

The Cleveland Clinic: a cardiac centre of excellence

Steve Nissen speaks of The Clinic's success and his hopes for the future to Emma Wilkinson.



Cleveland Clinic main entrance at dusk

It is pretty fair to say that the Miller Family Heart and Vascular Institute at Cleveland Clinic is one of the largest, and most highly rated, cardiovascular departments in the world. A quick look at the statistics shows that in 2009 alone, clinical staff saw almost 350 000 patients, carrying out many thousands of procedures, including 60 heart transplants.

A look back through its impressive history, starting with the development of coronary angiography in the 1950s, gives you some idea of the important role they have played in the improvements in heart care over the past decades. Other notable achievements include the introduction and refinement of coronary bypass surgery and, more recently, the implantation of the first biomechanically engineered mitral valve replacement. With so many impressive milestones on the résumé, it is difficult to single out an area where the Clinic particularly excels.



Steve Nissen

Prof. Steven Nissen, chairman of the Department of Cardiovascular Medicine at the Cleveland Clinic, says that there are a few factors which set them apart from their peers but the one that comes first to mind is how the unit is structured. 'It is a very large department with over 100 faculty members and we are organised differently from other traditional centres. We reorganised about two years ago when cardiovascular medicine, cardiac surgery and vascular surgery were linked together into a single Institute. We are now all together under one roof.'

He goes on to explain that the close ties between the medical and surgical teams, as well as other basic scientists carrying out cardiovascular research, make sense from both an academic and a clinical standpoint. 'Take, for example, a treatment like percutaneous aortic valve replacement—like so many of the things we do and so much of the research we do, it involves more than just cardiovascular medicine. So by coming together, we have a lot more in common and it makes much more sense than linking cardiology with traditional medical specialties'.

This collaboration has always been present at Cleveland—although maybe not as formally as it is now—but accelerated somewhat in 1991 when Eric Topol became chair of the department. Under his leadership, the clinic also oversaw some pivotal trials, including the impressively large GUSTO trial which showed a 14% reduction in deaths from heart attacks with the use of tissue plasminogen activator and heparin, and the EPILOG trial showing abciximab and low-dose heparin markedly reduces the risk of ischaemic complications in patients undergoing angioplasty. Under his direction, the Institute also became the first hospital in the USA to voluntarily release outcome data and mortality statistics to the public.

But let's talk about current projects. Nissen points to several areas of work that his department is involved in. 'We have the Cleveland Clinic Center for Clinical Research which is a classical coordinating centre for multi-centre clinical trials and has about 100 employees, including nurses and administration staff. This department has a dozen or more clinical trials ongoing, some of them involving up to 20,000 patients, covering a relatively wide spectrum of therapeutic areas. One I'm working on is the cardiovascular effects of NSAIDs, but we also do myocardial infarction trials and lipid trials. In addition, we are involved in core laboratory-type research, operating laboratories looking at echocardiography and nuclear medicine and biomarkers. Our intravascular ultrasound core laboratory is considered the most successful in the world'.

He also points to the preventive type work currently being done, specifically the work of Dr Stanley Hazen looking at cardiovascular risk factors such as hyperlipidaemia. That research includes understanding inflammation and oxidant stress in the development of atherosclerosis. Cardiovascular imaging and epidemiological research are two other areas that Nissen points to as being very strong within the department.

Looking to the future, one of the key developments could come from the completion of the PARTNER trial looking at the safety and effectiveness of transcatheter aortic valve replacement in select patients with severe aortic stenosis. 'Our groups have been part of the leadership of the PARTNER study', says Nissen. 'This is a rapidly evolving area and we have been involved right from the beginning in these new ways of replacing aortic valves—they're doing some really exceptional work.'

The other area I should point out is we have received a \$60m grant from the state of Ohio for an incubator facility as part of the Global Cardiovascular Innovation Center for Biotechnology. Plus, we obtained matching contributions from industry of \$180m. We have opened the building and are attracting companies interested in developing new devices and this will be a great area of future development. This incubator facility within the GCIC will enable start-up companies to develop cutting edge cardiovascular technology'.

Spin-off companies which benefit from this Center and its investment include Juventas Therapeutics which specialize in cell-based, regenerative therapies for treating heart failure and PrognostiX, a company developing molecular biomarkers for diagnosing and treating cardiovascular disease.

