

Next-Generation Transcatheter Aortic Valves

A preview of the latest devices that are expected to change the practice of transcatheter valve replacement.

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With the recent US Food and Drug Administration approval of the Edwards Sapien valve (Edwards Lifesciences, Irvine, CA) and initiation of the pivotal trial studying the CoreValve device (Medtronic, Inc., Minneapolis, MN), transcatheter aortic valve replacement is poised to become a common procedure for treating patients who are at high risk for surgical replacement.¹ Although these two devices have a significant market lead time over competitors, a number of innovative technologies promise to transform the field of transcatheter aortic valve replacement. These valves range from significant in-human experience (eg, Direct Flow [Direct Flow Medical, Inc., Santa Rosa, CA] and Lotus [Boston Scientific Corporation, Natick, MA]) to first-in-man proof of concept (eg, JenaValve [JenaValve Technology, Inc., Wilmington, DE] and Portico [St. Jude Medical, Inc., St. Paul, MN]) to early stage conceptual development (eg, ValveXchange [ValveXchange, Inc., Aurora, CO]). During the next several years, a number of these devices may enter pivotal clinical trials and change the landscape of transcatheter aortic valve replacement.²

Although the clinical experience with the Edwards Sapien and CoreValve transcatheter valves has generally been excellent, both devices have several limitations. Neither device is repositionable, making deployment a “one-shot” procedure with an attendant risk of suboptimal positioning or embolization. Both devices can also have significant paravalvular leak after deployment, which may be associated with heart failure and late

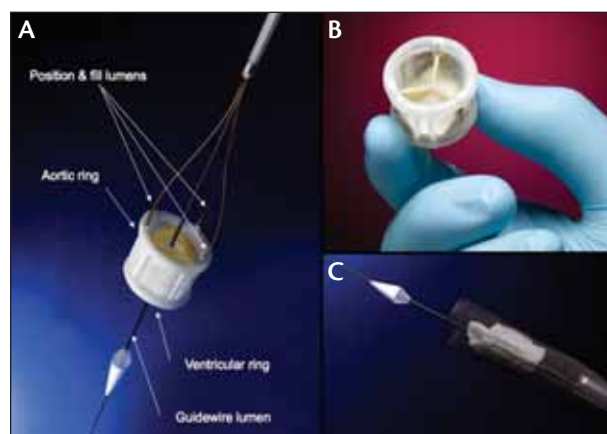


Figure 1. Direct Flow valve (A). The Direct Flow valve is constructed of bovine pericardial leaflets sewn into Dacron fabric. The ventricular ring is inflated first to allow seating in the left ventricular outflow tract, followed by inflation of the supra-ventricular aortic ring. The three position and fill lumens are initially filled with contrast material, which is then exchanged for an epoxy. The latest generation device with modified ring and strut construction is shown in profile (B). The device includes a basket that allows full retrievability (C).

mortality.³ Furthermore, some current valve technologies, especially the CoreValve, have an increased incidence of complete heart block necessitating pacemaker placement.^{4,5} Next-generation transcatheter aortic valves attempt to circumvent the limitations of currently available technologies in three ways: deliverability, retrievability, and anatomic positioning.

DIRECT FLOW VALVE

The Direct Flow valve dramatically differs from other valves that are under development (Figure 1). The leaflets consist of bovine pericardial tissue with an anticalcification treatment, but the support structure is nonmetallic and constructed from Dacron fabric.⁶ The aortic and ventricular cuffs are independently inflatable, allowing repositioning and retrievability before implantation. During deployment, the cuffs are initially inflated with diluted contrast to verify positioning and adequate expansion. Specifically, the ventricular cuff is inflated first and pulled against the ventricular aspect of the aortic annulus followed by inflation of the aortic cuff. Once positioning is confirmed, the diluted contrast is exchanged for an inflation medium composed of a radiopaque epoxy that rapidly solidifies and forms the support structure.

