond a focus on transcatheter aortic valve replacement (TAVR) to cover a range of new procedures and new devices that have emerged since the recommendations were published in 2011.



**EchoNavigator use during left atrial appendage closure: fluoroscopy and 3D live-echocardiography fusion.**
**For left atrial appendage (LAA) closure, fluoroscopy for catheter and device visualisation and echocardiography in 2 and 3D for anatomy and soft tissue imaging are most frequently used. A new navigation system (EchoNavigator, Philips Healthcare, The Netherlands) has been introduced that allows synchronisation and fusion of echocardiography and fluoroscopy images in real time, as an aid during structural heart disease interventions. In the image on the left we can see the 3D transoesophageal echocardiography image of the LAA closure device during introduction into the LAA. The image on the right shows fusion between the 3D echocardiography and fluoroscopy images with the same orientation, during LAA closure device implant. It allows visualisation in one same screen, fused and in real time of both imaging techniques, as well as what will help during procedure guidance and device deployment. (Prof. Zamorano, Dr A González-Gómez. University Hospital Ramón y Cajal, Madrid, Spain).**

This year, at the ESC congress in Barcelona, he will present his review of new imaging tools during the Spotlight Symposium on 1 September 2014, which aims to be devoted to 'Innovation in Interventional Imaging.'

'There are two innovations I will present that will have a high impact for interventional cardiology, and specifically for TAVR [transcatheter aortic valve replacement],' he explained. 'The first, a new 3D echography system, will show how interventions can be better planned and that the imaging information can go further to help guide the selection of the prosthesis.

'Then, once we move to the cath lab, I will show how interventions can be guided in real time guidance with synchronised image fusion of fluoroscopy and 3D echo.

The cardiology centre at the Ramón y Cajal University Hospital in Madrid, headed by the professor, is the European reference centre for both systems.

Developed by Siemens, cutting edge planning tool for TAVR procedures generates off-line a 3D image of a patient's native valve with an automatic generation of morphological data that are very relevant for an interventional cardiologist, such as the area of the valve, the area of the annulus, or the distance to the coronary arteries, he pointed out.

The immediate application of this tool is a major advance to address the critical issue of valve implantation, yet the power of this technology also inspires new possibilities, he confirmed.

'In a very near future, with all of this actual anatomical information and quantification, why not take it to a next step where we will be able to truly simulate the implantation of a specific valve in order to see what actually will happen, to see the positioning and the different aspects of the intervention in advance.'

Such modelling would become a predictive model for patient complications, identifying what is unique for each patient, and matching these conditions against a library of specific valve types and sizes. 'This is where we hope to go with this technology and I have already spoken with the engineers who see no reason it can't be done,' the professor revealed.

The second focus for his presentation of innovation in interventional imaging is the EchoNavigator developed by Philips Healthcare.

The real-time fusion of 3D cardiac ultrasound with fluoroscopy is 'something cardiologists have never seen before,' he said.

*Seeing the dynamics of blood flow into the heart is definitely a Wow!*

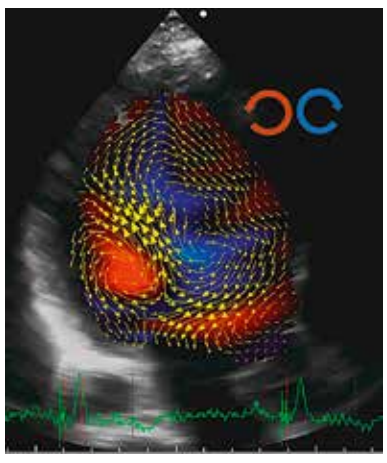
# Vector flow mapping via echocardi

**'There are aspects** of the heart's physiology that we know about, but now we can see them, and this is absolutely different,' said Patrizio Lancellotti, President of the European Association of Cardiovascular Imaging. 'It's definitely a "Wow!" to see the different aspects of flow motion, to see exactly the dynamics of blood flowing into the heart, its direction or magnitude. We can sometimes characterise an early stage of a disease, or an advanced stage. We can get an idea of the effect of cardiac resynchronisation therapy on the flow inside the heart. This is clearly new.'

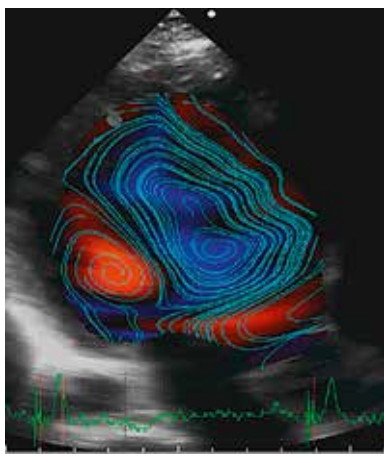
The head of the intensive care cardiology unit at the University of Liège Hospital Centre, Lancellotti is working on a new frontier in cardiac diagnostic imaging that has been opened by Vector Flow Mapping, or VFM.

Developed by Hitachi-Aloka Medical, VFM is an innovative application of the well-established cardiac imaging technologies for colour Doppler velocity data and speckle tracking combined with novel software that generates velocity fields on a 2D image.

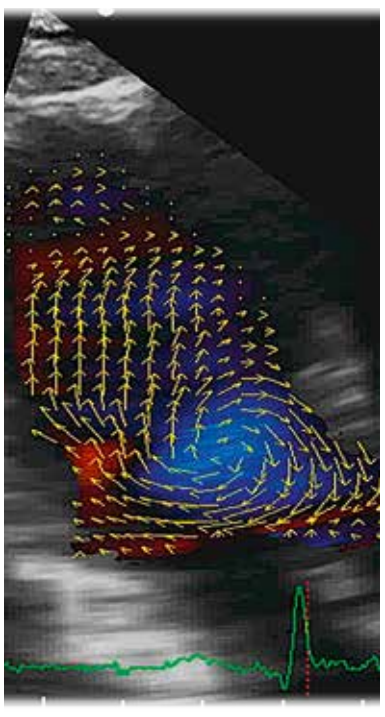
Simply put, this advanced technical prowess means a cardiologist can now assess cardiovascular blood flow distribution in real-time at a patient's bedside using the non-invasive and familiar examination of echocardiography.