But like any major (or minor for that matter) organization, the economic downturn has had a negative impact on funding and therefore the work they have been able to do. 'I know of no area that hasn't been affected', says Nissen. 'The pharmaceutical industries are struggling in terms of new drugs and government authorities are not overflowing with research dollars, so we have had to become more efficient at finding other ways. One thing we have done is looked to philanthropy and got foundations to support us but it has been challenging'.

In fact this is one of the primary challenges they face—along with many other research institutions—over the next few years; how to maintain these impressive academic and clinical standards and continue with groundbreaking research in such difficult financial times. But Nissen believes that with a little lateral thinking on potential funding sources and clever use of resources, the future of the Clinic is bright.

Emma Wilkinson, MA, freelance journalist

Recent pioneering cardiology developments in Japan

Japanese cardiologists have discovered Waon therapy for severe or refractory heart failure and extracorporeal cardiac shock wave therapy for severe angina pectoris.

Waon therapy is a soothing warm therapy for severe or refractory heart failure that was developed by Chuwa Tei, MD, FACC, FAHA, professor and chairman of the Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Japan.



Chuwa Tei

In 1989, Tei and his colleagues developed a form of thermal therapy for heart failure using a far-infrared-ray dry sauna with temperature maintained at 60°C (140°F). The temperature is lower than the traditional saunas of northern Europe (usually >80°C and sometimes >100°C) and the temperature is uniform throughout the room. Most sauna rooms experience temperature differences of around 30°C from the ceiling to the floor.

In 2007, they changed the name to Waon therapy to distinguish it from local hyperthermia therapy for cancer.¹ 'Wa means soothing, and On means warmth, hence Waon means soothing warmth which infers warmth that comfortably refreshes the mind and body', says Tei.

During the therapy, the entire body is warmed and deep body temperature is increased by ~1.0–1.2°C. Afterwards, patients rest supine on a bed outside the sauna where they are covered with blankets for an additional 30 min to continue the soothing effects, and drink ~150–300 mL water to compensate for weight loss through perspiration.

Tei says that the three main advantages to Waon therapy are: high medical value to cost ratio; safe and free from side effects;

and gentle and relaxing unlike western-style therapy which is often painful.

He has studied the effects of Waon therapy in more than 400 patients with moderate-to-severe heart failure including refractory heart failure. It has been shown to improve acute haemodynamics including cardiac output, mean pulmonary artery wedge pressure, and systemic vascular resistance.

Four weeks of therapy (once a day, 5 days a week) improves clinical symptoms and decreases cardiac size. Two weeks of therapy (once a day) reduce brain natriuretic peptide levels, improve endothelial function, decrease arrhythmia, and increase heart rate variability.

More recently, they have shown that Waon therapy improves autonomic nervous activity by increasing parasympathetic activity and decreasing sympathetic activity and that it decreases oxidative stress in patients and hamsters.

A prospective, multicentre clinical trial has confirmed that Waon therapy is safe, improves clinical symptoms and cardiac function, and decreases cardiac size in heart failure patients. A retrospective 5-year follow-up study has shown that when given twice weekly, it decreases hospitalization and mortality. '[This] indicates that Waon therapy is a promising non-pharmacological treatment for heart failure', says Tei.

He is now conducting a prospective clinical trial in 20 major cardiovascular centres in Japan to investigate the long-term effects of Waon therapy on the prognosis of moderate-to-severe heart failure.

Waon therapy was included in the Japanese Circulation Society Revised Guideline Update for Chronic Heart Failure in December 2010 and is set to be approved for severe or refractory heart failure by the Ministry of Health, Labour and Welfare as a highly advanced medical technology in Japan.

Its clinical applications extend beyond heart failure to peripheral arterial disease, fibromyalgia/chronic pain, and chronic fatigue syndrome. As society gets older, Tei believes that 'gentle medicine' will become increasingly important. 'Change the bedridden longevity to wellbeing longevity', he says.

Extracorporeal cardiac shock wave therapy for severe angina pectoris was discovered by Hiroaki Shimokawa, MD, PhD, FESC, FAHA, professor and chairman of the Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine in Sendai, Japan.

Shimokawa and his colleagues found that low-energy shock waves (~10% of the energy density used for urolithiasis) up-regulates the expression of vascular endothelial growth factor (VEGF) in cultured endothelial cells. They also reported that it induced angiogenesis through up-regulation of VEGF in ischaemic myocardium and ameliorated myocardial ischaemia and dysfunction in a porcine model of chronic myocardial ischaemia.²

'This was the first literature in the world that showed beneficial effects of cardiac shock wave therapy as a new non-invasive angiogenic therapy', says Tei.

