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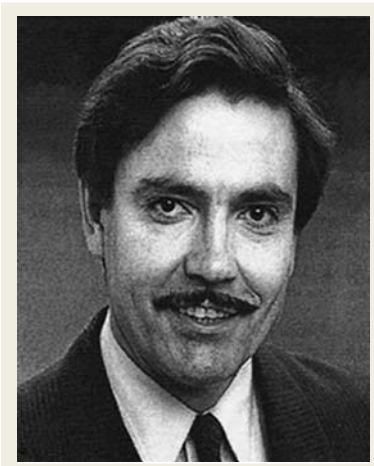
Pioneers in cardiology

The unlocking of the coronary arteries: origins of angioplasty

A short historical review of arterial dilatation from Dotter to the creative Gruentzig

Developments in the use of coronary catheters and the employment of angioplasty in the field of non-surgical vascularization owe much of its early success and indeed later developments to the young German cardiologist Andreas Gruentzig (1939–1985).



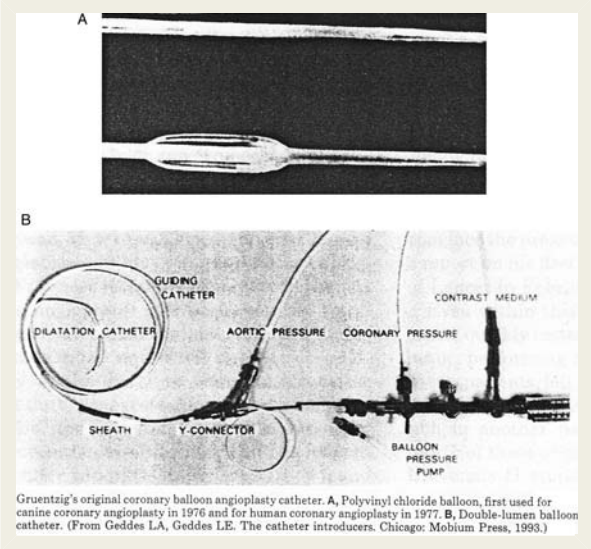
Andreas Gruentzig

From 1969 to 1970 Gruentzig spent time as a guest Fellow in the radiology department of the Aggertalclinic in Engelskirchen, Germany. It was there that the Head of Diagnostic Radiology, Eberhard Zeitler introduced Gruentzig to what was then known as the 'Dotter technique' so-named after its innovator Charles Theodore Dotter (1920–1985) a vascular radiologist. When operating in 1963 on a patient with renal artery stenosis, Dotter unintentionally recanalized an occluded right iliac artery. This was achieved by passing a percutaneous catheter retrograde through the blockage to achieve an abdominal aortogram. The therapeutic potential in the use of this procedure was immediately recognized by Dotter who subsequently carried out further studies on cadavers and later conceived of the possibilities in employing sequential dilators on arterial obstructions. He then envisaged constructing balloon-mounted dilating catheters and using endoluminal stents to aid recanalization.

In 1964, Dotter and Melvin Judkins undertook the first translumenal dilation on an 82-yr-old woman suffering from gangrene owing to a left popliteal artery stenosis. The woman refused amputation and so Dotter passed a guide wire through the stenosis and then continued dilation using double, coaxial rigid polyethylene catheters. The gangrene problem was resolved and the patient fortunately recovered well. Dotter and Judkins wrote up their results using such techniques on 11 patients and Judkins went on to pioneer percutaneous cardiac catheterization.

Although Dotter and colleagues published several papers on the procedure, its limitations were recognized, i.e. the necessity of introducing large-bore rigid dilators percutaneously and then the use of large instruments to remove the atherosclerotic plaque that made the technique cumbersome and risky with the possibility of additional damage to branch vessels. Dotter suggested balloon angioplasty and endoluminal stenting but sadly his ideas were not put into practice and in the USA interest in such work faded. As we see however, this was fortunately not the case in Europe.

