Title: Mid-term performance of a novel restorative pulmonary valved-conduit: preclinical results.

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Mid-term performance of a novel restorative pulmonary valved-conduit:

preclinical results

Running title: Outcome of a restorative pulmonary valved-conduit

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Abbreviations:

XPV, Xeltis pulmonary valved conduit
ETR, Endogenous tissue restoration
HPV, Hancock pulmonary valved bioprosthesis
PA, Pulmonary artery
PR, Pulmonary regurgitation
RV, Right ventricle
RVOT, right ventricular outflow tract
Abstract

Aims: A bioabsorbable pulmonary valved-conduit (XPV), designed to guide functional restoration patients own tissue, is potentially more durable than current pulmonary bioprosthetic valves/valved-conduits. The aim of this study was to assess the hemodynamic performance of the novel XPV implanted in an ovine model.

Methods and results: The XPV was surgically implanted in adult sheep under general anaesthesia and cardiopulmonary bypass (XPV-group, n=20). Sheep that received a Hancock bioprosthetic pulmonary valved-conduit served as a control group (HPV-group, n=3). Transthoracic echocardiography (TTE) from VARC-2 recommended time points at 3, 6, 9, 12, 18 and 24-months (XPV-group) and at 3 and 6-months (HPV-group) after the procedure were analysed in an independent core laboratory. The primary endpoint was favourable performance defined as: peak systolic pressure gradient <40 mmHg, no severe pulmonary regurgitation (PR), and a maximum conduit patency index of -20%. In the latter, negative values denote luminal narrowing and vice versa.

The valvular peak systolic pressure gradient (mmHg) was 25.6±9.7 (3-months), 19.6±7.1 (6-months), 10.0±9.2 (24-months) in the XPV-group and 18.4±6.6 (3-months), 17.7±4.6 (6-months) in the HPV-group. The patency index (%) of the conduit at the valvular level was +30.3±13.6 (6-months) and +64.1±1.4 (24-months) in the XPV-group and +2.0±15.9 (6-months) in the HPV-group. PR was trace or mild at all visits, except in one animal with persistent moderate PR in the XPV-group up to 24-months.

Conclusions: The XPV showed a favourable and durable hemodynamic performance (up to 2-years after implantation), without conduit narrowing/obstruction or severe regurgitation.
Condensed abstract

We sought to assess the hemodynamic performance of a novel biodegradable pulmonary valved-conduit (XPV) implanted in an ovine model and to compare short-term performance with the Hancock pulmonary bioprosthesis. Up to 2 years postoperative, the pressure gradient across the XPV leaflets was favourable and no luminal narrowing or severe regurgitation were seen. XPV animals demonstrated an increase in diameter and a decrease in pressure gradients over time in contrary to the Hancock animals. Short term morphologic and hemodynamic features in the XPV group were comparable to the Hancock control.
INTRODUCTION

Congenital defects involving the right ventricular outflow tract (RVOT) and the pulmonary artery (PA), such as tetralogy of Fallot, pulmonary atresia, or transposition of the great arteries with pulmonary stenosis, represent about 20-40% of patients with congenital heart disease who survive until adulthood (1,2). Reconstruction of the RVOT is part of the surgical repair of these conditions, and inevitably portends recurrent RVOT dysfunction requiring the implantation of a right ventricle (RV)-to-PA conduit or a prosthetic pulmonary valve. Unfortunately, the life span of these conduits is much shorter than the life span of the recipient patients due to the fact that they degenerate, resulting in pulmonary regurgitation (PR), with resultant progressive RV dilation and failure (3-6). In addition, these conduits do not allow for natural growth of the child. In order to overcome these limitations, the development of more biocompatible conduits that have the potential to grow has been a challenging quest in recent years. The approaches to engineering a biocompatible pulmonary valve with growth potential typically involve the seeding of cells (endothelial cells, stem cells, amniotic fluid-derived cells, or autologous progenitor cells) to populate various scaffolds composed of biodegradable polymers, autologous tissue, or allograft or xenograft matrixes (7-13). More recently, a new technology was developed based on a biodegradable polymer matrix designed to enable Endogenous Tissue Restoration (ETR) without the use of stem cells or animal-derived products (14). The novel polymeric valved conduit allows patient’s own cells to infiltrate and trigger a cascade of physiological events leading to gradual replacement of prosthetic material by native tissue. In this study, we sought to investigate the mid-term performance of a novel biodegradable polymeric pulmonary valved-conduit (XPV) in a sheep model.
METHODS

