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CARDIOLOGY 2015

NEWS AND TECHNOLOGY UPDATES FOR CARDIAC CARE

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Diffusion tensor MRI

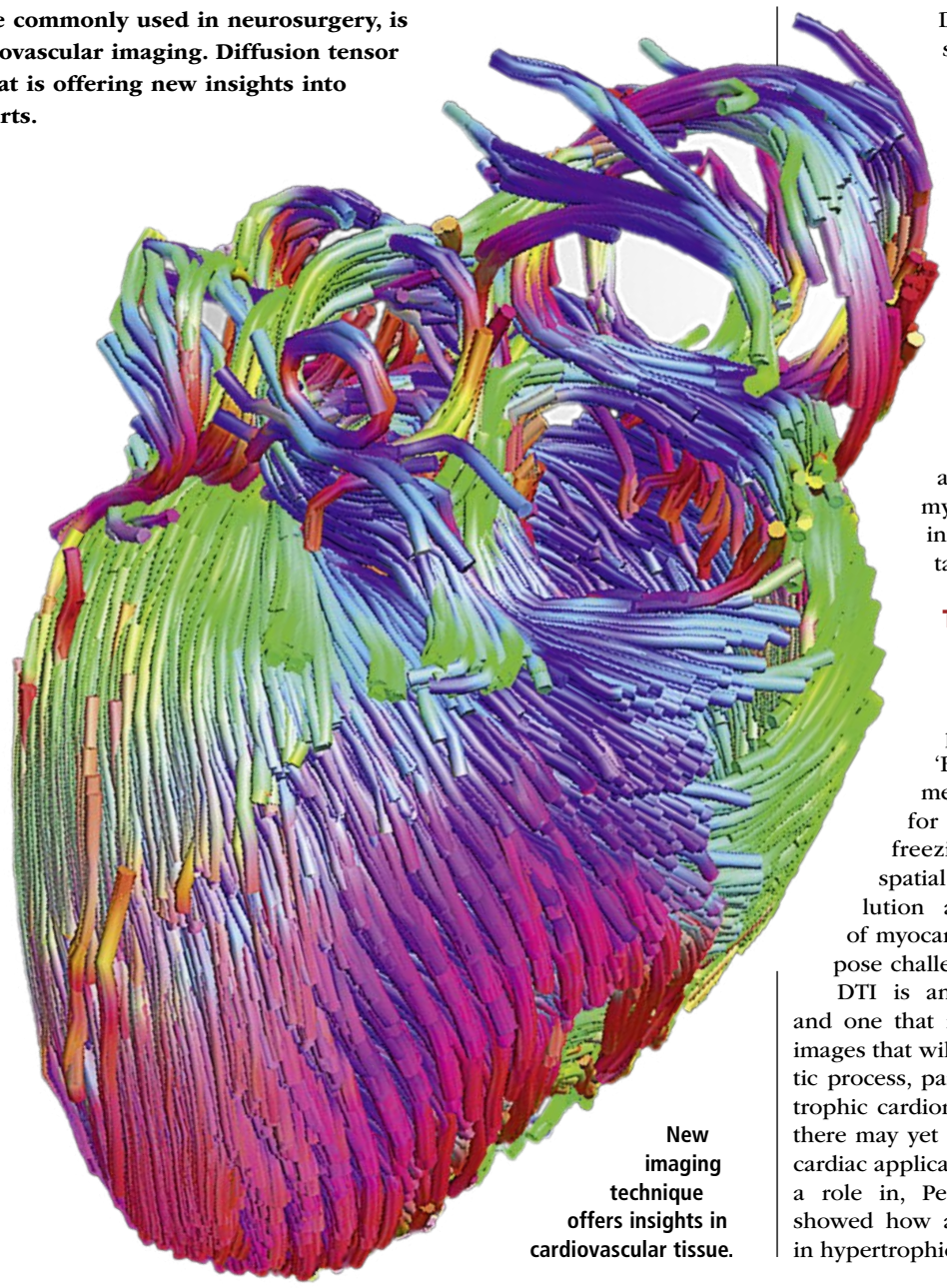
An innovative imaging technique, more commonly used in neurosurgery, is finding fresh applications within cardiovascular imaging. Diffusion tensor MRI is an evolving form of imaging that is offering new insights into tissue architecture, Mark Nicholls reports.

During a session focused on innovations in cardiovascular imaging, at the British Cardiovascular Society annual conference (Manchester in June), Professor Dudley Pennell, Director of the Cardiovascular Magnetic Resonance (CMR) Unit, and Director of Non-Invasive Cardiology at Royal Brompton and Harefield NHS Foundation Trust, outlined the background to diffusion tensor imaging (DTI). He explained how the technology yields information on water diffusion in tissue and is widely used by neurologists. It allows the mapping of the diffusion process of water molecules in biological tissues, in vivo and non-invasively, with the water molecule diffusion patterns revealing microscopic details about tissue architecture, either normal or in a diseased state.

Tractography

Through seven individual measurements taken by MRI, the DTI can map out the path of neurons and myocytes using an image processing technique called tractography.

'With brain tractography, the images are colour-coded for direction and it reveals amazing details in 3-D and is used by neurologists to map where the neurons are going,' Pennell explained. 'It also has an application for the heart and can image the organisation of myocardial cells.'



New imaging technique offers insights in cardiovascular tissue.

DTI has been around since the mid-1990s but until recently has been a slowly evolving technology.

It has taken huge steps forward with the use of accelerated imaging, advanced technology, and high field magnets (3-Tesla). Within cardiology, it has an application for cardiomyopathy, myocardial infarction and congenital heart disease.

The challenges

'There are, however, major challenges for cardiac DTI,' the professor added. 'Because of the movement, there is a need for advanced motion freezing techniques, for spatial and temporal resolution and the complexity of myocardial architecture also pose challenges.'

DTI is an evolving discipline and one that is revealing stunning images that will help in the diagnostic process, particularly with hypertrophic cardiomyopathy (HCM) and there may yet be a range of further cardiac applications that it may have a role in, Pennell suggested. He showed how abnormal contraction in hypertrophic cardiomyopathy has been shown to result from abnormally reduced rotation of blocks of myocytes, called sheetlets, which are organised contractile structures in the heart consisting of many myocytes.

Dudley Pennell is Professor of Cardiology at the National Heart and Lung Institute, Director of the National Institutes of Health Research Cardiovascular Biomedical Research Unit located at Royal Brompton Hospital, and additionally he directs the Cardiovascular Magnetic Resonance (CMR) Unit.

'With Cardiac DTI the current approaches appear promising and it is improving our understanding of normal cardiac structure,' he concluded.

During the same session, Derek Hausenloy, Professor of Cardiovascular Medicine at University College London and Duke-National University of Singapore, outlined the role of Hybrid PET/MR imaging in cardiac disease.

A technology that has only been available since 2011, he said it had the advantage in that the PET element images the biological process and MR the tissue characteristics. Hausenloy: 'Through that, we are gaining new pathophysiological insights into cardiac disease.'

Improved soft tissue definition and contrast

PET/MR is promising

PET/MR has long been studied for oncology but the technique also holds promise in cardiovascular applications, according to a panel of experts at the recent International Conference on Nuclear Cardiology and Cardiac CT (ICNCT), Mélisande Rouger reports.

A new kid on the block, PET/MR enables the acquisition of soft tissues definition and contrast unseen in PET/CT. The new hybrid combines both PET and MR strengths – excellent spatial resolution with molecular data – an alliance that has begun to tickle the interest of the cardiology community.

'What are we going to get when we put PET and MR together?' asks Bristol-based cardiologist Dr Chiara Bucciarelli-Ducci, who has used MR extensively in her work. 'Potentially a lot,' she added, 'but we still don't know because it's early days.' Cardiac imaging, she believes, is still very much a niche for PET/MR, but its potential in myocardial function makes it an attractive option. 'Although these machines were not developed for cardiac imaging, but rather oncology, their potential in myocardial infarction assessment represents an opportunity. Acute myocardial infarction is the nearer development and this is where cardiac MRI has really been worked on, to find some constraints that hopefully now, adding PET, we'll be able to understand better.' MR pictures of recent myocardial damage usually show a large scar with micro vascular structure on top. Adding PET to the formula, cardiologists can not only see a lack of metabolism in the damaged area itself, but also in surrounding segments.

'What it means is still a bit unclear, but it offers unprecedented pathophysiological opportunities to understand these complex processes,' Bucciarelli-Ducci said.

For the last few years, MR has been an exciting tool for interventional radiologists in myocardial salvage after primary percutaneous coronary intervention (PPCI) in acute ST-segment elevation myocardial infarction, to show the area at risk as end point for successful PPCI. Simply put, MR is increasingly used because it allows a reduction of miscalculation.

Stress MRI is excellent to image induced myocardial ischemia; combining it with PET could also increase diagnostic accuracy.

PET/MR also holds promise in sarcoidosis and acute myocarditis, an acute inflammatory disease of the heart. 'The potential here is really immense. The question is really how do we combine the information and how do we want to use these techniques,' she added.

A consultant cardiologist and lecturer at the UK's Bristol Heart Institute, **Dr Chiara Bucciarelli-Ducci** also co-directs the Clinical Research and Imaging Centre (CRICBristol) and leads creative medical research (CMR) at the Bristol National Institute of Health Research (NIHR) Biomedical Research Unit (BRU).

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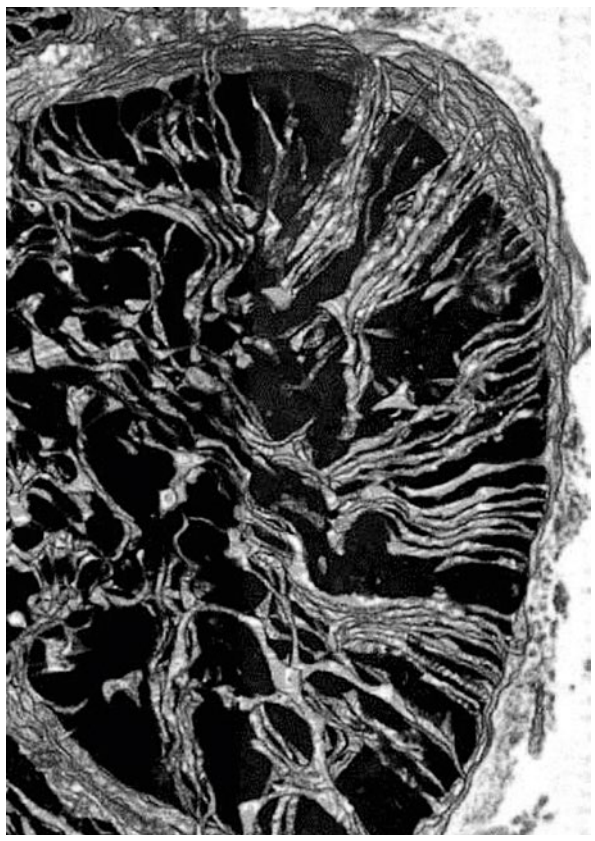
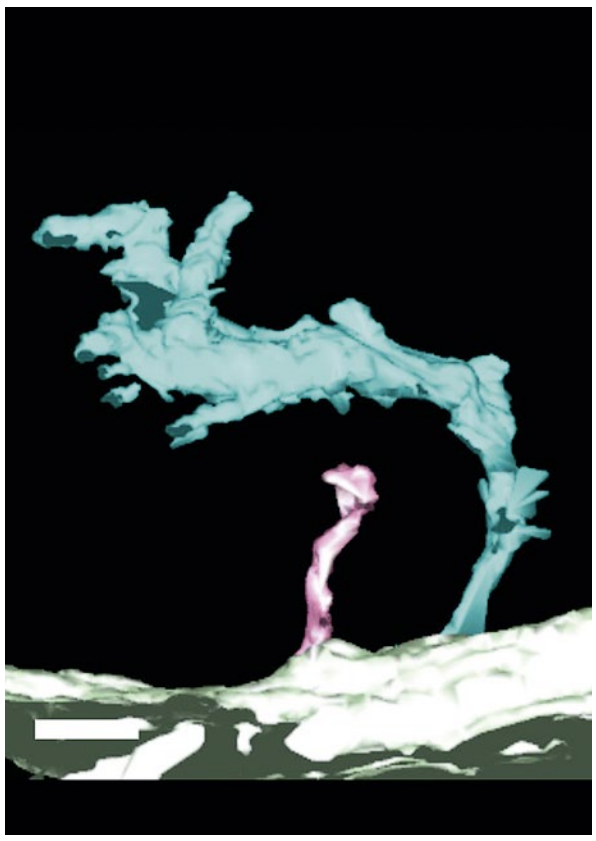
Brilliant 'bicycle spoke' images may hold clues to myocardial infarction

Advanced imaging techniques reveal T-tubules



Part of a healthy heart cell with a T-tubule 'bicycle spoke' structure

Part of a heart cell following a heart attack, where T-tubules have been lost.