Here, Andreas Gruentzig, who had learnt the Dotter technique from his tutor Zeitler, went on to use these techniques for renal arterial recanalization, when he relocated in the 1970s to the University Hospital in Zurich, Switzerland. A couple of years later he conceived the idea of adding a balloon to the Dotter catheter. Early prototypes of the balloons were made of latex but Gruentzig worked on different materials while experimenting in his home kitchen using polyvinyl chloride on the advice of a plastics engineer. In 1973 he performed peripheral balloon angioplasty on animals with his single-lumen catheter prototype. He then went on to perform the first of many human peripheral balloon angioplasties. He used a single-lumen catheter with the balloon being inflated through the central lumen into the patient's superficial femoral artery. Gruentzig continued experimenting in his home kitchen at night or over the weekends to develop catheters such as the double-lumen one, which was fitted with a non-elastic polyvinyl chloride balloon.



Gruentzig's original coronary balloon angioplasty catheter. **A,** Polyvinyl chloride balloon, first used for canine coronary angioplasty in 1976 and for human coronary angioplasty in 1977. **B,** Double-lumen balloon catheter. (From Geddes LA, Geddes LE. The catheter introducers. Chicago: Mobium Press, 1993.)

Gruentzig's original catheter

In 1976, production of the catheters was taken on by the Schneider and Cook Company in MN, USA. The latest catheter had a distal lumen so that pressure monitoring and contrast injections could be achieved. In 1975 this innovative design was a major advance with its flexibility and small profile.

Gruentzig went on to experiment with his double-lumen balloon in human peripheral angioplasty and by 1976 he had managed to make the equipment even smaller so that it could be used in the coronary arteries and he experimented with it in animal and cadaver studies. Sadly, at a meeting of the American Heart Association, the experimental results he presented received a less than favourable response—obviously, the time was not yet right for acceptance of such innovative procedures. One positive outcome of the event however was Gruentzig's meeting with R. Myler who was working in a similar field and hoped they could collaborate to achieve the ultimate goal, i.e. coronary angioplasty in humans. Thus the two together carried out the first of these procedures in May 1977 at St. Mary's Hospital, San Francisco. The procedure was undertaken intraoperatively with the retrograde passage of the catheter through an arteriotomy in the left anterior descending coronary artery, distal to the stenosis, prior to positioning of the bypass graft. After removal of the catheter, a cannula was inserted to flush out the coronary vessel effluent which was collected for examination and analysis.

In September 1977, Gruentzig carried out the first coronary angioplasty in a conscious 37-year-old male patient who was suffering from stenosis of a proximal left anterior descending artery. Although undoubtedly anxious that he would be the first to experience this treatment, the patient agreed to the procedure and fortunately the operation was successful with the lesion being swiftly dilated during two balloon inflations. A return to normal pressure in the distal coronary artery resulted and a pleasing reduction in the stenosis. During the procedure the one complication was a transient right bundle branch block: 'Gruentzig was prepared to diffuse the distal vessel through the catheter's central lumen with blood from the patient's contralateral femoral artery, a nuance that foretold future developments in perfusion catheters.'[1] Fortunately, this was not required as during the balloon inflation the patient remained in a stable condition.

Gruentzig reported on his first five cases in a letter to the editor of the *Lancet* in 1978. Fortunately, by now the medical fraternity was more prepared to accept percutaneous revascularization but the development of suitable equipment was still in its infancy, for example the guiding catheters were of solid Teflon which made cannulation of the targeted vessel difficult or even impossible. Balloons at this time were constructed of polyvinyl chloride which had a low rupture-pressure threshold. Gradually, improvements in instruments were achieved yet problems remained or gradually emerged and what Gruentzig had originally conceived of as a technique for the safe and simple dilation of virtually any lesion revealed the process of angioplasty as a more 'violent, somewhat unpredictable assault on the diseased vessel segment.'[2]

Gruentzig, who joined the Department of Medicine at Emory University School of Medicine in 1980 as Professor of Medicine and Radiology, and Director of Interventional Cardiology strove to popularize angioplasty by performing some 2500 procedures and even persuaded one of his colleagues, Dr Hall Whitworth to perform the technique on him in order to demonstrate his faith in the safety of the procedure. He did, however, recognize the problems inherent in such intervention and felt that bypass surgery still had its place for some patients. He also recognized the high rate of re-stenosis, more than 25% in 6 months, as a significant drawback.