This treatment approach has the advantage of accurate sizing and full retrievability before infusion of the inflation medium. There is no need for rapid pacing because the valve functions as soon as the ventricular cuff is inflated. A potential disadvantage of the technology is that, in some cases, the polyester cuffs may not exert sufficient radial force on the aortic annulus. It is therefore necessary to perform adequate balloon valvuloplasty before device deployment to ensure expansion of the stenotic leaflets and creation of a circular annulus.⁷

After extensive preclinical studies, first-in-man implantation of the Direct Flow valve was reported in 2006. A subsequent case series from Germany reported on 31 patients who underwent implantation in 2007 to 2008 as part of a clinical registry.^{8,9} Twenty-two of these patients had successful device implantation. Reasons for not achieving implantation included excessive tortuosity of the aorta, a bicuspid valve, or excessive calcification of the leaflets or annulus. The latest-generation device has recently been designed with an 18-F profile, increased radial strength, and a simplified retrieval mechanism. This device is now undergoing clinical testing in Europe for a CE Mark approval study.

LOTUS VALVE

The Lotus valve is a nitinol-based self-expanding aortic valve with bovine pericardial leaflets (Figure 2). The lower part of the prosthesis is coated with a polyurethane seal-

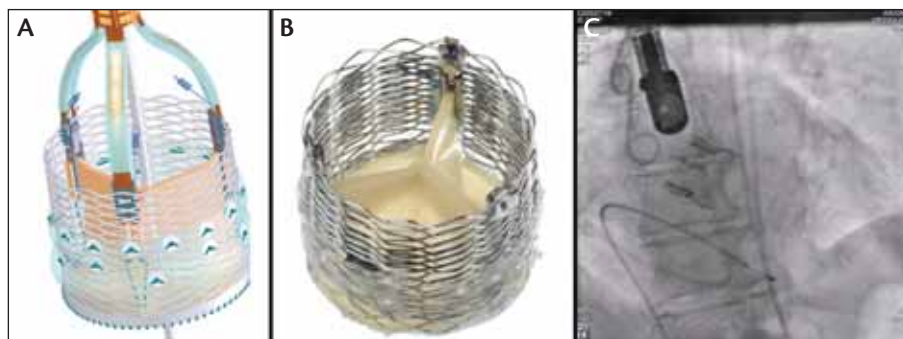


Figure 2. Lotus valve (A). The Lotus valve consists of bovine pericardial leaflets and a nitinol frame. Three arms assist in alignment, and during deployment, the device shortens and expands in diameter, thereby increasing radial strength. The nitinol frame encompasses the leaflets (B). Also note the lower polyurethane sealing membrane, which may minimize paravalvular leak. Fluoroscopy of a deployed device shows alignment with the aortic annulus and relative positioning of the three radiopaque arms (C).

ing membrane, which minimizes aortic paravalvular leakage. During device deployment, the device shortens in length thereby decreasing the nitinol cell areas, resulting in greater radial force and expansion. The valve is then locked into place using a buckle mechanism that is attached to the inner frame. It is fully retrievable until final deployment, and there is no need for rapid pacing during the procedure because there is flow around the valve or through the leaflets during positioning.

Successful implantation of the Lotus valve was first reported in Germany in 2007 in a 93-year-old woman with multiple comorbidities.¹⁰ The patient required implantation of a permanent pacemaker due to complete heart block but was doing well at 3-months follow-up. Subsequent refinement of device design resulted in a simplified and lower-profile 18-F system that underwent clinical testing in Europe in 2010, with 12 patients enrolled.¹¹ Based on these results, the device will soon enter testing for European CE Mark approval.

ENGAGER

The Engager transcatheter valve (Medtronic, Inc.) consists of bovine pericardial leaflets mounted to a self-expanding nitinol-based frame (Figure 3). The frame has three support arms that anatomically align the prosthesis in the aortic sinuses. These arms provide additional axial support to the valve prosthesis in addition to radial fixation. The frame also has a fluid dynamic shape that may also minimize pressure recovery across the valve.

