Next-generation cardiovascular health tech

The team will develop wearable technology that can be used in daily life to capture more data than ever before. From symptoms and physical activity to heart function and air quality, this information could be used alongside genetic and healthcare data to transform diagnosis, monitoring, and treatment of cardiac and circulatory diseases through the creation of a digital twin. Led by Professor Frank Rademakers, Chief Medical Technology Officer at University Hospitals Leuven, Belgium.

A cure for inherited, killer cardiomyopathies

The researchers will develop a treatment that targets and silences the faulty genes responsible for cardiomyopathies. By combining a deep understanding of underlying genetic mechanisms with new technologies, the team aims to stop the progression of the damage caused by genetic heart muscle diseases, or even reverse the damage. Led by Professor Hugh Watkins, BHF Chair of Cardiovascular Medicine at the University of Oxford, UK.

The teams will now start work on full applications, with a winner expected to be announced at the end of 2020.

The four shortlisted teams have been given a small amount of seed funding and will spend the next 6 months putting together their full applications. These will be reviewed by subject experts and the three panels, and the teams will be interviewed by the IAP. Together, they will decide which proposal has the most promising chance of delivering a revolutionary advance towards better cardiovascular health.

Dame Anne Glover, President of The Royal Society of Edinburgh and Independent Advisory Panel member, said: 'All four shortlisted applications have identified big problems that desperately need to be addressed. They've submitted ideas that are different to anything the BHF has funded before, and the raw ambition, boldness and creativity of all teams is inspirational. Each member of the IAP brings unique expertise and vision from the world of science, research, and beyond. We're intrigued to see the teams' ideas flourish into full proposals and decide who will be given the chance to write their names into history books by transforming cardiovascular disease research'.

Professor Sir Nilesh Samani added: 'This is high-risk, high-reward research. We whole-heartedly believe in the transforming potential of the Big Beat Challenge to save and improve lives, both here in the UK and around the world. It represents the single biggest investment in pioneering science in the BHF's 60-year history. In an ideal world, we'd like to fund all four as each one has the chance to make a monumental impact'.

About the Big Beat Challenge

The Big Beat Challenge is a unique research funding award of £30m (about €35m, US$39m) that has brought together world-leading researchers and innovators to look beyond incremental gains and accelerate breakthroughs in cardiovascular disease that could transform lives across the globe. The shortlisted teams are international and multidisciplinary, with experts from countries across the world spanning the domains of academia, industry, and technology.

Find out more at bhf.org.uk/bigbeatchallenge.

Acknowledgements

Press release from Sciad Communications Ltd, with permission.

Conflict of interest: none declared.

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doi:10.1093/eurheartj/ehaa112

Cardiac centre of excellence

Introduction to the Department of Cardiology in Nanjing First Hospital of Nanjing Medical University, China

History and current status of Nanjing First Hospital

Nanjing City, used to be the capital of China during a period of 10 dynasties, located at the Yantz Triangle area, a location named as the most active economic zone.

Nanjing First Hospital (NFH) was built in May 1935, just before WWII. As an only government-run hospital during WWII, NFH contributed very much to the national recovery and growth since the beginning of WWII. The splendid achievements and unique characteristics of the Nanjing population have nourished this city and encouraged NFH to catch up with innovation in medicine.

Nanjing First Hospital consists of three campuses, one campus for the original tertiary NFH and two for Nanjing Heart Center (NHC),

Figure 1 Main building of Nanjing Heart Center.

Figure 2 Staff of Department of Cardiology in Nanjing Heart Center.

the only cardiovascular centre in the Yantz Triangle territory (*Figure 1*) from 2003 with both affiliated to Nanjing Medical University. Nanjing Heart Center now has a total of 332 beds, of which the Department of Cardiology has 200 beds, one coronary care unit (CCU), clinical trial centre, cardiac biological and molecular Labs, and intravascular imaging Core Lab (*Figure 2*). By March 2020, a total of seven Cath Labs and 400 beds will be available for the cardiology department.

Acknowledging the rapid development in interventional cardiology, NHC has utilized many percutaneous treatments for patients. There are more than 3500 coronary interventional procedures performed annually, in line with the growth of coronary artery bypass grafting (CABG). Clinical studies are the key element to strengthen NHC. The first randomized trial led by Professor Shao-Liang Chen, chief cardiologist at the hospital, the comparison of autonomous bone marrow mesenchymal stem cells with placebo for ST-segment elevation myocaridal infarction (STEMI) patients, has been cited 1500 times since its publication in *American Journal of Cardiology* in 2008.