Based on these results, they conducted two clinical trials in Japan in which patients with refractory angina pectoris underwent a total of three sessions of therapy at intervals of 1–2 days.

In the first clinical trial, they reported that *cardiac shock wave therapy* improved symptoms and myocardial perfusion as assessed by stress scintigraphy. No adverse effect was observed. It was the first published clinical trial showing the beneficial effects of cardiac shock wave therapy, a treatment which does not require surgery or anaesthesia. The second clinical trial was a double-blind placebo-controlled study where they reported improved symptoms and cardiac function.

The cardiac shock wave therapy machine developed with a company in Switzerland (STORZ MEDICAL AG) received an EU CE marking in 2003. In July 2010, extracorporeal cardiac shock wave therapy for refractory angina pectoris was approved by the Ministry of Health, Labour and Welfare as a highly advanced medical technology in Japan.

As of 2010, the therapy has been performed in more than 10 countries in the world and has provided a new clinical approach to treating patients. Tei says: 'Extracorporeal cardiac shock wave therapy can improve symptoms and myocardial perfusion in "no option patients". Patients who are not candidates for PCI or CABG due to extensive disease'.

Two further clinical trials are underway in Shimokawa's group to investigate the effects of extracorporeal cardiac shock wave therapy on acute myocardial infarction (AMI) and peripheral artery disease (PAD).

In the AMI trial, the therapy is performed within 72 h after the onset of AMI for patients who are successfully treated with PCI. A reduction in left ventricular remodelling in the chronic phase after AMI is expected.

In the PAD trial, patients with intermittent claudication will undergo a total of nine sessions of therapy at intervals of 1–2 days. An extension of maximal walking distance and relief from leg pain are expected.

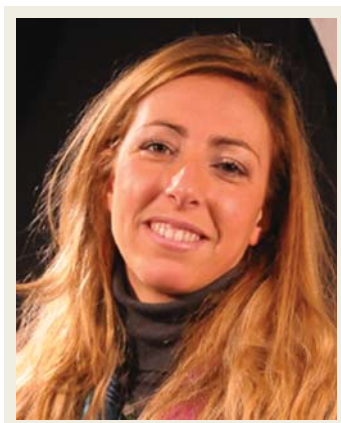
J. Taylor, MPhil

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A modern Roman landing in *Britannia*: 'UK, here I come'

The personal experiences of émigré cardiologist Chiara Bucciarelli-Ducci, MD, FESC, in England.



Born in Rome, Italy, in 1976 but raised in Tuscany, the eldest of four daughters, she is the quintessence of a European citizen that can fluently speak in three foreign languages, in addition to her native Italian.

Chiara decided that she wanted to be a cardiologist when, aged 12, she was fascinated by reading the description of a cardiac operation at school. Not without minor disappointment from her parents who pictured her as a lawyer, she entered medical school in Rome diverting from the family's professional traditions. Her grandfather was an eminent member of the Italian parliament for over 20 years, becoming President of the House of Parliament for a number of legislatures and then a judge of the Supreme Court. This example of high achievements at a time where honesty, respect, and loyalty to the State and others were non-negotiable values has always inspired her.

During her medical studies, she did not miss an opportunity to explore the world and where possible combine clinical medicine with travelling. As a result, she was an internal medicine intern at the Karolinska Institute, Stockholm, in 1997 and an intern in surgery in Vilnius University Santariskiu Hospital, Lithuania, in 1998. Then in 1999, she spent 6 months at the Hospital de la Virgen Macarena/University of Sevilla, Spain, with a European-funded ERASMUS scholarship.

Finally, in her last year of medical school, she received a research scholarship at the Texas Heart Institute, Houston, TX, USA, where she collaborated on an ischaemia–reperfusion study.

'I could never thank my parents enough for allowing me to grow up as a European long before the EU was a reality. I was only 6 when they sent me to summer school in Switzerland to learn French. Studying in the morning and playing with international kids for the rest of the day enabled me to develop social skills early in life'.

July in Switzerland and later in France became a regular schedule for 10 years.

