Biological heart valves

A technology on the verge of another breakthrough?

Valvular heart disease: the problem

Valvular heart disease represents an important clinical problem worldwide. The prevalence of heart valve disease is increasing globally due to degenerative valve disease accompanying the growing ageing populations in the western world and due to the still inadequate treatment of rheumatic heart disease in the developing world countries. As a result, the number of heart valve interventions is expected to increase further over the coming decades, reaching more than 800 000 annual procedures worldwide by 2050. The most commonly performed semilunar valve replacement is for aortic valve disease, the aortic valve replacement (AVR), which is the basis for the following discussion.

The ‘evolution’ of heart valve prostheses

The first heart valve prosthesis—a caged-ball device—was implanted by the pioneer Charles Hufnagel on 11 September 1952. It was the beginning of the era towards mechanical heart valve replacements, a revolutionizing therapy for valvular heart disease. However, all of them were and are, associated with a major clinical limitation: the significant risk for thromboembolic complications and the associated need for life-long anticoagulation therapy. These shortcomings have stimulated the development of ‘biological’ valve replacements that circumvent the need for anticoagulation, bringing the replacement a step closer to healthy native valves.

Currently, the most commonly used valve for AVR is stented tissue (‘biological’) valves, derived either from bovine or porcine pericardium. The major advantages of this type of valve include the ease of implantation and the absence for the need of anticoagulation therapy. However, the main disadvantage is the occurrence of structural valve deterioration (SVD) mainly due to progressive calcific degeneration of the surface-treated biological materials, a phenomenon that is age-dependent.

In the 1990s stentless bioprosthetic valves made from native porcine valves became available. The main advantage of these valves was the improved haemodynamics compared with the stented counterparts. Accompanying the development of biological valves based on xenogenic tissues, the use of human, allogenic tissue has also received particular attention.

It was Donald Ross in 1962, who pioneered implanting an aortic homograft into the aortic position. In contrast to xenogenic tissue valves, homografts are less immunogenic and are therefore usually not fixated with glutaraldehyde. Instead, they are frozen for preservation without denaturizing pre-treatment.

The perceived advantages of homografts include lower thromboembolic risk and a longer durability than glutaraldehyde-fixed (xenogenic) tissue valves. In addition, it is speculated that they have a higher resistance to infection, even if recent reports do suggest higher rates of SVD than initially expected.

In striving to reduce the antigenicity of homografts, the technology of decellularized homografts has shown promising experimental and also initial clinical results. However, in spite of these promising data, the technology of human cadaver valves, with or without decellularization, is severely limited by the widespread organ scarcity and does not hold potential for having a major impact on heart valve replacement in the near future for a wider population of patients.

Only technologies such as in vitro heart valve tissue engineering approaches would be completely independent of donor organs or tissues; however, this technology has not reached the clinical phase yet.

The right choice: mechanical vs. biological prostheses

Choosing the type of valve according to the patient’s age remains to be the standard of care, but also remains a controversial issue. That is because randomized clinical trials have revealed inconsistent data on long-term survival when comparing mechanical with bioprosthetic valves. While the Veterans Affairs Cooperative Study (VACS) showed improved 15-year survival with mechanical vs. biological valves,9 the Edinburgh Heart Valve Trial (EHVT) showed no significant difference in the 20-year survival rate.

Both the European11 as well as the USA American12 guidelines recommend bioprosthetic valves for patients older than 70 years, when age is the only factor considered. However, differences exist concerning additional recommendations related to the choice of biological valves in the case of reoperations. These differences uniquely illustrate the controversy that still exists on whether choosing mechanical or biological replacements in specific groups of patients.

In recent years a significant tendency towards using more biological substitutes has been observed. A major reason for this development can be found in the technological improvement of new-generation bioprostheses. Recent independent trials reported that the freedom from SVD in different biological valve replacements to be 61–63% depending on the system used.13–15 Another controversy exists as to which type of biological valve tissue—pericardial or native valvular—is to be used for valve replacement. In a recent trial Rahimtoola reported that bovine pericardial valves showed significantly lower rates of SVD than porcine valves.
The introduction of transcatheter aortic valve implantations: a new age in heart valve replacement

In addition to the improvement of biological valves developing SVD, another major technological advancement impacted on the AVR field: the introduction of transcatheter aortic valve implantations (TAVI). Although open surgical valve replacement offers the most excellent long-term results, an increasing number of patients have no access to conventional open AVR due to their excessive risk profile.17,18

This clinical dilemma stimulated the development of transcatheter implantation technologies. Following the pioneering work by Anderson et al. in animals,19 Cribier et al. were the first to implant a valve prosthesis via the transcatheter route in humans in 2002.20 Finally, Webb et al. introduced the retrograde arterial approach via the femoral artery,21 which today represents the standard of care.

