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European Journal of Cardio-thoracic Surgery xxx (2011) xxx–xxx

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

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Implantation of a catheter-based self-expanding pulmonary valve in congenital heart surgery: results of a pilot study☆

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Received 1 September 2010; received in revised form 14 November 2010; accepted 16 November 2010

Abstract

Objective: Dilatation of RV outflow after surgical patch repair represents a problem for seating a percutaneous valve. We present the data of a new catheter-based, self-expanding tissue valve with a diameter up to 31 mm. **Methods:** 7 Patients (median 9 years, range 2 to 24 years) with severe PR due to RV outflow tract dilatation after patch repair or percutaneous procedures were treated with a catheter-based, self-expanding porcine pulmonary valve (Biointegral®). Valve diameter ranged between 15 and 29 mm. Maximum follow-up was 40 months. Patients were postoperatively assessed on day 1 and 6 months after the procedure, including physical examination, 12 lead electrocardiography and cross-sectional echocardiography with color Doppler. **Results:** Valve implantation was successful in all patients. Implantation was performed using three different routes: RVOT after partial sternotomy, pulmonary artery after mini-thoracotomy, or via the RV apex. Median follow-up was 25 months (5–40) identifying no significant morbidity and no death. Echocardiography revealed competent valves, no paravalvular leaks, no valve migration and no significant gradient in the RVOT. **Conclusion:** The new, self-expanding, catheter-based pulmonary valve is easy to implant via an antegrade (RVOT, RV) or retrograde approach (PA) even in dilated RV outflow tracts. The procedure can be done without CPB under echocardiographic guidance.
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Keywords: Congenital; Pulmonary valve; RVOT; Transcatheter valves

1. Introduction

Severe pulmonary regurgitation (PR) and conduit failure are a common problem following surgical correction of the right ventricular outflow tract (RVOT). One of the indications for redo-surgery is severe PR with hemodynamic impairment of the right ventricle and obstruction of the RVOT or pulmonary artery/ies (right ventricular pressure >2/3 of systolic systemic pressure) [1]. Nevertheless, the invasive nature of re-do surgery is associated with the risk of major adverse events such as catastrophic hemorrhage [2]. Oechslin et al. described severe complications during resternotomy as more common in patients with 2 or more previous operations. Minimally invasive techniques for pulmonary valve replacement may circumvent such risks [3]. Bonhoeffer et al. reported pioneering work in transcatheter pulmonary valve implantation [4]. However, size limitation and the need for a calcified landing zone in order to anchor the transcatheter valve are central issues in percutaneous valve implantation. We report our initial experience with the catheter-based, self-expanding pulmonary valve (No-React® injectable pulmonic valve Biointegral Surgical Inc.®). Valve size ranges from 15 to 31 mm. Implantation is possible via the RV apex, RVOT, or trunk of the pulmonary artery with or without using cardiopulmonary bypass (CPB).

2. Material and methods

2.1. Patient population

Patients presenting for pulmonary valve implantation at our institution were evaluated regarding their suitability for the study by a multidisciplinary team consisting of a cardiac surgeon, pediatric cardiologist and interventional cardiologist. Patients were considered for valve replacement if they presented with severe PR and progressive RV dilatation in echocardiography, or MRI irrespective of symptoms. The diameter of the RVOT at the level of the pulmonary valve had

☆ Presented at the 24th Annual Meeting of the European Association for Cardio-thoracic Surgery, Geneva, Switzerland, September 11–15, 2010.

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doi:10.1016/j.ejcts.2010.11.041

Please cite this article in press as: von Wattenwyl R, et al. Implantation of a catheter-based self-expanding pulmonary valve in congenital heart surgery: results of a pilot study. Eur J Cardiothorac Surg (2011), doi:10.1016/j.ejcts.2010.11.041

Table 1. Patients' demographics.