She set off for a new adventure at 17, to attend a year of high school, destination USA. Wanting to be a doctor, English had to be learned. Landing in Portland, OR, USA, she lived for a year (1993–94) with a lovely host family she had never met before. It was a great life experience and fascinating to graduate from an American high school and have the chance to go to a prom.

She was then back in the USA 10 years later (2004) as a cardiology trainee to learn cardiovascular magnetic resonance (CMR) at the Feinberg Cardiovascular Institute of Northwestern University in Chicago with Profs Bonow and Klocke and Dr Ed Wu, thanks to Prof. Fedele's visionary career advice. 'If it wasn't for him, I wouldn't probably have pursued a career in cardiovascular imaging'.

After finishing her cardiology training back at 'La Sapienza' University in Rome the dilemma was whether or not to return to the USA. It was a great opportunity to work and train in the Cardiovascular MRI Unit of the Royal Brompton Hospital that brought her to London in 2006, where she enrolled in a 4-year PhD programme ('Role of CMR in acute and chronic myocardial ischaemia') at the National Heart and Lung Institute of Imperial College under the supervision and support of Prof. Dudley Pennell. 'I am grateful for the opportunity I was given to work in such an excellent centre, not only to learn a great deal about CMR, but also to enjoy myself at the same time.' Between 2008 and 2010, it was an honour to have been offered the opportunity to help set up the cardiovascular magnetic resonance imaging (MRI) service of the Heart Hospital, University College London. Although this additional commitment implied working alternate weekends, the enthusiasm for the project and the team amply paid back her efforts.

The worst and the best episode of her life was a very serious ski accident in 2009 in which she suffered multiple pelvic fractures. During the 1-month immobilization, she made good use of her time writing a paper and applying for the AHA imaging young investigator award for which she was shortlisted as a finalist. 'I was very proud of this achievement which proved that even negative events can be turned around as positive opportunities'.

A few months after rehabilitation, she was appointed Senior Lecturer and Consultant Cardiologist at the Bristol Heart Institute in Bristol, UK. The Bristol chapter started in April 2010, and in addition to her role as lead of the CMR theme of the Bristol National Institute of Health Research (NIHR) Cardiovascular Biomedical Research Unit, a few months later, she was also appointed co-director of the Clinical Research and Imaging Centre (CRIC) Bristol. The latter is a centre that hosts a state-of-the-art 3 T MRI scanner, two sleep study rooms, and other clinical rooms.

In 2010, she was also elected a nucleus member of the CMR working group of the European Society of Cardiology. Since 2009, she has been active in the Society of CMR (SCMR) with editorial responsibility.

In her spare time, she enjoys travelling the world, skiing, sailing, cooking, and gourmet dining. She is a member of the Italian Academy of Cuisine in London and a founder member (with Dr James Moon, Dr Anna Herrey, and Dr Flett) of London SkiMR, a social ski getaway with colleagues after the annual February CMR meeting. Since the accident, she has returned to the slopes and enjoyed them even more. 'As a Tuscan living in the UK I am asked recurring questions, one being, what could possibly have made me move from Tuscany to the UK. With the addition, it can't be the weather, can it? I explain that to be professionally happy and satisfied is a very important part of life'.

Being an Italian in the UK, another interesting question is whether I like English food. My answer is, I find it interesting and tasty but my palate still prefers Italian. Depending with whom I am interacting at this stage of the conversation and to be more persuasive, I usually offer a dinner invitation at my place to prove my argument and my cooking skills, in keeping with the evidence-based approach over and above medicine!

Interestingly, being in the UK hasn't stopped me working for Italy and in Italy. I have a number of ongoing scientific collaborations

with the Italian Society of Cardiology and other excellent Italian centres. I have Italian cardiology trainees come to the UK to train with me, and I am helping some centres set up their CMR service. I am indeed doing more than I would probably have done if I was working in Italy because as an expatriate you are somehow more respected.

One exquisite Anglo-Saxon feature that I am trying to learn is to control the Mediterranean temper and mask my emotions. But what would you expect from somebody whose name (Chiara) actually means 'clear'?

'Sometimes I miss Italy but I will never forget the frustrations of an academic system that doesn't leave enough room for the younger generations. The UK has been for me an incredibly welcoming and generous country, in which meritocracy is taken seriously and resources allocated accordingly. Since 2006 I have been discovering a beautiful country rich in traditions, history, and positive surprises. It wasn't for nothing that my fellow ancient Romans got here long before I arrived'.