While this switch to the even less-invasive route was a major achievement for patients, it also had another major impact: it shifted the previously fully surgical domain of heart valve replacement from the field of cardiac surgery to the field of interventional cardiology (for detailed discussion, see also22).

According to expert opinions22 the technique of TAVI will rapidly emerge in the near future and may eventually become a standard therapy. Already now, randomized trials are ongoing to determine the proper use of TAVI in patients with lower AVR-risk profiles. The increase of endovascular procedures will also have a major impact on the type of valve implanted. So far no robust endovascular mechanical valve system is clinically available. As a result the spread of the TAVI technology will further support a significant shift towards biological valve prostheses.

The future of biological valves: the reasons for a success story

Taken as a whole, we have experienced a dramatic change in the practice of aortic valve surgery, also affecting the type of prosthesis used. The introduction of the TAVI technology and the late term freedom from SVD in different xenogenic tissue valves have both shifted clinical practice towards a broader use of bioprosthetic valves. In addition, the adapted guidelines with a more profound role for the patient in decision-making on the type of prosthesis, further supported this development.2

While in 2001 ~64% of all AVRIs were bioprostheses, this number increased to ~82% in 2011 according to the Society of Thoracic Surgeons (STS) database (adapted from 2)—a trend that is expected to continue in the future.

However, the rapid shift towards TAVI replacements also stimulated discussions on possible complications associated with the technology including (i) structural deterioration of the biological prostheses due to the crimping at the time of implantation with reduction of valve longevity23,24 and (ii) possible association with increased stroke risk due to the endovascular retrograde approach.25 However, both of these possible adverse events remain to be confirmed by large multicentre trials before a final statement can be made.

Therefore, at the moment biological valve prostheses appear to be on the rise, given the above-mentioned recent developments a further relative increase of bioprosthetic vs. mechanical valves can be anticipated.

Conflict of interest: none declared.

References

References are available as supplementary material at European Heart Journal online.
used bioprostheses are still similar to the valves introduced in the 1970s. Also the valves used for the rapidly emerging transcatheter techniques are still based on conventional bioprosthetic valves of xenogenic origin (for a detailed discussion of biological valves, see also the Weber and Hoerstrup article above, Biological heart valves section) limiting their long-term durability and therefore use in younger patient populations.

Requirements for an ideal heart valve substitute

Already in the 1950s, Dwight E. Harken, a pioneer in cardiac surgery, defined the essential characteristics of an ideal heart valve substitute and summarized them in the ‘Ten Commandments’ of heart valve replacement therapy. This included growth potential, sufficient structural durability, absence of thrombogenicity, resistance to infections, and lack of antigenicity. In principle, these commandments are still valid and so far are not met by the currently used substitutes.

Tissue engineering technologies aiming to create living autologous heart valves, with regeneration and growth potential, have emerged in recent years to overcome the limitations of today’s mechanical and bio-prosthetic heart valve replacements. However, when considering the clinically relevant requirements for such next-generation replacement procedures, further essential characteristics have to be considered:

1. First, an ‘off-the-shelf availability’ of the constructs appears to be essential, as most current approaches to heart valve tissue engineering are focusing on the in vitro manufacture of autologous cell-based, living constructs. Such methodologies involve highly complex multi-step biotechnologies and ‘just-in-time’ clinical implantation logistics. Furthermore, today’s complex regulatory requirements (tissue engineered implants are classified as ‘Advanced Therapeutic Medicinal Products’) additionally prohibit the rapid translation of such a technology into clinical practice.

2. Second, an intrinsic ‘regenerative capacity’ would be another essential characteristic of the ideal substitute given the emergence of minimally invasive delivery approaches, which have shown to harbour a risk for structural impairment of biological valve substitutes during valve delivery and even increasing the occurrence of dysfunctional degeneration of the fixed biological tissues involved.

Decellularization: the renaissance of a long-standing technology?