Study description:

The study included 23 adult Swifter sheep (age: 2-4 years, weight: 60-90 kg). The pulmonary valved-conduit (Xeltis BV, Eindhoven, the Netherlands) was implanted in 20 sheep (XPV-group) while the 22 mm Hancock® bioprosthetic valved-conduit which consists of a porcine aortic valve sutured into the center of a woven fabric conduit (Medtronic Heart Valve Division, Irvine, CA, USA) was implanted in 3 control sheep (HPV-group). Two animals died early after implantation of the XPV because of arrhythmia and extensive clamping during the procedure. Nine animals have no data available. Nine animals eventually constituted the XPV-group available for follow up. The study flow chart is shown on Figure 1, and a third animal was sacrificed after 5-months due to infective endocarditis.

The study protocol adhered to the Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes and the Guide for the Care and Use of Laboratory Animals and was reviewed and approved by the Test Facility’s Ethical Committee for compliance with regulations prior to study initiation (EC approval n° EC MxCl 2014 - 027).

The biodegradable pulmonary valved-conduit description:

The XPV is a flexible, highly porous conduit with 3 leaflets, fabricated by electrospinning from a novel supramolecular elastomer. The XPV has a length of 5 cm and an inner diameter of 21 mm. The concept of XPV is based on ETR, in which gradual restoration of the absorbable leaflet and conduit wall by patient’s own cells takes place. The leaflet and conduit are infiltrated by inflammatory cells which release growth factors and promote smooth muscle cell infiltration and matrix (proteoglycans and collagen with focal elastic tissue)
production, while the same inflammatory cells also ensure the absorption of the polymeric implants.

**Surgical technique and postoperative management:**

The conduits (XPV 21 mm or HPV 22 mm) were surgically implanted under general anaesthesia and normothermic cardiopulmonary bypass on beating heart. The heart was exposed by a left anterolateral thoracotomy through the third intercostal space. After transection of the native pulmonary artery, the graft was implanted as an interposition pulmonary artery vascular graft 0.5-1.0 cm above the native pulmonary valve, the leaflets of which had been surgically removed. The antithrombotic regimen consisted of Enoxaparin (Clexane®, Sanofi Aventis, Diegem, Belgium) 20 mg twice daily and Aspirin (Aspegic®, Sanofi Aventis, Diegem, Belgium) subcutaneous injection 250 mg for 5 days.

**Echocardiographic acquisition:**

Echocardiographic acquisition was performed using a Vivid-I (GE Healthcare) ultrasound machine in accordance with a prespecified protocol in the Animal Test Facility (Medanex, Belgium). Transthoracic echocardiography (TTE) was performed on conscious animals at the following time points: pre-operative, 1 week after the procedure, every 4 weeks thereafter up to 2 years, and one week before animal sacrifice. Standard echocardiographic views were used to obtain two-dimensional, spectral Doppler, and colour Doppler interrogation of the pulmonary valve, RVOT, and the main PA. For the assessment of the pulmonary valved-conduit performance, echocardiographic acquisition included the following views: two-dimensional images of the entire conduit as well as pulsed-wave (PW) Doppler, continuous wave (CW) Doppler, and colour Doppler at the subvalvular, the valvular, and the distal conduit regions.
Core laboratory echocardiographic analysis:

As recommended by the Valve Academic Research Consortium (VARC)-2 guidelines, we choose mandated timelines for echocardiographic analysis (15). TTEs at 3-, 6-, 9-, 12-, 18- and 24-months (XPV-group) after implantation were analysed for XPV primary and secondary performance endpoints. Comparison between the XPV-group and HPV-groups was performed at 3- and 6-months after the procedure.