Transapical implantation of the Embracer valve was first performed in 2008.¹² A follow-up feasibility study of 30 patients was conducted from 2008 to 2009.¹³ Four patients in this study developed aortic dissections, with three requiring operative repair. These dissections result-

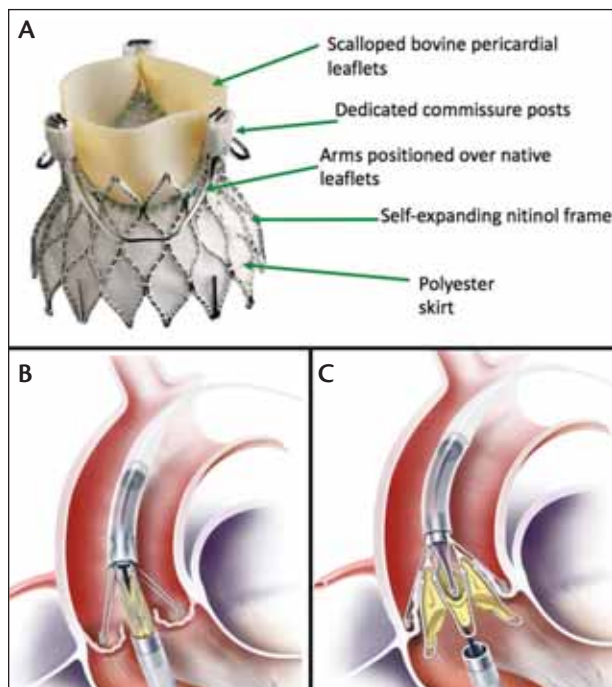


Figure 3. Engager valve and JenaValve. The Engager trans-catheter aortic valve has a self-expanding nitinol frame and a polyester skirt (A). The frame has arms that encompass the native leaflets. The JenaValve, as shown in transfemoral conceptualization, also has arms that engage the native leaflets (B). The JenaValve nitinol frame expands around the leaflets, resulting in an anatomic orientation and subcoronary positioning (C).

ed from one of the device posts injuring the posterior wall of the aorta during implantation due to acute ventriculoaortic angulation. These findings led to redesign of the device, with a more flexible delivery shaft and a protective cover over the device posts. The redesigned device is currently undergoing feasibility studies.

JENAVALVE

The JenaValve device has been developed for both transfemoral and transapical implantation, although, to date, only the transapical experience has been published. The device has a self-expanding nitinol frame with three “feelers” that orient the valve anatomically in a subcoronary position (Figure 3). Similar to the Engager valve, this positioning improves the axial and radial strength of the prosthesis. The feelers also act as a clip system to embed the native leaflets between the feelers and the stent body, which helps orient the device at the correct level and possibly minimize the development of conduction abnormalities. After initial animal experiments, the first-in-man results were recently published.^{14,15} A CE Mark pivotal study for the transapical device

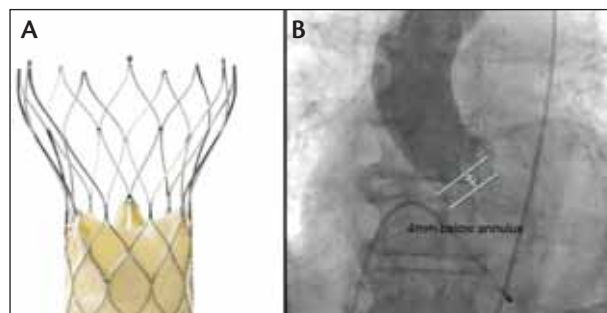


Figure 4. Portico valve (A). The Portico valve has an open-cell nitinol frame that rests along the aortic annulus. The valve is positioned low on the frame, thereby minimizing protrusion into the left ventricular outflow tract. Fluoroscopy of the first-in-human placement showing that the device rests only 4 mm below the annulus (B).

is currently underway, and the company plans to start a transfemoral program in 2012.

PORTICO VALVE

The Portico valve is a pericardial valve that is mounted on a self-expanding nitinol system (Figure 4). It is very similar in appearance to the CoreValve system; however, the leaflets and a tissue cuff are located low on the support frame, thereby minimizing device protrusion into the left ventricular outflow tract and reducing the incidence of paravalvular leak. The valve is resheathable and redeliverable before deployment. Although the support structure covers the coronary ostia, the open-cell design is meant to allow easy access to the coronary arteries. First-in-man experience with transapical implantation was reported in mid-2011, and European trials are anticipated to start in 2012.¹⁶ The device is currently designed as a 24-F transapical and 18-F transfemoral system; there are plans to initiate transfemoral studies in the next year.