A 'super-tubule' (cyan) compared with healthy T-tubule (pink)

Report: Mark Nicholls

Images revealing the 'bicycle spoke' structure of a heart cell may hold key clues to reducing damage from a heart attack.

Research conducted by Dr Ashraf Kitmitto and colleagues at the University of Manchester provides new information as to why some cells do not work properly following a heart attack. Their findings – illustrated with striking 3-D nano-images – were presented at the British Cardiovascular Society (BCS) Conference in Manchester in June in the session 'Unravelling the structural basis of cardiovascular disease through the application of advanced imaging techniques'.

Using serial block face scanning electron microscopy (SBF-SEM), Kitmitto and her team produced the 3-D images of a healthy heart cell at nanoscopic scale, which shows that part of their structure is arranged like spokes on a wheel.

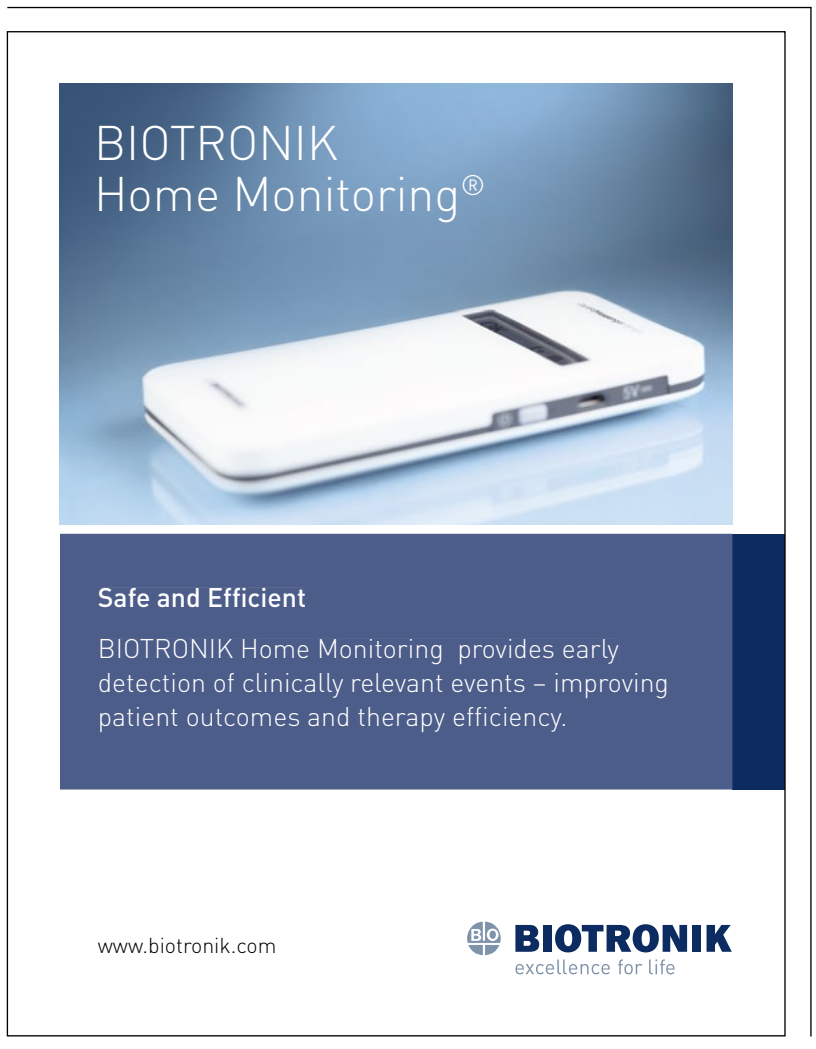
During her talk, '3-D views of myocyte remodelling in heart failure and MI', Ashraf Kitmitto discussed how the spoke-like structures, called T-tubules, carry an electrical signal from the outside the cell to the inside and are necessary for the coordinated transmission of the electrical impulse through the cell, enabling cardiac cells to contract and thus the heart to pump blood around the body.

However, following myocardial infarction, the T-tubules are lost in many areas and the electrical signal cannot be carried properly through the cells. The cardiac myocyte death triggers a healing response or remodelling with extracellular matrix, fibrous tissue deposition within the surviving myocardium.

The remaining T-tubules appear to fuse and clump together forming very large, but distorted, 'super-tubules'.

Funded by the British Heart Foundation (BHF), the research has offered what Kitmitto described as 'the most detailed images of the T-tubule network to date' – promising new insights into the structural changes that may contribute towards the development of heart failure and dangerous irregular heartbeats. The next step is to find out why this process happens following a heart attack and develop strategies to intervene to stop it from happening, for improved outcomes.

With an estimated 550,000 people in the UK living with heart failure following a heart attack, Kitmitto said: 'We've made major advances in treating people following a heart attack, so more people are surviving, but the treatments don't address changes to the structure of the heart.' For the first time, we've been



PET/MR is promising in cardiology

Continued from page 1

Researchers hope they will be able to use PET/MR in many more applications. Bucciarelli-Ducci: 'The ambition for PET/MR is that it represents a one-stop shop where you can measure precisely myocardial function, but also viability assessment with FDG, which is the gold standard on top of tissue revascularisation and weak cardiac MR.'

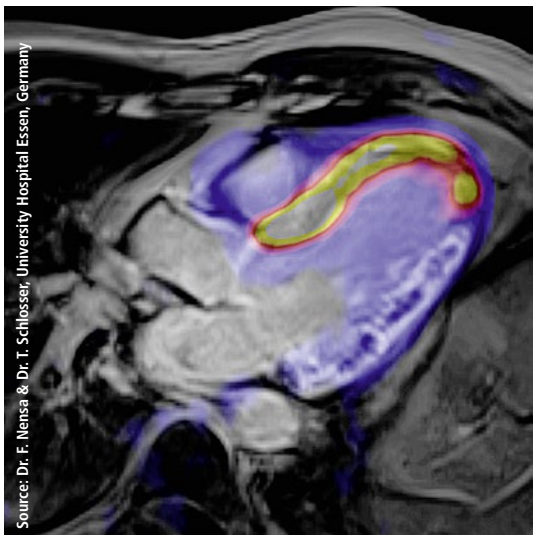
Simultaneous acquisition by PET/MR studies is another advantage, since it facilitates workflow and image registration significantly.

Choosing PET/MR over PET/CT leads to a dose reduction of 80% by leaving CT alone – a strong argument in they system's favour, especially in child imaging.

Although data on PET/CT or PET/MR for cardiac applications is almost non-existent, a paper published by Catalano et al. in Radiology in 2013, can be used as a reference. The study compared the use of the two hybrids in cancer patients and concluded that data found by PET/MR revealed additional findings not similar to PET/CT in 41% of the patients. 'It's very relevant because it did impact on clinical management in about 18% of patients, and influenced decisions on whether they should receive additional chemotherapy and surgery or not' she points out.

Despite numerous promises, a series of very real weaknesses continue to restrain development of the new hybrid. First, the price of the modality is dissuasive and means doctors will have to justify the cost. Then, PET/MR equipment is scarce, and only very few centres worldwide do cardiac PET/MR. Siemens recently published a map of its Biograph mMR (which enables to do 3-T) global distribution; Even if they were present on four continents as of January 2015, they only had about 60 machines in total.

Additionally, the level of expertise demanded by the modality is very high and remains an obstacle to its widespread use among cardiologists. 'Once you do PET/CT, it's



Siemens' Biograph mMR provides MR and PET data as one dataset – molecular MR acquisition data. Although this machine was not developed for cardiac imaging, but rather oncology, its potential in the cardiac field represents an opportunity

Dr Ashraf Kitmitto is a Reader in the Institute of Cardiovascular Sciences, University of Manchester. Having established her own research group she worked on structural studies of proteins mediating excitation-contraction coupling, leading to the determination of the first 3-D structure for the L-type voltage-gated calcium channel. This research has now developed to encompass the morphological changes that occur to the cellular structure of the heart as cardiac failure develops, using state-of-the art 3-D electron microscopy imaging methods.

able to look, in 3-D, at the nano-architecture of the cells around the damaged area of the heart and see the changes following a heart attack.

'The regular pattern of T-tubules – like spokes on a wheel – is really important because it means the whole heart cell can receive the same information and it can contract together. But, following a heart attack that regular structure is lost, so some parts of the cell will get the signal and other parts won't.

'Now, we can see what's going on; the next step is to find out why and how we can intervene to prevent heart failure development.'

BHF Associate Medical Director Dr Mike Knapton said: 'This interesting research and the beautiful images may hold key clues to reducing the permanent damage caused by a heart attack.'

Other talks in the session included clinical imaging for vulnerable plaques: VH-IVUS, CT and OCT by Professor Martin Bennett; Materials Science in Cardiovascular Research: a new perspective (Dr Sergio Bertazzo); and how SICM microscopy/FRET reveals molecular and cellular basis of heart failure (Professor Julia Gorelik).

not so much trouble. But for me, if I want to learn about PET/MR, I have a lot of work to do to understand the PET part. The opportunity is there to have a lot of data, but what can you do without the skills?' Bucciarelli-Ducci underlines.

Last, but not least, a number of issues come up with 3-T cardiac MR: artefacts can ruin pictures and patients with non MRI-conditional devices or metallic cerebral clips cannot be screened with 3-T.

Robert Gropler from St Louis, USA, who also spoke during the session, summed up the situation and outlined the perspectives for the near future. 'PET MR is slowly being introduced in the clinic and it will remain slow for a while. It's challenging but strategies are coming. We have to keep the industry involved. The most money is going to oncology, so we need to make it shift to cardiac.

'Finally, radiation exposure is not trivia. CT strategies are reducing radiation but, in the US, you can see that risk areas, such as vaccines, food, etc. are getting pushed back. I could see that for radiation exposure as well,' Gropler warned.

Stable chest pain and suspected CAD

Seeking CT's role

Coronary artery disease (CAD) is the major killer worldwide. Its early detection can save the lives of many. Computed tomography (CT) has shown tremendous results in this area, but its advantage over more invasive techniques remains to be demonstrated, especially in patients with low to moderate risk. Across Europe, a large team of investigators decided to do just that through the new DISCHARGE study. Mélisande Rouger interviewed team member Marc Dewey, Professor of Radiology at the Charité University Hospital in Berlin, about the study's aims and design.