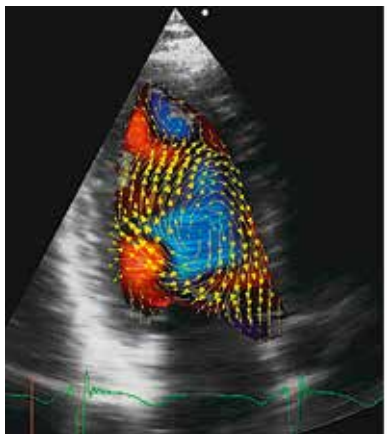
Dilated Cardiomyopathy
Vector + Energy Loss Display



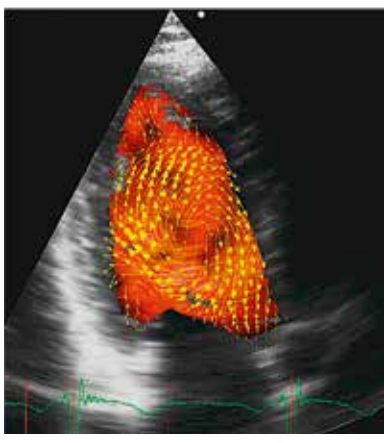
Dilated Cardiomyopathy
Streamline + Vorticity Display



Dilated Cardiomyopathy
Vector + Energy Loss Display



Aortic Regurgitation
Vector + Vorticity Display



VFM in Valvular Heart Disease
Vector + Energy Loss Display

'Flow motion has been described in the past mainly using MRI,' Lancellotti pointed out. 'Cardiologists know that we can see beautiful images from MRI, that we can even see the heart in three dimensions; but the issue is the availability and the high technical requirements for MRI. It is very difficult to get these images so, to this point, cardiac imaging for flow motion has been done primarily for research, not for routine clinical use.'

In contrast, he said, 'echo is very simple, readily available and with the VFM software, once we are able to define patterns, cardiologists can easily use it'.

Here lies the challenge on the frontier of a new science. Understanding the new VFM images and the significance of dozens of parameters of heart performance the software is capable of generating is where Lancellotti said help is needed. 'VFM allows us to associate a visual aspect to a condition we suspect, which is amazing,' he said. 'We now see so many new things regarding flow; but what's behind flow direction, vectors, vortices, energy loss, or shear stress? This is very complex and we do not yet really understand the expanding vocabulary. We don't know exactly which of these different measurements can be used to improve our decision-making and the clinical outcome for the patient.'

A core group of European and Japanese cardiologists have formed a VFM task force with the goal of creating a homogenous nomenclature that links specific measures to visual patterns in order to identify a specific disease state. 'Once we have a pattern for a disease, we'd be able to define different degrees and extents of the disease process, which would allow us to stage the disease,' he said. 'Once we can stage a disease, we could follow the progression or regression changes in the heart. This will allow us to better follow-up the patient.'

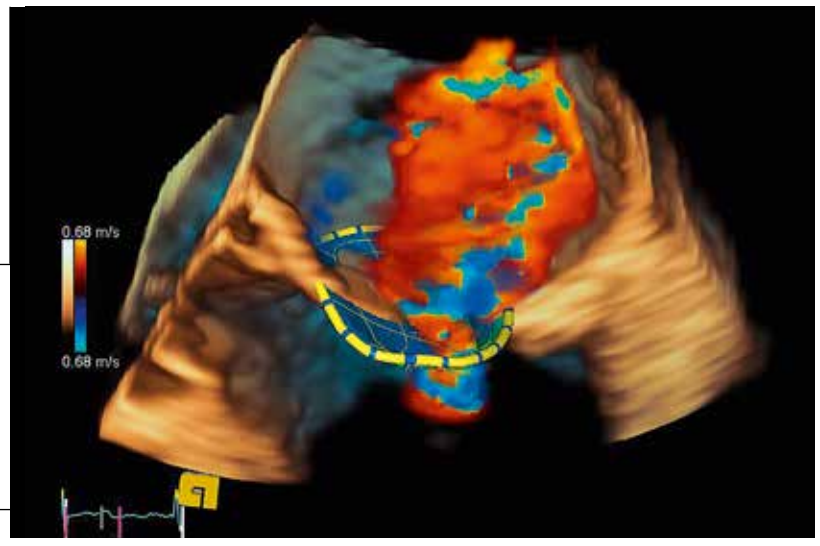
The VFM consortium is currently discussing the design of a large-scale study that would begin with the assessment of normal heart per-

# ne heart

In 99.9% of cardiac interventions, the interventionist is guided by conventional angiogram that requires interpretation of where the wire and prosthesis are located by watching a flat greyscale image that never actually shows the interventionist the heart.

By placing on the same interventional monitor a synchronised image of the heart, the use of 3D echo guidance becomes more intuitive.

'With EchoNavigator we can now superimpose over the angiogram the anatomical structure at the same moment as the angiogram shows the wire for positioning the valve prosthesis. There is no longer any question of interpreting the image,' Prof. Zamorano confirmed, 'because we are seeing the anatomy exactly the way it is.'




**A 3D echography data set is reconstructed with the cutting edge planning tool by Siemens Healthcare to show color Doppler flow across a reconstructed mitral valve. (Courtesy of University Hospital Ramón y Cajal in Madrid)**

**Professor Jose Luis Zamorano Gomez** is Head of Cardiology at the University Hospital Ramón y Cajal in Madrid. A Fellow of the European Society of Cardiology (ESC,) he currently chairs the ESC Guidelines Committee and he is a past-President of the European Association of Echocardiography of the ESC. He is also on the editorial board of many leading journals, including the European Heart Journal and JACC Cardiovascular Imaging.

