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Percutaneous Transvenous Melody Valve-in-Ring Procedure for Mitral Valve Replacement

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Objectives The purpose of this study was to demonstrate the feasibility of percutaneous transvenous mitral valve-in-ring (VIR) implantation using the Melody valve in an ovine model.

Background The recurrence of mitral regurgitation following surgical mitral valve (MV) repair in both adult and pediatric patients remains a significant clinical problem. Mitral annuloplasty rings are commonly used in MV repair procedures and may serve as secure landing zones for percutaneous valves.

Methods Five sheep underwent surgical MV annuloplasty (24 mm, n = 2; 26 mm, n = 2; 28 mm, n = 1). Animals underwent cardiac catheterization with VIR implantation via a transfemoral venous, transatrial septal approach 1 week following surgery. Hemodynamic, angiographic, and echocardiographic data were recorded before and after VIR.

Results VIR was technically successful and required <1 h of procedure time in all animals. Fluoroscopy demonstrated securely positioned Melody valves within the annuloplasty ring in all animals. Angiography revealed no significant MV regurgitation in 4 and moderate central MV regurgitation in the animal with the 28-mm annuloplasty. All animals demonstrated vigorous left ventricular function, no outflow tract obstruction, and no aortic valve insufficiency.

Conclusions This study demonstrated the feasibility of a purely percutaneous approach to MV replacement in patients with preexisting annuloplasty rings. This novel approach may be of particular benefit to patients with failed repair of ischemic mitral regurgitation and in pediatric patients with complex structural heart disease. (J Am Coll Cardiol 2011;58: 2475–80) © 2011 by the American College of Cardiology Foundation

Mitral valve (MV) repair with an annuloplasty device is the preferred surgical therapy for mitral regurgitation (MR) (1). Recent studies have called into question the durability of MV repair for functional, degenerative, and congenital etiologies (1–3).

The recurrence rate of significant MR after undersized annuloplasty for ischemic MR approaches 30% 6 months after surgery. Recent studies have documented the development of recurrent MR after repair for degenerative etiologies to be 2% to 4% per year. Because of very complex pathologies, recurrence of MR following valve repair for congenital anomalies is also common (4).

Recently the development of novel valve technologies has made the percutaneous replacement of the aortic and pulmonary valves possible (5–7). However, percutaneous replacement of the MV is not currently possible because of inherent anatomic features of the MV that make fixation and perivalvular seal with currently available devices a challenge. Recent clinical reports and animals studies have demonstrated that the presence of a surgically placed annuloplasty device or a bioprosthetic valve makes MV replacement with valved stents feasible. This technique has been termed the valve-in-ring (VIR) or valve-in-valve (VIV) procedure and has been performed surgically via transatrial (8) and transapical (9–11) approaches using the Sapien transcatheter heart valve (Edwards Lifesciences, Irvine, California). Given the growing awareness of the limitations of valve repair durability, VIR offers a potential remedial procedure for high-risk adult and pediatric patients who develop recurrent MR after MV repair.

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Abbreviations and Acronyms

ASD = atrial septal defect
LV = left ventricle/ventricular
MR = mitral regurgitation
MV = mitral valve
PA = pulmonary artery
VIR = valve-in-ring
VIV = valve-in-valve

In this study, we report on the feasibility of performing VIR via a completely percutaneous approach using the Melody transcatheter valve (Medtronic, Minneapolis, Minnesota) in a sheep model of MV repair.

Methods

Surgical mitral annuloplasty. Surgical MV annuloplasty was performed on 5 sheep with CE-Physio devices (24 mm, n = 2; 26 mm, n = 2; 28 mm, n = 1; Edwards Lifesciences) using standard techniques.