All TTEs were analysed in an independent core laboratory (Cardialysis, Rotterdam, the Netherlands) using the Image Arena version 4.6.3 workstation (TomTec, Munich, Germany). Measurements of Doppler velocities and 2D dimensions were performed in accordance with published guidelines (16-19). Figure 2 displays the locations at which the echocardiographic measurements of the conduit diameters and performance indices were performed.

Conduit function: Hemodynamic assessments included: peak velocity (m/sec) and mean and peak pressure gradients (mmHg) at the subvalvular and the valvular levels of the conduit. Mean and peak pressure gradient (PG) were derived from PW or CW Doppler by manual tracing the spectral systolic velocity curves.

Severity of pulmonary valve regurgitation (PR) was graded on a 5-grade scale as none, trace, mild, moderate, or severe based on jet width criteria (Table 1) and/or color Doppler flow reversal criteria (Table 2)(20). Clinically relevant PR was defined as at least mild PR.

Conduit morphology: Measurements of the conduit diameter at early to mid-systole was intended at the level of the conduit leaflets (valvular), 5-10 mm proximal to the leaflets (subvalvular), and >10 mm distal to the leaflets (distal).

The conduit patency index (CPI) was calculated to assess narrowing or expansion of the conduit at the subvalvular and valvular levels from 3-month post-implantation to a given
follow up time point (=[conduit diameter at follow up – conduit diameter at 3-months] / conduit diameter at 3-months%). A negative CPI value suggests conduit narrowing due to e.g. neo-intimal hyperplasia; and a positive CPI suggests conduit expansion.

The primary endpoint of the study was the XPV performance at postoperative 3-, 6-, 9-, 12-, 18- and 24-months. A favourable performance of the XPV was defined as freedom from all of the following: 1) a transvalvular peak systolic pressure gradient >40 mmHg, 2) conduit narrowing as demonstrated by a reduction of the CPI of 20% or more, and 3) severe PR.

Statistics

Continuous variables with normal distribution were expressed as mean ± SD, while continuous variables with non-normal distribution were expressed as median and interquartile range (IQR). No formal statistics were performed in this study due to the small sample size and the exploratory nature of the study.
RESULTS

As shown in Supplementary Table 1, all echocardiographic parameters were measurable in the majority of cases (88-100%), except for the distal conduit diameter which could be reliably measured in only one third of cases. Therefore, measurements at the subvalvular and valvular conduit levels are reported in the results.

Study primary endpoint (Table 3)

A favourable valve hemodynamic performance was achieved in all study animals. The average peak systolic PG at the valvular level was 25.6±9.7 mmHg (3-months), 10.0±9.2 mmHg (24-months) in the XPV-group and was 18.4±6.6 mmHg (3-months), 17.7±4.6 mmHg (6-months) in the HPV-group. Except for a single case that showed a temporary rise of peak PG >40 mmHg at the 3-month evaluation, all other cases did not show a significant rise (>40 mmHg) at any time point and tended to decline overtime (Figure 3). Therefore, although tended to be higher early post-procedural, peak PG values were eventually lower in the XPV-group at the end of follow up than in the HPV-group at 3- and 6-months (Table 3).

The CPI (%) in the XPV-group was +27.6±9.8 at 6-months and +50.8±6.1 at 24-months post-procedure at the subvalvular level, while it was +30.3±13.6 at 6-months and +64.1±1.4 at 24-months at the valvular level. The CPI in the HPV-group were at 6-months +2.0±15.9 at valvular level and +5.7±16.3 at subvalvular level (Table 3). None of the animals in the XPV-group had a narrowing >20% across the conduit at any time point (Figure 4).