## iography

**Patrizio Lancellotti MD PhD FESC FACC**, is a Board Member of the European Association of Echocardiography, of the European Society of Cardiology and an active contributor to several professional journals, including as an editorial adviser for the European Heart Journal and the European Heart Journal – Cardiovascular Imaging. Cardiologists interested in participating in a large-scale study for Vector Flow Mapping are invited to contact a member of the consortium or Prof. Lancellotti at the University of Liège, Belgium, where he is a Professor of Cardiology.

formance and then add a cohort of patients with cardiac dysfunctions and diseases.

'We need to involve more heart centres, and certainly we welcome people who are interested in participating. The more centres we can involve,' he said, 'the larger the community of echocardiographers, the better this study will be.' (JB)

# It's cool, Man!

**Evidence is scant on the cooling of comatose patients who have suffered cardiac arrest, stroke or traumatic brain injuries; nevertheless, new methods for cooling patients are continuously being developed.**

**Therapeutic hypothermia** is also being used in the cardiac catheter laboratory to prevent re-perfusion injury during revascularisation of coronary vessels, EH correspondent Matthias Simon reports, although noting that its use has not been documented sufficiently for this purpose. Currently available cooling methods are used either invasively (venous cooling catheters, cold infusions) or superficially (cooling pads, ice packs), or by utilising natural body orifices, such as the administration of perfluorocarbon into the nasal cavity.

There are many different views on the point at which cooling should be initiated: during re-animation, during transport to the hospital, or even only once the patient has arrived at a hospital. There are also different recommendations as to the correct target temperature: A study published in 2002 by the European Hypothermia After Cardiac Arrest Study Group showed an improved six-month survival rate (59% v. 45%) and improved neurological outcome (55% v. 39%) in 275 patients who had suffered out-of-hospital cardiac arrest (OHC) and ventricular fibrillation or tachycardia when they were treated with therapeutic hypothermia (target temperature range between 32°C - 34°C) compared to those given normothermic treatment [*N Engl J Med 2002; 346:549-56*].

However, Australian medics found a significantly improved neurological result (49% hypothermic v. 26% normothermic) in 77 patients after OHCA with ventricular fibrillation if they were treated with therapeutic hypothermia to 33°C. However, there was no significant advantage to the survival rate with 49% v. 32%. 'After adjustment for base-line differences in age and time from collapse to the return of spontaneous circulation, the odds ratio for a good outcome for hypothermia as compared with normothermia was 5.25.' [*N Eng J Med 2002; 346:557-63*].

In 2005 these results led to the development of a guideline recommending the treatment of patients with therapeutic hypothermia (32°C – 34°C over a period of 12-24 hours) after OHCA with shock-able rhythm.

However, the initial high hopes for the treatment were replaced by disillusion in 2013, when Nielsen et al published the results of the Targeted Temperature Management (TTM) Trial, a prospective randomised multi-centre study on patients after OHCA, with or without shock-able rhythms. 950 patients in 36 European and Australian hospitals were randomly cooled to either 33°C (Hypothermia group) or 36°C (TTM group).

The respective temperature was maintained for 28 hours; if patients developed a temperature after rewarming, fever-reducing medication was administered for 72 hours. There was neither an improved neurological outcome nor a significant difference in survival [*N Engl Med 2013; 369:2197-2206*].

## New goal: Cath Lab

In 2007 Dr Derek Yellen of the Hatter Cardiovascular Institute in London, UK, wrote that the potentially fatal reperfusion injury, which can occur with any percutaneous coronary intervention, can be avoided through therapeutic hypothermia before, during and shortly after the intervention [*New Engl J Med 2007; 357:1121-35*], basing his view on the results of a study involving 220 patients, with a subgroup who had suffered anterior myocardial infarction and had been treated with induced hypothermia below 35oC showing a reduction in the size of the infarction by 39% compared to those in the normothermic control group [Presented at Transcatheter Cardiovascular Therapeutics 2004, Washington, DC].

Dr Mathias Götberg of the Skane University Hospital in Lund, Sweden, showed a significant reduction of the size of infarction in a pilot study of 18 patients when the target temperature was below 35°C (with an initial 4°C cold infusion with endovascular cooling catheter) [*Circ Cardiovasc Interv. 2010; 3:400-7*].

Dr David Erlinge, also from Lund, recently published different results. 120 patients were examined in nine centres in Sweden, Denmark, Austria and Slovenia, with 61 patients in the hypothermia group and 59 in the control group. Therapeutic hypothermia did not result in a significant reduction in the infarction size, or in a subgroup-analysis either. The only benefit was seen in patients with anterior myocardial infarction who were re-perfused very early and showed a significant risk reduction [*J Am Coll Cardiol 2014; 63:1857-65*].

Therapeutic cooling of patients in cardiogenic shock is also being discussed: in animal experiments, Göttingen and Freiburg researchers showed an increase in cardiac contraction capacity with an increase in stroke volume under hypothermia [*Basic Res Cardiol 2001; 96:198-205 and Circ 2004; 110:A1639*].

However, the central questions remained unanswered: How quickly should the temperature be lowered? When should cooling commence? What is the right temperature to cool to? For how long should the target temperature be maintained? At what speed should rewarming be carried out?

One needs to literally keep one's cool not to lose track here!