Patient	Age (yrs)	Sex	Weight (kg)	BSA (m^2)	Diagnosis
1	8	M	38	1.21	TOF
2	8	F	24.5	0.96	TOF/PFO
3	17	M	54	1.64	PS/TI
4	9	M	30	1.09	PS/VSD/PFO
5	15	M	46	1.43	PS/AS/AI
6	24	F	52	1.62	TOF
7	2	M	8	0.4	AVSD/PS/PDA

TOF = tetralogy of Fallot, PFO = patent foramen ovale, PS = pulmonary stenosis, TI = tricuspid valve insufficiency, VSD = ventricular septal defect, AS = aortic valve stenosis, AI = aortic valve insufficiency, AVSD = atrioventricular septal defect.

to be at least 15 mm but not over 30 mm. We excluded patients with unfavorable RVOT morphology (i.e. significant RVOT obstruction due to hypertrophied muscles bundles) requiring open surgical repair. Between April 2007 and March 2010 a total of 7 patients with significant PR were included in this pilot study for implantation of a catheter-based, self-expanding pulmonary valve. The patients' demographics are summarized in Table 1. All procedures were performed under general endotracheal anesthesia. Physical examination, 12-lead electrocardiography and cross-sectional echocardiography with color Doppler were assessed prior to surgery, postoperatively and at least 6 month after the procedure.

2.2. Prosthesis and the delivery system

The No-React® Injectable Pulmonic Valve (Biointegral® Surgical Inc.) is a conduit consisting of a porcine pulmonic valve mounted inside a tubular self-expandable nitinol stent covered by No-React® treated pericardium (Fig. 1). The valve design is based on the Shelhigh Injectable Pulmonic valve System®, which was distributed until 2007 in Germany.

The valve is available in sizes from 15 up to 31 mm. The delivery system is comprised of three parts (Fig. 2). We upgraded the rigid part of the trocar barrel with a new flexible trocar barrel. The new delivery device is designed to allow the system to be guided inside the RV by a guidewire. A

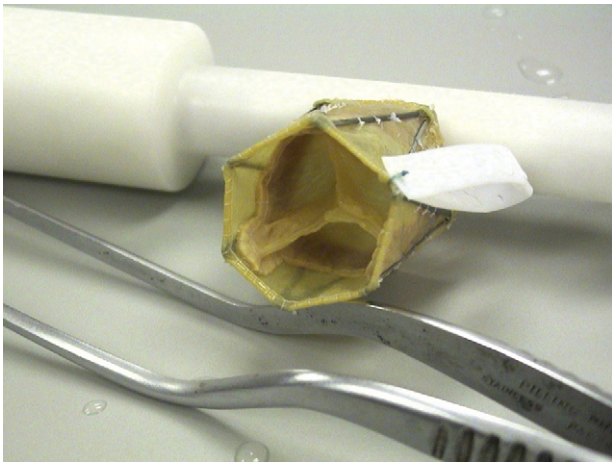

Fig. 1. Biointegral valve is a conduit consisting of a porcine pulmonic valve mounted inside a tubular self-expandable nitinol stent covered by No-React® treated pericardium. Copyright by Biointegral®.

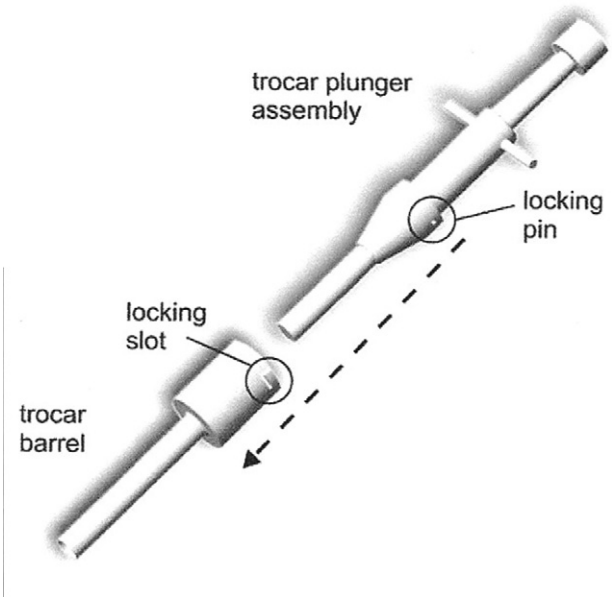

Fig. 2. Overview of the classic delivery system showing the trocar barrel and trocar plunger assembly. Copyright by Biointegral®.

special introducer tip allows gentle introduction of the delivery system into the RV (Fig. 3A and B). The valve expands while the trocar plunger is depressed (Fig. 4), and gently anchors at the desired destination (Fig. 5). Unfortunately, the delivery system is currently available in only one size. This makes implantation of the valve without the use of CPB impossible in small patients (i.e. those under 30 kg bodyweight).