'DISCHARGE is a large multicentre randomised trial that aims to determine whether CTA helps to reduce myocardial infarction, stroke and cardiovascular death,' explained Professor Marc Dewey, a team mem-

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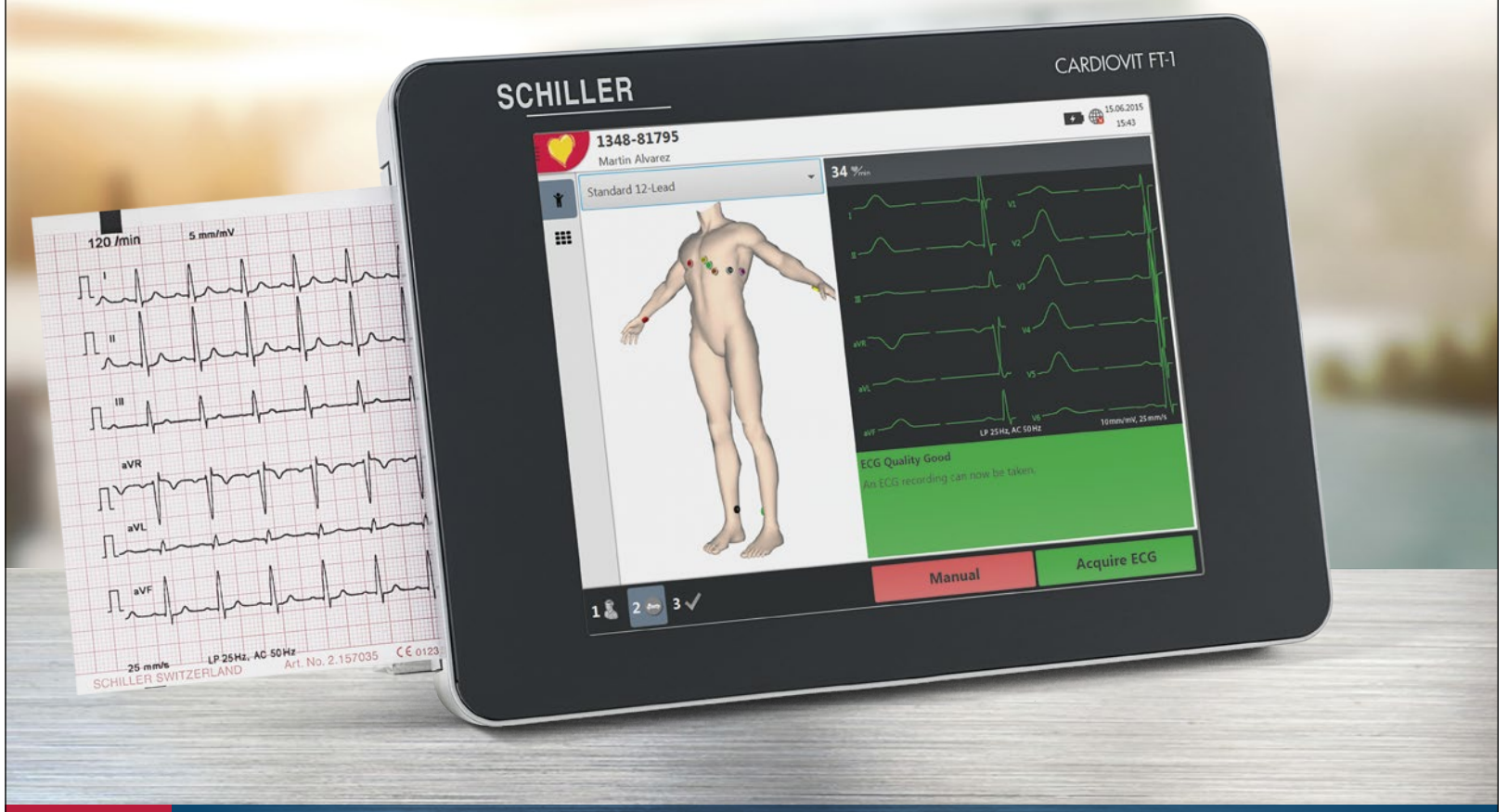

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The Art of Diagnostics

From the International Conference on

Dose reduction strategies

World-renowned cardiologists reviewed the latest trends and dose reduction strategies in cardiac CT during the International Conference on Nuclear Cardiology and Cardiac CT (ICNC) that unfolded in Madrid in May. Mélisande Rouger reports.

During this year's International Conference on Nuclear Cardiology and Cardiac CT, Dr Marcio Bittencourt, from Sao Paulo, Brazil, offered an overview of the newest available technology, namely GE Healthcare's Revolution, Siemens Force, Toshiba's Aquilion ONE ViSION, and Philips' Brilliance and IQon Spectral Detector CT scanners.

New scanners must do four things: improve image quality, acquisition speed and coverage, and reduce radiation dose, Bittencourt explained.

Temporal resolution – the time needed to acquire one image – should be <15% of the cardiac cycle to minimise motion artefacts. Thus, acquisition time, a challenge in the cardiac setting, must be as low as possible. Faster rotation is one way to achieve that, and most new scanners have indeed increased speed up to 0.25s per rotation. Other options are dual source CT and multi segment reconstruction.

To improve spatial resolution, users can either do sharper reconstruction, although some recent changes in detector technology and flying or dynamic focus spot have also improved spatial resolution.

For z-axis coverage, cardiac imaging usually required about 14 cm. Some new scanners now allow this to be performed in a single heartbeat, though this technology is not available for all vendors, Bittencourt pointed out.

New technology enables selection of the best scan mode and protocol for each individual examination, which contributes to reducing radiation dose. Besides protocols, other features, such as automated exposure control, reduced target noise and iterative reconstruction, may also lower dose significantly.

One recent technology, spectral energy imaging, has the potential to do calcium subtraction, myocardial perfusion or iodine map, and beam-hardening correction for perfusion.

However, not all these options are necessary if users are not doing top-notch research, Bittencourt believes. 'If you can't afford newer technologies, any 64 detector scanner allows adequate diagnostic image quality for most patients. Anything newer will cost more. If you ask me whether any of the new scanners better, I think they certainly have improved temporal resolution and spatial resolution, which are interesting and may allow evaluation of more complex patients. So, if you can pay for these new toys, my answer is yes, they are better. But if you ask if they are a cost effective replacement for a 64 detector scanner, from a health perspective, the answer is probably no.'

Dr Stephan Achenbach from Erlangen, Germany, focused on methods for low-dose coronary CTA. 'CT made its way into European guidelines on stable coronary disease and acute coronary syndrome, so it should really be considered in patient management,' he said.

There is tremendous potential for dose reduction. A 2007study at 50 sites across Europe compared 1,965 CTA examinations in 2,000 individuals. It showed tremendous differences in estimated radiation dose associated with CT angiography, with some sites using doses of up to 13 mSv on average and others 4.6 mSv.

Image quality, however, did not correlate to dose. 'This study from the past clearly shows that radiation dose can be lowered without sacrificing image quality, and today we

Professor Stephan Achenbach is Chairman of the Department of Cardiology at the University of Erlangen, Germany and Vice President of Global Affairs and Communication at the European Society of Cardiology (2014-2016). With major clinical interests in cardiac CT, imaging of atherosclerosis and interventional cardiology, he was president of the Society of Cardiovascular Computed Tomography between 2007 and 2009, and is currently its secretary. He is also a fellow of the European Society of Cardiology, the American College of Cardiology and the Society of Cardiovascular Computed Tomography, and a member of the European Academy of Sciences and Arts.

Dr Marcio Sommer Bittencourt is Assistant Physician at the Division of Internal Medicine, University Hospital of Sao Paulo, Brazil, where he obtained his PhD in 2014. He also gained a Masters Degree in Public Health from Harvard Medical School in 2013, and carried out a post-doctoral research fellowship in cardiovascular imaging at Brigham. His main clinical interests lie in cardiovascular disease, epidemiology, internal medicine, public health, biostatistics, medical and biomedical image processing and cardiac MRI.
He is one of the Fellow and Resident Leaders of the Society of Cardiovascular Computer Tomography SCCT and has over 100 publications to his name. Dr Bittencourt obtained a Masters in Public Health at Harvard Medical School in 2013, and gained his PhD in cardiology from Sao Paulo University in 2014.

Seeking CT's role

Continued from page 3

ber in this pan-European study. 'Procedural complications will be a secondary outcome.

'The study design was presented at the last ECR, during a late-breaking clinical trial session. The study has only just begun and is being conducted in 30 sites across Europe so far. We also plan to include large and small hospitals in the project.

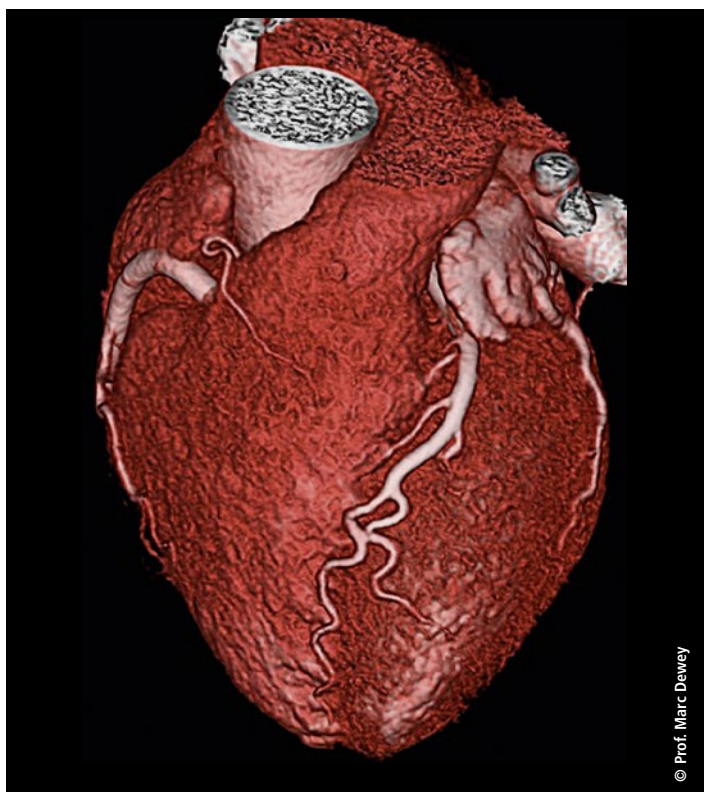
'Ultimately, DISCHARGE aims to provide the basis for new guidelines in cardiac imaging. Therefore, we are collaborating closely with clinical sites as well as non-clinical partners to optimise the impact of the study for the benefit of the different European health systems.

'This study has been granted six million euros through the 7th Framework Programme of the European Union (EC-GA 603266). It will actively recruit for two years with a maximum follow-up of four years.'

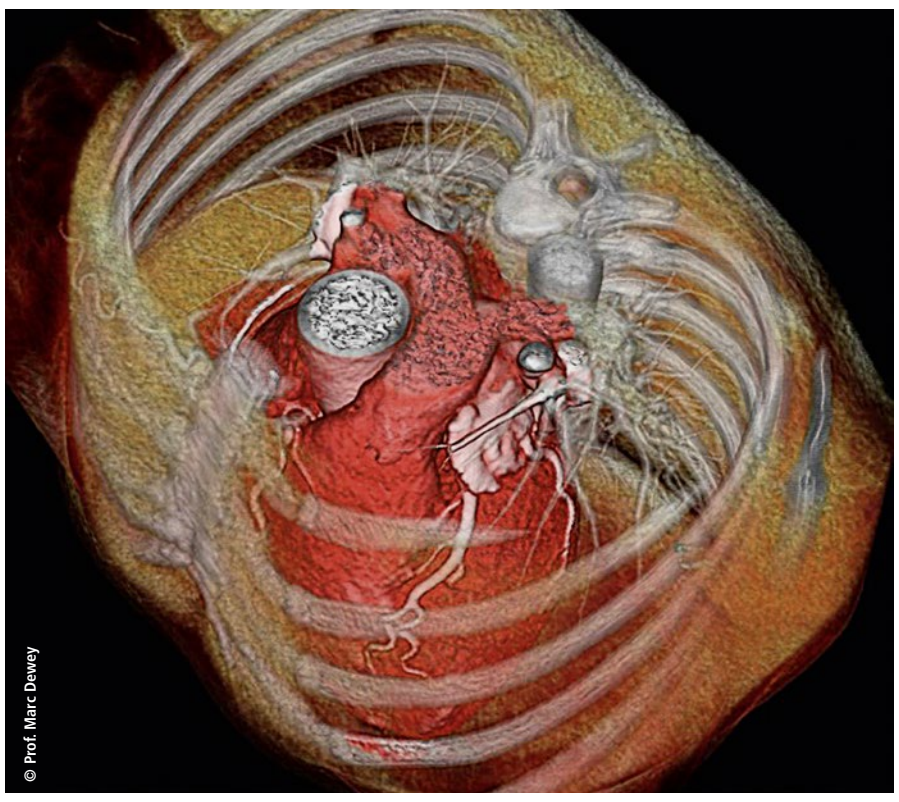
Today, where is CT placed in assessing suspected CAD?

'Currently, CT has little role and is not reimbursed for this purpose. Despite its proven high diagnostic accuracy, CT's full diagnostic potential is not being used, mainly because the comparative effectiveness of CT versus invasive coronary angiography (ICA) has not been shown in patients with stable chest pain and suspected CAD.

'In most European countries, ICA is the final reference standard to detect CAD, but it only allows minimally invasive treatment of coronary stenosis during the same procedure. However, approximately two million ICAs, done in Europe every year, do not detect CAD. It is thus the focus of our research efforts to analyse in which cases CT could replace these invasive tests.'



Cardiac CT without CAD



Cardiac CT with 3-D reconstruction of the chest

Does CT have diagnostic value in stable chest pain and suspected CAD?

'ICA is an invasive technique. As a diagnostic tool for patients with suspected CAD, especially with a low to moderate risk (10-60%), alternative tests that are non-invasive might provide a better risk/benefit ratio in favour of the patient.

'CT, because it is non-invasive, also grants potentially higher patient safety if used in appropriate clinical situations – but currently we do not know which ones.