Melody VIR procedure. One week following surgery, animals were brought to the catheterization laboratory for the Melody VIR procedure. Vascular access was obtained in the usual fashion. Under intracardiac echocardiographic guidance, an atrial septal defect (ASD) was created. Next a pre-shaped, super-stiff 0.035-inch guidewire (Lunderquist wire, Cook Medical, Bloomington, Indiana) was introduced and looped in the left ventricular (LV) apex (Figs. 1A and 1B), creating a railway from the iliac vein to the LV via the ASD.

Melody valves were crimped onto 22-mm diameter angioplasty balloons (22 mm × 4 cm BIB balloon catheter, NuMed Inc., Hopington, New York). The crimped Melody valve was advanced over the wire through the 22-F sheath and centered within the annuloplasty ring. Once in position, the device was deployed via standard balloon inflation technique (Fig. 1B). Following deployment, the small ASD was device closed (Helex, Gore Medical, Flagstaff, Arizona). Post-deployment angiography was performed to assess valve position and function. Follow-up hemodynamics and echocardiography were recorded and compared with baseline values. Procedure time, defined as beginning after vascular access was established and ending with ASD closure, was recorded for all animals. After a period of observation (6 h), animals were euthanized. Necroscopy was performed, including gross inspection of the VIR complex. All experiments were approved by the University of Pennsylvania's animal use committee.

Statistical analysis. Hemodynamic measurements before and after VIR were summarized using standard descriptive statistics and reported as mean ± SD. Comparisons were made using paired student *t* test. Statistical significance was defined as $p < 0.05$.

Results

All animals underwent successful surgical placement of an annuloplasty device.

The only significant difference between the pre- and post-VIR hemodynamic measures was an increased systolic (and mean) pulmonary artery (PA) pressure (33.8 ± 3.7 mm Hg vs. 38 ± 4.8 mm Hg; p = 0.008) and a trend toward increased cardiac output (4.1 ± 0.4 mm Hg vs. 5.2 ± 0.9 mm Hg; p = 0.06). Otherwise no significant differences were noted, as shown in Table 1. The greater and lesser diameters of the "D-shaped" rings (Fig. 2) were recorded for all animals and are listed in Table 2. All VIR procedures were successful, and each required <1 h of procedure time (Table 2). Although engineered to be circular upon full deployment, the Melody device conformed to the "D-shaped" annuloplasty ring in all cases (Fig. 2). Despite this conformational change, the valves functioned well in the 24- and 26-mm rings. Follow-up angiography and echocardi-