PR severity was trace or mild at all follow-up time-points in 8 animals and consistently moderate in one animal in the XPV-group, while PR was trace in the HPV-group animals up to 6-months (Table 4 and Figure 5). In the XPV-group, the PR jet width to RVOT ratio was <20% in 5 animals and >20%, in 2 animals 12-months after implantation. According to the flow reversal criteria, PR severity was trace or mild in 6 animals and moderate in 1 animal
12-months after procedure in the XPV-group. There has been a discrepancy of the PR severity between jet width criteria and flow reversal criteria in a single animal, in which PR was eventually adjudicated as mild.

Other study endpoints:

Other parameters of valve performance were examined in the XPV-group at 12- and at 24-months after the procedure and compared to the respective measurements performed at 3- and 6-months in the HPV-group. Mean systolic PG at the valvular level was 15.1±6.5 mmHg (3-months), 10.9±3.9 (6-months) and 5.4±4.7 mmHg (24-months) in the XPV-group and was 10.6±3.6 mmHg (3-months) and 9.7±2.0 mmHg (6-months) in the HPV-group. Mean systolic PG was <20 mmHg in all XPV-group animals at both the subvalvular and the valvular levels of the conduit 12-months (n=7) and 24-months (n=2) after the procedure. Mean systolic PG decreased over time in the XPV-group while it did not change in the HPV-group between 3- and 6-months after implantation (Figure 6).

None of the animals in the XPV-group had a peak velocity >3 m/s at subvalvular or valvular levels of the conduit 12- and 24-months after the procedure (n=7). Although one animal had a peak velocity >3 m/s at the valvular level 3-months after the procedure, the peak velocity at 6-months decreased to <3 m/s. Peak velocity decreased over time in XPV-group (Figure 7 and Table 3) while peak velocity in the HPV-group did not change between 3- and 6-months (Table 3).

The subvalvular conduit diameter of XPV increased from 18.7±2.0 to 27.2±2.8 and 24.6±0.2 at 3-, 12- and 24-months, respectively. In contrary, the subvalvular conduit diameter in the HPV-group was 18.6±1.3 and 19.5±1.7 at 3- and 6-months, respectively. Similarly, the valvular conduit diameter of XPV increased from 18.4±2.4 to 27.1±2.0 and 25.8±1.3 at 3-,
12- and 24-months, respectively; while in the HPV-group it was 18.4±1.2 vs. 18.7±1.9 at 3- and 6-months, respectively (Figure 8 and Table 3).

**Discussion**

In 20-40% of adults with congenital heart disease, there is an RVOT abnormality requiring implantation of an artificial conduit between the RV and the PA (1,2). Regardless of the technique used to reconstruct the RVOT, conduit dysfunction is common and freedom from degeneration at 10 years is 51% in case of homografts implanted before the age of 10 years (5). Accordingly, many patients have their third RVOT intervention by the age of 20 years (21). Re-intervention is associated with discomfort, disfigurement, cost, morbidity, and mortality.

Attempts have been made over the last 3 decades to develop tissue-engineered heart valves, which generally consist of a 3D scaffold seeded with autologous cells to produce a new extracellular matrix in a bioreactor. This biological construct can be implanted enabling further in vivo tissue growth and remodeling(22). The scaffold can be made of polymers, decellularized scaffolds, or non-valve tissue biological scaffolds (e.g. collagen)(23). Decellularized xenogenic scaffolds (e.g. ovine(24), porcine(25,26), and allogenic human(7) pulmonary valves) have been tested in lamb(24), dog(25) and sheep(26) models, as well as in human pediatric cases(7). Polymeric scaffolds (especially poly ε-caprolactone-based scaffolds) are characterized by suitability for electrospinning, balanced strength and speed of resorption, and, accordingly, less vulnerability to leaflet compaction and retraction(27). In an ovine model, Schmitt et al reported the mid-term results of a transcatheter stented decellularized valve implanted to replace the pulmonary valve(28). The valve was based on a polymeric scaffold seeded with ovine vascular cells, then decellularized and implanted 8.5±5.9 weeks after manufacture. Serial echocardiographic assessment until explanation...
(after 8, 16 or 24 weeks), revealed a normal transvalvular pressure gradient of all implants (n=15), but stent ovality led to progressive regurgitation. Complete endothelialization and rapid cellular repopulation and remodeling of the entire matrix as well as freedom from endocarditis, calcification and graft rejection were demonstrated in all cases.