'Early detection and improved characterisation of coronary plaques in the entire coronary artery tree is possible with CT. Certain unique high-risk plaque features have been shown to predict subsequent events and outcomes if assessed by CT. However, it's not known from a randomised trial whether such high-risk plaques should lead us to recommend intensified risk factor modification or certain medications.

'Another advantage is that CT images the tissues surrounding the heart, whilst ICA is limited to the coronary arteries. Therefore, CT has the possibility to check the lungs, oesophagus and spine, which may result in a diagnosis that explains chest pain and suggests appropriate treatment, but could be overlooked by ICA.

'In conclusion, ICA is the best way to treat known CAD; but in a situation where ruling out diagnosis of CAD is likely, CT, with its tremendously improved image quality, might prove to be the best method available.'

Other imaging modalities to rule out CAD

'We also use imaging ischemia tests, such as stress MRI, PET/CT, SPECT and stress echocardiography. These tests, while they allow the detection of CAD, are so-called functional tests and thus have a different purpose than CT.

'These perfusion-imaging tests enable a search for stress-induced ischemic myocardial areas, which play an important role in clinical decision-making in case of anatomic coronary stenosis found by CT with unclear functional relevance.'

Future promising techniques

'For all the above-mentioned non-invasive techniques (CT, MRI, PET/CT, SPECT, and echocardiography), dedicated research groups are working in Europe to further improve these diagnostic tests from a technical and clinical perspective.

'The main goal would be to develop a comprehensive imaging test that would allow accurate stenosis detection, characterisation of coronary plaques and myocardial perfusion assessment.

Due to CT's high diagnostic accuracy for stenosis detection and plaque visualisation, CT itself, which is broadly available, and more costly

s in cardiac CT

have many more options to do so,' Achenbach said.

The first strategy to limit exposure is to modify the mode of acquisition and to avoid spiral or helical scanning with continuous radiation exposure, which results in a dose in the 25-30 mSv range. 'That is really inappropriate for most patients who undergo CTA and can easily be modified because, in most cases, we want image reconstruction only in diastole. Most technology enables limitation of the full output of the X-ray tube during the diastolic segment of the cardiac cycle, thanks to ECG-correlated tube current modulation, often called ECG pulsing,' he explained.

Achenbach recommends using ECG pulsing systematically when spiral/helical acquisition is performed, as this will lead to a dose reduction of 40 to 50%.

Prospectively ECG triggered acquisition avoids spiral acquisition and combines step-wise table movements with short periods of data acquisition, typically in diastole. Therefore the dose is low, between 3 and 5 mSv.

High-pitch spiral acquisition, sometimes called Flash mode, is a combination of spiral l acquisitions and prospective ECG triggering. Thhis is only possible with dual source scanners and spends low dose, between 1.5 and 2 mSv. However, it requires low and very regular heart rates.

Lowering tube voltage also helps to reduce dose. Traditionally 120 kV were used in cardiac CT, but in many cases this can be lowered to 100 kV. Doing so will reduce the dose by 40%, even in patients who have high body mass index (BMI), according to Achenbach. '100 kV should be used in patients less than 85 to 100 kg – some say with BMI < 30 or 25, some combine the two, there are no strict guidelines,' he pointed out. By combining 100 kV tube voltage with prospectively ECG triggered axial acquisition, dose can be lowered to 2-3 mSv, and to as little as 0.9 mSv with high-pitch acquisition. 80 kVp work in very thin patients (<70 kg), and can lower dose to 0.6 mSv.

Some studies have combined all possible modes for dose reduction and performed coronary CTA with doses as low as 0.1 mSv. However, image quality can be seriously hampered in such an approach.

'Very low doses are possible, but I have to say I am not a fan for continuing this race for lower doses because we really risk sacrificing image quality and makinf misdiagnosis if we put too much weight on dose. Cardiac CT imaging is not a race to achieve the lowest possible dose; you always have to make sure you retain image quality to evaluate even those patients who have complex situations such as calcified plaque, etc.

hybrid imaging techniques such as PET/CT, are most promising to comprehensively assess CAD.'

For further information please go to:
DISCHARGE Trial
www.dischargetrial.eu

Department of Radiology
http://radiologie.charite.de

Prof. Marc Dewey MD
www.marcdewey.de

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Marc Dewey MD is the Heisenberg Professor of Radiology and Vice Chair of the Department of Radiology at Charité University Hospital, Berlin, Germany. He studied medicine at Charité and Johns Hopkins universities.
His research focused on non-invasive cardiovascular imaging, cardiac MRI and CT, radiation dose, experimental radiology, meta-analyses, cost-effectiveness and patient-centred imaging. Publications number over 150 and he has produced 65 original papers as first or last author, and given more than 70 invited lectures, including at the RSNA and ECR.

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[1] Business Strategy: Analytics Leads, Accountable Care Investment Priority, IDC Health Insights, Cynthia Burghard, March 2013
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Hypertrophic cardiomyopathy

Experts: Echocardiography is an invaluable tool

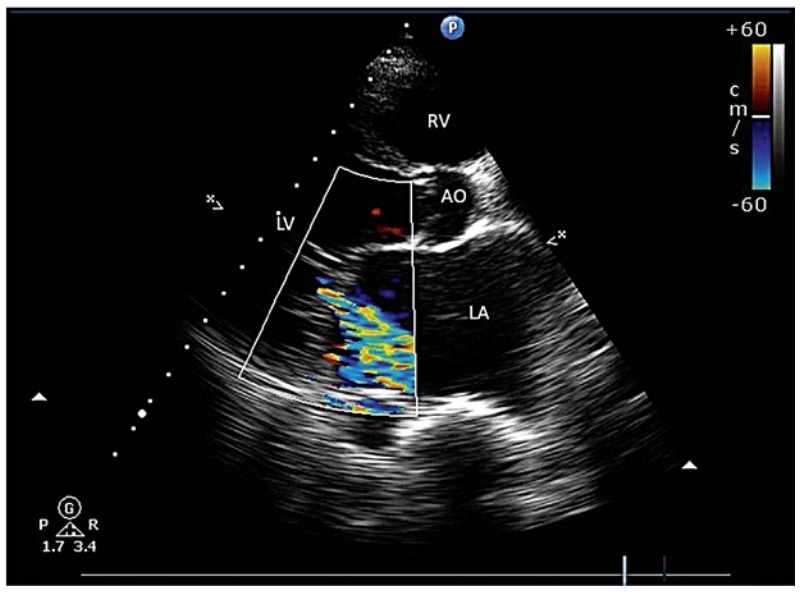
The challenges and advantages of using echocardiography as an invaluable tool in the assessment of Hypertrophic Cardiomyopathy have been highlighted at a major UK cardiology conference. A key benefit of echocardiography is its ability to accurately measure important aspects of cardiac structure and function related to hypertrophic cardiomyopathy (HCM), explained cardiac physiologist Dr Martin Stout.

Speaking at the British Cardiovascular Society Conference, held in Manchester this June, during a session that examined the use of cardiac ultrasound in diagnosis, Dr Stout looked at the advantages, challenges and factors in using echocardiography to assess HCM.

A primary disease of the myocardium, where a portion becomes abnormally thickened and fibrosed, HCM has a prevalence of 0.02-0.23% in adults and, in children, prevalence estimates are 0.3-0.5 per 1,000 – although data is more limited in this population.

Dr Stout: 'Diagnosis in adults is a wall thickness of 15mm or above in one or more myocardial segments. Echocardiography plays a central role in diagnosis but both cardiac MR and cardiac CT may also be relevant.'

Giving examples of different phenotypic patterns of HCM, Stout explained the importance of using contrast media in patients where diagnosis with echocardiography alone was difficult, particularly for a better view of the apex in potential apical HCM. 'It's very important in these cases to use contrast to aid diagnosis and there's real benefit in patients with apical HCM,' he added.



Echocardiography: Ultrasound examination of the heart

Viewing from different imaging planes

Working with current ESC 2014 guidelines on HCM, he stressed the importance of viewing from different imaging planes and the particular need to assess for right ventricle (RV) involvement and measure left atrial (LA) dimensions /volume (a particularly powerful indictor of prognosis).

With echocardiography in HCM, he pointed out, factors also to be aware of include mitral valve abnormalities and left ventricular outflow tract obstruction (LVOTO). He also added the importance of assessing LVOTO at rest, during valsalva manoeuvre (exhalation against a closed airway), and during exercise.

'The problem,' Stout warned, 'is that not everyone will have outflow tract obstruction at rest: only one third of patients with HCM will have outflow obstruction at rest, and another third will have obstruction during provocative manoeuvres.' However, he stressed that not only SAM (systolic anterior motion) might result in LVOTO in HCM. Other factors to consider are papillary muscle abnormalities and MV leaflet or apparatus abnormalities; so it remains important to rule out other causes of LVOTO.

According to Stoute, there are additional challenges in using echocardiography for HCM.

'Monitoring LV diastolic function in HCM is not always that straightforward either, it's difficult because of the phenotypic variation of hypertrophy and fibrosis. You must use all available technologies including LA volume and assessment of PA systolic pressure.'

LV systolic function in HCM can be monitored using advanced strain technology to look at subtle aspects of LV mechanics, which he said was particularly important when ejection fraction is usually normal or supranormal in these patients.

'Strain imaging can help in the clinical management of a patient and is also useful in patients with apical HCM,' he said. His Echo HCM "checklist" includes: assess presence and distribution of hypertrophy; think about use of contrast agents; assess for RV involvement; assess LV systolic function in detail; LV diastolic function; LA volume; PA systolic pressure; LVOTO, MV, and the extent of MR and papillary evaluation.

The session also heard from Paediatric Echo Cardiographer Dr Saleha Kabir, from the Evelina London Children's Hospital, who highlighted the role of echocardiography in inherited conditions, in particular left ventricular noncompaction, which, although rare, is increasingly recognised primarily through advances in imaging technology.

Dr David Oxborough, reader in cardiovascular physiology at John Moores University, in Liverpool, discussed echocardiographic assessment of ARVC, a genetically determined heart disease. He said ECG is crucial for this diagnosis and stressed the importance of multi-angle views.

Dr Martin Stout is Clinical Researcher in Cardiac Physiology at University Hospital South Manchester Cardiology Department and at the Manchester Metropolitan University School of Healthcare Science, where he performs advanced echocardiography techniques, physiologist-led exercises and dobutamine stress echo services for routine and more complex cases. He is also programme director for the modernisation of scientific careers, academic pathways in cardiac, critical care, vascular and respiratory and sleep sciences. An active member of the British Society of Echocardiography Education and Research he also takes part in Audit committees and is a regular presenter at national and international conferences.

The British Cardiovascular Society Conference

Music reaches the heart

British Cardiovascular Society

Report: Mark Nicholls

Innovative presentations, groundbreaking science and inspirational lectures underlined the diversity of sessions at the British Cardiovascular Society 2015 conference held in Manchester this June.

Professor Cliff Garratt, the conference programme committee chair, pointed to an evolving programme as key in the event's success. 'From my point of view it has been very exciting and energising to see so many people in the cardiovascular community involved in various ways in the meeting.'

Renowned scientist and TV personality Professor Robert Winston set the tone during the opening ceremony, with his presentation 'Where are we going with molecular medicine?'

With the conference theme "Hearts to Genes" a number of sessions focused on new genetic tests for cardiac disease and how these are being applied.

Among research presented was the discovery of a faulty gene that can cause fatal abnormal heart rhythms that are brought on by exercise, while another session suggested that fat surrounding blood vessels may actually help fight heart disease to reduce the risk of a cardiac attack.

The conference also offered unusual sessions, notably one by Professor Peter Sleight, from the University of Oxford, on music and the cardiovascular system, highlighting the therapeutic potential of music on the heart rate, blood pressure and wider well-being. This session attracted widespread national media interest in the UK.

Cliff Garratt is Professor of Cardiology at the Institute of Cardiovascular Sciences, Professor of Cardiology at Manchester University and Hon Consultant Cardiologist at Central Manchester University Foundation Trust. His research and clinical interests focus on the mechanisms and management of atrial fibrillation and familial sudden cardiac death syndromes. He is co-chair of the Heart Rhythm UK Working group on Clinical Management of Familial Sudden Death syndromes and Vice-President (Education and Research) of the British Cardiovascular Society

Professor Garratt, who is also BCS vice president (education and research), said the increasing involvement of the British Heart Foundation (BHF) in the meeting was pivotal in its success and development: 'The BHF is a key supporter of the meeting and had a number of sessions devoted to research that it funds,' he pointed out.

