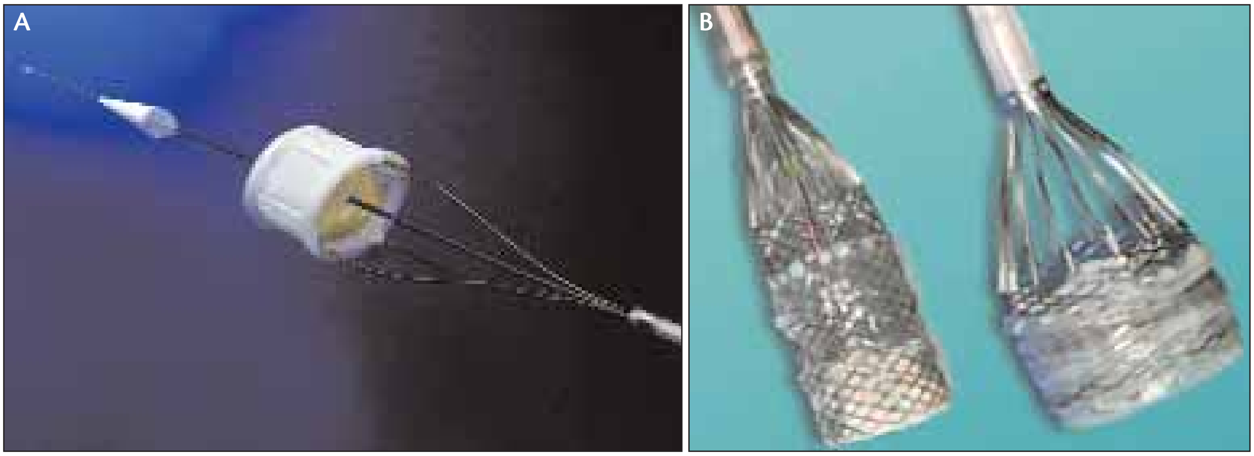
# The Next Generation of Transcatheter Aortic Valve Devices

Which new technologies will become the gold standard for treating aortic valve disease?

BY PETER C. BLOCK, MD

The Edwards first-generation transcatheter valve (Edwards Sapien, Edwards Lifesciences Corporation, Irvine, CA) is currently used in clinical trials in the United States and routine patient care in Europe. The CoreValve system (Medtronic, Inc., Minneapolis, MN) is also being used for routine care in Europe and will likely be tested in clinical phase I and II trials in the United States in 2010. However, a relatively large catheter size, difficulty in crossing the stenotic native valve, limited variance in proper placement, presence of paravalvular leak, risk of heart block, and the need for pacemaker implantation have characterized the drawbacks of these valves. Despite the downsides, approximately 10,000 patients have been successfully treated with these devices worldwide. To separate these valves from those that have been designated as second-generation devices is, perhaps, inaccurate. As newly designed, more sophisticated, and possibly more successful devices are launched, the Edwards Sapien and CoreValve technologies are themselves morphing into their second-generation iterations. The newest version of the Edwards Sapien valve has a smooth leading tip, smaller dimensions that allow an 18-F insertion, and a continued ease of transition across the transverse arch, which will keep it competitive. CoreValve has been tested further, and new data allay fears of strut fracture. With its 18-F (and possibly lower) profile, CoreValve also boasts true percutaneous femoral and even axillary artery insertion to help deal with the problems of limited access because of peripheral atherosclerotic disease. However, neither of these valves, once deployed, can be repositioned, and perhaps more importantly, they cannot be recaptured by the delivery device and removed. It is these characteristics




(Courtesy of Direct Flow Medical, Inc.)

(Courtesy of Sadra Medical, Inc.)

**Figure 1. Next-generation valves that are currently in clinical trials: Direct Flow valve (Direct Flow Medical, Inc., Santa Rosa, CA) (A) and the Lotus valve (Sadra Medical, Inc., Campbell, CA) (B).**

that separate the CoreValve and the Edwards Sapien from the newer generation of valves.