Sadly, this determined and inventive scientist died tragically on 27 October 1985 when piloting his personal plane on a return journey to Emory with his wife from their holiday home in Georgia. In a tribute to him, his former colleague from Emory, J Willis Hurst MD wrote: 'I cannot close this tribute without pointing out that he (Gruentzig) lived in the present as few have dared to live. He saw the future and in fact moulded it to his liking. We are still grieving his loss but he would be impatient with us. He would say, "It is time to move on."'[3]

Diana Berry, medical historian and writer

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Changes in the research landscape require a new approach, while continuing to fund the highest scientific priorities

Jennifer Taylor talks with Dr Elizabeth Nabel, Director of the National Heart, Lung, and Blood Institute at the National Institutes of Health (NIH)

National Library of Medicine, © NIH

NIH campus director's office, © NIH

With a budget approaching $3 billion, the National Heart, Lung, and Blood Institute (NHLBI) is a giant funder of cardiovascular research. Like the other institutions of the National Institutes of Health (NIH), it receives its money on a yearly basis as appropriated funds from the US Congress.

The funds available to the NHLBI have increased dramatically since 1950, when less than $16 million was allocated. Notably, the NIH had its budget doubled during 1999–2003, and since then has largely been flat. 'It was a very obvious effort during the Clinton administration to increase funding for biomedical research in this country,' says Dr Elizabeth Nabel, MD, director of the NHLBI.

Historically, the NIH has devoted the majority of its funds for research to US universities and academic health centres, which make up the extramural grant programme. In that spirit, the NHLBI spends about 95% of its funds on the extramural programme and 5% on the intramural programme, which is on its own campus, somewhat like a university.

About 70% of the money directed at extramural research goes towards investigator-initiated research in which researchers spontaneously send their proposals to the Institute. Its another aspect that is rooted in tradition at the NIH of the way the government has funded biomedical research, and one that Dr Nabel says would cause an outcry among research investigators if it was changed.

'Investigator-initiated research has been a fundamental principle of US funding of biomedical research, really since the conception of the NIH and there is a good deal of consensus that that is the right thing to do for this country and we would like to continue it,' she says.

'Scientifically, those grants really do reflect very exciting and promising areas of science.'

The NHLBI does devote some its money each year to develop initiatives it is particularly interested in or that it feels may be missing from some of the investigator-initiated research, but it does not budget a certain number of dollars to any particular disease or subject matter.

Dr Nabel says: 'We aspire to fund the best science, done by the best scientists, with the least administrative burden. What we really

do is we look for the best scientific opportunities in all areas and we strive to achieve a balanced portfolio.'

The extramural research programme is managed by separate divisions for cardiovascular diseases, lung diseases and blood diseases, plus a Division of Prevention and Population Sciences (DPPS).

The Division of Cardiovascular Diseases (DCVD) is responsible for research on the causes, prevention and treatment of atherothrombosis, coronary artery disease, myocardial infarction and ischaemia, heart failure, arrhythmia, sudden cardiac death, adult and paediatric congenital heart disease, cardiovascular complications of diabetes, obesity, and hypertension. Biotechnological research is also covered, including genomics, proteomics, nanotechnology, imaging, device development, cell-, and tissue-based therapeutics and gene therapy.

Artificial heart, © NIH

In the fiscal year 2007, DCVD received 49.1% of the NHLBI's extramural funding, with lung diseases receiving 22.5%, blood diseases and resources 16.2%, and DPPS 12.1%. Heart and vascular diseases—which includes DCVD and DPPS—received 61.3% altogether. One of the most famous studies on heart disease funded by the NHBLI is the Framingham Heart Study (see box text).

All research proposals submitted to the Institute undergo an independent peer review process and are assigned a priority score. 'We fund all grants that have fundable priority scores and we don't cherry pick to fund X number of heart, X number of lung, X number of blood,' says Dr Nabel. 'We fund excellence.'

The Institute aims to keep the administrative burden for investigators to a minimum and is currently shortening the grant application. It also tries to keep timescales short, so that investigators are not left hanging for many months to hear about the status of their grant. And once a funding decision is made, the money is distributed swiftly.