This included a highlight session of hypertrophic cardiomyopathy, which focused on research from a single clinical research department, showing how it works in terms of vision and scope. 'For that reason we were keen that the cardiology trainees who attend the meeting went along because soon they will be looking to see whether they are interested in cardiovascular research as a career, or part of their career, and the session gave them an insight into what might be involved," Garratt added.

The UK Genetic Testing Network (UKGTN) was involved in a session on the new genetic tests for cardiovascular disease that helps cardiologists to treat inherited conditions more effectively while the Strickland Goodall Lecture, topic "wellness and its causes", was given by Sir Harry Burns, professor of global public health at the University of Strathclyde and former Chief Medical Officer for Scotland.

Other highlight lectures covered issues such as the transplant cycle, the medico-legal minefield. There were also hands-on interactive training, popular hot topic sessions, a strong focus on cardiac imaging and exhibitors.

One of the more popular sessions, said Professor Garratt, was the 2015 hypertension update for cardiologists, which drew a large audience with discussions outlining why cardiologists should be interested in hypertension.

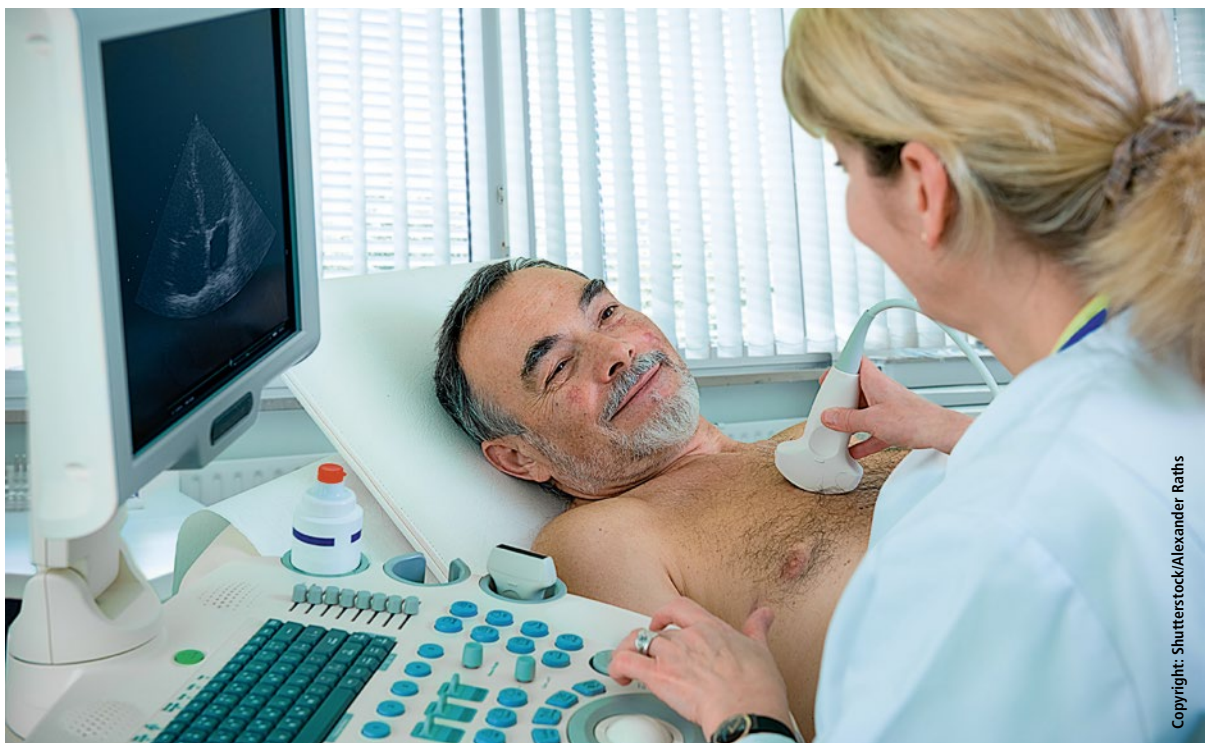
'The aim of the British Cardiovascular Society Conference is to deliver the best basic and clinical science sessions in such a way that is relevant to everyone,' Garratte concluded. 'We think we have achieved it, but will continue to build on that for 2016*.'

*For the diary: 6-8 June 2016
BCS conference. Manchester, UK

When should this procedure be performed?

Transthoracic echocardiography

The role transthoracic echocardiography plays in a number of common clinical scenarios was discussed by leading cardiac imaging experts at this year's British Cardiovascular Society Conference, Mark Nicholls reports.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Posing the question of when transthoracic echocardiography should be used, four senior figures in cardiac imagery examined its value in atrial fibrillation, chemotherapy, hypertension and stroke.

Speaking in this session, Dr Dipak Kotecha, a clinician scientist in cardiovascular medicine at the University of Birmingham and consultant cardiologist specialising in cardiac imaging, said transthoracic echocardiography had a significant role to play in atrial fibrillation (AF). 'AF,' he said, 'is becoming more prevalent and echo is important and essential in the patient management pathway. Incidence is expected to double in the next 20 years and by 2030 there will be 15-20 million people in Europe with AF. 'We have to do echo in AF for ejection fraction but it is important for choosing what rhythm control drug you may use or whether it's safe to use rhythm control in the first place.

'Echo should be considered for all AF patients, as we are looking for LV function, risk of stroke, safety of rhythm control drugs and interventional support.'

Within hypertension Professor Jamil Mayet – who heads the Surgery, Cardiovascular and Cancer clinical, educational and research programmes at Imperial College Healthcare NHS Trust in London – outlined how transthoracic echocardiography can be used to try to support patients, to decide which ones receive treatment and for risk stratification.

He explained that it can be used to assess whether there is left ventricular hypertrophy (LVH), diastolic dysfunction, LV systolic dysfunction, aortic valve issues or to assess myocardial ischemia.

Concluding that transthoracic echocardiography has a role to play in hypertension, he said: 'With patients who have stage one hypertension, we need to decide whether to treat the risk factors, lifestyle, or with drugs, and we can use echo if we are going to change the management of patients.

'Patients who will benefit from referral for routine echocardiograph are those with borderline blood pressure, where LVH may have an influence on the decision to treat; possibility of white coat hypertension; risk stratification in patients with multiple risk factors or routine reasons for echo, such as shortness of breath.'

Dr Leonard Shapiro, consultant structural interventionist at Papworth Hospital, Cambridge, suggested that the use of transthoracic echocardiography was not critical in all cases of stroke, but had value if it made a contribution to the management of patients.

Dr Thomas Mathew, consultant cardiologist at Nottingham University Hospitals NHS Trust discussed the role of transthoracic echocardiography in patients undergoing chemotherapy in the context of cardio-toxicity. With patients suffering cellular destruction, biopsy changes, cumulative dose-related effects and permanent damage as a result of chemotherapy, echocardiography had a role in their assessment.

'We should use the best form of echocardiography available and, on the evidence it is 3-DE as 2-DE fails to detect small changes in contractility. If 2-DE has to be used, it should be with GLS or Troponin, which is the best biomarker in this context.'

Mathew is concerned that all heart failure trials have excluded patients with cancer and there are no proper studies in this evaluation group. 'Using echocardiography is important,' he underlined. 'The main purpose is to decide whether to continue or stop chemotherapy because of the risk.

Dr Dipak Kotecha MD is a clinician/scientist in cardiovascular medicine at the University of Birmingham and a Consultant Cardiologist at Queen Elizabeth Hospital, Birmingham, specialising in cardiac imaging. An Honorary Research Fellow at the Royal Brompton Hospital, London, and the Monash University Centre of Cardiovascular Research & Education, Melbourne, he is a Task Force member for the European Society of Cardiology Guidelines on Atrial Fibrillation, and is currently writing the next set of practice guidelines that will be published in 2016. His main research interests are heart failure and atrial fibrillation.

Dr Thomas Mathew is the clinical lead for cardiac imaging at Nottingham University Hospitals and specialises in echocardiography, cardiovascular magnetic resonance imaging and nuclear cardiology. He is also the training programme director for East Midlands North Deanery and a member of the BCS training committee. An elected council member of the British Society of Echocardiography and a member of the BSE educational committee, he is also an editorial board member of the British Journal of Echocardiography. With more than fifteen years' experience in cardiovascular imaging, his interests include non-invasive imaging of ischaemic heart disease, valve assessments and cardiomyopathies.

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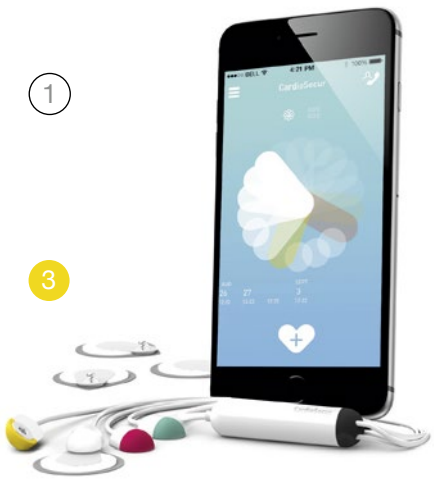

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Test predicts myocardial infarction outcome

Researchers have identified a new test that can be used to predict the likelihood of a patient developing heart failure, or even dying following a heart attack, Mark Nichols reports.

Known as the index of microvascular resistance – or IMR – a new test to predict myocardial infarction outcome uses a pressure-sensitive and temperature-sensitive wire that can be used to accurately work out the extent of injury in a blood vessel supplying blood to the heart.

Findings from a study from the University of Glasgow and funded by the British Heart Foundation (BHF) were presented at the British Cardiovascular Society (BCS) Conference, held in Manchester this June. The researchers showed that a wire inserted into the coronary artery, after someone has a heart attack, can predict if they will go on to develop heart failure.

Professor Colin Berry, lead researcher and cardiologist from the University of Glasgow and Golden Jubilee National Hospital, said: 'Heart attacks lead to heart failure, which is a big problem in the UK, and has a huge impact not only on the individual, but on the families and carers of those suffering – affecting whole communities.

'Thanks in large part to the work of the British Heart Foundation, 70% of people who have a heart attack now survive, but this means we now see an increased number of people surviving but left with damaged hearts and heart failure.

'We want to improve the outlook for people after they have a heart attack and develop new treatments to limit heart damage, reducing the burden of heart failure.'

Around 175,000 heart attacks occur in the UK each year; survivors could find the heart has been damaged and could lead to heart failure (HF). As is known, early treatment after a heart attack can reduce the chance of HF.

After a suspected myocardial infarction a patient is routinely given a coronary angiogram to identify any narrowed blood vessels – but although this can identify narrowed vessels, it cannot show if, or how much, cardiac blood vessel damage has occurred.

The Glasgow researchers now say the new wire technique can be used to work out the level of arterial damage, enabling doctors to quickly identify patients at a high risk of HF after their heart attack, based on damage to the arteries.

Patients were enrolled in this new research at the Golden Jubilee National Hospital in Glasgow. All will have life-long follow-up to check whether the IMR result predicts survival in the long term.

Professor Colin Berry is Chair of Cardiology and Imaging in the University of Glasgow and academic lead in cardiology and consultant cardiologist at the Golden Jubilee National Hospital and Western Infirmary, Glasgow. With specialist interests lie in interventional cardiology and imaging, and research focus on injury and repair pathways in coronary heart disease, Berry is a committee member of the British Cardiovascular Society Academic & Research Committee, the British Society of Cardiovascular Research and the British Society of Cardiovascular Magnetic Resonance. He is also a Fellow of the Royal College of Physicians and Surgeons of Glasgow, the Royal College of Physicians of Edinburgh and the American College of Cardiology

Cardiac exploration gains tool to access hidden areas

New mobile ECG gives 360-degree view

The conventional 12-lead ECG has certainly proved its worth in displaying rhythm disorders or ischemia. Nevertheless, as the display possibilities of a 12-lead ECG are limited to only about 110 degrees of the heart, an exact location of a cardiac event often cannot be determined.