## NEXT-GENERATION VALVES

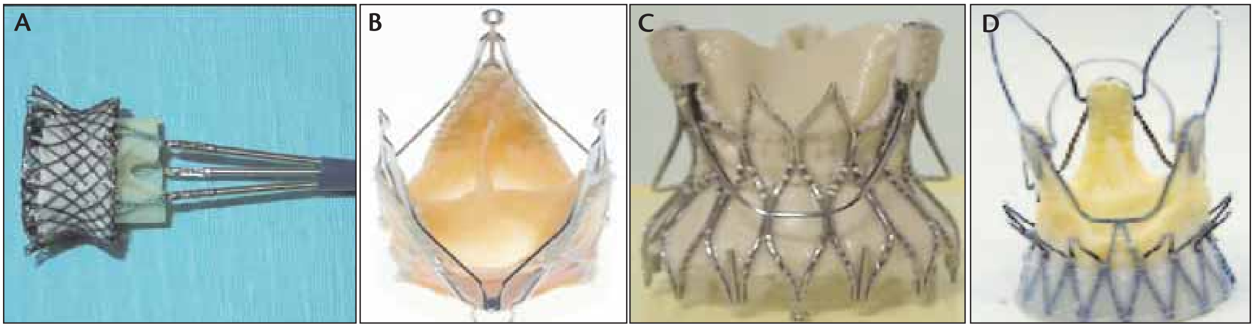
New transcatheter valves that are under development and are currently in, or soon to be entering, clinical trials in humans have common characteristics: small diameter (usually 18 F or less), ease of passage through the stenotic native aortic valve, repositionability, self-seating, the ability to be aligned in a coaxial fashion during deployment, and finally, the ability to be recaptured and removed after deployment, if necessary. The actual number of next-generation valves that fit these criteria is steadily increasing. It is not the aim of this article to provide a complete review, but rather to point out those technologies that are already in early human trials and to indicate the future designs that are slated for implantation in humans in the relatively near future.

## THE DIRECT FLOW VALVE

The Direct Flow valve has been evaluated in approximately 40 patients worldwide during the past 2 years. The valve is uniquely designed in that it has no metallic parts. Rather, the bovine pericardial valve is supported by two expandable tubular cuffs that are in turn supported with polyester and are positioned just below the aortic annulus and just above the tips of the native valve leaflets (Figure 1A). The device is sequentially expanded with saline; the first cuff within the left ventricular outflow tract frees the valve and allows it to function immediately upon deployment. Because the prosthetic valve is functional upon expansion of the distal cuff, there is hemodynamic stability throughout deployment and rapid pacing during deployment is not needed. The expanded cuff is then withdrawn until it rests just below the aortic annulus, creating a seal to minimize paravalvular leaks. Size and position can be evaluated, and if coaxial alignment is not ideal, control lumens with identifying radiopaque markers allow adjustment. Once the distal cuff and valve are appropriately positioned, the proximal cuff and waist supports are expanded, which seats the valve within the annulus. Valve function, paravalvular leak, and positioning are then evaluated by echocardiography. If the valve is not ideally positioned or paravalvular leakage is present, the valve can be collapsed, repositioned, or withdrawn. A second valve can then be introduced, or the procedure can be abandoned. If the valve is positioned well and the hemodynamic function is optimal, then the saline in the balloon-supported polyester cuffs is replaced with a water-soluble epoxy inflation medium that hardens in situ in a few minutes, allowing for immediate detachment of the valve. The favorable features of this valve are that it is stentless, can be repositioned, allows hemodynamic assessment before detachment, simulates a surgical valve design, is made of polyester fabric that supports tissue ingrowth, and currently comes in 23- and 25-mm diameter sizes with only a 17- to 18-mm height. The initial report of 15 patients by Schofer and colleagues[1] has been followed by abstract presentations of a larger intent to treat group of 31 patients at 2 centers in Europe.[2] A total of 22 patients underwent implantation in this feasibility study. Nine patients did not have the valve implanted due to either iliac atherosclerosis (n = 2), functionally bicuspid valve (n = 2), excessive outflow tract calcification (n = 3), large annular size (n = 1), and excessive valve calcification (n = 1). Two patients were converted to surgical correction because of mis-sizing with an increasing gradient (n = 1) and misplacement (n = 1). Two patients died postimplantation: one had a pericardial effusion, which resulted in a myocardial infarction on postoperative day 2, and one experienced heart failure immediately after the procedure. Of the 18 patients who were implanted with the device and discharged from the hospital, two died within the 6-month follow-up period: one from respiratory failure (adjudicated nondevice- or procedure-related) and one due to unknown causes (adjudicated as indeterminate). The remaining patients continue to be followed clinically with the longest now at > 18 months. Aortic gradients are approximately 20 mm Hg with an effective valve area by transthoracic echocardiography of 1.5 $cm^2$. Patients are in New York Heart Association class I or II with a paravalvular leak grade of 1 or less. A European trial using the 18-F system is scheduled to begin in the second half of 2009, and a 16-F device is also being developed.

## THE LOTUS VALVE

The Lotus valve is made of bovine pericardium, has a delivery system for guidance and placement, and is placed percutaneously. Also, this valve is deployed without the need for rapid pacing. A nitinol self-expanding ring holds the valve and is designed to adapt to variations in annular geometry while it is deployed. There is a proprietary seal on the outer diameter that is designed to minimize paravalvular leakage (Figure 1B). Deployment is performed by phased expansion within the annular landing zone, which allows for changes in positioning, if needed. Final expansion produces rigid support of the valve. If repositioning or removal is necessary, the valve can be retracted into the delivery sheath at any time before final separation of the delivery device. The first clinical deployment of the Lotus




(Images courtesy of Heart Leaflet Technologies, Inc., JenaValve Technology, Inc. Medtronic, Inc., and Symetis SA)

**Figure 2. Next-generation valves that are in development or in early safety and efficacy trials: the porcine pericardial valve by Heart Leaflet Technologies, Inc. (Maple Grove, MN) (A), the JenaValve system (JenaValve Technology, Inc., Wilmington, DE) (B), the Ventor valve (Medtronic, Inc.) (C), and the Symetis valve (Symetis SA, Lausanne, Switzerland) (D).**

valve was performed in July 2007 in Germany.[3] A feasibility trial of 10 patients was conducted to evaluate this device. After its initial clinical use, the delivery system was re-engineered to simplify the deployment process. Plans for a larger clinical experience are set to begin in late 2009.