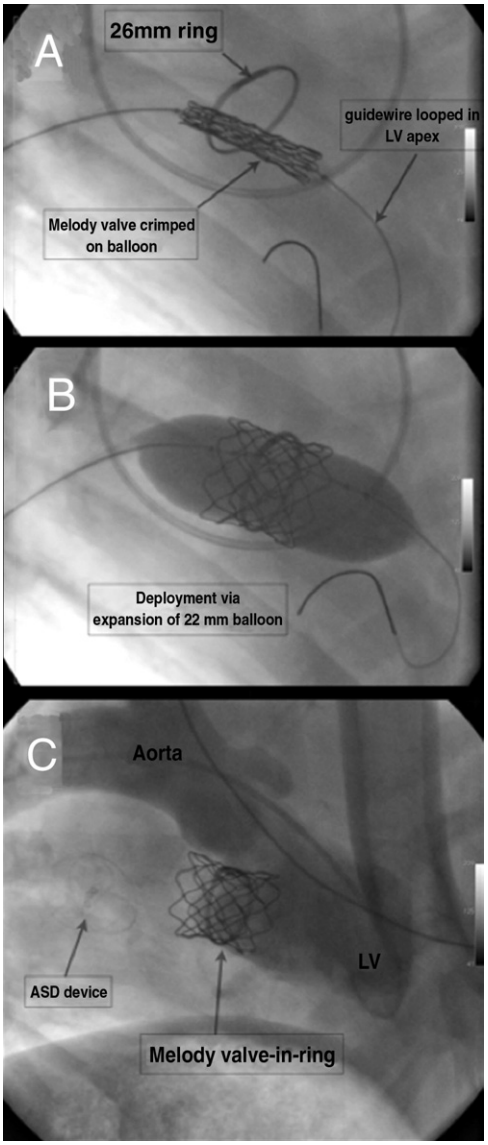

Figure 1 Transvenous, Transseptal Approach to Melody VIR Delivery

(A) The Melody device is crimped on the delivery balloon and advanced from the femoral vein across the atrial septum and positioned centrally in the annuloplasty ring. **(B)** Deployment of the Melody valve via balloon inflation. **(C)** Follow-up left ventriculogram. There is no mitral regurgitation and no left ventricular (LV) outflow tract obstruction. A device was used to close the small atrial septal defect (ASD). VIR = valve-in-ring.

Table 1 Hemodynamics*

Variable	Before VIR (n = 5)	After VIR (n = 5)	p Value
Aortic systolic pressure, mm Hg	98.8 ± 11.8	93.0 ± 5.8	0.44
Aortic diastolic pressure, mm Hg	60.4 ± 7.9	52.4 ± 11.1	0.25
Mean aortic pressure, mm Hg	73.6 ± 9.7	65.4 ± 5.9	0.23
Heart rate, beats/min	99.2 ± 16.8	97.8 ± 18.9	0.64
LV systolic pressure, mm Hg	100.4 ± 12.8	97.0 ± 8.3	0.64
LV diastolic pressure, mm Hg	11.2 ± 2.6	10.8 ± 2.4	0.65
Mean LA pressure, mm Hg	17.0 ± 4.0	17.8 ± 2.6	0.55
Mean PCWp, mm Hg	16.2 ± 2.9	16.8 ± 2.8	0.67
PA systolic pressure, mm Hg	33.8 ± 3.7	38.0 ± 4.8	0.008
PA diastolic pressure, mm Hg	19.6 ± 3.1	20.8 ± 4.0	0.21
Mean PA pressure, mm Hg	24.8 ± 1.9	28.0 ± 3.0	0.02
Mean RA pressure, mm Hg	7.6 ± 2.5	10.2 ± 1.5	0.07
Cardiac output, l/min	4.1 ± 0.4	5.2 ± 0.9	0.06

*There were no significant differences between the hemodynamics measured before surgical annuloplasty ring placement and after valve-in-ring (VIR) placement.

LA = left atrial; LV = left ventricular; PA = pulmonary artery; PCWp = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RA = right atrial; RV = right ventricular.

ography revealed excellent LV systolic function. There was MR through a central coaptation defect in 3 animals: trivial to mild in 2 and moderate to severe in 1 (Fig. 3). In this animal, the 28-mm annuloplasty ring appeared too large for secure anchoring of the Melody device when it was expanded to 22 mm. Therefore, this valve was expanded beyond the listed maximum diameter to approximately 24 mm, resulting in malcoaptation of the valve leaflets and moderate to severe central MR. There was no LV outflow tract obstruction, aortic insufficiency, or perivalvular regurgitation in any animal (Table 1, Fig. 4).

Following euthanasia, necropsy demonstrated that all Melody valves were anchored securely within the annuloplasty, with a tight seal formed between the Melody device and the ring circumferentially (Fig. 5).

Discussion

In this report, we described the first transvenous, transatrial, septal VIR implantation using the Melody device. Via standard vascular access and transseptal techniques, we successfully deployed the Melody valve into the mitral position from the venous circulation in all animals, without difficulty or complication. The Melody valves were securely seated in all cases. Importantly, although there was a conformational change noted in the Melody valves from "round" to "oval" or "D-shaped" when implanted into the annuloplasty rings, there was no perivalvular leakage and only trivial to mild central MR (except in the 1 animal in which we intentionally oversized the device) (Fig. 4). The only significant hemodynamic change noted following VIR was an increase in PA pressure ($p = 0.008$). The exact cause of this difference is unclear; however, it was likely due to a trend toward increased cardiac output secondary to sympathetic upregulation ($p = 0.06$) after VIR. Theoretically, increased PA pressure could also be secondary to pulmonary vein obstruction or an increase in left atrial pressure caused by MR and/or mitral stenosis. However, the pulmonary veins were unobstructed, and the mean left atrial pressure did not increase following VIR ($p = 0.55$). The success and relative ease of this procedure highlighted the potential for this approach in patients with ongoing MV dysfunction despite prior surgical repair.