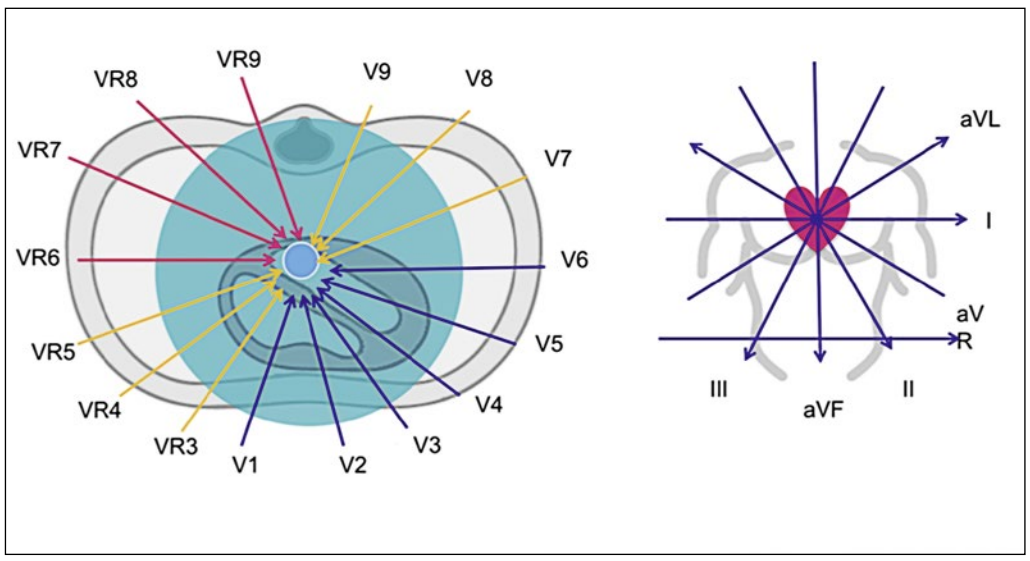
Personal MedSystems has produced a brand new combination of smartphone, or tablet PC, and ECG technology to reveal a significantly greater area of the heart. This is the next generation of ECG devices. A broader display is gained via ten supplementary leads, calculated for a 360-degree view. Combined with the free CardioSecur pro app – and using only four electrodes – the mobile 22-lead ECG shows V7-V9 as well as VR3-VR9, in addition to all 12 standard leads. Thus it allows diagnosis of the left and right lateral as well as posterior cardiac wall.

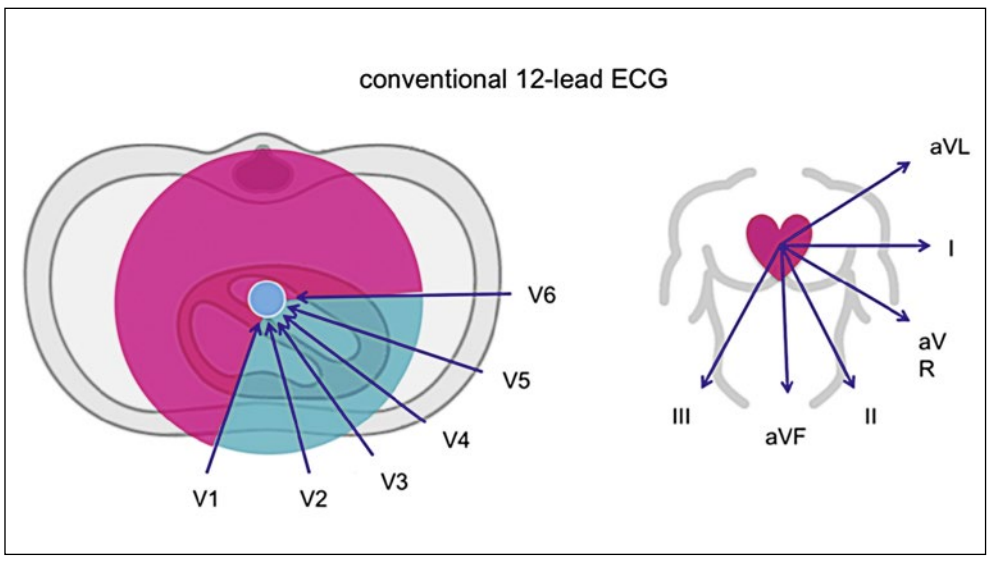
CardioSecur pro also provides unrivalled communication and mobility options, the manufacturer points out.

Faster precise diagnosis

Distinguished in the Best Medical App contest at MEDICA 2014, CardioSecur pro ECG technology is a reduced electrodes system based on the EASI standard first developed in the 1960s and described by Dower in the 1980s. Numerous publications scientifically acknowledge that EASI is a highly precise alternative to conventional ECG systems, the maker reports. 'The outstanding quality and accuracy of CardioSecur pro has been validated in numerous clinical studies against conventional 12-lead ECG systems with 10 electrodes, and evidences a 99% plus match regarding specificity on the heart's activity.

'Using only the four electrodes mitigates artefacts to a bare minimum ensuring maximum signal quality and exceptionally stable lead depiction. As the four electrodes are placed on very marked positions of the thorax lead misplacement, often consequential to highly diverse anatomies, is eradicated.' The originality of the professional mobile ECG system lies in its mobility and simple communication system, the firm adds. 'Due to its small size and light weight (50 grams), it can be taken anywhere easily, without taking up much space. Time saving is significant due to swift electrode application and intuitive ECG report export options in PDF format via email, iMessage or AirPrint. ECG reports can be easily e-mailed to fellow professionals or attached to the patient's electronic records, serving the increased need of efficiency.'





ECG readings with CardioSecur pro do not take up much space on a mobile device, as 10,000 minutes of ECG can be recorded per 1GB. Optionally, Personal MedSystems offers an automatic interpretation.

Details: www.mobile-ecg.com
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Ultrasound is at the heart of Spanish strategy

Chest pain units

Imaging modality complements a stress test in diagnosing the aetiology of chest pain, according to an expert speaking at the International Conference on Nuclear Cardiology and Cardiac CT (ICNC) held this May in Madrid.

Report: Mélisande Rouger

Chest Pain Units (CPUs) have spread through Europe, and Spain is no exception. Almost every large hospital offers this service to rule out acute coronary syndrome and diagnose unspecific chest pain, according to Professor Ivan Nuñez, a cardiologist at the San Carlos Hospital in Madrid and Chairperson of the Ischemic Cardiopathy and Acute Cardiovascular Care Section of the Spanish Society of Cardiology.

'CPUs can either be physical or virtual, i.e. work with dedicated personnel or on-call physicians – the latter being the most common scenario. Services offered within the units are heterogeneous and depend mainly on the hospital and region,' Nuñez explained. A stress test, highly available and reproducible, remains the most widely used examination in Spain's CPU setting.

When the aetiology of chest pain is unclear and the patient doesn't come for cardiac trauma, ultrasound (US) can be a powerful ally, according to Daniel Rodriguez-Muñoz, a cardiologist at the Hospital Ramon y Cajal in Madrid, and a speaker at the International Conference on Nuclear Cardiology and Cardiac CT (ICNC).

'Our main strategies are CT; nuclear cardiology following either exercise test or stress test with drugs; and exercise or stress dobutamine test using alterations in wall motion with echo detection,' he continued. 'In general, we choose echo when we have to use drug-induced stress. When the patient is obese, or a heavy smoker, the acoustic window may be bad and alter image quality, so you would rather use nuclear tests or CT".

Do we need to run?

In his presentation Rodriguez-Muñoz tried to answer the main questions a cardiologist faces in the CPU setting, the first and foremost being: 'Do we need to run?'

Patients in shock, or presenting with myocardial infarction, or pulmonary embolism, are all situations in which physicians must act immediately: 'We need to run whenever we believe that clinical symptoms and the ECG are suggestive of acute coronary syndrome.'

Echo will help to show whether the patient is suffering from hypovolemic, cardiogenic or septic shock. Rodriguez-Muñoz recommends using echo when the suspicion of pulmonary embolism is high and the patient presents with shock or hypotension, or when CT can't be performed.

Echo will also work for distinguishing cardiac vs. non-cardiac aetiology of dyspnoea when clinical and lab clues are ambiguous, and for guiding therapeutic option in patients with intermediate risk.

The next step is to determine whether the patient has angina or acute coronary syndrome, or not, by focusing on the negative predictive value of echo, i.e. by looking at regional wall motion abnormalities, depressed LV function, and other data. When the symptoms are atypical, a common situation in this setting, echo will also help to confirm or take decisions about where to refer the patient next. 'We rely on echo to make the final call. In on-call shifts, we see many patients with chest pain that is non suggestive of acute coronary syndrome based on the symptoms alone. Echo helps us to discharge patients when we have doubts – for example when the patient is a 75 year-old hypertensive, diabetic and obese man, so the likelihood for coronary disease is high, but the symptoms are atypical and the ECG is normal.'

An increasing number of emergency physicians use US to assess patients in the emergency department, especially in small hospitals that may not have on-call cardiologists. Ramon y Cajal is one of Madrid's largest hospitals, with 1,000 beds, including 50 in cardiology and 14 in the acute coronary unit. The CPU has an average two patients per on-call shift, amounting to 700 to 800 patients per year, Rodriguez-Muñoz estimates.

'The number of patients referred for additional cardiac examination from the CPU is not very high. When it's clear that it's acute coronary syndrome, patients go directly to the cath lab. Patients presenting with heart failure or other associated clinical problems that require further treatment, go directly to the cardiology ward – and, when there is highly suggestive clinical evidence that it's not acute coronary syndrome, patients will undergo other tests in the emergency department.'

Spanish are unique

At the ICNC the panel concluded that most CPU strategies of detection of ischemia or coronary artery disease eventually include patients with very low probability of having acute coronary syndrome; around 95% of the tests are usually negative.

Spanish CPU organisation is unique. Spain has not one but several public healthcare systems managed by the comunidades autonomas, or regions. Protocols are not always the same and they may impact on patient care differently.

'Each region's network, resources and mortality rates are different. Studies on infarction showed that the mortality rate in Valencia was higher than in Madrid or Barcelona. This was relayed in the media and pushed the national government to issue measures to improve infarction prognosis. However, apart from that, the national Health Ministry has very little power,' Nuñez pointed out.

'There is a very different prevalence of coronary artery disease between Japan and the USA, so it makes sense to have different approaches there; but it doesn't seem to make much sense to have different approaches in Andalusia, Madrid or Catalonia. It's really an administrative and political issue,' Muñoz believes.

However, Spanish hospitals tend to follow the European recommendations, which smoothes out differences, experts suggested.

In 2009 **Daniel Rodriguez-Muñoz** qualified in medicine at the University of Málaga and later (2015) completed his residency at the Department of Cardiology, Ramón y Cajal University Hospital, in Madrid. Now a medical doctor at the Unit of Electrophysiology and Arrhythmias, at the same department, he is completing his work towards a Masters degree in medical education at the University of Barcelona and PhD on Intra-cardiac Flow Parameters to guide Atrio-Ventricular Delay Optimisation in Resynchronisation Therapy at the University of Alcalá de Henares, Madrid. With his experience in peer-education, formal/non-formal training, and design of training programmes, Rodriguez-Muñoz's main interests are the design and development of projects and publications, and medical education.

An extra asset in the diagnostic toolkit

New cardiac genetic testing panels

Cliff Garratt is Professor of Cardiology at the Institute of Cardiovascular Sciences, Professor of Cardiology at Manchester University and Hon Consultant Cardiologist at Central Manchester University Foundation Trust. (See profile on page 6)

Report: Mark Nicholls

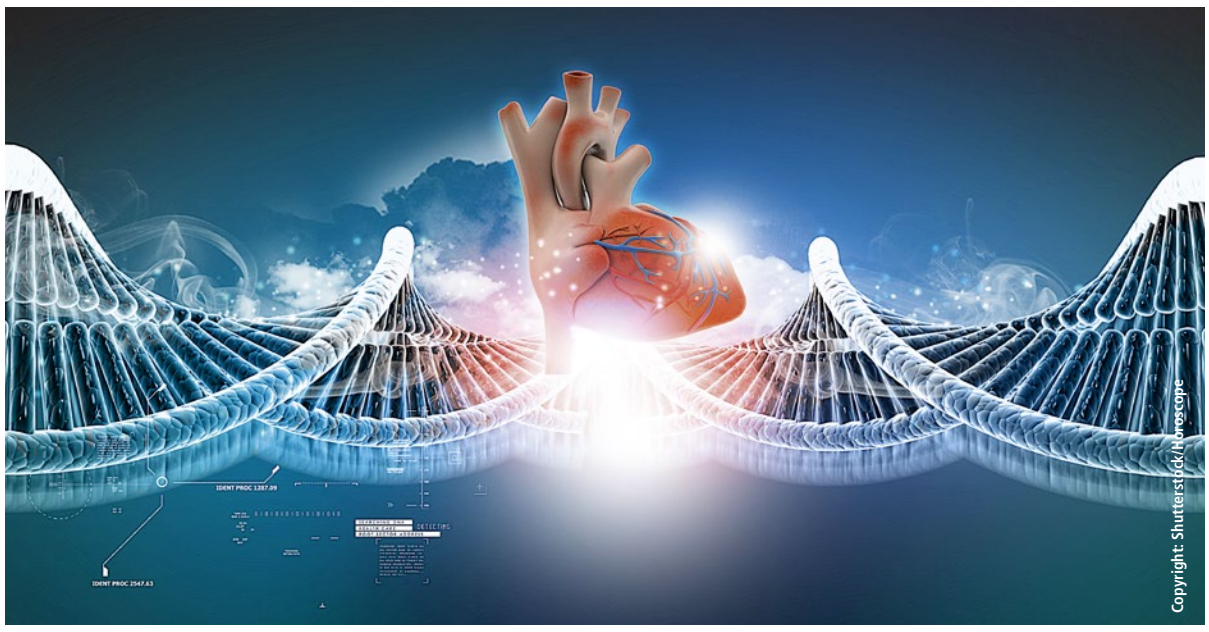
As new cardiac genetic testing panels become available, cardiologists have been warned not to lose sight of the importance of comprehensive clinical evaluation. While genetic testing is helping to identify more people at risk of inherited conditions, experts stress they are only part of the diagnostic toolkit.