## OTHER VALVE SYSTEMS

A number of other valve systems are not yet at the first-in-man stage, but they are slated to begin initial clinical safety and efficacy trials soon. The porcine pericardial valve by Heart Leaflet Technologies, Inc. is 17 F and is designed to be repositionable and retrievable. The valve tissue is suspended within a nitinol wire form, which fits inside a nitinol support structure lined with polyester fabric. After crossing the stenotic aortic valve, a backstop device is first expanded just below the aortic annulus. The outer support structure is advanced up to the backstop and expanded within the aortic annulus. The upper half of the support structure is inverted to increase the radial strength of the deployed valve (Figure 2A). The valve is then exposed and becomes functional. After valve placement, the backstop device is collapsed, pulled into the deployed valve, and used as a dilator to fully expand the valve before release. Human trials for this device are expected to begin in the third quarter of 2009.

The JenaValve system is also currently being evaluated. First-in-man deployment has not yet been done but is expected to take place in the third quarter of 2009. The valve structure is less bulky than the valve systems that are presently used. It has centering loops of nitinol that are placed within the coronary sinuses when the valve is deployed, theoretically ensuring proper height position and centering of the new valve in the aortic orifice (Figure 2B).[4] The Paniagua[5] (Endoluminal Technology Research, Miami, FL) and AorTx (Hansen Medical, Inc., Mountain View, CA) valves have both been implanted in humans, but there are currently no clinical trials underway to test these valves in the United States.

## TRANSAPICAL VALVE PLACEMENT

Because of the high incidence of peripheral atherosclerosis in elderly patients with aortic stenosis, or simply because the size of the pelvic vessels is inadequate to accommodate the relatively large sheaths needed to place transcatheter valves, other approaches are being explored. Thus, the Edwards transcatheter valve can be implanted via a transapical ventricular route, antegrade into the stenotic native valve. The procedure requires a 5- to 10-mm incision in the intracostal region just over the left ventricular apex, which is exposed after the pericardium is opened. A purse-string suture line allows safe placement of the sheath through the left ventricular apex, and the transcatheter valve is then advanced into the appropriate position. The safety and efficacy of this route of valve implantation is being tested in one arm of the current PARTNER trial, but its appeal has generated a number of newer valve designs that deserve mentioning.

The Ventor valve has already been implanted in approximately 20 patients. It has self-seating qualities, is self-expanding, and has supravalvular hoops that are placed over the coronary sinuses, ensuring proper positioning of the expanded valve (Figure 2C).

The Symetis valve has not yet been tested in man, but it is also a self-expanding valve design with relatively large hoops that are first deployed in the ascending aorta just above the native valve. The hoops align the valve in the proximal aorta and left ventricular outflow tract, and the valve, which self-centers within the aortic annulus, is then deployed (Figure 2D). Both of these uniquely designed valves are currently designed for transapical deployment, but subtle design changes in the delivery systems, may

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allow them to be deployed retrograde as well.

Looking into the future, one might hope for a transcatheter valve that could be implanted through 8- or 10-F catheters. This would allow many patients who are presently not suited for transcatheter therapy to have valve replacements. Conceptually, nanotechnology would allow such a valve replacement to be constructed. Ion-transfer technology and flexible nitinol-valve material 10 µm in thickness have already been manufactured, and valve replacements in animals have been performed. The valve material endothelializes within weeks, is apparently minimally thrombogenic, and essentially produces a new valve within the diseased annulus as it endothelializes. Clearly, these new materials will have considerable regulatory hurdles to cross before safety, efficacy, and long-term durability are proven, but the promise of this technology continues to capture the imagination.

## CONCLUSION

It is important to point out that in describing these next-generation valves, only representative technologies have been listed. Certainly, there are other valve systems with promise that have not been detailed in this review, primarily because of a paucity of recent reports. In the coming years, as transcatheter valve replacement therapy becomes a strategy for selected patients with aortic valve disease, some of the newer valves will be clinically successful and will become "winners," and others will lose appeal and will no longer be contenders. For interventional cardiologists and cardiac surgeons who are watching the rapidly changing landscape of this technology, it seems best to keep an open mind about new designs and concepts, and to recognize that there may be pleasant and unexpected surprises along the way. ■

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