Irrespective of the cause, surgical repair of systemic atrioventricular valve regurgitation (mitral, common atrioventricular, or tricuspid valves) carries a significant risk for recurrence in both adult and pediatric patients (4,12). Despite this risk, in most circumstances, valve repair is still preferred over replacement, due to durability concerns associated with tissue valves and to the reduced need for

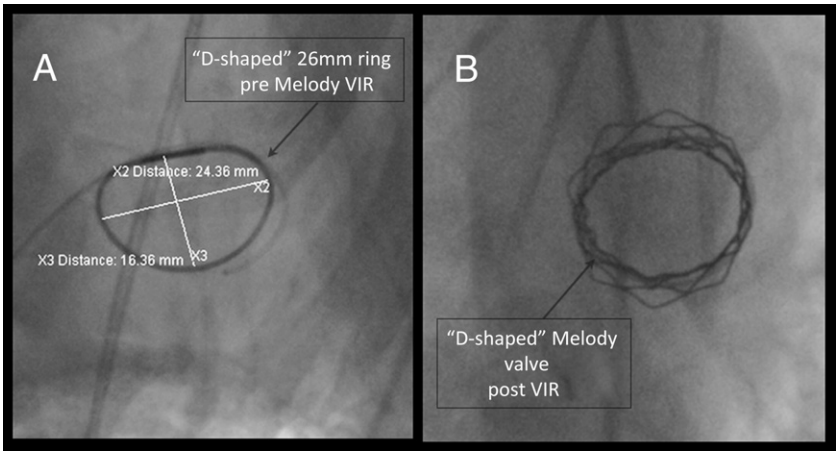

Figure 2 En Face View, Pre- and Post-Melody VIR Procedure

The Melody device conformed to the "D shape" of the annuloplasty ring upon valve-in-ring (VIR) implantation.

Table 2 Procedural Variables

	Animal				
	1	2	3	4	5
Weight, kg	39	48	52	63	43
Nominal annuloplasty ring size, mm*	24	24	26	26	28
Greater ring dimension (largest diameter), mm†	22	22.7	24.4	24	25
Lesser ring dimension (shortest diameter), mm†	17.9	16.3	16.4	17.3	19.6
Melody valve size, mm	22	22	22	22	22‡
MR grade before VIR (ECHO 1–4)	0	0	2	0	3+
MR grade after VIR (ECHO 0–4)	1+(central coaptation)§	0	0	2+(central coaptation)§	3+(central coaptation)§
MR grade (angiography 0–4)	0	0	0	0	3+
ASD size, mm‖	7	9	8	8	8
ASD device size (Helex), mm	20	20	20	20	20
Procedure time, min¶	60	50	55	45	50

*Size as listed by the manufacturer (Edwards Lifesciences, Irvine, California). †Given the "D" or "oval" shape of the annuloplasty ring, there are greater and lesser diameters (as measured fluoroscopically) to be considered when sizing for Melody valve implant. ‡This valve was deployed on a 22-mm balloon but post-dilated to 24 mm to ensure secure anchoring in the 28-mm ring. §Three of the 5 animals had residual mitral regurgitation (MR), although it was significant only in animal 5 in which the Melody valve was oversized to fit securely in the 28-mm annuloplasty ring. The mechanism of MR was through a central coaptation defect in the Melody valve in all animals (Fig. 3). There were no perivalvular leaks noted. ‖Atrial septal defect (ASD) diameter was determined using intracardiac echocardiographic imaging with color flow. The maximum diameters are listed. ¶For the purposes of this study, procedure time was defined as beginning after vascular access was established and ending after Melody VIR implantation and ASD closure.