The first decellularized native and tissue engineered valves had already been investigated pre-clinically as well as in first clinical trials in the 1990s. The technology then experienced a setback following the failure of decellularized animal-derived heart valves in a series of children in 2003. However, stimulated by the ease of manufacture and the obvious advantages of the technology, the decellularization approach has experienced some renaissance in recent years for heart valve replacement therapy. This included mechanistic investigations in large animal models as well as implantation into paediatric patients.

However, the current nomenclature is somewhat misleading as the term ‘decellularized tissue engineered valve’ is partly used for both in vitro engineered neo-tissue valves based on isolated human cells, as well as native xenogenic or allogenic decellularized valves. It is misleading because in native decellularized valves no neo-tissue is ‘engineered’, it is rather a ‘recycling’ of already existing native tissue. Therefore, a more stringent use of the word ‘tissue engineered’ seems mandatory.

As part of this renaissance of the decellularization technology, controversial discussions are ongoing on whether these decellularized matrices are repopulated and remodelled in vivo resulting in an autologous tissue with regeneration and growth potential or, whether a decellularized homograft is ‘just another bioprosthetic heart valve’. Discussions on these questions are in full swing and at this point more scientific data on these specific aspects is obviously needed.

Decellularized in vitro engineered valves based on allogenic cells

Even if the use of decellularized homogencic or xenogenic valves holds its promise, they are associated with significant limitations. In homogenic valves, widespread scarcity of donor organs limits broad scale use. In xenogenic valves, remnant immunogenicity, and potential transmission of zoonoses remains an issue of debate. Therefore, recent studies have focused on creating homologous tissue engineered heart valves (based on human cells) followed by decellularization. These would represent ‘off-the-shelf’ replacement valves of human origin with an unlimited supply.

In the first preclinical trials, these valves have shown promising results in different large animal models, including sheep and non-human primates. Interestingly, in a direct comparison with human native decellularized valves, substantially more host cell infiltration was observed after only about a month in vivo, suggesting a higher and/or faster remodelling capacity of these matrices in the early stage.

In spite of these encouraging results, several obstacles still have to be overcome prior to clinical use, in particular optimizing the valvular design of in vitro engineered valves. However, given the above-mentioned shortcomings of allogenic/xenogenic decellularized tissue valves, this approach could provide a superior and clinically feasible solution to the availability of heart valve replacements for a larger patient population in the future.

Outlook for the future

Taken as a whole, the technology of decellularizing native tissues holds major potential for future therapeutic strategies in many fields of regenerative medicine. It seems that host cells have the ability to repopulate acellular tissues and thereby create viable, functional tissues in situ. However, independent of the current experimental and clinical success of human cadaver or animal-derived native decellularized tissue valves, these valves are still associated with the inherent limitations of xenogohomografts consisting of donor organ scarcity, calcific degeneration, residual immunogenicity, as well as zoonotic risks. Also, their potential for ‘growth’ and ‘in situ regeneration’ has not yet been clearly demonstrated by independent trials.

On the contrary, tissue engineered decellularized valves, even if being steps away from routine clinical use, do have the potential to overcome such limitations and may represent a significant step
towards a more ideal heart valve substitute according to the Ten Commandments of Dr Harken.

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References
References are available as supplementary material at European Heart Journal online.

Executive summary of the position paper of the German Cardiac Society on quality criteria for the implementation of transcatheter aortic valve implantation (TAVI)

Introduction
Accumulating scientific evidence and the current discussion on structural prerequisites for transcatheter aortic valve implantation (TAVI) in patients with aortic stenosis (AS) have prompted the German Cardiac Society to update its 2009 position paper.1 In particular, the discussion centred around performing TAVI without on-site cardiac surgery but with an on-site cardiac surgery service, which is practised in 6% of all TAVI procedures in Germany, gave reason for this document. The aims of this paper are to define the standards of good-quality care in the presence of a growing number of procedures and sites based on both the current reality of patient care and the updated scientific evidence. Since the German Society of Cardiothoracic Surgery did not contribute, the specific surgical aspects are not covered in detail.

Current transcatheter aortic valve implantation evidence
In 2010, the Placement of Aortic Transcatheter Valves (PARTNER) Cohort B trial demonstrated the superiority of TAVI over standard medical therapy in inoperable patients with high-grade AS.2 In AS patients adjudicated by cardiac surgeons as being operable but with high surgical risk, TAVI and surgical aortic valve replacement (AVR) were shown to be equivalent with respect to hard clinical endpoints in the PARTNER Cohort A trial.3,4 The US CoreValve High Risk trial actually revealed superior 1-year survival associated with TAVI as opposed to surgical AVR in elderly medium-risk patients.5

The German Aortic Valve Registry (GARY) reported in-hospital mortalities of 5.1 and 7.7%, and 1-year mortalities of 20.7 and 28.0%, in patients who underwent transvascular and transapical TAVI in 2011, respectively.6,7 The federally mandated German AQUA (Institut für Angewandte Qualitätsförderung und Forschung im Gesundheitswesen) registry recently documented an overall TAVI in-hospital mortality of 5.7% (transvascular 4.7%, transapical 8.3%) in 10 441 patients.