## CURRENT AND NEW DEVICES FOR MILD THERAPEUTIC HYPOTHERMIA, WITHOUT CLAIMING COMPLETENESS (OWN COMPILATION)

| | | | | of use at | | of use for (Manufacturer-promoted) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Type | Company | Product | how it works | Ambulance | Hospital | stroke | traumatic brain injury | circulatory arrest | volume management | Delta T / hour [K/h], measured at | Concept |
| body surface | Emcools AG, Traiskirchen, AT | Brain.Pad Flex.Pad | Pre-frozen cooling pads filled with HypoCarbon® - a substance made from carbon - with 15 times more heat conductivity than ice. * In combination with Flex.Pad also for cooling of the upper body (extremities) after cardiac arrest. | ✓ | ✓ | ✓ | ✓ | * | | ~ 1 K/60-90 min 3,3 K/h | Disposable product |
| | MedCooling GmbH, Apolda, DE | CaroCooler | Selective Brain Cooling (SBC). The activation of cooling occurs through pressing and shaking of the fluid-filled pads. Cooling results from a phase change of the substances "Phase-Change-Materials (PCM)". | ✓ | | ✓ | ✓ | ✓ | | n/a | Disposable product + resusable holder |
| | Cryothermic Systems Inc., Cleveland, OH | Exel® Cryo Cooling System | Neck brace as holder for disposable cool element. On activation, this achieves a temperature reduction of -3°C to -5°C and ensures a tympanic temperatue drop of 1.73°C. Used also by first responders after cardiac arrest. | ✓ | ✓ | | | ✓ | | 1.73 K/h @ Tympanum | Disposable product + resusable holder |
| invasive | Advanced Cooling Therapy, Chicago, IL | Esophageal Cooling Device | A triple lumen, disposable catheter (water in- and out, stomach access) is inserted into the orogastric tube and lets water circulate by being pumped into, and then being sucked out of the stomach.Airways are secured via an endotracheal tube (not included). Used only for unconscious and intubated patients. | | ✓ | | | ✓ | | 1.37 K/h @ Rectum (animal lab) | Disposable product + Water temperature control unit |
| | Seiratherm GmbH, Herzogenaurach, DE | tempedy | The principle is based on infusion technology and combines volume management with temperature control. The patient's target temperature is regulated through a mix of warm and cold infusion solutions which are fed into the device and applied venously. Information on cooling capacity or CE mark is not yet available. | | ✓ | ✓ | ✓ | ✓ | ✓ | n/a | Console + Infusion tube system |

*The intra-aortic balloon pump*

# Shocked by the Shock t

**No need to ask who was really shocked by the Halle Shock trial, followed by the multi-centre Shock II trial. It was the cardiologists, of course – and heart surgeons – but mainly the manufacturers. Several million Euros worth of lost sales are no small matter. Ah, but, that's not the end of the story. European Hospital correspondent Holger Zorn observes the emergence from a state of shock**

**Almost exactly** a decade ago, Dr Roland Prondzinsky, then a consultant at the Martin Luther University Hospital in Halle, Germany, prospectively randomised 45 Patients with Acute Myocardial Infarction (AMI) complicated by Cardiogenic Shock (CS), who had to undergo Percutaneous Coronary Intervention (PCI) with or without an additional Intra-aortic Balloon Pump (IABP). He had no idea of the repercussions this would present. In 2010 he published his results: 'The addition of IABP to standard therapy did not result in a significant improvement in Multi-Organ Dysfunction Syndrome' and '… mechanical support was associated only with modest effects on reduction of APACHE II score as a marker of severity of disease' [*Crit Care Med. 2010; 38:152-60*].

Although he observed some haemodynamic improvements, these were not significantly better than those achieved by medication. Conclusion: 'The use and recommendation for IABP treatment in CS remain unclear.' [*Shock. 2012; 37:378-84*].

An unclear recommendation despite the fact, up to that point, that the IABP had a Class I indication in the relevant guidelines for the treatment of cardiogenic shock – a result like this had to be checked. From June 2009 to March 2012, 600 patients with CS-AMI, who were due to undergo PCI, were prospectively, multi-centrically randomised into the IABP group, or the control group, in 37 German hospitals for the Shock II trial.

The study's endpoint was 30-day survival, and here again: 'At 30 days, 119 patients in the IABP group (39.7%) and 123 patients in the control group (41.3%) had died' - no significant difference [*NEJM 2012; 367:1287-96*]. The one-year results confirmed: 'Of 595 patients completing 12-month follow-up, 155 (52%) of 299 patients in the IABP group and 152 (51%) of 296 patients in the control group had died. IABP did not reduce 12-month all-cause mortality' [*Lancet 2013; 382:1638-45*].

## The No Growth disaster

Several well publicised studies, a downgrade in the German-Austrian S3-guidelines on the treatment of CS-AMI to the lower status of a 'can' recommendation [*Dtsch Arztebl Int 2012; 109:343–51*], all this led to a slow and then increasingly faster decline of usage in these two countries (see table).

Not only the authors of the studies quoted above talked about the end of the IABP; European Hospital reported about this extensively (*EUR HOSP Vol. 22 issue 4/2012 page 20-21*).

Still, the world does not seem that impressed. From the month of the Shock II trial results publication to now, another ten studies on the IABP have been published. There are also some new, large studies.

Dr Ludhmila Abrahão Hajjar, Professor for Cardiology at the University of Sao Paulo, will study the effect of counterpulsation on 180 patients due to undergo heart surgery. Dr Nico Pijls, Professor for Cardiology at the Catherina Ziekenhuis Hospital in Eindhoven, the Netherlands, will recruit 100 patients, to find out if a potential persistent ischaemia following PCI can be alleviated with the help of an IABP-implantation. And Dr Philippe Grieshaber, heart surgeon at the University Hospitals in Giessen and Marburg, plans to prophylactically, pre-operatively fit 856 Patients with an IABP for surgical high-risk revascularisation, to see if the clinical outcome, and first and foremost the 30-day-mortality, can be further improved.

The state of shock in the community seems to have been overcome for now.

# Renal denervation moves beyond the HTN-3 disaster

**Clinicians and companies remain committed to a procedure that failed to demonstrate efficacy against a sham-control group in pivotal clinical trial, John Brosky reports**

**One year ago** the enthusiasm for treating resistant hypertension with renal denervation was festive. 'That party is over,' laughed Mano Iyer, founder and COO for ReCor Medical, one of the dozen companies offering novel devices to ablate nerves in the renal artery. 'Last year everyone was riding on the coat tails of Medtronic,' he said. 'Now the playing field has been levelled and we all have an opportunity to differentiate with what we believe is a superior technology.'

The transforming event that trashed the party came in January this year when Medtronic reported that its SYMPLICITY-HTN 3 pivotal trial of renal denervation in the United States failed to meet its primary endpoint for efficacy against a sham-control group of patients.

In March 2014, at the meeting of the American College of Cardiologists, the trial investigators revealed details that confirmed Symplicity HTN-3 was indeed the most rigorous renal denervation clinical trial conducted to date, and that the validated data did indeed show the therapy was no more effective than compliance to medications to lower blood pressure.

