Chapter 30: The History and Evidence base for Transcatheter Pulmonary Valve Replacement

Varun Aggarwal MD[1], Athar M. Qureshi MD[1], and Lauren C. Kane MD[2]
The Lillie Frank Abercrombie Section of Pediatric Cardiology[1] and Congenital Heart Surgery[2], Texas Children's Hospital and Baylor College of Medicine, Houston, TX.

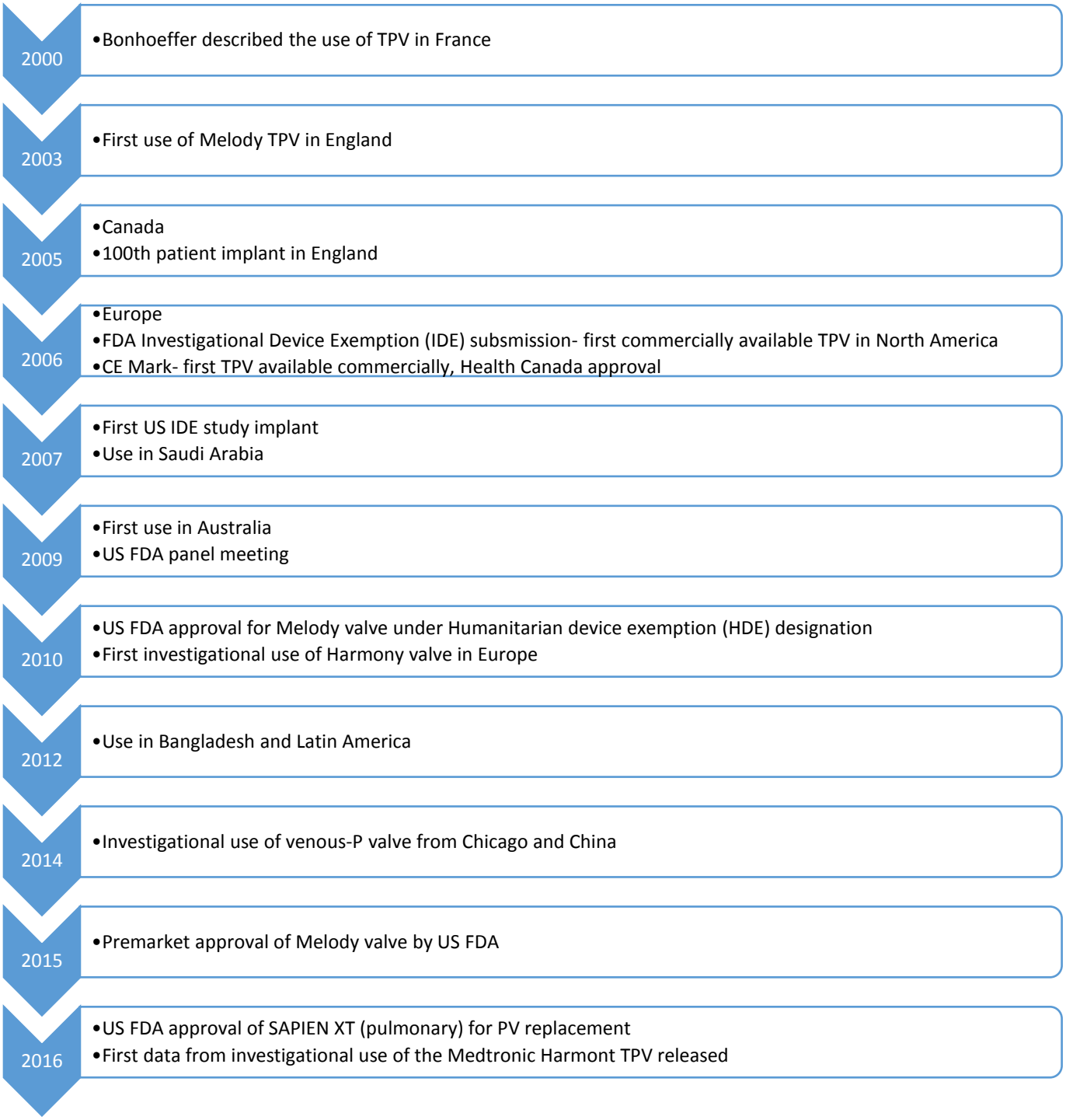
With improved cardiac surgical and perioperative management strategies, there is a growing population of patients who survive well into adulthood after pediatric congenital heart surgery. In the follow up of children after various surgical palliative procedures involving the right ventricular outflow tract (RVOT), long standing RVOT stenosis or regurgitation is common. These patients can be broadly classified into two groups. The first group consists of patients who underwent transcatheter or surgical intervention on the pulmonary valve (PV) or RVOT and now suffer from a *dysfunctional native RVOT*. The other group includes patients who received a right ventricle to pulmonary artery (RV-PA) conduit or a bio-prosthetic pulmonary valve and now suffer from a *dysfunctional conduit/bio-prosthetic pulmonary valve.*