Clinical research on coronary bifurcation stenting

While functioning as a National and Provincial Training Center from 2003, more and more patients with complex coronary artery disease

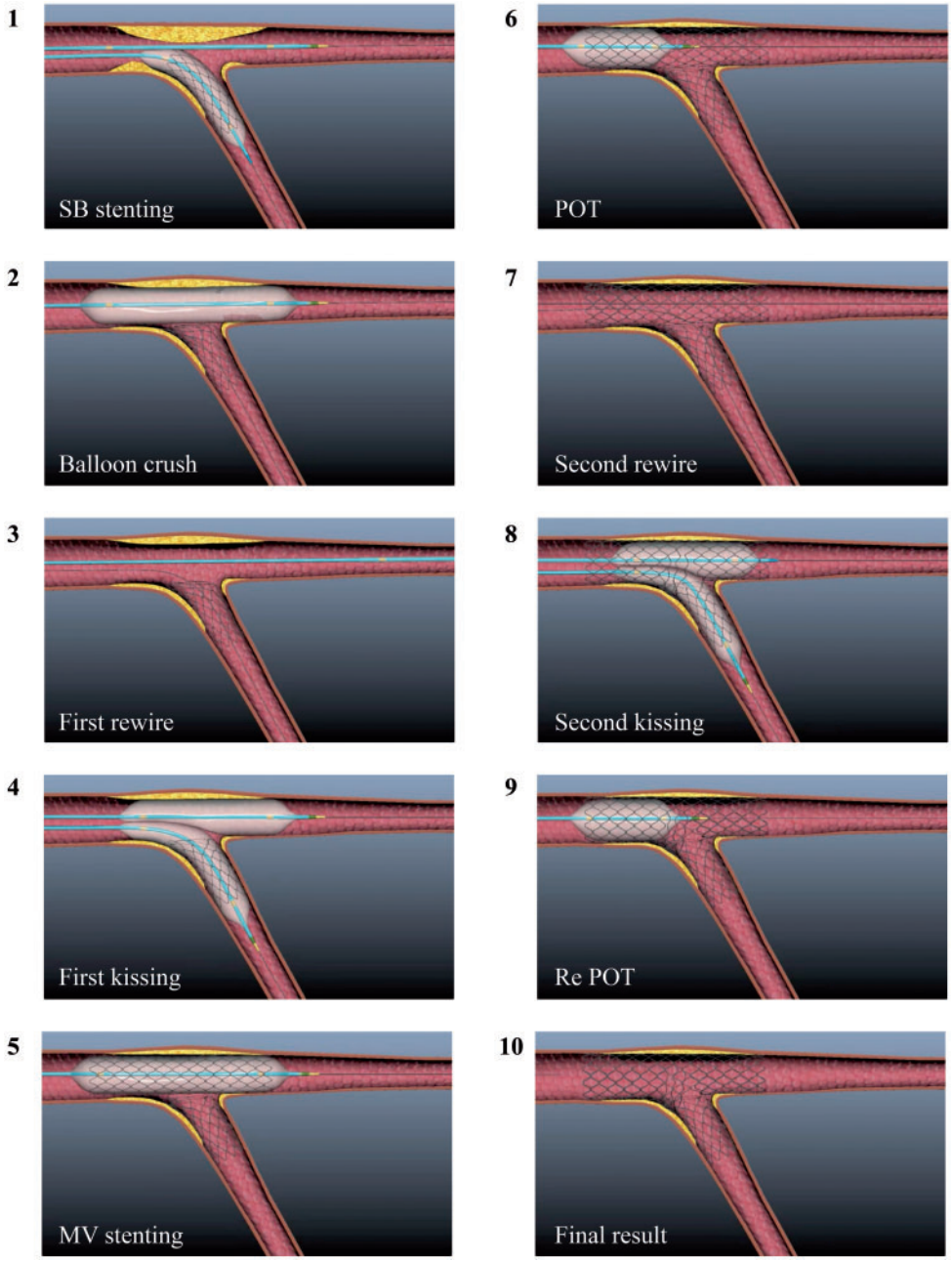

Figure 3 Central illustration of DK crush stenting.