ACURATE VALVE

The Acurate valve (Symetis, Ecublens, Switzerland) is a porcine valve that is mounted on a nitinol stent (Figure 5). The stent has stabilization arches that extend into the aortic root for optimal positioning. To minimize paravalvular leak, the device also has a polyester skirt that lines the ventricular end of the prosthesis. Initial transapical experience with 40 patients has been reported in Germany, with 38 patients having successful device implantation. A multicenter pivotal trial is currently planned for European CE Mark approval.¹⁷

HEART LEAFLET TECHNOLOGY

The Heart Leaflet Technology valve (Bracco Diagnostic, Inc., Princeton, NJ) consists of a porcine pericardial valve mounted on a nitinol support structure (Figure 5). The

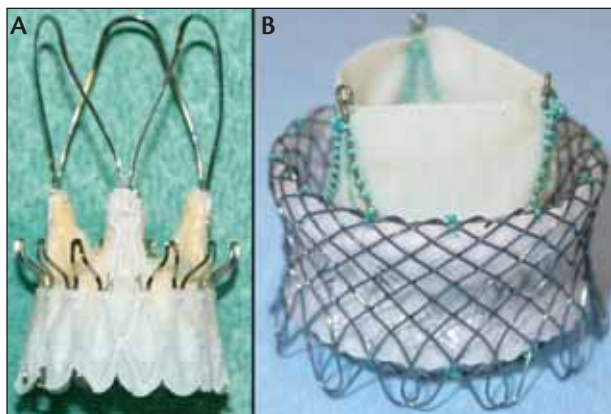


Figure 5. Acurate and Heart Leaflet Technology valves. The Acurate valve has a nitinol frame and a polyester skirt to minimize paravalvular leak (A). The Heart Leaflet Technology valve consists of a nitinol support structure and a braided polyester liner (B).

valve leaflets are embedded in a braided polyester liner. This design separates the valve from the support structure, resulting in a lower-profile (17 F) device. Initial human studies have been reported in four patients. During the initial experience, the backstop used to position the device caused mitral leaflet entrapment and left ventricular perforation, and the device is currently undergoing redesign and testing before initiation of further human implantations.

OTHER AORTIC VALVE TECHNOLOGIES AND CONCEPTS

A number of other transcatheter aortic valve concepts are under development and nearing first-in-man status. The ValveXchange system is based on a permanent implant support system with exchangeable leaflets. Other valves, such as the AorTx (Hansen Medical, Inc., Mountain View, CA), Enable (ATS Medical, Inc., Minneapolis, MN), and Perceval (Sorin Group, Milano, Italy) valves, involve surgical removal of the degenerative aortic valve but a sutureless implant. Alternative surfaces in devices such as the PercValve (Advanced Bioprosthetic Surfaces, Ltd., San Antonio, TX) include nanosynthesized nitinol membranes, which may endothelialize more rapidly. Although most of these valves have passed the proof-of-concept stage, extensive clinical testing with rigorous endpoints will be necessary before these and all other devices in development reach widespread clinical use.

SUMMARY AND FUTURE DIRECTIONS

A number of next-generation transcatheter aortic valves will undergo pivotal clinical trials in Europe and the United States during the next few years. Each of the valves under development represents potentially significant innovation

that could simplify transcatheter aortic valve implantation and improve clinical outcomes. Despite significant technological advances, next-generation transcatheter aortic valves have still not addressed other important niche areas of aortic valve disease. Future areas of innovation will include technologies specifically designed for treatment of bicuspid aortic valve stenosis, transcatheter valve implantation for treatment of aortic regurgitation, transcatheter aortic valve stent grafts, and valve-in-valve technologies. Ultimately, these new technologies will improve patient care and provide treatment options to patients who were previously thought to be too high risk for any surgical intervention. ■

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