The news recalled for many interventional cardiologists the Black Tuesday in Barcelona in 2006 when the then-emerging practice of implanting stents for coronary revascularization failed to match the efficacy of coronary artery bypass graft surgery (CABG) in the landmark SYNTAX trial.

Despite that setback, stenting of arteries has grown to become a standard of care for revascularisation. Both clinicians and companies invested in the development of renal denervation expect that the procedure will similarly overcome the disappointment of the Symplicity trial to find its place as a therapy.

The field of renal denervation is 'too interesting and too young to be written off,' stated Felix Mahfoud MD, an interventional cardiologists at the Saarland University Hospital (Homburg, Germany) who has consulted with Medtronic, St. Jude Medical (St. Paul, Minnesota), and Recor.

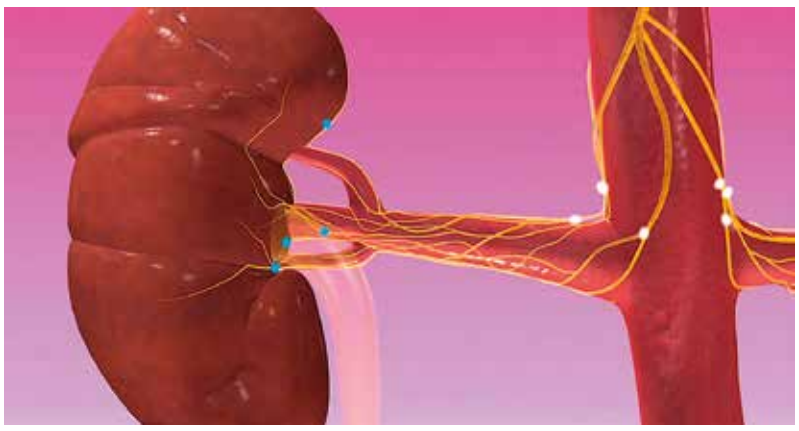
Speaking as a course chairmen for the newly formed Resistant Hypertension Course, he said in a statement at EuroPCR, 'We see the results of this trial [Symplicity-HTN 3] as neutral and after a careful assessment of this study have identified various potential procedural and methodological considerations that could partly account for the study's results.'

The General Manager for Renal Denervation (RDN) at Medtronic, Nina Goodheart stated in an email, 'As the leader in RDN Medtronic will continue to support our global HTN [hypertension] clinical program to better understand the potential of RDN in uncontrolled HTN. '

'We are continuing our analyses of Symplicity HTN-3 and are committed to better understanding the confounding factors observed in this trial. We believe there are many factors that may have contributed to the observed efficacy results in Symplicity HTN-3, including key variables that have arisen such as population differences and medication and procedural variability in Symplicity HTN-3 versus other Symplicity studies,' she stated.

St. Jude Medical is just as heavily invested in renal denervation as its rival Medtronic, and through the vice president for corporate relations, Rachel Ellingson, said that it is also 'committed to this space'.

'True innovation takes time and persistence to develop,' she said. 'The good news is that industry, academics and regulators are interested in talking about how to develop evidence that is supportive of the therapy, and whether new trial designs might help bring this therapy to patients with severe high blood pressure.'



Depicting renal denervation

The parade of trial results for a variety of new devices continues from Boston Scientific, Terumo and the Cordis unit of Johnson & Johnson. While the causes of Symplicity-HTN 3 failure to prove efficacy may be confounding, one clear result of that study, according to Mahfoud, is that all clinical trial in the field moving forward will require a control arm.

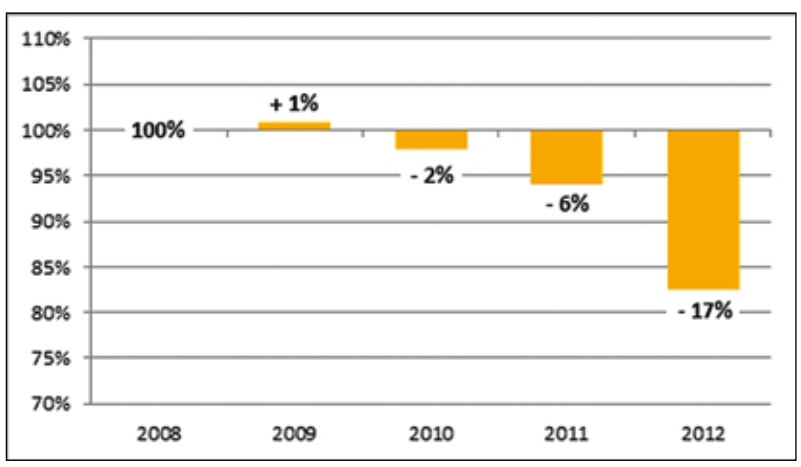
'Sham-control arms will be a real problem in Europe,' he said, declining to elaborate.

Separately, Iyer with ReCor, who is based in Amsterdam, explained. 'If you talk to European physicians they will tell you that a sham-control may be scientifically important but not clinically relevant and that practically it is very difficult,' he told European Hospital. 'They are not believers here in Europe that a sham is necessary. They will ask how they can ethically prescribe a sham procedure if there is a procedure for a patient coming in who is suffering, with no alternatives. They will tell you this patient is going to come back with a significant cardiovascular event if we don't get their blood pressure down. Meanwhile here is a technique that is proven to be safe that might help.'

Roland Schmieder MD, a nephrologist specialising in hypertension at the University of Erlangen in Germany, told European Hospital that 'Moving forward with renal denervation means two things. First we need to move forward with more robust study designs. It does not need to have sham-control, but it does need to be randomized with a real control group.'

'As for the technology, we have heard of new technologies for a more reliable delivery of the energy, such as ultrasound, or 360-degree radiofrequency. What will become important are technologies for making the procedure less operator-dependent with reproducible effects. We are not there yet.'

trials?