Indication
The indication for the treatment of patients with AS, aortic regurgitation, or degenerated surgically implanted bioprostheses is based on existing guidelines. Owing to the rapid development of the technique, the indication for TAVI vs. surgical AVR can no longer be made exclusively via the assessment of perioperative risk.

Assessment of perioperative risk
The German Cardiac Society endorsed the recommendation of the ESC Working Group on Valvular Heart Disease.8 Currently available scoring systems (STS, EuroSCORE) should be used for decision-making only as part of an integrated approach that includes an assessment of the patient’s overall clinical situation as well as comorbidities.

Differential indication
The joint clinical assessment by a heart team of cardiologists and cardiac surgeons is crucial to the indication for TAVI.

• Younger patients (<75 years) with a logistic EuroSCORE <10% and an STS score <5% should primarily be assigned surgical AVR.
• Patients ≥75 years with a high logistic EuroSCORE (≥20%) and an STS score ≥10% as well as patients ≥85 years (regardless of a risk score) should primarily be assigned TAVI.
• For all patients who do not meet the criteria outlined above, the therapeutic decision should incorporate the patient’s wish and be made by interdisciplinary consensus within the heart team.
• Currently, TAVI is regarded as the first-line therapy in many patients with a degenerated surgically implanted aortic valve bioprosthesis. An increased risk of repeat surgery is also present in many elderly patients with prior cardiac surgery.

The indication for TAVI must be established by consensus within the heart team. The interdisciplinary decision-making must be documented such that the final decision can be understood by all concerned parties, including the patient.
Transcatheter aortic valve implantation complications

Paravalvular leaks and higher-grade atrioventricular (AV) conduction blocks necessitating subsequent implantation of a permanent pacemaker are currently the most prevalent side effects of TAVI procedures. Initial studies with prostheses of the latest generation have shown that higher-degree paravalvular regurgitation is extremely rare. New AV conduction disturbances occur after TAVI in 4–65% of patients and necessitate pacemaker implantation in 6–27% of cases. Vascular complications or bleeding from the arterial access site are specific problems of transvascular TAVI interventions. The AQUA registry noted an 8.5% incidence of vascular complications. The majority of vascular complications do not require surgical intervention.

Peri-interventional neurological events and severe intraprocedural complications such as annular rupture, obstruction of the coronary ostia, or embolization of the valve prosthesis are rarely observed. The risk of periprocedural stroke or transient ischaemic attack was 2.9 and 3.3% in two meta-analyses of >10,000 TAVI patients each.9,10

Surgical conversion for serious complications during transfemoral TAVI occurs in 0.4–1.3% of cases. Mortality after conversion in the usually elderly and frail patients is high (28–67%).

TAVI harbours the risk of contrast-induced nephropathy. Newer prosthetic valves and increasing experience have been shown to markedly reduce contrast agent volume and associated nephrotoxicity.

New percutaneous valve designs

Recent years have witnessed various new valve designs as well as iterations of existing valves. Specific characteristics of new prostheses are a reduction in catheter diameter, enabling the implantation via smaller sheath systems, and increasingly improved control of valve positioning, including retrievability and repositioning of the prosthesis. Most importantly, new valve types have almost completely eliminated aortic regurgitation due to paravalvular leaks.

Criteria for transcatheter aortic valve implantation centres

Transcatheter aortic valve implantation centres need to meet certain personnel, technical, structural, and organizational requirements.

Personnel

Heart team

Transcatheter aortic valve implantation mandates comprehensive patient care within an interdisciplinary heart team. The core of the heart team comprises cardiologists and cardiac surgeons with adequate experience in the implementation of TAVI procedures and the management of complications. In addition, anaesthesiologists, intensive-care physicians, and specially trained medical support personnel should be on the heart team. To ensure the continuity of the TAVI programme, at least two cardiologists and cardiac surgeons each with TAVI experience must be part of the heart team.