Investigators submit an annual report on what they have done during the past year. While brief, it includes research findings, publications, patent applications that have been submitted or patents that have been issued.

Grants include Funding Opportunity Announcements, the Small Business Innovation Research/Small Business Technology Transfer Programme, plus targeted standalone workshops that generate research recommendations from the extramural research community.

These workshops are held when NHLBI staff identify an area of interest to the Institute and want to gain information from the scientific community about what is known in the area, what scientific knowledge gaps exist, and, whether or not it would be worthwhile for the Institute to be involved. If it transpires that there is an opportunity, the results of the workshop may feed into development of an initiative that would then be done extramurally.

Framingham Heart Study

The Framingham Heart Study, http://www.framinghamheartstudy.org/index.html is one example of the influential cardiovascular disease research funded by the NHLBI. It began in 1948 at a time when World War II veterans were returning to the US and rejoining the workforce. People were contracting heart disease but the aetiology was not clear, so the public health service decided to conduct a long-term epidemiology study to examine factors which contribute to heart disease in a community population. Framingham, MA, USA was chosen because there had been a high degree of community participation in the area for previous studies on tuberculosis.

Three generations of families are involved, who enrolled in 1948, 1971 and 2002, amounting to more than 10 000 subjects. Of the 5209 original subjects, about 500 are still alive.

The study was moved administratively to the NHLBI in the 1950s and in the fiscal year 2007 it was funded to a tune of nearly $3 million.

Dr Nabel says: 'Over the years there have been a number of landmark papers that have been published from the Framingham Heart Study that have really defined the base of prevention, diagnosis and treatment of cardiovascular disease.'

One of the first studies was a paper published in the 1960s by the first Framingham Heart Study director, Dr William Kannel.[1] 'It was the first paper to define heart disease risk factors – smoking, diabetes, cholesterol, blood pressure, family history,' says Dr Nabel. 'That was a hallmark paper which at least in this country has evolved over the years to influence education programmes such that I think you could probably stop anybody on the street now and ask them "what are the risk factors for heart disease?" and they'd probably be able to cite you at least two or three of them.'

While most of the NHLBI's extramural research funding does go to US bodies, anyone can submit a research project grant proposal, which will then undergo peer review and receive a priority score. Non-US applications that receive a priority score that places it in a fundable range will have their pay plan reviewed by the NHLBI's advisory council, which is comprised of outside experts. The aim is to determine whether it is in the best interest of the US taxpayer to have those monies go to an institution outside of the United States for its investigation.

Dr Nabel says: 'Often the factors that the advisory council consider is the innovation or novelty of the proposal—is this research that can't be done in the United States [or] is not being done in the United States—[and] that information gained from this proposal will lend useful information to the field. The intent is not to support research that is trying to duplicate work that is already being done in the United States.'

Dr Nabel believes it is a 'very hopeful and optimistic time' in biomedical research, especially for cardiovascular diseases. But with such big advances already made in cardiovascular research, won't the next steps be smaller and slower? 'I think it's hard to read at this juncture,' says Dr Nabel. 'Science moves forward by consensus, it moves forward by people sharing data, sharing insight. Sometimes progress is slow and then there is a discovery that suddenly appears that takes science to the next level and then progress is rapid.'

She adds: 'That's to me one of the exciting aspects of scientific research, that the process of discovery is exciting, and that there is always something new to learn, a new insight to be made. Conversations with colleagues are never dull.'

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Success stories

Actelion 'You need to follow the innovation where the innovation leads you'

Jean-Paul Clozel, CEO and founding member of Actelion, talks to Emma Wilkinson about how a vision for a different approach to research and development became a model for success

When four researchers at Hoffmann-La Roche decided to take the brave step of starting their own biopharmaceutical company they had little idea of the success they would have achieved a decade down the line. Yet according to the annual report for 2008, Actelion, based near Basel, Switzerland, produced operating profits of CHF 371.4 million (€245.1 m). Not at all a bad achievement for a company which at the start had no outside funding and relied solely on the savings of those four researchers. It is an even greater achievement when you consider the founding members started with a vision and a strategy, but no product.