IABP in Germany. In 2008, used here as the base date, more than 10,000 catheters were inserted for the first time. In 2009, the year when patients were first recruited for the Shock II study, the number increased slightly – only to then decrease consistently, and then dramatically by the end of 2012. The numbers for 2013 are expected in November; experts anticipate a decline to < 5,000. (Own graphic representation, based on data obtained from the Federal Statistical Office (Destatis) and personal interviews.)

*Cardiology in smaller EU nations*

# Malta needs to nurture collaborations

**Imaging has progressed at vertiginous paces since X-rays were invented, not only as a diagnostic tool but also as an invaluable partner in the realm of non-invasive medical intervention. This progress has not only sharpened the cutting edge in many medical and surgical specialities but has also served as a very valid bridge or alternative between the two. Cardiology is but one example of this scenario, writes Moira Mizzi**

**'Nowadays one of** the hallmarks in choosing between one imaging technique and another is its capacity for higher resolution,' explains Dr Kevin Schembri, a resident specialist in cardiothoracic surgery at Mater Dei Hospital, the sole public hospital in Malta. 'At present the buck lies with high resolution CT imaging and MRI, although ultrasound is fast becoming a very valid alternative in the field.' These advances in cardiac imaging have spelt a major exponential growth in cardiology and cardiac surgery in Malta in the last quarter of a century since the first surgical and cardiological interventions (namely open heart surgery and coronary angioplasty) took off. 'Prior to that, such interventions were carried out either abroad or by visiting consultants,' Dr Schembri reminisces. 'Nowadays our cardio-thoracic centre carries out well over a thousand imaging-assisted interventions per year and some, like percutaneous coronary interventions, have substantially cut down the number of open heart surgery interventions from around 450 per year to 300.'

Dr Schembri goes on to describe another recent investment in local cardiac imaging technology, namely the FFR (Fractional Flow Reserve Measurement). 'With this technology a coronary artery stenosis visible on coronary angiography is not only quantified on anatomical criteria, or percentage stenosis, but also physiologically by measuring the drop in pressure across the narrowing,' he explains with enthusiasm.

The latest addition to the armamentarium of the local interventional cardiologist is a TAVI, or transcutaneous aortic valve implantation, a procedure carried out under X-ray imaging. With this technology the cardiologist can deliver a crimped or shrunken biological aortic valve through the common femoral artery and into the diseased native valve squashing it to the aortic wall and taking over its function.

Despite these advances, working in such a small island has its obvious limitations. 'The Health Department does not have the financial resource to invest in the very latest cardiac imaging technology and, even if it did, it would not be such a cost-effective exercise considering the size of the population and the small parallel diagnostic turnout,' Dr Schembri explains. 'The particularly minuscule population size not only limits the financial resource but also puts a boundary on the level of expertise.

'Buying the latest in cardiac imaging technology is fruitless if there is no resource and expertise to complement it,' Dr Schembri asserts. 'Unfortunately locally we have the knack of investing in "half-baked packages" where the investment in the technology is not suitably paralleled by the availability of trained personnel both to use the said technology and interpret the results,' he regretfully adds. Obviously, this not only reduces drastically the potential of the imaging technique but also stretches the limit in an already stressed resource.

Dr Schembri believes that another hurdle stemming from Malta's size, and thus limited resources, is the paucity of research centres. 'Research drives people and spurs innovation,' he asserts. 'Unfortunately, we do not invest enough in basic science research as much as we do in epidemiological research and this hinders greatly our academic growth.' He adds that our tight resource should not inhibit or limit us in any way but we need to understand that collaborations with larger, more advanced European, or indeed transatlantic, cardiology centres could go a long way in supporting us to make the best out of the wealth of ever-growing resource available in the field.

Dr Kevin Schembri, resident cardiothoracic specialist at the Hospital Mater Dei in Malta

For Malta, being part of the European Community should go beyond geographical location, financial stakeouts and political affiliations. We need to keep up with the health services in other member states because the Maltese patient does not deserve inferior care. We need to invest more in research and technology to boost primary prevention and strengthen the general practitioner service.

Finally, we need to understand our limitations and nurture collaboration with bigger European centres lest we fall into the trap of insulation defeating the idea of being part of a European family.

