

## Need for new materials, biofunctionalization and non-surgical heart valve technology

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### INTRODUCTION

A number of recent reviews and original papers have demonstrated that transition from non-surgical heart valve defect repair from bench to bedside is a reality. Although this is also the case for atrioventricular valves, research and clinical applications are clearly prevalent among tubular system valves<sup>[1]</sup>. In any case of new catheter-based technique, a precise imaging technique is essential (e.g. magnetic resonance imaging and/or transesophageal echocardiography).

### VALVES PLACED WITHIN TUBULAR SYSTEMS

Bonhoeffer was the first to perform transcatheter implantation of a prosthetic valve into the pulmonary valve position in 2000<sup>[2]</sup>. Cribier is credited with pioneering the concept of transcatheter aortic valve implantation (TAVI), with the first such procedure performed in 2002<sup>[3]</sup>. Although TAVI has not gained worldwide acceptance, several thousands of these percutaneous prostheses have been implanted. Although there are several modifications, they are all bioprostheses with the dual components of a metallic carrier (i.e. the stent) and a prosthetic valve of animal origin. To date, almost 10 different designs of these prosthetic valves have been developed for catheter-based implantation. Of these, the CoreValve ReValving system has become the most widely used<sup>[4]</sup>. Its design derives from original experiments by

### Abstract

Transition from non-surgical heart valve defects repair from bench to bedside is a reality. Some biological material-based designs for transcatheter aortic valve implantation are ready for use. Their drawback, however is their unknown functional as well as structural durability. Moreover, research on new non-biological materials is essential to replace classical animal-derived sources of human heart valve prostheses.

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**Key words:** Biomaterials; Aortic valve; Non-biological materials; Heart valve prosthesis

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Andersen *et al*<sup>[5]</sup> undertaken in 1992. The only difference is that the current valvular prostheses are self-expandable and do not use the hydraulic force of the balloon catheter to expand. The only justifiable indications include the impossibility of employing a standard heart surgery technique, or too high surgical or anesthesiology-related risks as determined by the hospital's institutional review board. Considering the fact that a target group of such patients no doubt exists, surgeons have sought to minimize the operating field by creating the transapical approach. However, it should be kept in mind that the conventional cardiac surgical procedure definitely serves as a gold standard. In terms of valve prosthesis durability, mechanical components are clearly superior to biological ones, even at the cost of risks associated with permanent anticoagulant therapy. As all biological materials including surgically implanted prostheses are subject to degeneration (e.g. leaflet thickening, calcium deposition or loss of physical properties), it is mostly elderly patients who are indicated for bioprosthesis implantation. With biological prostheses inserted using a catheter, emphasis is initially placed on increased mechanical trauma during the crimping process, and its subsequent catheter-based passage to the ultimate position. It was for this reason that all pilot studies enrolled patients of advanced age with limited life expectancy, which made it impossible to define valve durability clearly.

In conclusion, the design of current valves intended for placement in tubular structures has been refined and is functional and justified for a limited period of time. Moreover, there is no evidence of extensive randomized comparison between more valve designs, even if they have the same principle of action (i.e. Edwards Sapien *vs* CoreValve, when both are derived from Andersen's original model). The task in the years to come is to search for novel materials that are not prone to degeneration in the way that denatured tissues of animal origin are. These will most likely be polymers employed in the manufacture of biofunctional nanofibers. These materials are expected to offer prolonged durability compared with that seen in current biological valves, and feature all the possible attributes of the ideal implant in blood flow (biocompatibility, fatigue resistance, elimination of the risk of valve apparatus fracture, resistance of immunity-mediated processes, resistance to calcium deposition, and antithrombogenic surface). It would then be sufficient if the novel material possesses at least the properties identical to those seen in current components of mechanical valves<sup>[6,7]</sup>. Several materials that have shown promise to meet these requirements are currently available<sup>[8,9]</sup>. The introduction and widespread use of such materials will most likely change the position of bioprostheses, whatever their design, in the area of cardiac valve surgery, as well as TAVI. Efforts are also being made to miniaturize the biotechnology<sup>[10]</sup> so that it could be combined with polymer engineering, thus giving additional biofunctionalization. The goal is thus set, the needs are defined, and the process is underway, but the product has not yet

been developed<sup>[11]</sup>. However, it seems it is just a matter of time before one becomes available.

## NON-TUBULAR SYSTEM VALVES: ATRIOVENTRICULAR VALVES

This issue is addressed here only for the sake of providing a comprehensive overview. Unlike tubular valves, those placed in between two moving compartments are much more complicated. Although the left heart is much more important than the right, the tricuspid valve is the most intricate structure (reduced wall thickness compared with the left heart, three papillary muscles, a larger annular area, different coaptation geometry). Still, it is the mitral valve that has long attracted more attention, both in experimental and clinical studies designed to manage valve repair non-surgically. Interest in balloon mitral commissurotomy, on the other hand, has waned completely as attention has mainly focused on defects with regurgitation. Also, major technical advances have been made in the mechanical, mostly metallic, components. It seems no progress has been made to date in the field of biomaterials. Non-surgical catheter-based techniques seem to be feasible *via* the left ventricular apical approach or the classical trans-vessel approach. The first approach has been attempted at mitral valve stabilization in the presence of papillary muscle rupture in a patient who developed cardiogenic shock after acute myocardial infarction<sup>[12]</sup>. Other techniques that have found widespread use include those that connect both mitral leaflets using a clip or suture (Evalue edge-to-edge clip, and the Edwards MOBIUS system) and give rise to a double orifice mitral valve<sup>[13,14]</sup>. Also relatively frequent are techniques that are designed to shift the anterior mitral leaflet towards the center of the annulus, thus making use of the deformation force of a body advanced into the coronary sinus. A number of modifications of the approach and a variety of devices have been reported; however, relative functionality has only been achieved in cases that do not involve annulus dilatation. Other catheter-based approaches are only of marginal importance and still under development, as are mini-surgical procedures. Although attempts at anchoring the bioprostheses in the stent carrier have been made, they are associated with excessive risks of stent migration, embolization, endoleak and interference with surrounding structures. Added to this are all the drawbacks of biomaterials listed in the section addressing the issue of bioprostheses placed within tubular structures.

The all-out effort within this exciting area of research, experiments, and initial clinical experience is far from being over. A true breakthrough will not come until a novel material is discovered that has the properties of biological tissue coupled with the durability of mechanical prosthetic valves currently used in cardiac surgery. This is as yet an unrealized goal for the coming years.

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