2.3. Implantation technique

The valve can be implanted via three different routes: (1) the right ventricular outflow tract [5,6], (2) pulmonary artery trunk (PT) [7] and (3) right ventricular apex [8]. The valve's implantation technique via the RVOT and PT were previously published [5–7] and described in detail. Both access routes allow implantation without CPB use. However, small patient

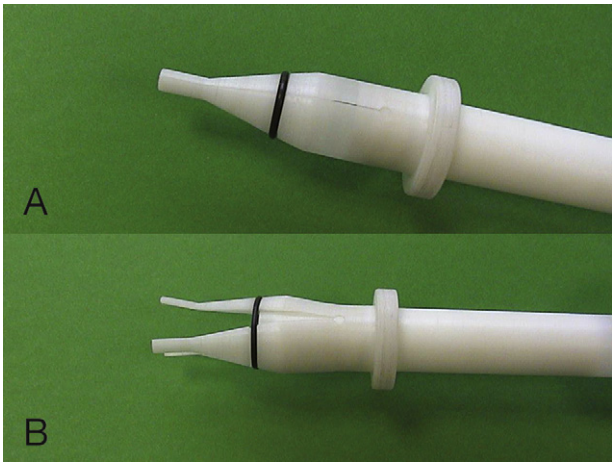

Fig. 3. Introduction tip for easier penetration of the tissue wall (A); tip of the delivery system while the valve expands (B). Copyright by Biointegral®.

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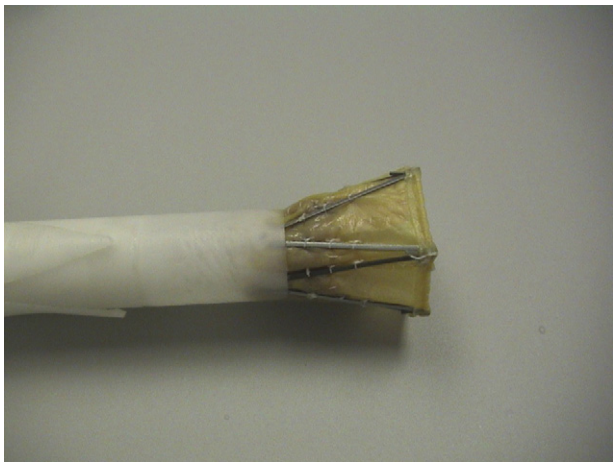

Fig. 4. The valve expands while the trocar plunger is depressed. Copyright by Biointegral®.

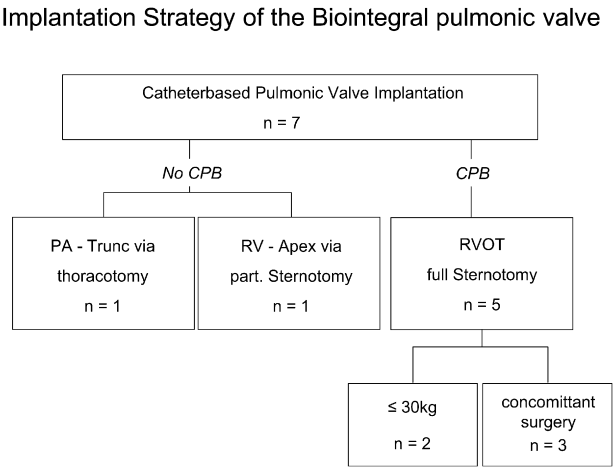

Fig. 6. Overview of the valve implantation strategy in our 7 patients.

size, and simultaneous repair of concomitant intracardiac defects may necessitate CPB application. To date there is only one size of the flexible delivery system available irrespective of valve diameter. As a consequence, the delivery system's introducer tip, in which the self-expanding valve is mounted, cannot be completely inserted into the right ventricle cavity in small patients (i.e. those under 30 kg of bodyweight). To avoid unnecessary blood loss, we therefore recommend using CPB in patients weighing under 30 kg (Fig. 6). The pulmonic valve can be implanted via the RV apex using subxyphoidal access. After dissection of the subxyphoidal tissue and (optionally) partial lower sternotomy, the RV apex is exposed and purse-string sutures, which are reinforced with felt, are placed on the RVOT's diaphragmal plane. From the right ventricular apex, a stiff guidewire is introduced under transesophageal and fluoroscopy guidance through the RVOT into the peripheral pulmonary artery. Once the guidewire is in the correct position, the RV apex is incised with an 11 blade, and the introduction tip is inserted into the ventricle. The flexible delivery system can be positioned across the introduction tip on the pulmonary valve level using gentle rotation. An additional mini-thoracotomy of the left third intercostal space allows the positioning of the delivery trocar under digital control. Simultaneous transesophageal echocardiographic guidance ensures correct positioning of the device. After ensuring that the valve's angle and level were aligned within the patient's anatomy, the valve is 'injected' under digital control, and additional fluoroscopic guidance for positioning the valve is usually unnecessary. Once the valve has been completely expelled from the trocar, the delivery trocar is slowly withdrawn. Valve positioning is completed by using two to three single sutures at the stent posts at the inflow part of the valve using 4–0 polypropylene sutures for external fixation to prevent valve migration. Successful positioning of the valve and competent valve function are monitored by transesophageal echocardiography in the operating room.