are transferred to NHC. In particular, coronary bifurcation lesions rank number 1 among patients referred to Nanjing. Stenting coronary bifurcations is technically challenging and is usually suboptimal. The birth of classic crush stenting seems not to improve clinical outcomes much, as confirmed by later serial studies. From a pilot study by NHC showing lower rate of final kissing with subsequent higher rates of stent thrombosis and target lesion revascularization (TLR), Chen's team created the spectrum of novel double kissing (DK) crush stenting (*Figure 3*) in the autumn of 2004. The strength of DK crush over other mature two-stent techniques should be confirmed by clinical trials, a requirement paving the way of DKCRUSH I~DKCRUSH VII clinical studies.

Insight analysis into the DKCRUSH studies, DKCRUSH II was boldly designed to compare DK crush with provisional stenting, as the latter is still the main treatment recommended by modern guidelines. Although the primary endpoint at 1-year follow-up was comparable between studied groups, DKCRUSH II however, demonstrated a lower rate of TLR by DK crush. From this study, the NHC team first realized the importance of the bifurcation's complexity in bifurcation stenting trials. Since then, the DKCRUSH V study went to the podium on which DK crush stenting started to improve provisional stenting in patients with left main distal bifurcation lesions. Here, a very clear roadmap was emerging into our thoughts—that a simple but practical criterion differentiating really simple from real complex bifurcation

Figure 4 Live demonstration of left main bifurcation stenting from NHC to EuroPCR 2015.

lesions is mandatory. To this end, the NHC team performed its first step and introduced the utility of DEFINITION criteria, beyond previously proposed New Risk Stratification (NERS) and NERS II scores for left main distal bifurcation lesions. DEFINITION-based Phase II DEFINITION trial tested the reality of such friendly used criteria and reported significant reduction of mortality after DK crush stenting for patients with real complex bifurcations. This study unmasked the questions: were all bifurcation lesions complex lesions and if not, which bifurcations should be classified as complex?

Unfortunately, the next critical question is whether systematic two-stent (mainly DK crush) is better than provisional stenting for such complex bifurcation lesions? To address this concern, DEFINITION II trial will unblind the 1-year follow-up by November 2019. One reality we have to accept is the difference in stenting technique selection for complex bifurcation lesions between Eastern and Western countries, as reflected in our DKCRUSH serial studies and others. For example, side branch lesion lengths were longer from DKCRUSH serial studies than from other studies.

The left main coronary artery is different. While stenting left main ostial disease for lesions localizing at its body is equivalent to CABG, percutaneous treatment of left main distal bifurcation lesions is associated with an increased requirement of revascularization, supported by recently published EXCEL and NOBEL trials. The NHC team in 2011 proposed NERS score to stratify patients with left main disease, this score was further modified and simplified to NERS II score in 2013. Fundamentally, combination of or individual NERS and NERS II scores and DEFINITION criteria has shown a clue to help physicians select appropriate stenting techniques. In this regard, DKCRUSH III was designed and compared to DK crush with culotte stenting for left main distal bifurcation lesions. The improvement in clinical outcome by DK crush was sustained until 5-year follow-up.

DKCRUSH V is an RCT designed to compare DK crush with provisional stenting. We found a higher rate of target lesion failure in a provisional group, compared to DK crush, mainly due to increased events of target-vessel myocardial infarction (MI) at 1-year follow-up. More recently, 3-year clinical data will be soon published in *Journal of the American of College of Cardiology (JACC): Cardiovascular Interventions*, which shows a sustainable improvement in primary endpoint in DK crush group while compared to provisional stenting. Particularly, TLR at 3-year follow-up is also significantly reduced in DK crush group, consistent with our previous report in DKCRUSH II trial.

Taken together, serial DKCRUSH trials have clearly provided the solid evidence that for complex left main bifurcation lesions according to DEFINITION criteria, DK crush gives long-lasting results. Of course, intravascular imaging guidance for bifurcation stenting is critical to benefit patients, as identified by the ULTIMATE trial.

Some international colleagues are still praying for 'provisional' lesions that look like very complex and are reluctant to admire the stronger functions of DK crush, this follows one Chinese saying, 'deputing makes your mind wiser'.