It has been recognized that long standing pulmonary regurgitation is detrimental to right ventricular hemodynamics, and is associated with worse outcomes such as heart failure, arrhythmias and death[1]. Surgical strategies for reconstruction of RVOT include bio-prosthetic valves and valved conduits with or without patch augmentation[23]. Long term durability of these interventions is highly variable and repeated surgical interventions are typically required over a lifetime[4]. Considering this and the advent of transcatheter techniques, the principles of management have evolved, although there are certain limitations of existing transcatheter pulmonary valve technology (particularly with regards to native right ventricular outflow tracts). In this chapter, we aim to review the history and evidence behind the transcatheter pulmonary valve replacement (TPVR).

Evolution of transcatheter pulmonary valve replacement

In the year 2000, Philipp Bonhoeffer was first to report the TPVR in an ovine model[5] and subsequently in a 12 years-old boy[6] with pulmonary atresia and ventricular septal defect who had an 18 mm RV-PA conduit placed at the age of 4 years. Since its revolutionary introduction in 2000, TPVR has gained widespread acceptance and usage as a non-surgical alternative among patients who have dysfunctional RV-PA conduits.

Figure 1: Historical timeline of the development of transcatheter pulmonary valve (TPV)



TPVR for patients with RV-PA dysfunctional conduit

Melody valve (Medtronic, Minneapolis, Minnesota, USA)

The valve designed by Bonhoeffer was later acquired by Medtronic and named 'Melody valve'. Khambadkone et al[7] from London documented successful Melody valve implantation in 58 patients in 2005. The first US implantation of the Melody valve was in 2007. FDA approved the use of Melody valve under humanitarian device exemption in January 2010 and subsequent pre-market approval was given in February 2015. Currently available Melody transcatheter pulmonary valves in US are 16 mm and 18 mm bovine jugular vein tissue which can be deployed up to diameters of 20mm and 22mm respectively (Table 1). In a recent meta-analysis, Virk et al[8] reported an overall peri-procedural mortality of 1.4%. Procedural complications included conduit rupture (2.6%), valve embolization (2.4%), coronary artery compression (1.2%) and pulmonary artery obstruction (1.2%). Conversion to surgery was reported in 2.8% of patients. The incidence of stent fracture and infective endocarditis were 12.4% and 4.9% respectively. The long-term outcome of the US Melody investigational device exemption trial[9] demonstrated five-year freedom from re-intervention and explantation to be 76±4% and 92±3%. The main cause of valve dysfunction was stent fracture (which decreased once pre-stenting prior to Melody valve placement was adopted).