Actelion Research Centre, Allschwil, Switzerland

Back in the 1990s, Dr Jean-Paul Clozel was heading a drug discovery group in the cardiovascular department at Hoffmann La Roche and along with his wife Dr Martine Clozel, a researcher also in the cardiovascular department, and two colleagues Dr Walter Fischli, a researcher, and Dr Thomas Widmann, head of clinical development in the cardiovascular department, he was considering going it alone. They shared a dream of a biopharmaceutical company that could quickly and efficiently develop new drugs for unmet clinical needs. One major difference they wanted to achieve was to avoid pigeon-holing a potential new drug into a disease before the science was clear. The idea was to have all the research and clinical development in one place so that sharing of ideas and decision-making could be done quickly and easily.

'At Roche, when we left, and it was true in many companies, there were very separate and isolated business units, for cardiovascular disease, and the central nervous system, and metabolism, and so on,' Dr Clozel explains. 'But when you do not know what a new receptor or target is doing, you should look at all the potential uses. You need to follow the innovation where the innovation leads you and so very often when you have a new drug you don't know where that drug is going to lead you.'

The team finally made the break with Roche—albeit a very amicable break—when the company decided not to pursue clinical trials with two very promising compounds they had been working on. At this point, the team knew what they wanted to achieve but did not have a product. Such was their belief that they had left well-paid jobs without any signs of funding

for their new venture and were heavily reliant on their own savings.

Actelion founders from left to right: André J. Mueller, Jean-Paul Clozel, Martine Clozel, Walter Fischli, Thomas Widmann

Fortuitously, they soon had a major stroke of luck that was to be the key to their success. Roche had decided to leave the cardiovascular arena and allowed Actelion to purchase the license for the two drug candidates they had developed while at the company—bosentan and tezosentan.

It was Dr Martine Clozel, working alongside Dr Fischli, who had realized the potential of a potent vasoconstrictor now known to be endothelin and had spent many years searching for antagonists as well as identifying the human receptors.

Bosentan and tezosentan, were the final result of that research and a year after the initial launch, the team at Actelion finally had compounds to work with and to show investors. It was the start of the development of Tracleer (bosentan)—now a cornerstone treatment for pulmonary arterial hypertension (PAH).

Tracleer

Dr Clozel is very clear that when they left Roche they did not have anything from the company—they were not a spin-off and the fact they were later able to obtain a license for the two compounds was a surprising development. 'We couldn't believe it, it was like a miracle,' he says. But it would not be accurate to paint a completely rosy picture from this point on. Although Tracleer proved useful in PAH, in the much larger market of chronic heart failure, the drug did not produce the expected results.

'We really believed that our drug would work in heart failure and the failure of the trial was a very big surprise for us. When we started the company it was something we really thought would work. That was our biggest hurdle.'

As a small company they had the advantage of being able to work fast; and since the first clinical trial to marketing of Tracleer it only took 26 months. But therein lay the next hurdle—at the time PAH was a little-known condition and the team had to get good at spreading the message. 'We realised that even if we have a very good drug, we need to spend money on marketing to inform the doctors because back then the market for PAH didn't exist. Even if you get a breakthrough, you still need to have the energy to communicate it.'

Dr Clozel is particularly proud that the company, which now employs 1900 staff worldwide, still follows that original vision.

'We have stuck to everything which was written in our first business plan, and it worked—innovation, science, and discovering only new drugs which would make a difference, not doing "me toos". A lot of failures happen because people try to adapt or change their strategy.'

He adds: 'You have to make your decisions based on the science—you should never make a decision based on financial reasons. PAH looked like a very small market when we started but the drug was so effective in this area it was a good decision. You have big financial constraints when you start a company and some people would like very fast returns but it does not pay because it's a long-term business, you have to think long-term.'

It may seem unbelievable now that the extent of their success caught them almost by surprise but the founders of Actelion knew there had been very few such successes in Europe compared with their US counterparts.