Additional personnel and structural requirements must be met by a TAVI centre:

- At least two anaesthesiologists with at least 1 year of experience each in anaesthesiology during TAVI or cardio-surgical procedures.
- If the centre provides a cardiac surgery department, the interdisciplinary processes with the other members of the heart team must be arranged such that they meet the criteria of this position paper. As an alternative, a contractually documented cooperation with an external cardiac surgery department must exist that meets the criteria of this position paper.
- Documented standard operating procedures (SOPs) as well as experience must exist
  - in percutaneous or surgical treatment of vascular complications;
  - in multi-modality imaging for the planning and implementation of TAVI procedures;
  - in the diagnosis and treatment of neurological complications
- Experience in intensive care of cardiovascular or high-risk patients must be documented.

Cardiac surgery

(a) Serious complications requiring immediate surgical intervention occur rarely.
(b) Complications occurring belatedly after TAVI and requiring immediate surgical conversion are extremely rare.

Therefore, a postinterventional on-call surgical team that can arrive on site within 30 min is adequate.

Cardiology

Complications requiring the immediate percutaneous intervention by a cardiologist occur predominantly during the TAVI procedure itself. After TAVI, on-call service by an interventional cardiologist experienced in TAVI and the arrival of the interventional team within 30 min is adequate.

Other medical disciplines

Medical disciplines that should be available on-call for 24 h after TAVI and be on site within 30 min:

- Anaesthesiology
- Vascular surgery
- Neurology
- General surgery
- Radiology

In the intensive care unit, the continuous presence of a physician with a consultant on background service must be ensured by shift work.

Rooms

High-resolution X-ray imaging commensurate with a cardiac catheterization laboratory is a basic prerequisite for TAVI. A mobile angiography C-arm is not sufficient for TAVI procedures.

Adequate space must be provided to accommodate a heart-lung machine, workbenches for the preparation of the prosthetic valve, and an echocardiography unit. Transapical/transaortic TAVI necessitates a hybrid operating theatre.
During TAVI, left-heart circulatory support must be available in close vicinity.

Transcatheter aortic valve implantation procedures should be performed preferably in a hybrid catheter laboratory/operating theatre so that surgery can be performed immediately in the same room.

If no hybrid operating theatre is available on site, TAVI procedures may also be performed in a heart catheterization laboratory on the condition that it meets the hygiene requirements (at least clean-room air class Ib). The laboratory must be fully equipped for cardio-surgical intervention.

**Structural requirements**

At a TAVI centre, SOPs should be in effect ensuring that all patients with AS or a degenerated surgical bioprosthesis are discussed within the heart team. This applies irrespective of to which department the patient is admitted.

An intensive care unit with experienced personnel and equipment to treat cardiovascular diseases, particularly in the elderly, must be available on site.

**Organizational requirements**

For the optimal treatment of intra- and postprocedural complications it is necessary to establish emergency plans in the form of SOPs for the most frequent complications.

After the intervention, patients need to be monitored for at least 24 h in an intermediate or intensive care unit. Afterwards, telemetric ECG or ECG monitoring is required for at least 3 days.

**Criteria for transcatheter aortic valve implantation operators**

At least two cardiologists with comprehensive, long-standing (>5 years) experience in percutaneous coronary intervention and percutaneous treatment of valvular heart disease, TAVI in particular, should head the transvascular TAVI programme at a TAVI centre.

To qualify as a TAVI operator, at least 25 supervised transvascular TAVI procedures as first operator must be documented. In an ongoing TAVI programme, every operator must perform at least 25 TAVI procedures annually to document continuous practical expertise. A TAVI operator must have particular experience in the management of acute complications.

For emergency cardiac surgery, a cardiac surgeon and a perfusionist must be available without delay and nearby during any TAVI procedure.

**Certification process**

Certifications are necessary for the TAVI centre as well as the TAVI operators and must be renewed every 3 years. Participation in an independent national quality registry (e.g. GARY) is obligatory for any registered TAVI centre.

The minimum number of TAVI procedures performed at the centre should be 50 per year.

If there are to be staff changes within the heart team or structural changes within the TAVI centre, this information must be provided to the certification board of the German Cardiac Society within 12 weeks.

These recommendations on quality criteria for the implementation of TAVI procedures should be updated on a regular basis in accordance with current scientific evidence or at least every 2 years.