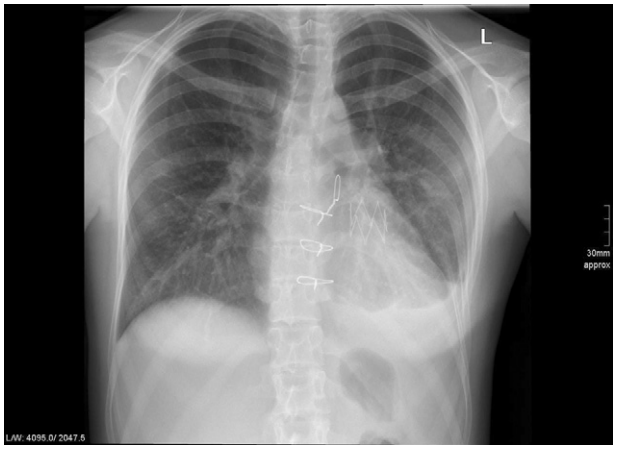

Fig. 5. Postoperative chest X-ray showing the valve in the RVOT. The procedure was performed in an adult presenting a repaired TOF with lower mini-sternotomy.

2.4. Statistics

Normally distributed and not normally distributed values are presented as median and range. We used the Student's paired *t*-test to compare preoperative to postoperative variables. The computer-based analysis was done using MS Excel (Microsoft Corporation, CA). $p < 0.05$ was considered statistically significant.

3. Results

Five males and two females, ages ranging between 2 and 24 years (median 9 years), weight ranging between 8 kg and 54 kg (median 38 kg), underwent successful implantation of the Biointegral pulmonary valve. Three patients had variant TOF, 3 suffered from congenital pulmonary valve stenosis (PS), and one had a complete AVSD combined with a PS. All of the patients had undergone surgery or interventional procedures previously and had developed severe PR. The valve was implanted via the RV apex, RVOT or PT. Five of 7 procedures were carried out with using CPB. However, additional cardiac malformations were repaired simultaneously in 3 patients; another two patients were too small (< 30 kg bodyweight) for off-pump implantation (see Section

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Table 2. Pre- and postoperative parameters from the echocardiographic evaluation are given as median and range.

	Pre-OP	Post-OP	*p*-Value
RV Dd [mm]	33 (17–59)	23 (12–40)	<0.001
RVSP + CVP [mmHg]	28 (25–80)	26 (20–45)	0.13
PAP diast. [mmHg]	4.5 (4–8)	0 (0–0)	<0.001

RV Dd = diastolic diameter of the right ventricle; RVSP + CVP = measured value for right ventricular systolic pressure plus central venous pressure; PAP diast. = diastolic pressure in the pulmonary artery.

2.3) [Fig. 8]. Median CPB time was 62 min (12–168); median procedure time was 295 min (182–333); cross-clamp was used in only those 3 patients requiring additional surgery. Valve diameters used were 15 mm, 23 mm, 25 mm, and 29 mm.

Pre- and postoperative echocardiographic parameters are summarized in Table 2. In follow-up echocardiography 6 months after valve implantation, RV systolic pressure dropped from 28 (25–80) to 26 (20–45) mmHg ($p = 0.13$). RV diameter decreased from 33 (17–59) to 23 (12–40) mm ($p < 0.01$). Median intensive care unit stay was 21 (18–85) h. Median total hospital stay was 7 (4–20) days. The post-operative courses of the 6 patients were uneventful; patient number 7 suffered from a urinary tract infection successfully treated by antibiotics. None presented a neurological impairment after surgery. Median follow-up was 25 (5–40) months. All seven patients are doing well. We have not observed any late post-operative complications. Follow-up echocardiography revealed competent valve function and no valve migration in all seven patients.