This was outlined in a session entitled 'The new cardiac genetic testing panels: implications for the clinical cardiologist' held during the British Cardiovascular Society Conference in Manchester this June.

With the emergence of new genetic tests for cardiac disease, Professor Cliff Garratt raised issues 'the cardiologist needs to know' in making the modern diagnosis.

Sanger Sequencing remains the standard to confirm a single genetic variant but new tests – next generation sequencing – which can be applied to a large number of genes, are now facilitating more testing, more cheaply and in the same timescale with panels of genes.

Garratt, who is Professor of Cardiology at the Institute of Cardiovascular Sciences, Professor of Cardiology at Manchester University and Hon Consultant Cardiologist at Central Manchester University Foundation Trust, explained: 'We can have them highly targeted at 5-15 genes for LQT, for example, or a less targeted panel for 20 genes, though the disadvantage of the panel approach is that you have the problem of background genetic noise.'



Advances in genetic and genomic technology are enabling many more patients with a rare disease to benefit from genetic tests, either to establish or confirm a diagnosis; or assess the genetic status of other family members and gene panel tests are now making it possible to test simultaneously all the genes known to be associated with a condition.

Despite having the benefits of genetic testing, Garratt issued a clear warning that, whilst genetic testing is proving valuable, it is not an alternative to making a clinical diagnosis. 'It will not solve your clinical problems but will help management of patients who you have a proper diagnosis for,' he said.

During the same session Dr Shehla Mohammed outlined the work of the UKGTN (United Kingdom Gene Testing Network) in the evaluation process for genetic tests.

The role of UKGN is strategic; it involves healthcare commissioning and evaluating new genetic tests for clinical utility and validity with screening for 698 disorders, 872 genes and 46 panel tests. 'It's about promoting equity of access of genetic tests for individuals who have, or are, at risk of genetic disorders,' Mohammed explained.

UKGTN works with 30 member laboratories across the UK, many affiliated to regional genetic centres and some linked with specialist services and follows the ACCE model process for evaluating genetic tests of: Analytic Validity; Clinical Validity; Clinical Utility; and Legal and Ethical and Social implications. 'The reasons for doing genetic testing is for diagnosis, treatment, prognosis and management, pre-symptomatic diagnostic testing and genetic risk assessment,' Mohammed added. 'The UKGTN promotes high quality, equitable and appropriately identified genetic tests.' It has the capability to deliver effective cascade testing in inherited cardiac disorders.

Dr Kay Metcalfe, NHS Consultant Clinical Geneticist at St Mary's Hospital Manchester, discussed panel testing for Sudden Cardiac Death SCD syndromes.

Underlining Garratt's point, she added: 'Family screening helps identify those at risk, but the challenges of the exome and genome sequencing approach are the large amount of data generated. Genetic testing is probabilistic and forms part of a comprehensive clinical evaluation.'

Dr Paul Clift, from Queen Elizabeth Hospital, Birmingham, spoke about genetic testing in the context of Marfan syndrome and other familial thoracic aortic aneurysm syndromes but stressed the importance of physical and clinical assessment in such conditions in association with genetic testing.

According to Clift, Marfan remains a clinical diagnosis but fibrillian-1 (FNB1) gene testing aids that diagnosis and there are advantages with panel testing giving rapid genotyping allowing a detailed management strategy for patients.

'Panel testing in aortopathy allows for early genotyping for suspected hereditary aortopathy, risk stratifies management strategy for patients and families.'

UK progresses genetic testing to identify FH

Familial hypercholesterolaemia

A ground-breaking genetic testing programme for an inherited and potentially-deadly high cholesterol condition has been extended to more United Kingdom health trusts, Mark Nicholls reports.

The faulty gene associated with Familial hypercholesterolaemia (FH) is found in an estimated one in 200 UK families – making this the country's most common genetic mutation, with possibly as many as 320,000 people affected, including around 68,000 people under 18 years old.

FH is caused by a genetic fault that leaves people with abnormally high cholesterol, which significantly increases their risk of heart disease, including a heart attack and, on average, shortens life expectancy by 20 to 30 years if untreated. If one person in a family is found with FH, on average half of their brothers and sisters and half of their children will also have the faulty gene and be at high risk of early heart disease.

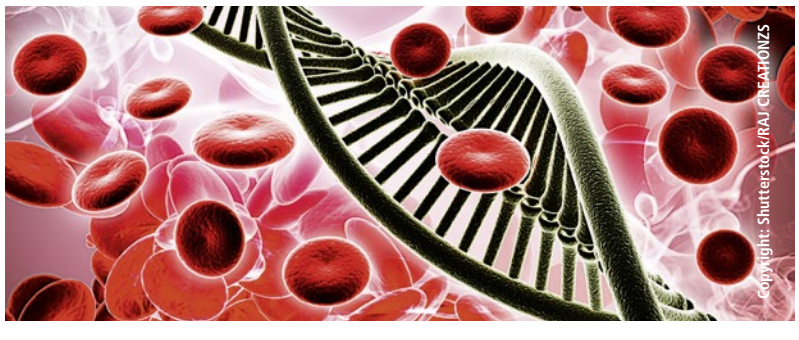
Most FH cases are never diagnosed, putting them at significantly higher risk of dying young from a heart attack. Now funding of over £900,000 from the British Heart Foundation (BHF) is enabling the availability of FH testing in five further UK areas. With a simple DNA blood test, a specialist nurse can identify whether an individual with a clinical diagnosis of FH carries the faulty gene. If discovered, they are then referred for family cascade testing with all immediate first-degree relatives also invited for testing and treatment at their local clinic.

If diagn#osed, early statin treatment, lifestyle advice and careful monitoring, mean that an individual's life expectancy goes up to match the average of the general population.

The additional FH cascade testing funding – extended to University Hospitals Birmingham, York Teaching Hospitals Foundation Trust, NHS Western Isles, Gloucestershire Hospitals NHS Foundation Trust, and the Royal Brompton & Harefield NHS Foundation Trust – was announced in June at the British Cardiovascular Society Conference.

These follow the initial roll-out across eight sites – Royal Free London NHS Foundation Trust, Guys and St Thomas National Health Service Foundation Trust, South Yorkshire Cardiothoracic Centre, Greater Manchester and Cheshire Cardiac and Stroke Network, University Hospitals Bristol NHS Foundation Trust, City Hospitals Sunderland NHS Foundation Trust, NHS Grampian / North of Scotland Cardiac Network, and University Hospital Southampton NHS Foundation Trust – which has already identified 500+ FH people.

Jo Whitmore, the FH Clinical Lead at the BHF, said: 'If high cholesterol is left unchecked, fatty materials can build up in your arteries, increasing your risk of heart disease. The problem with FH is that it dramatically increases the LDL cholesterol in the person's blood, causing a heart attack, commonly at a very young age. We know that cascade testing within families works, and the challenge is now to engage with NHS organisations and commissioners across Britain so that no family falls through the cracks.



'FH is easily treated, so no family should have to go through the pain of seeing a loved one have a heart attack that could have been prevented.'

The National Institute for Health and Care Excellence (NICE) estimates that if 50% of the predicted relatives of people with FH are diagnosed and treated, the NHS could save £1.7 million per year on healthcare for heart disease by preventing cardiovascular events.

From a clinical commissioning perspective, FH has not been on the 'radar' of general healthcare commissioners, but has not been seen as small enough to do specialist commissioning either.

However, screening is a cost effective option, Whitmore confirms: 'For the first person in the family identified the cost is about £200 for the DNA test but, once you've identified the gene you are looking for, the test comes down to £75 for other family members.'

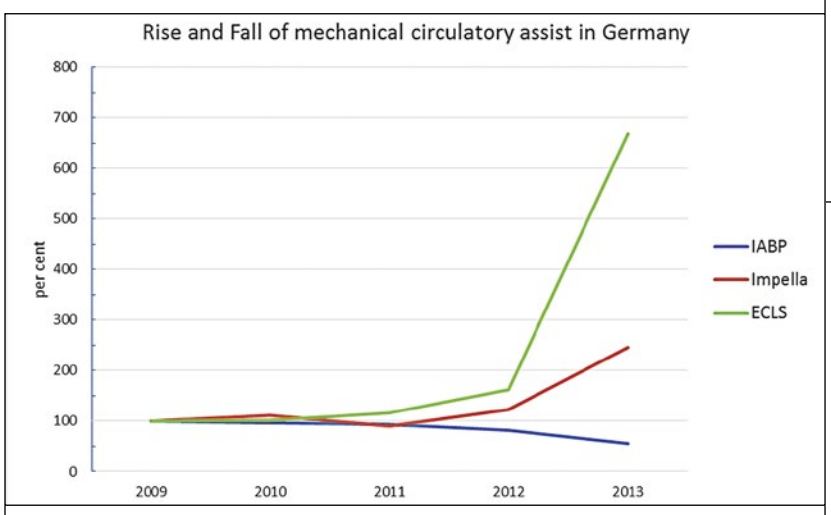
Jo Whitmore has worked within cardiovascular nursing for over 20 years in roles that include managing a Coronary Care Unit and being a specialist nurse in Cardiology involved in acute chest pain management and thrombolysis.
More recently she has been involved in a number of projects in relation to CVD, working for the British Heart Foundation Clinical Lead for Familial Hypercholesterolaemia sites. She is a member of the Primary Care CVD Leadership Forum in the UK, which works alongside Public Health England, NHS England, Royal College of General Practitioners and the British Heart Foundation.

IABP: Aortic counter-pulsation reduced hospital mortality

Evidence at last

Cardiac surgeons have finally found what cardiologists had reported missing three years ago: evidence to support the use of the oldest mechanical circulatory assist devices: IABP. Nevertheless, EH correspondent *Holger Zorn* expects the findings to have only limited impact.

A small study at the small University of Halle (Saale), Germany, triggered the most significant business kill of the current decade. Confirmed by a multi-centre study, the IABP Shock II trial, it prompted the worldwide revision of guidelines: the recommendation regarding the use of intra-aortic counter-pulsation (IABP – intra-aortic balloon pump) was downgraded from a Class I 'strong' recommendation to a simple recommendation (see European Hospital, 4/2013 p. 20-21 and EH 4/2014 p. 14-15). Why: There was no difference in 30-day and one-year mortality between patients who had received IABP in addition to conventional therapy after infarction-induced cardiogenic shock and those who had not received IABP (30d, 40% vs. 41%; 1a, 52% vs. 51%). Consequently, in Germany, the number of implantations decreased by almost one third (see figure).



Development of the use of circulatory assist devices in Germany. In 2009, 10,205 percutaneously implanted IABPs were recorded (2009 was chosen as the base year because the first patients for the IABP shock II trial were recruited in that year). In 2013, the year following the publication of the results, the figure had fallen to 5,712. In the same period the number of Impella implantations had risen from 153 to 372, and of ECLS (without purely perioperative use) from 273 to 2,268.

*** Source: own illustration, based on data provided by Statistisches Bundesamt (Destatis) and personal conversations.**

Meanwhile, the sister clinical discipline cardiac surgery, where in the early 2000s significantly more IABPs had been implanted, made renewed efforts to assess the oldest and most easily implantable mechanical circulatory assist device and published a specific S3 guideline on the use of intra-aortic counter-pulsation in cardiac surgery (S3 Leitlinie zum Einsatz der intraaortalen Ballongegenpulsation in der Herzchirurgie [Source: www.awmf.org/leitlinien/detail/ll/011-020.html, viewed 30.07.2015].