We thank all friends and partners in the bifurcation community and educational platforms, such as Coronary Bifurcation Summit (CBS), Serbian conference on INtERventional cardioloGY (SINERGY) cardiovascular imaging and drug therapy, European Bifurcation Club (EBC), Transcatheter Cardiovascular Therapeutics (TCT), and Congress of the European Association of Percutaneous Cardiovascular Interventions (EuroPCR) (*Figure 4*), who are working with and supporting us in conquering coronary bifurcations.

Clinical research on pulmonary artery denervation

Similar to most developing countries, huge population and imbalanced economic status are two major factors limiting the nationwide promotion of healthcare policy in every corner. This is reflected by higher rate of diagnosis and treatments not complying with current guidelines. An example is the lower rate of target drugs for pulmonary arterial

hypertension (PAH), mainly because of an extremely high unfordable cost. Furthermore, controversies exist regarding the treatment effect of the target drugs for different pulmonary hypertension (PH) types, demonstrated by the unknown effect of PAH-targeted drugs for combined pre- and post-capillary PH secondary to left heart failure. Taken together, more aggressive and non-medication-based treatment may be useful for PAH or PH. To do so, the NHC team first proposed and reported on pulmonary artery denervation (PADN) for both PAH and PH in 2013. Then a follow-up study confirmed the improvement in 6-min-walk distance, haemodynamics and exercise capacity.

Experimentally, PADN induces sympathetic nervous injury and subsequently inhibits pulmonary arterial remodelling, a major pathology of PAH. We are very happy to announce that a national FDA-oriented PADN-CFDA study is ongoing and will report the benefits of PADN for Group I PAH in a randomized fashion. Any innovation is accompanied with concerns, suspicion, and questions. Those points are thought to be the main forces driving the scientific workflow.

Recently, Professor Hao Zhang reported significant improvement of surgical PADN for PAH animals, a finding that provided additional evidence for PADN within our community. Moreover, our PADN-V study has reported preliminary data showing significant improvements in 6-min-walk distance, haemodynamics, and mortality in Cpc-PH patients who are refractory to medication. However, it seems a long way to go before PADN will be approved by government(s).

Conflict of interest: none declared.

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doi:10.1093/eurheartj/ehaa233

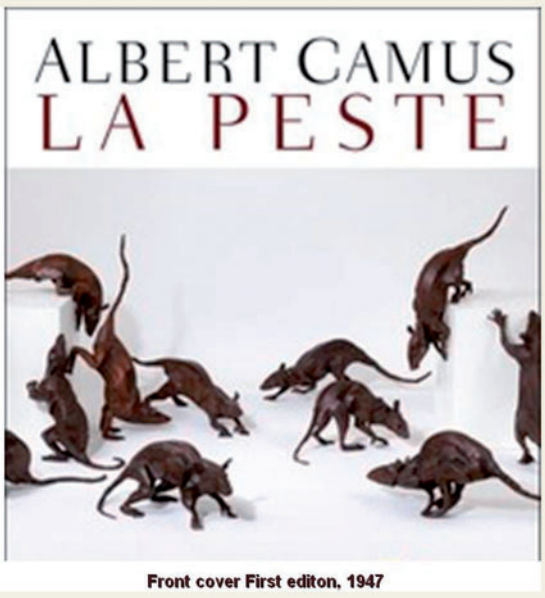
The Cardiologist at the time of Coronavirus: a perfect storm

> "When leaving his surgery on the morning of 16 April, Dr Bernard Rieux felt something soft under his foot. It was a dead rat, lying in the middle of the landing": The Plague (La Peste) by Camus[1]

This is the beginning of one of the most famous novels of the 20th century (The Plague by Albert Camus). The rats quickly became two, three, tens, and then hundreds, accumulating inside buildings and on roads. People became unsettled, but then finally, the death of the rats stopped them. 'The town breathed' says Camus, but only briefly. Before long humans began falling ill and as the number of sick increased, the scenario became more ominous.

The novel (as is often the case with a true masterpiece) is strikingly contemporary, not only regarding the dynamic of the infection, but especially to the spectrum of psychological and anthropological consequences this has on the protagonists. Indeed, every epidemic has profound effects on the social fabric and the psychology of the individual that we should reflect upon.

The Triumph of Death, Pieter Bruegel, 1562



Front cover First editon, 1947