4. Discussion

Transcatheter heart valve implantation is currently very much in vogue in innovative cardiovascular heart surgery. While there is a great deal of literature describing transcatheter aortic valve implantation (TAVI), little has been published concerning transcatheter pulmonic valve implantation. Pulmonic valve implantation mainly affects patients with congenital heart disease, especially those with severe pulmonary regurgitation. Severe pulmonary regurgitation is a common finding after surgical or percutaneous treatment for pulmonary stenosis. Possible causes of PR are transannular patch plastic of the RVOT (especially in TOF patients), conduit failure, absent pulmonary valve syndrome, and RVOT aneurysm. Boone et al. [9] recently published a small case series of transcatheter pulmonary valve implantation using the Edward Sapien® transcatheter valve (Edward Lifesciences) in congenital heart disease, reporting encouraging early results. Momenah et al. [10] reported on 13 patients who underwent successful percutaneous pulmonary valve implantation using the Melody valve® (Medtronic Inc.). However, an outflow diameter greater than 26 mm rules out the percutaneous valve delivery approach using the Edward Sapien or Melody valve. In addition, both valve types require a calcified landing zone for safe anchorage of the housing stent (e.g. calcified homograft). The absence of calcification, which is common in congenital heart disease patients requiring a new pulmonic valve (e.g. TOF with transannular patch), makes the safe positioning of the transcatheter valve difficult and pre-stenting of the RVOT mandatory. However, pre-stenting means downsizing the outflowtract, which stands in opposition to the cardinal desire to leave the RVOT as wide as possible. The Biointegral Injectable Pulmonic Valve can be considered as the next generation of the Shelhigh Injectable Pulmonic Valve System®. In 2007 there were arguments regarding potential bacterial contamination of the Shelhigh products including the Shelhigh pulmonic valve. After solving this problem, Biointegral licensed the technology to manufacture the pulmonic valve in accordance with the model we used in our study. Our hybrid approach allows the implantation of large valve diameters up to 31 mm even in patients with dilated and non-calcified outflow tracts. The valve can be implanted via the RVOT after partial or full sternotomy, via the pulmonary artery after mini-thoracotomy [7], or via the RV apex [8]. Transventricular implantation of a self-expanding bioprosthesis (Shelhigh® Model NR-4000MIS) for pulmonary valve replacement has been described by Berdat and Carrel [5] and Schreiber et al. [6]. They succeeded in implanting the bioprosthesis via the RVOT without CPB use. Ferrari described a transcatheter stent-valve implantation (Edwards Sapien®) in a stenotic pulmonary conduit via a subxyphoid access [8], Huber et al. emphasized already in 2006 direct-access valve replacement (DAVR), and in 2009 introduced an experimental device for transapical pulmonary valve replacement [11,12]. The decision to use CPB in our study depended on two issues. First, if the pulmonic valve was implanted as an additional procedure during more complex cardiac repair surgery, CPB was mandatory. In this scenario, implantation of the self-expanding valve into the opened RVOT has various advantages: it saves time, avoids suture lines inside the pulmonary arteries (which can trigger suture line stenosis during follow-up), and it offers surgeons the opportunity to implant a larger valve size thanks to it self-expanding character. Second, since there is only one size of the delivery system available, it cannot be fully inserted into the right ventricular cavity in small hearts. To prevent unnecessary blood loss, we therefore recommend using CPB in patients weighing less than 30 kg. In all other cases, the Biointegral pulmonic valve can be implanted without using CPB. The new flexible barrel piston of the delivery system makes the NRIP® easy to position and deploy. Although the main part of the delivery trocar's barrel is not visible during positioning, the device is easy to feel through the pulmonary artery so as to ensure correct three-dimensional positioning. In case of a malpositioning or dislodgement, repositioning is easy. External fixation at the level of the inflow part concludes the valve's implantation and prevents potential valve migration. However, those additional stiches might not be necessary due to the combination of oversizing and the self-expandable character of the valve in a low pressure system, which is currently under experimental investigation.