**References**

References are available as supplementary material at European Heart Journal online.
Computing in Cardiology (CinC)

A report from the 41st Annual CinC meeting in Cambridge, MA, USA, held on 7–10 September 2014

The European Society of Cardiology, through its Working Group 15 (e-Cardiology), has had a long association with Computers in Cardiology which it has recently been renamed Computing in Cardiology (CinC). Indeed, the annual Computing in Cardiology meeting is endorsed by the ESC through WG15. Professor Paul Hugenholtz, a former President of the ESC, helped to establish the CinC Annual Meeting.

This year, the 41st Annual CinC Meeting was held in Cambridge, Massachusetts. The local organizing committee, guided by Dr Roger Mark following the illness of George Moody, was mainly drawn from the staff of MIT/Harvard University. Approximately 350 delegates attended the meeting, which was the largest number yet held outside of Europe. This is a reflection on the meeting itself and the importance which computing techniques now play in everyday cardiology.

From automated ECG interpretation to MRI, echocardiography and support for interventions and ablations among other things, computer-based methodologies have an enormous role to play. The annual meeting of CinC is therefore a time when engineers and clinical scientists gather to discuss how such investigative technologies can be enhanced.

Prior to the opening of the 2014 meeting, there was a Sunday Symposium at which leading presentations on Data-driven Learning, Discovery, and Innovation were delivered by leading world authorities. Traditionally, CinC begins with presentations by four competitors, selected this year after peer review of over 50 entries for the Rosanna Degani Young Investigator Award, which was won by Matthijs Cluitmans (Maastricht, Netherlands).

This opening plenary session was then followed for 3 days by four sessions in parallel, which covered a large number of topics. There were sessions on cardiac arrhythmias, blood pressure, infarction and ischaemia, modelling, etc. There were two large poster sessions, as many engineers and research students opt to present their results in this way. This is one of the characteristics of CinC. Another is that the Proceedings of each annual meeting are freely available on-line at http://www.cinc.org/archives.shtml.

One other special item is the PhysioNet Challenge where a problem is set many months in advance of the meeting giving competitors time to develop a solution. This year the challenge related to Robust Detection of Heart Beats in Multimodal Data gathered from bedside monitors and similar devices that record a variety of physiological signals. This annual PhysioNet/CinC challenge (http://physionet.org/challenge/2014/) always proves immensely popular and the databases used by competitors are of worldwide importance to researchers and industry in the development of robust algorithms for incorporation into products. There were three winners, Marcus Vollmer (Greifswald, Germany), Thomas De Cooman (Leuven, Belgium), and Alistair Johnson (Oxford, UK).

The Chairman of WG15 has been an ex-officio member of the Board of Directors of CinC for many years and lately, Professor Marek Malik, the previous Chairman of WG15, suggested that reciprocity should be sought. This has recently been agreed by the ESC and now the President of CinC will in future attend the WG15 Nucleus meetings. Thus, the links between WG15 and CinC have been strengthened even further.
People’s corner: Prize award

Dan Atar receives Norway’s Storstein Prize for 2014

The Storstein Prize, the highest Norwegian scientific medal of honour in cardiology, was presented to Dan Atar, Professor of Cardiology at the Oslo University Hospital, Norway. This distinction is given annually by the National Cardiac Society of Norway.

According to the statutes of the prize, this merit is granted to an active, preferably young researcher who has spearheaded cardiovascular research in Norway. The prize is named after the late Professor Ole Storstein recognized as the mentor of Norwegian cardiology.

During his laudatio, held at the 2014 annual autumn meeting of the NCS in Oslo, Dan Atar recalled the landmarks on his way leading to his most important research findings. While at The Johns Hopkins University in Baltimore, MD, USA in the early 1990s, as well as during his subsequent training positions in Basel and Zürich, Switzerland, he discovered that the troponin molecules showed degradation following myocardial reperfusion after a mild and fully reversible episode of myocardial ischaemia, the so-called reperfusion injury phenomenon.

This was long before the troponins were introduced and used in clinical practice as today’s most important biomarkers of myocardial injury. In his subsequent research, Dan Atar has led large research consortia in order to elucidate—in a multicentre setting—whether patients suffering from myocardial infarction would be amenable to protection from reperfusion injury in their myocardium.

In his final reflections, the clinician-scientist thanked the entire cardiology community in Norway for having offered him outstanding research opportunities.

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The Storstein Prize 2014, painting by artist Dag Hol was presented to Prof. Dan Atar by Prof. Svend Aakhus, Chair of the Scientific Committee of the NCS