'In Europe we have very few of the huge universities like Stanford and Yale, which have a high level of discoveries and create a lot of opportunities to form these companies. Also Europe is not a unified market—we do not have the huge internal market they do in the USA. In the US people are used to success like Actelion, but in Europe people are more pessimistic—we need to be more optimistic, entrepreneurship is not as developed in Europe as in the US.'

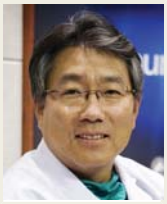
When asked what achievement highlights the level of success the company has now reached, Clozel points to the recent announcement that Dr Elias A Zerhouni, who late last year was director of the US National Institutes of Health (NIH), has been proposed as a new board member of Actelion.

'We are very pleased and very honoured. It's the best recognition that someone like Elias Zerhouni, who was head of the NIH under President Bush, has accepted the invitation to join our board.'

Emma Wilkinson, BSc MA, freelance medical journalist

Portrait statements of the International Associate Editors of the *European Heart Journal*

Seung-Jung Park, MD, PhD, Director of Interventional Cardiology at the Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea



Dr Park's major interest is interventional cardiology, but his experience also extends to coronary imaging.

In interventional cardiology, he is working on projects around the development of new coronary interventional devices and testing their clinical impact. 'In spite of an enthusiasm on the efficacy of drug-eluting stents, current stent systems still have problems of long-term safety, such as very late stent thrombosis,' says Dr Park. 'Therefore, I am trying to play an important role in the creation of the basic idea of a new stent system and the clinical trial to test its systems as an experienced clinician.'

In addition to the work in Dr Park's lab, worldwide there have already been important advancements in new coronary stent systems that avoid stent thrombosis, along with devices to treat structural heart disease, and imaging modalities to detect unstable plaques.

Dr Park believes that a new biodegradable stent may be able to eliminate the need for the metal portion of the stent or drug-polymer, subsequently leading to complete healing of the coronary vessel without the persistent inflammation shown with the current generation drug-eluting stent.

He also anticipates that, in addition, new percutaneous device systems for structural heart disease and for congenital heart disease, acquired valvular heart disease or arrhythmic disorders are about to be available in clinical practice.

As for coronary imaging, Dr Park says that new imaging modalities with invasive or non-invasive approaches now open a new era in detecting vulnerable lesions in patients who are apt to have heart attack and in predicting long-term outcomes of treatment. 'I hope our efforts may make our dream to completely treat and prevent coronary heart disease in the near future come true,' he concludes.

Stefano Taddei, MD, Professor, and Head of the Hospital Department of Internal Medicine, University of Pisa, Italy

Professor Taddei is conducting animal studies on the relationship between cyclo-oxygenase activity, angiotensin II, and endothelial function in experimental models of microcirculation.

His clinical studies cover three areas. First, the relationship between endothelial factors and atherothrombotic factors. 'We have recently demonstrated that there is a compensatory role of hyperpolarizing factors in determining not only vascular responses to endothelial agonists including acetylcholine, but also a compensatory role on tissue plasminogen activator (TPA) release in hypertensive patients, which is a condition characterizing reduced nitric oxide availability.'

The relationship between hypertension and arterial stiffness is another topic being investigated in clinical studies. This kind of alteration can represent a marker of cardiovascular events, and the aim is to understand whether arterial stiffness could be a clear target for antihypertensive treatment if longitudinal studies will demonstrate that improvement in stiffness is specifically associated with a better prognosis.

'The same concept can be applied, for instance, to the restoration of endothelium-dependent vasodilatation,' says Prof Taddei. 'At the present time we treat hypertensive patients according to the presence of global cardiovascular risk and the presence of classical target organ damage, including left ventricular hypertrophy or microalbuminuria. In the future its necessary to establish whether other markers, including vascular stiffness or endothelium-dependent relaxation, can be used as surrogate markers of clinical events.'

A third area of clinical research is left ventricular dysfunction, mainly diastolic dysfunction, in hypertensive patients and patients with heart failure. Again, the overall aim is to analyse and treat patients early to avoid the development of cardiac alterations that could lead to clinical heart failure.