In conclusion: we believe that the easy application, improved biocompatibility, and wide range of prosthesis sizes offer an auxiliary treatment option for patients with severe PR. Implantation of this catheter-based, self-expanding pulmonary valve is a safe procedure and a time-saving alternative to conventional pulmonary valve replacement

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References

[1] Oechslin EN, Harrison DA, Harris L, Downar E, Webb GD, Siu SS, Williams WG. Reoperation in adults with repair of tetralogy of fallot: indications and outcomes. J Thorac Cardiovasc Surg 1999;118(2):245—51.
[2] Follis FM, Pett Jr SB, Miller KB, Wong RS, Temes RT, Wernly JA. Catastrophic hemorrhage on sternal reentry: still a dreaded complication? Ann Thorac Surg 1999;68(6):2215—9.
[3] Lurz P, Bonhoeffer P, Taylor AM. Percutaneous pulmonary valve implantation: an update. Expert Rev Cardiovasc Ther 2009;7(7):823—33.
[4] Bonhoeffer P, Boudjemline Y, Quereshi SA, Le Bidois J, Iserin L, Acar P, Merckx J, Kachaner J, Sidi D. Percutaneous insertion of the pulmonary valve. J Am Coll Cardiol 2002;39(10):1664—9.
[5] Berdat PA, Carrel T. Off-pump pulmonary valve replacement with the new Shelhigh Injectable Stented Pulmonic Valve. J Thorac Cardiovasc Surg 2006;131(5):1192—3.
[6] Schreiber C, Hörer J, Vogt M, Fratz S, Kunze M, Galm C, Eicken A, Lange R. A new treatment option for pulmonary valvar insufficiency: first experiences with implantation of a self-expanding stented valve without use of cardiopulmonary bypass. Eur J Cardiothorac Surg 2007;31(1):26—30.
[7] Dittrich S, Gloeckler M, Arnold R, Sarai K, Siepe M, Beyersdorf F, Schlensak C. Hybrid pulmonary valve implantation: injection of a self-expanding tissue valve through the main pulmonary artery. Ann Thorac Surg 2008;85(2):632—4.
[8] Ferrari E, Sulzer C, Rizzo E, von Segesser LK. Transcatheter stent-valve implantation in a stenotic pulmonary conduit via a sub-xyphoidian access. Eur J Cardiothorac Surg 2009;36(3):595—7.
[9] Boone RH, Webb JG, Horlick E, Benson L, Cao QL, Nadeem N, Kiess M, Hijazi ZM. Transcatheter pulmonary valve implantation using the Edwards SAPIEN transcatheter heart valve. Catheter Cardiovasc Interv 2010;75(2):286—94.
[10] Momenah TS, El Oakley R, Al Najashi K, Khohhal S, Al Qethamy H, Bonhoeffer P. Extended application of percutaneous pulmonary valve implantation. J Am Coll Cardiol 2009;53(20):1859—63.
[11] Huber CH, von LK, Segesser. Direct access valve replacement (DAVR)—are we entering a new era in cardiac surgery? Eur J Cardiothorac Surg 2006;29(3):380—5.
[12] Huber CH, Hurni M, Tsang V, von Segesser LK. Valved stents for transapical pulmonary valve replacement. J Thorac Cardiovasc Surg 2009;137(4):914—8.

Appendix A. Conference discussion

Dr C. Schreiber (*Munich, Germany*): I call it quite a coincidence that I am helping out on this discussion because I implanted 9 valves, as you know, a few years ago. We abandoned it mainly because of valve-related issues. We had cases of endocarditis, and I also felt that the introduction mechanism was not safe enough.

In which patient group do you really think this valve with its available introducing mechanism has a place? Edwards is currently introducing its pulmonic program. There have been thousands of SAPIEN valves implanted. In addition, I found it quite interesting that you inserted your valves on-pump in quite a few cases, whereas we have not done it in a single case.

Maybe you can just elucidate which patients will benefit from your proposed approach.

Dr von Wattenwyl: Yes, it is a good point, but we are convinced that the main advantage of this valve is that we can go up to 31 mm. And it often occurs, for example, in tetralogy of Fallot patients that they have a dilatation of the right ventricular outflow tract. And according to my knowledge, I think that in the Edward SAPIEN valve, the highest range is 26 mm. So we still have 5 mm more to implant the valve.

Why we did so much on on-pump? It was a feasibility and safety study. So as you see, at the end we started with off-pump procedures, trying to get a little bit less invasive to get to the RVOT.

I am convinced that we can use this valve in the increasing number of patients, the grown-ups with congenital heart disease, which we will see more and more now.

Dr Schreiber: Any questions from the floor? If not, I might add that in addition to the pulmonic program from Edwards, cardiologists have increasingly used the 'Melody' valve. There are attempts reported at bringing down the size of the RVOTwith special stents. I am not sure to what extent your approach will gain acceptance in the future.

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