SAPIEN valve (Edwards Lifesciences Inc., Irvine, CA)

A major limitation of the Melody valve is the relatively small size. Initially introduced for aortic valve replacement, the first use of SAPIEN valve in the pulmonary position was reported in 2006[10]. The COMPASSION[11] trial demonstrated the successful deployment of SAPIEN valve in 34 attempts in 33 patients. Valve migration was noted in 3 patients. Freedom from re-intervention was 97% with one patient undergoing elective placement of a second valve due to conduit-induced distortion of the initial implant. Initially SAPIEN valve was available in US in 23mm and 26mm sizes for use in the RVOT range of 18-25 mm (Table 1). In March 2016, FDA approved the use of SAPIEN-XT valve for pulmonary position in patients with dysfunctional RVOT conduits with a clinical indication of intervention. This valve is available in size of 20-29 mm for landing zones varying from 16-28 mm in diameters (Table 1).

TPVR for patients with native RVOT

In most patients requiring PVR for RVOT lesions with significant pulmonary regurgitation (PR), the native RVOT is large and dilated. As mentioned above, the currently available TPVR options are somewhat limited due to small sizes that are inappropriate for native RVOT. Therefore, it is still challenging to perform TPVR in patients with large native dysfunctional RVOT.

Off-label use in dysfunctional native RVOT

Native RVOT, small diameter conduits (< 16mm) and relatively large RVOT with a dynamic outflow aneurysm are currently considered off-label uses of TPVR. There are some reports of expanding the use of TPVR in selected patients with native RVOT. Stenting the native RVOT to create a stable

"landing-zone" of acceptable dimensions for TPVR has been employed. Meadows et al[12] and Malekzadeh-Milani et al[13] have reported the use of Melody valve in patched non-circular RVOT after careful patient selection. In some instances, the Melody valve may be over-dilated to up to 24 mm (outer diameter of at least 26 mm) with good results[14]. This dimension is similar to the 26 mm SAPIEN valve. Experience with the SAPIEN valve in the native pulmonary position remains limited[15]. Placement of Melody valves in both branch pulmonary artery positions has also been reported in patients in whom the dimensions of the RVOT are prohibitive from percutaneous pulmonary valve placement[16,17]. Gupta et al[18] recently described per-ventricular Melody valve placement without a sternotomy in three patients <20 kg.

Hybrid procedure

Boudjemline et al[19] described the use of a hybrid approach for placement of pulmonary valve in native RVOT in an animal model. Surgical PA banding was done using two rings made of nitinol wire and subsequently pulmonary valve was placed either percutaneous or trans-ventricular in eight ewes[18]. They also described the use of intravascular reducers in seven animals[20]. Travelli et al[21] described a hybrid method of modifying the RVOT by placing a pulmonary artery band followed by successful percutaneous placement of Melody valve. Philips et al[22] described the use of hybrid approach to remodel the RVOT in patients with native RVOT using commercially available products supported by pre-procedural 3-D model planning.

Venous P-valve (Venous Medtech, Shanghai, China)

The Venous P-valve (Table 1) is a novel self-expanding percutaneous stent valve (available in 20-32 mm diameter) with flailed ends to conform to the dilated native RVOT. Initial report on five patients by Cao et al[23] demonstrated excellent short-term pulmonary valve function in patients with chronic severe PR in native RVOT. Garay et al[24] and Hussain et al[25] were able to reproduce these findings.

Other TPV (investigational use)

Schievano et al[26] reported safe and successful implantation of a new percutaneous pulmonary valve in a dilated pulmonary trunk, using patient specific data to influence the design of the device and ensure patient safety. Named as 'Harmony' transcatheter pulmonary valve (Medtronic, Minneapolis, Minnesota, USA), this is a self-expandable transcatheter pulmonary valve with subsequent feasibility study in an ovine model[27]. The valve used in the study was a self-expanding nitinol stent with a woven polyester covering and a porcine pericardial valve sewn into its center (proximal diameter 43mm, valve housing 22mm, distal diameter 33mm, and length 53mm). Early feasibility study using Medtronic Harmony valve is ongoing and the device is currently available only under investigational use (Table 1).