Chiara Bucciarelli-Ducci, Consultant Cardiologist, Bristol Heart Institute

The endovascular stent graft raises vascular stiffness and changes cardiac structure within a very short time

Dr Yasuharu Takeda, MD, from the Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine in Japan, won the poster session on catheter-based and surgical interventions at the American Heart Association conference in November 2010.

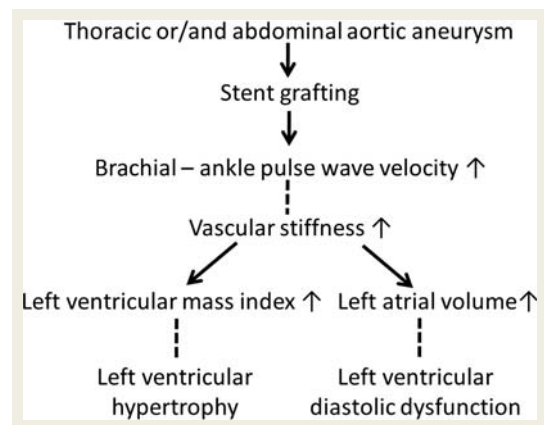
His finding that the endovascular stent graft raises vascular stiffness and changes cardiac structure within a very short time was made after an initial observation in a patient.¹

A 76-year-old female patient had developed heart failure 2 months after endovascular long stent grafting for thoracic and abdominal aortic aneurysm. There was no evidence of coronary artery disease. 'Stent grafting might induce vascular stiffening and development of heart failure, because she showed a high brachial-ankle pulse wave velocity (baPWV)', says Takeda. 'Thus, we thought that we needed to clarify the effects of the endovascular stent grafting on vascular and cardiac function and cardiac geometry'.

They collected data on 45 patients before and a week after endovascular stent grafting. Echocardiographic data were recorded, along with blood pressure, heart rate, and baPWV (measured using a non-invasive automatic waveform analyser).

They found that baPWV was significantly elevated after the grafting, although systolic blood pressure was not increased. Left ventricular mass index (LVMI) significantly increased at post-op status, although there was no difference in LV end-diastolic volume. The changes in LVMI were positively correlated with

those in baPWV. Left atrial volume significantly increased at post-op status.



Proposed course of events

"We found that the endovascular stent graft raised vascular stiffness and induced LV hypertrophy and left atrial enlargement within a very short time after stent grafting without elevation of blood pressure," says Takeda. "We think that this left atrial enlargement is diastolic dysfunction".

The results were a surprise. They had predicted that baPWV might be elevated after stent grafting but they did not think that

the elevation of baPWV would lead to LV hypertrophy within a very short time.

A previous paper reported that LV hypertrophy appeared within a few days in mice with transverse aortic constriction (TAC). There are of course many differences in the heart between mice and humans and in the load for LV between TAC and stent grafting. However, in Takeda's data, LVMI increased 5% due to stent grafting. He believes that LV hypertrophy is introduced as compensated hypertrophy for LV afterload even in a very short time.

In the study, it became clear that stent grafting might affect LV geometry and LV diastolic function. If there is a relationship between LV dysfunction and vascular stiffening, Takeda's hypothesis is that it may be necessary to give medication for vascular stiffening after or before stent grafting. They need to confirm their results in the long term after stent grafting, and then want to test medications on patients or animals. There was no evidence of improvements in heart failure using a vasodilator, so a new medication may be required.

An observational study is needed to acquire information about risk factors for the onset of heart failure after stent grafting. Short-term data after stent grafting show the importance of diastolic function and the change of baPWV in the onset of heart failure.

A long-term observational study is also required to assess the effects of stent grafting on vascular and cardiac function. 'We need to clarify what changes vascular stiffness and [the] possibility of drug intervention', says Takeda.

He also wants to use animal models with stent grafts to determine the relationships between vascular stiffness, LV systolic function, and diastolic function.

What questions do the findings raise?

- Is there a relation between stent grafting and LV systolic function?
- Was the increase in vascular stiffness due only to the physical influence of the stent graft? Do vasoactive substances have an influence?
- What elements influence the onset of heart failure after stent grafting? LV diastolic function? LV systolic function? Vascular stiffness? Or other elements?
- Is this change of vascular stiffness and diastolic function prevented by drug intervention?