Abbreviations as in Table 1.

systemic anticoagulation when compared with mechanical valves (13). In the last decade, the advent of percutaneous valve replacement has resulted in new minimally invasive therapeutic options for patients with dysfunctional aortic and pulmonary valves (5–7). Although many promising percutaneous MV repair technologies have been developed (2,14), percutaneous MV replacement with a single device remains elusive. The inherent anatomic features of the MV make fixation and perivalvular seal a troublesome challenge. In particular, the mitral annulus lacks a uniform "landing zone" for secure deployment of a percutaneous device. Despite these challenges, promising steps toward 1-stage percutaneous MV replacement are being made (15,16). In the meantime, minimally invasive surgical MV replacement via VIV and more recently VIR procedures have been described in which the Edwards Sapien device was deployed into previously placed bioprosthetic tissue valves (9,10) and/or annuloplasty rings (8,11) via a *surgical* transapical or transatrial approach. These procedures are intended to extend the functional life of the surgical valve in a manner analogous to Melody and Sapien valve treatment for dysfunctional surgical conduits in the pulmonary position. The VIR and VIV procedures have the potential to change the way in which MV patients are managed, especially as percutaneous valve technologies undergo further refinements that optimize their performance in these new settings.

Study limitations. The Melody valves used in this experiment were previously handled and cosmetically flawed, thus not viable for commercial use and not optimal for functionality

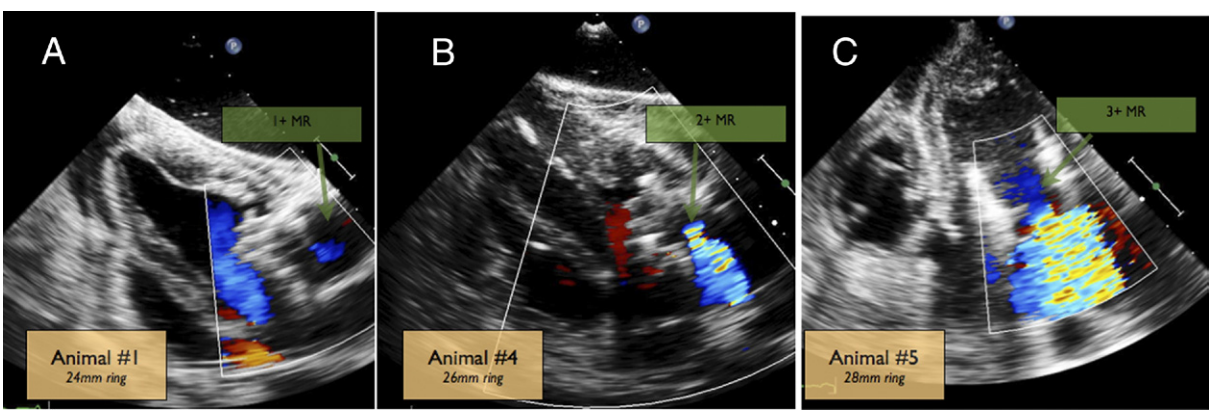

Figure 3 Doppler Echocardiography Following Melody VIR Procedure

Three of the 5 animals had residual mitral regurgitation (MR) following the valve-in-ring (VIR) procedure. The ECHO grade was trivial to mild for 2 animals **(A and B)** and moderate to severe for 1 animal (animal 5) **(C)**, in which a 28-mm annuloplasty ring was used, requiring "overdilation" of the Melody valve for secure anchoring. The mechanism of MR was via a central coaptation defect in the Melody device in all animals as shown above. There were no perivalvular leaks.