Recently Kim BG et al[28] from South Korea recently developed a self-expandable percutaneous pulmonary valve with cooperation of the TaeWoong Medical Company (Gyeonggi-do, Republic of Korea). The stent is made of knitted nitinol wire and the ends of the stent are flared to 4 mm more than the valve diameter to provide stable positioning and the wall is coated with de-cellularized porcine pericardium. The valve diameter ranges from 18-20mm (in 2mm increments) and currently not available in US.

Studies have shown that TPVR is comparable if not superior to surgical PVR. Further data on long term need for re-intervention after TPVR will guide the decision making in future. Further advances in device availability and expertise is needed for patients dysfunctional native RVOT.

Table 1: Table of currently available transcatheter pulmonary valves with their salient characteristics

Valve	**Description**	**Approved indication**	**Off-label use**	**Valve Diameter (mm)**	**RVOT treatment range**	**Sheath size (transfemoral, Fr)**	**Other**
Melody valve (Medtronic)	Bovine jugular vein with valve sutured inside 8-zig, 28 mm covered Cheatham platinum-iridium stent	Dysfunctional RVOT conduits > 16 mm	Native RVOT, small conduits	16 mm 18 mm	≤ 20 mm ≤ 22 mm (*may be over dilated up to 24 mm)	22 Fr Ensemble delivery system with the valve mounted on an 18, 20 and 22mm balloon in balloon.	-
Edwards SAPIEN valve (Edwards)	Bovine pericardial tissue valve sutured in a stainless steel stent with polyethylene terephthalate (PET) fabric skirt placed on the ventricular side covering half of the frame, limiting stent expansion and decreasing para-valvular insufficiency.	Replaced with SAPIEN-XT and SAPIEN 3 newer generation of valves		23 mm 26 mm	18-22 mm 21-25 mm	23 Fr 24 Fr	Larger effective orifice area and better hemodynamic profile than surgically implanted valves, but higher incidence of para-valvular leak. Short height of 14.5– 16 mm, therefore requires pre-stenting of the RVOT for safe delivery
SAPIEN-XT (Edwards)	Bovine pericardial tissue leaflets sutured inside a cobalt chromium frame stent	Aortic (trans-femoral, trans-apical or trans-aortic routes) and mitral valve (trans-apical access only) replacement. Approved for	Native RVOT	20 mm 23 mm 26 mm 29 mm	16-18 mm 18-22 mm 22-25 mm 24-28 mm	16 Fr 16 Fr 18 Fr 20 Fr	Modified and improved version of SAPIEN. Commercialized in Europe in 2009 and approved in US in 2014.

		use at RV-PA conduit in March 2016 by FDA					
SAPIEN-XT pulmonic (Edwards)	Bovine pericardial tissue leaflets sutured inside a cobalt chromium frame stent	Approved for use at RV-PA conduit in March 2016 by FDA	Native RVOT	23 mm 26 mm 29 mm	20-23 mm 23-26 mm 26-29 mm	16 Fr 18 Fr 20 Fr	Modified and improved version of SAPIEN. Commercialized in Europe in 2009 and approved in US in 2014. Approved for use in RV-PA conduits by FDA in March 2016.
Edwards SAPIEN-3 valve (Edwards)	Bovine pericardial tissue valve sutured inside a cobalt chromium alloy stent. A Polyethylene terephthalate (PET) skirt added at the base of the valve to minimize the leakage around the valve	Aortic (trans-femoral or trans-apical routes)	RV-PA conduit, native RVOT	23 mm 26 mm 29 mm	18-22 mm 21-25 mm 24-28 mm	14 Fr 14 Fr 16 Fr	Newest iteration of the SAPIEN family of valves designed to minimize para-valvar leak and reduce the diameter of the delivery system.
Harmony valve (Native outlflow tract device) (Medtronic)	Porcine pericardial valve mounted on nitinol stent	-	Native RVOT (investigational use)	Diameter: 20-32 mm	-	25 Fr	-
Venous-P valve[29] (Venous Medtech Inc., Hangzhou, China)	Laser cut nitinol self-expanding stent with flared proximal and distal sections. Valve leaflets made of porcine pericardium are hand-sewn to the stent		Native RVOT (investigational use)	Diameter: 22-36 mm (2 mm increments); Length: 25, 30 and 35 mm		22-26 Fr	

Table 2: Indications for pulmonary valve replacement in patients with dysfunctional RVOT[30].