# Research: Seeking radiological routes to cure cardiac diseases

## Stereotactic radiotherapy for hypertension and radiosurgery for AF

Report: Cynthia E. Keen

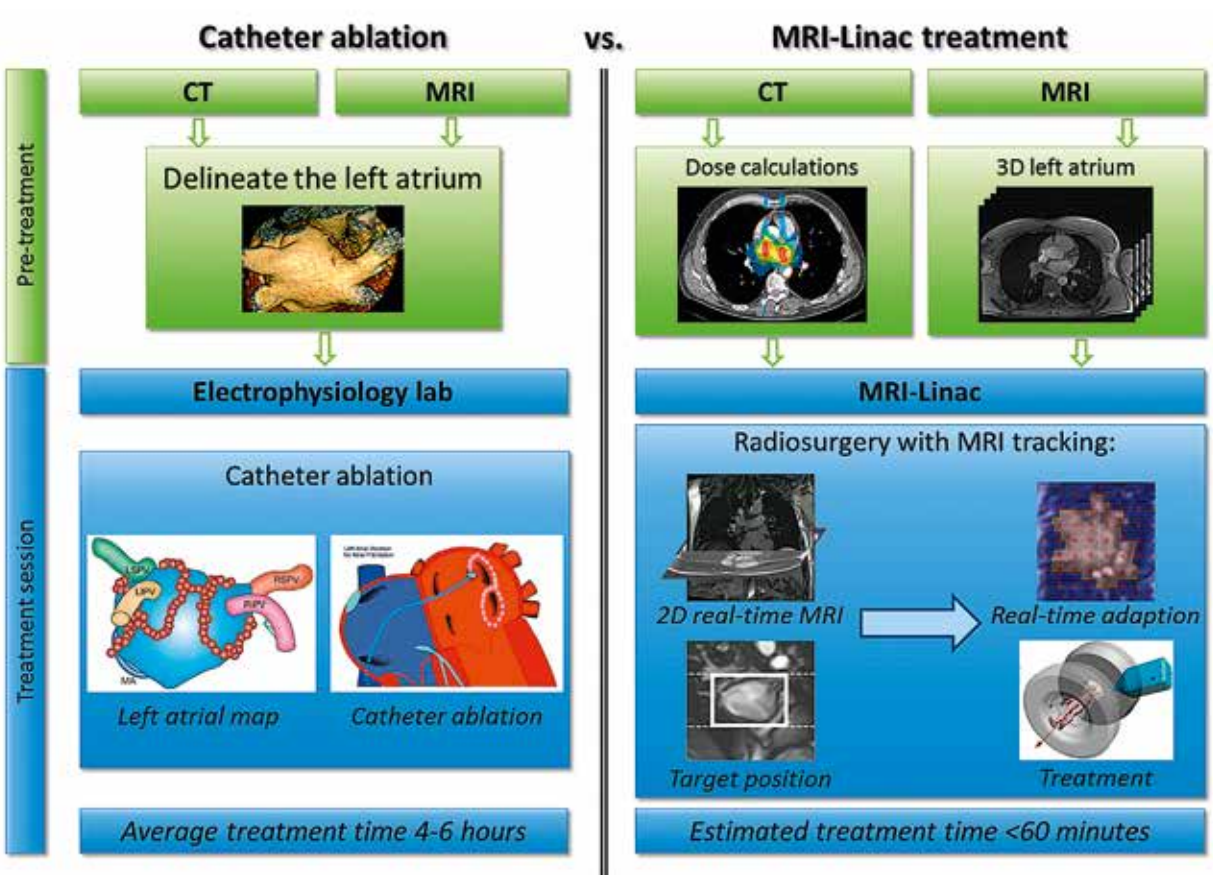
**Radiotherapy is being** proposed to treat heart diseases, specifically for hypertension and atrial fibrillation (AF). Attendees at the annual meeting of the American Association of Physics in Medicine (AAPM), held in Austin, Texas, learned this about current and on-going research.

The impact of this potential treatment could be huge. Atrial fibrillation affects more than 4.5 million Europeans and more than 2.5 million North Americans.

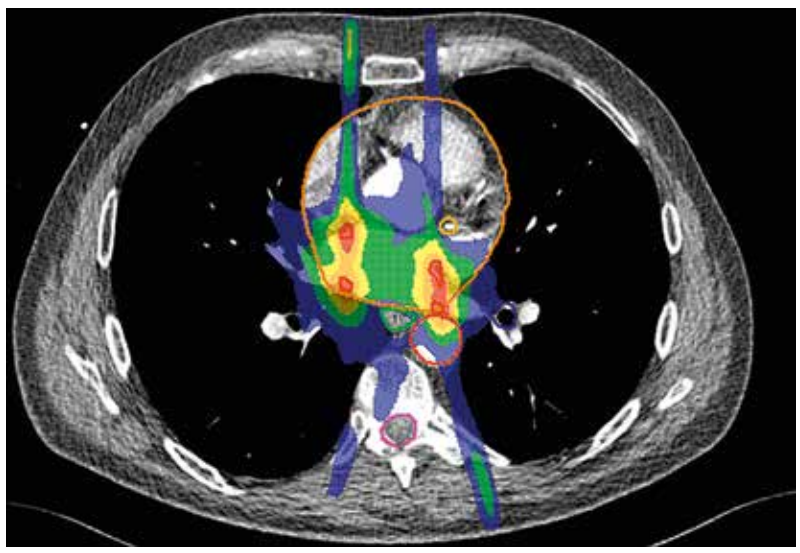
About one third of the adult population in many countries have hypertension. Uncontrolled hypertension substantially increases the risk of ischaemic stroke, ischaemic heart disease, and kidney failure. About 25% of patients do not respond to standard therapy.

### Stereotactic radiotherapy for renal sympathetic ablation

Peter G Maxim PhD, assistant professor of radiation oncology at Stanford University School of Medicine & Cancer Institute, reported that the use of stereotactic radiotherapy delivered to the renal sympathetic plexus of swine has been safe and effective in reducing hypertension. Maxim, and his colleagues at the institute, hope to have a safety study approved by fall or winter 2014 to test this treatment with a small group of very high risk patients with refractory hypertension for whom medication has not worked.




**The figure compares the current interventional treatment, catheter ablation, with the proposed MRI-Linac treatment. For catheter ablation, after the pre-treatment imaging and planning, a catheter is inserted into a vein and guided into the right atrium of the heart. The catheter then pierces the septa between the right and left atrium and is used to ablate tissue near the pulmonary vein. The procedure is invasive, requires anaesthesia and typically takes five hours.**
**For the proposed MRI-linac treatment, after the pre-treatment imaging and planning, the MRI images the heart in real-time. From the images, the target region in the left atrium is identified, and the linac treatment beam is adjusted so that the beam is continuously hitting the target region, thus reducing any damage to surrounding healthy tissue. The procedure is non-invasive, does not require anaesthesia and we estimate it could be completed in less than one hour.**



**This is a dose distribution of a patient with 11 IMRT fields and 1mm margins added to the target. (The team reports: Margins of up to 5mm were added to cover a range of potential tracking uncertainties. The dose limitations of nearly all organs at risk could be met, except for the heart dose, which was exceeded in all plans. An increase of the mean and maximum heart dose with growing margins was observed. The relatively high cardiac dose will require further investigation in terms of late effects.)**

**Professor Paul Keall PhD, director of the radiation physics laboratory at the University of Sydney, Australia**

**Peter G Maxim PhD, assistant professor of radiation oncology at Stanford University School of Medicine and Cancer Institute**

'A huge body of evidence has demonstrated that kidney-brain connection to nerve communications plays a major role in controlling hypertension. The kidneys are responsible for creating and sustaining high blood pressure. Previous studies have shown that if the renal nerves are ablated – through surgical removal or damage to them – it is potentially possible to control high blood pressure,' he said in a media teleconference. 'These were invasive procedures; radiotherapy treatment is non-invasive,' he observed.