J. Taylor, MPhil

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The Finnish Cardiac Society

The history and achievements of cardiology in Finland are discussed by the Society's president.

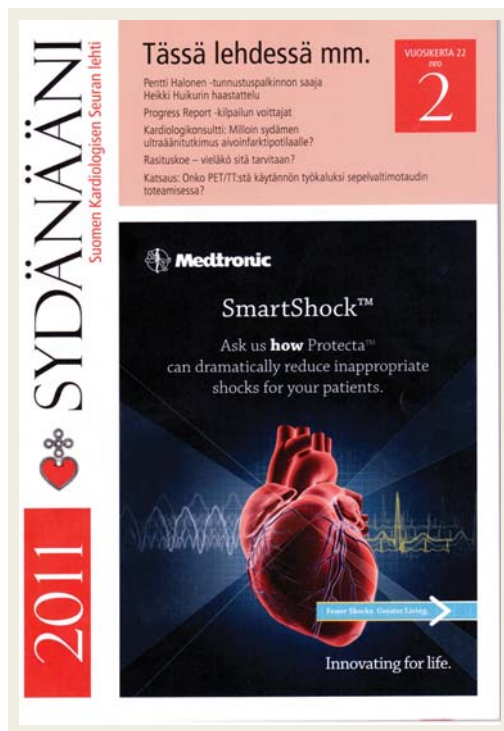
The Finnish Cardiac Society (FCS) was founded on 13 November 1967 in Helsinki, Finland. The 'grand old man' of the FCS, Prof. Pentti I. Halonen, was one of the fathers of the European Society of Cardiology (ESC). 'Finland was the second Scandinavian country to join the ESC in 1968. In addition, the FCS is an affiliated member of the World Heart Federation and has close co-operation with the other Nordic and Baltic countries', says Prof. Pekka Raatikainen, MD, PhD, FESC, professor of cardiology in the Heart Center of Tampere University Hospital and President of the FCS, who like many other members of the FCS, has been actively involved in the work of the ESC and the European Heart Rhythm Association (EHRA). In addition, he is responsible for the training of medical students as well as cardiology and electrophysiology Fellows.



Pekka Raatikainen

Members

Currently, the FCS has about 760 members. Most of them are either cardiologists or internal medicine specialists with particular interest in the treatment of cardiac patients. The remaining members are cardiac surgeons, anaesthesiologists, paediatric cardiologists, and other professionals actively involved in treating cardiac patients. In addition, the FCS has 38 industrial members representing the pharmaceutical and medical technology companies in the field of cardiology. The Board of the FCS is composed of nine voting members and the non-voting Editor-in-Chief of the membership journal *Sydänääni* ('Heart Sound'). The *Sydänääni* has five regular issues and one or two themed issues every year.



Finnish Cardiology Society Journal

Educational and research activities

The major aims of the FCS are to arrange high-quality educational events in the various fields of cardiology and to support cardiac research at the national level. The society has 12 active Working Groups (WGs), which are dedicated to a variety of specific areas in cardiology. Each WG has a nucleus composed of chair, vice chair, and secretary, who are actively involved in the planning of education activities with the FCS Board, Office Manager, and the Administrative Secretary of the Society. The FCS arranges more than 100 events with up to 4300 participants annually. The main meetings are the Autumn Meeting in October and the Spring

Meeting in March. The meetings' official language is Finnish, but there are usually some sessions in English with a foreign speaker. The exhibitions at the main meetings are popular with industry and provide a good view of the latest innovations in cardiology. In addition, the Society has been actively disseminating the ESC Guidelines and developing national guidelines for the management of cardiac diseases. The society also works closely with the Finnish Heart Association to promote cardiovascular health among the general population.

The Finnish Cardiac Society awards ~€100 000 for cardiovascular research annually. The grants are mainly aimed at supporting young investigators to present their data in the ESC and other major international congresses. Besides that, the FCS sponsors Fellowship training and some research projects every year.

Cardiology in Finland

In the past, coronary heart disease mortality was extremely high in Finland. Since launching the North Karelia Project in 1972, the annual mortality rate of coronary heart disease in North Karelia among the working age population has fallen ~75%, compared with the rate before the project (<http://www.ktl.fi/portal/265>). This landmark project showed that a determined and well-conceived intervention can have a major impact on cardiovascular mortality rates and improve the health of a population.