These guidelines clearly recommend the following:

For haemodynamically stable patients with high surgery risk, IABP implantation is recommended, based on the second-highest evidence category IB.

For patients with pre-surgical cardiac decompensation, implantation should be taken into consideration. This is a class B recommendation – just like the one mentioned above – however, evidence is three classes lower: class IV rather than I.

Evidence is equally weak regarding the recommendation on the point in time of implantation: early if HLM weaning of the patient is difficult or impossible.

Very strong evidence (IA) - and strong recommendation – for the operation of IABP: Pre-surgery implanted IABP is recommended for use during the actual cardiac surgery, to transform non-pulsatile flow of the HLM to pulsatile flow.

Dr Kevin Pilarczyk, cardiac surgeon and coordinator of the guideline, which was drafted in cooperation with the national professional organisations for cardiology, intensive and trauma medicine and extra corporeal techologies, sums up the recent data: 'The results of the IABP shock II trial, with patients who almost exclusively had received interventional treatment, cannot readily be applied to cardiac surgery patients.

Considering pathophysical conditions

'A patient in infarct-induced cardiogenic shock who has to undergo balloon dilatation or stent implantation in the cardiac cath lab cannot be compared to a comparatively stable non-infarction patient who has an increased perioperative risk profile due to reduced pump function. Surgery involving general anaesthesia, heart-lung machine and temporary cardiac arrest differs fundamentally from cardiac therapy.'

Such pathophysiological considerations are supported by a recent meta analysis assessing several randomised studies on preoperative IABP in high-risk cardiac surgery patients: it showed that aortic counter-pulsation is associated with reduced hospital mortality and reduced length of stay – even when limited to more recent studies [DOI: 10.1093/ejcts/ezv258]. Data regarding the continuation of IABP-induced pulsatility during HLM are equally reliable [Source: Int J Artif Organs. 2009;32:50-61]. In contrast, IABP in high-risk patients before stent implantation does not seem to have any benefits [DOI: 10.1016/j.ijcard.2012.12.027]. Dr Pilarczyk concludes: 'While there are no dedicated studies for this particular setting, we recommend considering IABP implantation in infarction-induced cardiogenic shock with surgical revascularisation due to the differences to cardiology.'

It remains to be seen to what extent these data will lead to an increase in implantations. Today, cardiologists are familiar with other, more difficult to implant systems – with remarkable results: attacked as business killers two years ago, they have now turned into business boosters. All other relevant systems – Impella, TandemHeart and ECLS – are significantly more expensive than IABP. The reimbursement a hospital receives for ECLS is at least ten times the amount reimbursed for IABP.

The implantation figures of all other systems totalled and projected into the future indicate that these other systems will overtake IABP in 2017 – despite the fact that, to date, no randomised study has demonstrated an advantage over – shown to be useless – IABP.

Following medical studies in Giessen, Essen and Houston, **Kevin Pilarczyk MD** became a researcher at the Mayo Clinic Rochester. He is now senior resident at Westdeutsches Herzzentrum, the West German heart centre in Essen, Germany. His clinical and research focus is cardio-surgical intensive care, particularly extracorporeal cardiac and pulmonary support systems. He is secretary and coordinator of the interdisciplinary S3 guideline for the use of intra-aortic balloon counter-pulsation in heart.

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The Lab2Go project

POC test detects myocardial infarction

Philips Minicare delivers rule-in/rule-out readings for heart attacks in 10 minutes. It takes a lot of hard work to make things easy, John Brosky reports.

Philips' Minicare I-20 POC system is designed to help physicians, nurses and paramedics identify patients at high risk for acute cardiac events– right at the bedside or in pre-hospital settings.

Biomedical experts at Royal Philips have spent more than 10 years developing a simple test for the emergency department that, in less than 10 minutes, may indicate whether a patient suffering chest pains is having a heart attack.

The company's new Minicare I-20 point-of-care (POC) system is now undergoing field evaluation at six prominent European hospitals as part of Lab2Go, the three-year European Union-funded project. If successful, this handheld, bedside device would open a new pathway for rapid, reliable diagnosis that responds to a long hoped-for, critical need in emergency medicine.

Professor Volkher Scharnhorst PhD, from the Catharina Hospital in Eindhoven, the Netherlands, presented the preliminary results of the Lab2Go evaluation to colleagues at EuroMedLab 2015. According to him, Minicare Acute has the potential to support near-patient testing for people suffering acute coronary syndrome when they arrive at the Emergency Department; and therefore would enable faster diagnosis or treatment.

If it sounds simple so far, here comes the fun part – making it work. The widely accepted test for a rule-in/rule-out decision on heart attacks is the Troponin I (cTnI) assay. A physician draws a patient's blood and the sample is sent to the central lab and after 60 minutes, the answer comes back. While the patient has to wait, often distressed, until the results return and the physician can then determine what treatment to provide.

To cut that window for treatment from 60 minutes to 10 minutes, Philips had to overcome a series of technical challenges. First, the simple finger prick to draw a droplet of blood for the POC test means drawing capillary blood, which is different from venous blood used in today's lab tests. Would the results be comparable?

Second, to reduce work for emergency departments, the Philips POC test needs to be user friendly and reliable by relying on microfluidics and chemistry that require no additional steps for staff.

Third, all the complexity of a laboratory instrument needs to be reduced to a hand-held device that anyone can operate without special training. To solve the miniaturisation challenge, Philips brings together an unexpected combination of nanotechnology with a compact disc player. It turns out that the optics used for reading music and film, an early Philips invention, work with a precision and reliability that can be applied to chemical testing. By mixing magnetically charged nanoparticles in the blood sample, the optics can detect and quantify the prevalence of a given biomarker – in this case, the cTnI protein indicating acute coronary syndrome.

At Philips, the potential was discovered long ago. The work to create a handheld diagnostic reader instrument began in earnest in 2009 by looking at ways to enhance the sensitivity of the detection and reduce the sample concentration required.

According to Michel Simons, Marketing Director of Philips Handheld Diagnostics in Eindhoven, 'no one else can deliver these high quality results from a finger-prick sample in less than 10 minutes.'

Jos Rijntjes, Head of Commercial Operations for Philips Handheld Diagnostics in Eindhoven

Michel Simons, Marketing Director of Philips Handheld Diagnostics, in Eindhoven

Looking beyond this first cardiac test, he sees a wider range of potential applications in the emergency department for the Minicare system. 'We will be able to measure all the different proteins in less than 10 minutes. We can do multiplexing on our device to test different parameters so that, with one drop of blood on the same cartridge with a nano-dispensing technology, we will be able to conduct up to 20 different tests at the same time.'

Jos Rijntjes, who leads Commercial Operations for Philips Handheld Diagnostics said that 'with the successful implementation of this first assay for chest pain, we can go on to apply the same technology and methodologies to additional assays. In one square millimetre we might, for example, be able to load tests for high fever, trauma, brain injury, or mental disorders – offering a series of assays to help emergency physicians understand which patient needs immediate attention and treatment when rapid results are critical.'

The second challenge for ease-of-use for the device is at the heart of the current test in the Lab2Go project. In addition to clinical results, the aim of the project is to gather evaluations of real-world use and identify where the workflow or usability can be improved. Rijntjes explains that the Minicare I-20 cartridges use dry chemistry without the liquid reagents found in central laboratories. 'The only fluid in the disposable cartridge comes from the tiny droplet of the patient's blood,' he said. 'There is no need to add agents, no need to wash, to dilute – no need for the staff to do anything but put the patient's finger on the cartridge and then insert it in the Minicare Acute reader.'

Returning to the first challenge, after all the engineering and technological marvels, the entire success for this break-through approach comes down to that finger prick and the micro droplet of blood from the patient. As one physician said, if there is not a strong correlation between results from a capillary blood sample and the traditional troponin results using venous blood, 'out go the finger-pricks and the utter simplicity.'

Scharnhorst is cautiously optimistic, reporting what he called a correlation that is 'very comparable and offers the potential to interchangeably use both capillary and venous samples.'

The full results of the evaluation from hospitals in Austria, France, Germany, Netherlands and the United Kingdom are not expected until 2016.

Meanwhile, Philips faces one more critical challenge, clinical trials that will put the Minicare Acute troponin assay up against laboratory results in a head-to-head comparison. Simons explained: 'We plan to start in Europe, but aim to have parallel trials running in the US as soon as possible. Discussions are currently underway with the FDA (Food & Drug Administration) to determine what our clinical trial needs to look like. Several sites in the U.S. have already expressed interest in joining the trial.'

Mechanical thrombectomy performs like a 'corkscrew'

Stroke is a surgical disease!

Cardiologists call for the establishment of 24/7 centres for rapid surgical interventions to remove blood clots in the brain, John Brosky reports

They did it for heart attacks. Can cardiologists now lead an effort to speed up the emergency medical response for stroke?

Over the past five years, the Stent for Life initiative organised by interventional cardiologists has pushed majors medical centres to assure 24/7 coverage and reduce the time to treatment for patients showing up with severe chest pain.

Now armed with fresh evidence that a mechanical intervention to pull out blood clots is more effective to halt devastating damage to the brain than the slower treatment with drugs to dissolve the clot, the European Association of Percutaneous Cardiovascular Interventions (EAPCI) has formally issued a call to action to mobilise its growing army of interventional cardiologists.

'We need to build healthcare systems for early intervention in stroke,' Jean Fajadet MD, the outgoing president of EAPCI.

Qualified physicians are needed

Even a quick glance at the number of interventional neuroradiologists in Europe compared to the number of stroke patients shows there are far too few qualified physicians to offer such a service everywhere, all the time.

'To offer this intervention rapidly, the question becomes whether cardiologists can help,' suggested Kenneth Snyder MD, from the State University of New York in Buffalo, who joined Fajadet at EuroPCR 2015 in calling for next-generation stroke centres.

A consensus statement issued this year by the European Stroke Organisation (ESO; Basel, Switzerland) unequivocally recommends rapid percutaneous intervention within 4.5 hours with a clot retrieval device.

ESO developed the statement with the European Society of Minimally Invasive Neurological Therapy (ESMINT; Zurich, Switzerland) and the European Society of Neuroradiology-Diagnostic and Interventional (ESNR; also Zurich).

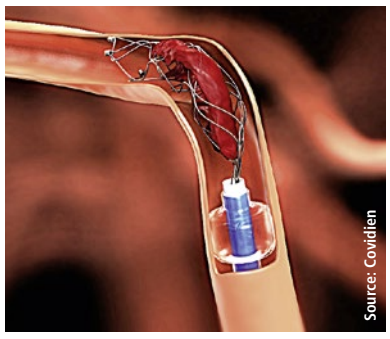
'Stroke is a surgical disease,' Snyder declared.

This bold statement challenges the current standard of care and is based on new scientific evidence from four major stroke studies presented this year at the International Stroke Conference in Nashville, USA. Those studies showed that rapid mechanical thrombectomy using a new generation of clot retrieval devices improves patient function after acute ischemic stroke.

'Five clinical trials have been halted because the new technology is better, because it works,' said Snyder. The current standard of care for stroke patients is an intravenous (IV) injection of a tissue plasminogen activator (t-PA) meant to dissolve a clot blocking blood circulation in the brain. The new procedure for mechanical thrombectomy is a surgical intervention, in which a device is used to pull out the blood clot immediately and directly. The procedure is performed without general anaesthesia as the patient is not aware of the catheter snaking through blood vessels to arrive in the brain with a device some call simply a cork-screw.

Surgeons have reported that patients in some cases have sat up on the operating table after the clot was removed and began speaking with them.

Catheter operators trained through EAPCI have the basic skill set needed for the procedure, and with additional training could maintain the 24/7 coverage for this time-critical procedure, according to Fajadet.



Solitaire is a mechanical thrombectomy device used to retrieve a clot in patients experiencing acute ischemic stroke

Membership in EAPCI has grown rapidly since it was founded in 2006. In the first five years 2,700 cardiologists joined to train for angioplasty and stenting procedures. That number nearly doubled again so that, in 2014, there were 5,500 members. There are almost 13,000 interventional cardiologists attending EuroPCR events in 2015.

New devices that are generating the excitement surrounding this procedure include the Solitaire revascularisation device from Covidien and the Trevo from Stryker Neurovascular.