1	Presence of symptoms from dysfunctional RVOT
2	Indexed RVEDV > 150 ml/m^2 ± regurgitation fraction > 40%
3	Indexed RVESV > 80 ml/m^2
3	RVOT peak instantaneous gradient > 50 mmHg
4	Moderate-severe accompanying tricuspid regurgitation
5	Risk of long term arrhythmia and progressive LV dysfunction, QRS ≥ 180 msec

References:

1. Gat Gatzoulis MA, Balaji S, Webber SA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicenter study. Lancet 2000;356:975–81.
2. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2008;52:e143 – 263.
3. Yuan SM, Mishaly D, Shinfeld A, et al. Right ventricular out fl ow tract reconstruction: valved conduit of choice and clinical outcomes. J Cardiovasc Med (Hagerstown) 2008;9:327 – 37.
4. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Transcatheter implantation of a bovine valve in pulmonary position. Circulation 2000; 102: 813–16.
5. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. Lancet 2000;356:1403–5.
6. Khambadkone S, Coats L, Taylor A, et al. Percutaneous pulmo- nary valve implantation in humans: Results in 59 consecutive patients. Circulation 2005;112:1189–1197.
7. Virk SA, Liou K, Chandrakumar D, Gupta S, Cao C. Percutaneous pulmonary valve implantation: A systematic review of clinical outcomes. International Journal of Cardiology. 2015;201:487–489.
8. Cheatham JP, Hellenbrand WE, Zahn EM, Jones TK, Berman DP, Vincent JA, McElhinney DB. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US melody valve investigational device exemption trial. Circulation. 2015 Jun 2;131(22):1960-70.
9. Garay F, Webb J, Hijazi ZM. Percutaneous replacement of pulmonary valve using the Edwards-Cribier percutaneous heart valve: first report in a human patient. Catheter Cardiovasc Interv. 2006 May;67(5):659-62.
10. Kenny D, Hijazi ZM, Kar S, Rhodes J, Mullen M, Makkar R, Shirali G, Fogel M, Fahey J, Heitschmidt MG, Cain C. Percutaneous implantation of the Edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position: early phase 1 results from an international multicenter clinical trial. Journal of the American College of Cardiology. 2011;58(21):2248–56.
11. Meadows JJ, Moore PM, Berman DP, Cheatham JP, Cheatham SL, Porras D, Gillespie MJ, Rome JJ, Zahn EM, McElhinney DB. Use and performance of the melody transcatheter pulmonary valve in native and postsurgical, nonconduit right ventricular outflow tracts. Circ Cardiovasc Interv 2014;7:374–380.
12. Malekzadeh-Milani S, Ladouceur M, Cohen S, Iserin L, Boudjemline Y. Results of transcatheter pulmonary valvulation in native or patched right ventricular outflow tracts. Arch Cardiovasc Dis 2014;107:592–598.
13. Cheatham SL, Holzer RJ, Chisolm JL, Cheatham JP. The Medtronic Melody® transcatheter pulmonary valve implanted at 24-mm diameter--it works. Catheter Cardiovasc Interv. 2013 Nov 1;82(5):816-23.