The research team used high-resolution CT images of six hypertensive pigs to develop treatment plans for each renal artery and nerve. A single 40 Gy fraction dose of radiation was delivered bilaterally by stereotactic radiosurgery to the renal nerves using a state-of-the-art linear accelerator. The animals were observed for six months. Clinical and behavioural exams were performed, blood pressure was measured, and a urinalysis and serum laboratories were conducted. Plasma norepinephrine levels (ng/ml) were obtained at 30-day intervals.

'We are very pleased that the animals showed a 63% reduction in norepinephrine and none of the animals showed any evidence of renal dysfunction,' Maxim pointed out. 'Pathology showed evidence of moderate nerve damage, but there was no histological or immunohistochemical evidence of damage to nearby organs such as the kidneys and spinal cord. The renal artery also was not damaged.

'Because of these very successful findings, we believe the treatment will be safe and effective for people.'

### MRI-guided radiotherapy for cardiac radiosurgery

Australian and German researchers have demonstrated that it is possible to image the beating heart accurately enough to guide radiation therapy to treat AF arrhythmias. In AF, electrical signals that control the heartbeat become disorganised, making the heartbeat irregularly. The team's previous research found that targeted cardiac radiation therapy can isolate the source of the arrhythmia, but the complex respiratory and cardiac motion patterns makes radiosurgery difficult due to the risk of damaging the heart.

Professor Paul Keall PhD, director of the radiation physics laboratory at the University of Sydney, and colleagues, believed that an integrated MRI and linear accelerator could solve this difficult real-time targeting and adaptation problem. He reported on a study involving four individuals who underwent real-time cardiac MRI under free breathing. The target motion on coronal and axial cine planes was analysed using a template-matching algorithm. The team quantified target motion ranges on cardiac MRI and analysed the dosimetric benefits of margin reduction, assuming that real time MRI tracking was applied.

'Accurate image guidance for high-dose AF radiosurgery is essential since safety margins covering untracked target motion will result in unacceptable treatment plans,' he said.

'Real-time MRI guidance and beam targeting are the enabling technologies that will make AF radiosurgery feasible. Our approach combines these to see the beating heart and treat the AF, by hitting the AF while avoiding critical structures near the heart, such as the oesophagus, blood vessels, and the spinal cord.'

The advantage of being able to utilise this non-invasive treatment will be enormous. The standard treatment, catheter ablation is a five-hour long surgical procedure, requiring anaesthesia and involving fluoroscopy.

In the United States the cost is approximately $50,000. Up to 6% of patients experience side effects. By comparison, the researcher's proposed procedure will take less than one hour to perform and cost substantially less.

**EUROPEAN HOSPITAL**

EUROPEAN HOSPITAL Publisher,
Theodor-Althoff-Str. 45,
45133 Essen, Germany
Phone: +49 (0)201 87 126 850
Fax: +49 (0)201 87 126 864
E-mail: info@european-hospital.com

www.european-hospital.com

**Editor-in-Chief**: Brenda Marsh
**Art Director:** Olaf Skrober
**Managing Editor:** Chrissanthi Nikolakudi
**Editor:** Brigitte Dinkloh
**Senior Writer:** John Brosky
**Executive Director:** Daniela Zimmermann
**Founded by** Heinz-Jürgen Witzke

**Correspondents**
**Austria:** Michael Kraßnitzer, Christian Pruszinsky. **France:** Annick Chapoy, Jane MacDougall. **Germany:** Anja Behringer, Annette Bus, Bettina Döbereiner, Matthias Simon, Axel Viola, Cornelia Wels-Maug, Susanne Werner, Holger Zorn. **Great Britain:** Brenda Marsh, Mark Nicholls. **Malta:** Moira Mizzi. **Poland:** Pjotr Szoblik. **Russia:** Olga Ostrovskaya, Alla Astachova. **Spain:** Eduardo de la Sota. **Switzerland:** Dr. André Weissen. **USA:** Cynthia E. Keen, i.t. Communications, Jacquie Michels

**Subscriptions**
Janka Hoppe, European Hospital, Theodor-Althoff-Str. 45, 45133 Essen, Germany
**Subscription rate**
6 issues: 42 Euro, Single copy: 7 Euro.
Send order and cheque to:
European Hospital Subscription Dept
**Printed by:** Margreff Druck, Essen, Germany
**Publication frequency:** bi-monthly
European Hospital ISSN 0942-9085

**Representatives**
**China & Hongkong:** Gavin Hua, Sun China Media Co, Ltd, Room 802, 15th Building, BinJiang Residential Quarter, Dongyuan Road, Futian District, Shenzhen, Guangdong, China, Code: 518031
Phone: +86-0755-81 324 036
E-Mail: gh@european-hospital.com
**Germany, Austria, Switzerland:**
Ralf Mateblowski, Hintergasse 1, 55234 Hangen-Weisheim, Germany
Phone: +49 6735 912 993
E-Mail: rm@european-hospital.com
**France, Italy, Spain:** Eric Jund, 2264 Chemin de Sainte Colombe, 06140 Vence, France Phone: +33 493 58 77 43
E-Mail: ej@european-hospital.com
**GB, Scandinavia, BeNeLux:** Simon Kramer, Willem Alexander Plantsoen 25, 2991 NA Barendrecht, The Netherlands
Phone/Fax: +31 180 6200 20
E-Mail: sk@european-hospital.com
**Israel:** Hannah Wizer, International Media Dep. of El-Ron Adv. & PR Co., Ltd., 7, Leteris street, Tel-Aviv 64166, Israel
Phone: +972-3-6 955 367
E-Mail: hw@european-hospital.com
**South Korea:** CH Park, MCI, Room 103-1011, Brown Stone, 1330, Baekseok-dong, Ilsan-Ku, Goyang-si, Gyunggi-do, Korea 410-360
Phone: +82 2 730 1234
E-Mail: chp@european-hospital.com
**USA & Canada:**
Hanna Politis, Media International, 8508 Plum Creek Drive, Gaitherburg, MD 20882, USA
Tel: +1 301 869 66 10
E-Mail: hp@european-hospital.com