Finland is a large and sparsely populated country which makes the treatment of myocardial infarction and other acute cardiovascular problems challenging. About 15 years ago, the FCS started a long-term goal to improve cardiology training and to increase the number of cardiologists in Finland. The goal has been reached, and now all the central hospitals have invasive cardiology units. However, 24/7 invasive cardiology service is currently available only in the Helsinki and Tampere area. At the moment, the FCS is working intensively with the Ministry of Social Affairs and Health in order to improve the night-time access to invasive treatment in the other university hospital districts.

The other substantial challenge for the FCS is to increase the knowledge of invasive treatment for cardiac arrhythmias among the referring doctors. According to the EHRA White Book, the rate of cardiac resynchronization therapy implantation in Finland is extremely low, despite the fact that Finland has been one of the best performing economies within the Europe in the recent years. On the other hand, access to catheter ablation of atrial fibrillation has improved rapidly as four out of the five university hospitals in Finland have built new electrophysiology laboratories with modern remote magnetic navigation equipment during the last 2–3 years.

For further information on the Finnish Cardiac Society, visit www.fincardio.fi.

Pekka Raatikainen

Heart, formerly the British Heart Journal

Heart is based in the UK but is an international journal that encourages submissions from around the world.

Heart was launched in 1939 and is co-owned by the British Cardiovascular Society and the *British Medical Journal (BMJ)* Group. It is the specialist cardiac journal within *BMJ* publishing. Formerly called *British Heart Journal*, it gained its current name in 1996, 'in order to emphasise its status as an international journal, as distinct from a national Society journal', says editor Adam Timmis, professor of clinical cardiology at the London Chest Hospital.

In common with most of its major competitors including *European Heart Journal*, in 2009, *Heart* changed from monthly to twice monthly editions. It had little impact on staffing requirements since the journal is supported by the entire infrastructure of *BMJ* publishing.

The day-to-day editorial work is Timmis' responsibility, who has a team of around 15 associate editors drawn not only from England but also from Scotland and many other parts of the world including Germany, the Netherlands, the USA, Hong Kong, and Singapore.

A core group of London-based associate editors meet at BMA House every week to deal with editorial issues and to select which papers will be published.

Each associate editor has a subspecialist expertise and decides whether papers submitted in their speciality area merit peer review. The journal sends ~55% of its original research submissions out for peer review; the remaining 45% are deemed unsuitable for the journal and are rejected without peer review.

The journal receives a total of ~2500 manuscripts per year, including 1400 original research papers of which only 13% were accepted in 2009. The diversity of the published research reflects *Heart*'s international scope with 19% of papers coming from the UK and the remainder coming from other Western European countries (41%), North America (14%), Australasia (7%), and the Far East, including Japan, China, Korea, and Singapore (18%).

The impact factor has been steadily rising and currently stands at 5.385. 'We're looking all the time for high quality material because we know that high quality material will be cited and that's what pushes up the impact factor', says Timmis.

Unlike *European Heart Journal*, the *Journal of the American College of Cardiology*, and *Circulation*, *Heart* does not have national society guidelines to publish. Guidelines are heavily cited and tend to exaggerate differences in impact factor between the major cardiovascular journals.

Timmis took over as editor in 2007 and is using a number of ways to attract submissions. Increasing the scientific impact is one way, as is broadening the scope from a clinical journal to one which incorporates cardiovascular science. 'We're aware that *Heart*'s image is very much that of a clinical cardiac journal', says Timmis. 'We're happy with that image but want also to reflect our interest in translational science'. To that end, *Heart* has been running a series of translational review articles which have been well received by researchers.

Heart encourages submissions not only from Western Europe and the USA but also from all around the world including the third world. It has tried to give a platform for cardiology as it is practiced in developing countries and is running a Global Burden of Cardiovascular Disease series which has featured review and research articles from sub-Saharan Africa, India, South America, and various other parts of the world. Timmis says: 'We believe that's an important function of our journal, to look at the global impact of cardiovascular disease, and not to restrict ourselves to its local impact in western economies'.

Timmis and his team are very conscious of the metrics that are important to authors when it comes to handling their papers. Over the past 5 years, they have improved lead times in order to attract more submissions. The average time it takes for a first decision to be delivered is now 24 days for all papers (49 days for reviewed papers), and the time from final decision to paper publication is 3–4 months (3–4 weeks for online publication).

J. Taylor, MPhil

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