14. Guccione P, Milanesi O, Hijazi ZM, Pongiglione G. Transcatheter pulmonary valve implantation in native pulmonary outflow tract using the Edwards SAPIEN transcatheter heart valve. Eur J Cardiothorac Surg. 2012;41(5):1192–4.
15. Gillespie MJ, Dori Y, Harris MA, Sathanandam S, Glatz AC, Rome JJ. Bilateral branch pulmonary artery melody valve implantation for treatment of complex right ventricular outflow tract dysfunction in a high-risk patient. Circulation Cardiovascular interventions 2011;4:e21-23.
16. Qureshi AM, Krasuski RA, Prieto LR. Percutaneous pulmonary valve implantation in left pulmonary artery branch in a patient with a functional single lung. The Journal of invasive cardiology 2012;24:e202-204.
17. Gupta A, Kenny D, Caputo M, Amin Z. Initial Experience with Elective Perventricular Melody Valve Placement in Small Patients. Pediatr Cardiol. 2016 Dec 20. [Epub ahead of print] doi:10.1007/s00246-016-1550-0.
18. Boudjemline Y, Schievano S, Bonnet C et al.: Off-pump replacement of the pulmonary valve in large right ventricular outflow tracts: a hybrid approach. J. Thorac. Cardiovasc. Surg. 2005;129(4):831–837.
19. Boudjemline Y, Agnoletti G, Bonnet D et al.: Percutaneous pulmonary valve replacement in a large right ventricular outflow tract: an experimental study. J. Am. Coll. Cardiol. 2004;43:1082–1087.
20. Travelli FC, Herrington CS, Ing FF. A novel hybrid technique for transcatheter pulmonary valve implantation within a dilated native right ventricular outflow tract. J Thorac Cardiovasc Surg 2014;148:e145–e146.
21. Philips ABM, Nevin P, Shah A, Olshove V, Garg R, Zahn EM. Development of a Novel Hybrid Strategy for Transcatheter Pulmonary Valve Placement in Patients Following Transannular Patch Repair of Tetralogy of Fallot. Catheterization and Cardiovascular Interventions. 2016;87:403–410.
22. Cao QL, Kenny D, Zhou D, Pan W, Guan L, Ge J, Hijazi ZM. Early clinical experience with a novel self-expanding percutaneous stent-valve in the native right ventricular outflow tract. Catheter Cardiovasc Interv. 2014;84:1131-7.
23. Garay F, Pan X, Zhang YJ, Wang C, Springmuller D. Early experience with the Venus p‐valve for percutaneous pulmonary valve implantation in native outflow tract. Neth Heart J. 2017;25(2):76-81.
24. Hussain J, Praichasilchai P, Gilbert Y, Qureshi SA, Morgan GJ. Early European experience with the Venus P-valve ®: filling the gap in percutaneous pulmonary valve implantation. Eurointervention 2016;12:e643-e651.
25. Schievano S, Taylor AM, Capelli C, et al. First-in-man implantation of a novel percutaneous valve: A new approach to medical device development. EuroIntervention 2010;5:745–750.
26. Schoonbeek RC, Takebayashi S, Aoki C, Shimaoka T, Harris MA, Fu GL, Kim TS, Dori Y, McGarvey J, Litt H, Bouma W, Zsido G, Glatz AC,Rome JJ, Gorman RC, Gorman JH, Gillespie MJ. Implantation of the Medtronic Harmony Transcatheter Pulmonary Valve Improves Right Ventricular Size and Function in an Ovine Model of Postoperative Chronic Pulmonary Insufficiency. Circ Cardiovasc Interv. 2016 Oct;9(10). pii: e003920.
27. Kim GB, Kwon BS, Lim HG. First in Human Experience of a New Self-Expandable Percutaneous Pulmonary Valve Implantation Using Knitted Nitinol-Wire and Tri-Leaflet Porcine

Pericardial Valve in the Native Right Ventricular Outflow Tract. Catheter Cardiovasc Interv. 2017 Feb 1. doi: 10.1002/ccd.26910. [Epub ahead of print]

28. Husain J, Praichasilchai P, Gilbert Y, Qureshi SA, Morgan GJ. Early European experience with the Venus P-valve®: filling the gap in percutaneous pulmonary valve implantation. EuroIntervention. 2016 Aug 5;12(5):e643-51.
29. Tretter JT, Friedberg MK, Wald RM, McElhinney DB. Defining and refining indications for transcatheter pulmonary valve replacement in patients with repaired tetralogy of Fallot: Contributions from anatomical and functional imaging. Int J Cardiol. 2016 Oct 15;221:916-25.