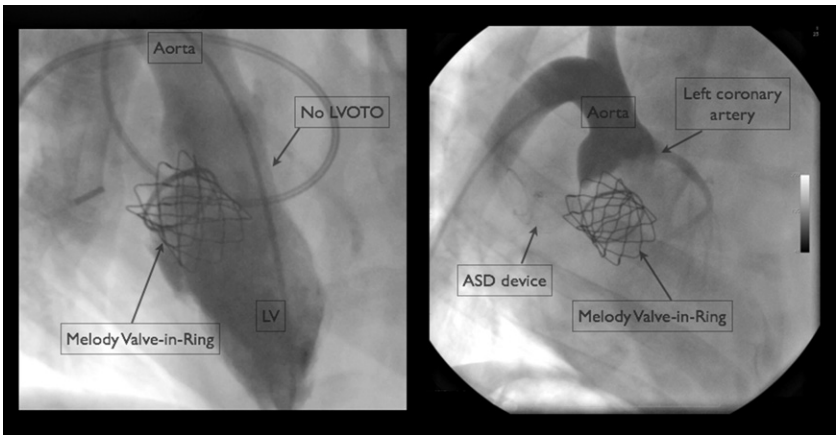

Figure 4 **Left Ventriculogram and Aortogram Status After Melody VIR Implantation**

There is no left ventricular outflow tract obstruction (LVOTO) and no aortic valve insufficiency. Abbreviations as in Figure 1.

testing. Furthermore, these devices are engineered for implantation into the pulmonary circulation. They are undersized relative to the normal adult mitral annulus (maximum functional diameter 22 mm) and are not intended for use in the systemic circulation, where the afterload is generally much higher. Despite these limitations, these results were a proof of concept sufficient to demonstrate the feasibility of the transvenous VIR procedure.

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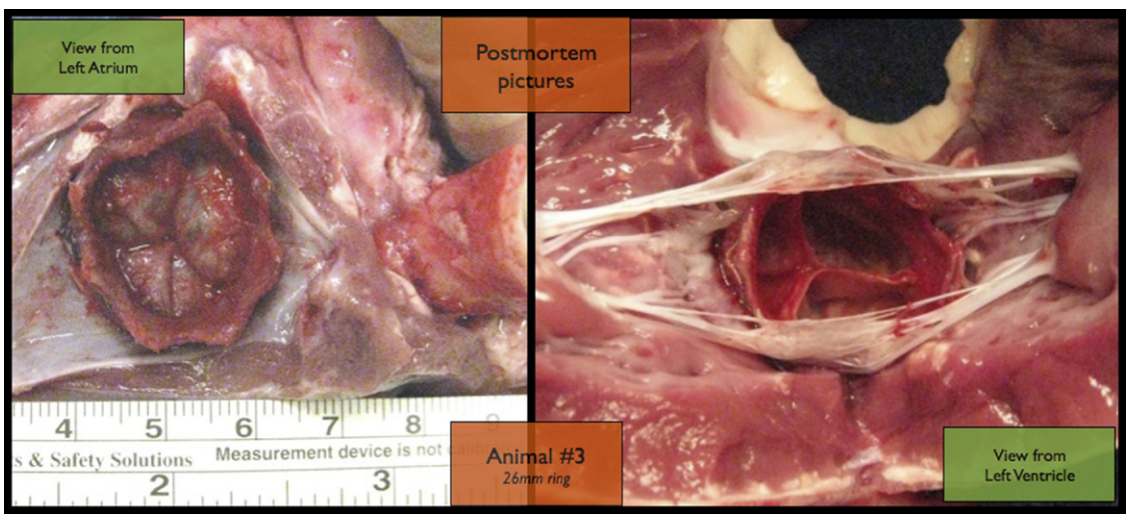

Figure 5 **Necropsy**

In all animals, the Melody device was securely anchored within the annuloplasty ring, forming a tight circumferential seal. The figure shows representative views from the left atrial and left ventricular sides.

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Key Words: annuloplasty ring ■ Melody valve ■ mitral valve ■ mitral valve insufficiency ■ mitral valve repair ■ mitral valve replacement ■ percutaneous valve replacement.