Early detection of cardiovascular risk factors, especially subclinical organ damage, is very important, says Prof Taddei. 'We need very early markers of structural alteration because we are able to characterize patients by biochemical analysis of blood for diabetes and hypercholesterolemia and measure blood pressure for hypertension to establish if there are cardiovascular risk factors, but we don't know exactly why one patient will develop heart failure; another one will develop atherosclerosis or will develop renal dysfunction.' More mechanistic and genetic studies are needed to understand which combinations of genetic predisposition and risk factors will lead to coronary artery disease, he says.

Professor Cheuk-Man Yu, MD, FRCP, FRACP, FHKAM, MBChB, Professor of Medicine; Director (Clinical Sciences), Institute of Vascular Medicine; and Head, Division of Cardiology, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong

Professor Yu's research includes the assessment of new imaging technologies, especially new echocardiography techniques. He says: 'We would like to have more echo-related parameters that could help us to characterise disease in an earlier stage so that we

may help physicians and cardiologists for early disease prevention and to consider early initiation of treatment for the right diagnosis.'

The pathophysiology of heart failure is another interest, in particular the differences and similarities between systolic and diastolic heart failure. Although they share somewhat similar pathophysiology pathways, there are differences in terms of aetiology, severity of the disease, and prognosis after initiation of treatment.

In device therapy, Prof Yu says his group has been at the forefront of cardiac resynchronization therapy (CRT) for heart failure. 'We have performed a substantial amount of research in the assessment of cardiac mechanical dyssynchrony, reverse remodelling of the heart, exploring new indications, as well as assessing the relationship between electrical and mechanical dyssynchrony.'

Prof Yu's group is the first outside the US and Europe to conduct clinical studies on a new device called cardiac contractility modulation. The device is able to improve myocardial function in patients with advanced heart failure without any effect on systolic dyssynchrony.

In basic research, Prof Yu is looking at the pathophysiological pathway of myocardial fibrosis. He says: 'We are studying what are the cytokines that will stimulate fibrosis and exploring potential therapeutic options that will prevent myocardial fibrosis from happening'. They are also assessing the treatment efficacy of traditional Chinese medicine, which has anti-fibrotic properties.

Plans are underway for new projects in animal models that explore cell therapy, including stem cells and other types of cells, for end-stage heart failure.

A Chinese Genome project of more than 1000 patients with coronary heart disease is also being planned. It aims to identify whether there is any particular genetic locus that might contribute to the development of accelerated atherosclerosis and coronary heart disease.

Jens-Uwe Voigt, MD, PhD, FESC, Professor of Cardiology and Head of Echocardiography, Research Group of Myocardial Function and Haemodynamics, Department of Cardiology, University of Leuven, Leuven, Belgium

The group of Professor Voigt and his colleagues is working in the field of myocardial function imaging, mainly on echocardiographic strain and strain rate imaging.

A current focus of research is myocardial function in ischaemic heart disease and cardiomyopathies. His group conducts experimental as well as local and large multicenter clinical trials in these fields. In addition, they want to develop a robust method of estimating myocardial function in three dimensions, and a good and accurate model of describing ventricular wall stress, also in three dimensions.

Echocardiography particle image velocimetry is a fairly novel area, with just two or three groups in the world involved. Prof Voigt investigates the physiological and pathological flow patterns in the heart in the hope of having an impact on the treatment of valve disease and diastolic dysfunction in the heart.

Prof Voigt's aim is to gain a better understanding of myocardial function and the physiology of the heart. 'It's about finding better ways of assessing myocardial function in clinical settings so that you can diagnose and follow up even subclinical heart disease,' he says.

All of the activities are a cooperative effort, Prof Voigt says, and take place in the Medical Imaging Research Centre that works with many different departments, including cardiology, radiology, nuclear medicine but also physicists and engineers. Fellows from all over the world contribute to the work of the group.

'Echocardiography is now the acknowledged working horse of cardiology imaging, but it still has some constraints. Our work not only helps to better understand how the heart works, but also to improve the imaging techniques to assess its function.'

And while some colleagues hesitate to use the new imaging techniques, he believes the methods are gaining ground. 'There are, of course, always believers and non-believers, [but] I think the group of believers is growing [and] people are becoming convinced.'

Jennifer Taylor, medical journalist