Another concept of valves with regenerative capacity is based on the extracellular matrix derived from decellularized porcine small intestinal submucosa (SIS-ECM) used as a biological scaffold for cardiac/vascular repair. CorMatrix (CorMatrix Cardiovascular, Inc., Roswell, GA, USA) is the most commonly used SIS-ECM scaffold owing to its absorbability, favorable remodeling and immunologic properties, and its potential to promote endogenous tissue regeneration and growth(29).

Preclinical results of pulmonary valve transcatheter/surgical replacement were mostly promising(30,31), but some were somewhat alarming to that the rate of growth of the biological conduit might not match that of the adjacent native tissues, leading to a relative narrowing of the conduit(32). Clinical outcomes in 103 patients with congenital cardiac defects who received different CorMatrix-based repair/reconstruction techniques were generally favorable, with no calcification detected up to a median follow-up of 23.3 months(33). Interventions involving the pulmonary valve and/or pulmonary artery were associated with a relatively high rate of need for re-intervention, likely due to imperfect surgical techniques; e.g. valve repair by leaflet extension.

The XPV is a next generation conduit fabricated from a novel supramolecular elastomer that enables endogenous cells to populate the scaffold and to produce matrix. In the present study, echocardiographic analysis by an independent Core Laboratory showed a favourable hemodynamic performance as well as an acceptable regurgitation severity of the XPV, sustained up to 2 years after implantation. Morphologically, the XPV showed no narrowing or abnormal growth during the follow-up period. The definition of a favourable
valve hemodynamic performance in this report was based on the best clinical judgment, published data on established pulmonary prosthetic valves/conduits, and practice guidelines (19,34,35).

In two animals, hemodynamic findings warrant more discussion. Animal #99798 initially had a high peak systolic PG at the valvular level at 3-months, which was consistently improving on later echocardiograms, eventually approaching acceptable values. The peak transvalvular gradient decreased to <30 mmHg at 6-month and to <20 mmHg on the ’12-month echocardiogram. There is no clear echocardiographic findings, or otherwise clinically, to explain this temporarily high PG. However, a transient thrombus is a likely explanation.

Moderate PR was consistently seen in animal #66242 up to 24-months after the procedure. This animal has shown a CPI of up to +70%, denoting a considerable increase in the conduit diameter during follow-up, ranking highest among all animals in terms of luminal expansion. In the contrary, the actual diameter of the XPV in that animal (#66242) was 25 mm, which is the same diameter of the other animal (#21732) at the latest follow-up at 24-months. These values are, in fact only 4 mm larger than nominal implantation diameter of 21 mm. Likewise, another animal (#99972) with even more increased diameter at 12-months follow-up have only trace PR.

There is limited data on precise echo-Doppler cut-off values to define prosthetic pulmonary valve dysfunction. The American Society of Echocardiography guidelines recommend using RV-to-PA peak velocity as well as peak and mean PG for the evaluation of prosthetic pulmonary valve function. A normal performance of pulmonary prosthetic valve is defined by a peak transprothetic velocity of <3.2 m/s and a mean transprothetic pressure gradient <20 mmHg (18). In the Melody Transcatheter Pulmonary Valve Post-Approval Study (NCT01186692) a mean pressure gradient ≤30mmHg and PR <moderate at 6-months
were used as the intended transcatheter valve performance criteria (36). Procedural success was defined as transcatheter pulmonary valve implanted in desired location, and RV-PA peak gradient <35 mmHg (derived from invasive measurement), no more than mild PR on angiography, and freedom from explantation at 24 hours post-implantation (36). Structural valve deterioration of the surgically implanted Medtronic Freestyle bioprosthesis was defined as a composite of significant stenosis (a peak transvalvular gradient of >50 mmHg or a mean transvalvular gradient of >35 mmHg), or significant regurgitation (moderate or greater) on echocardiography (37).

In line with the hemodynamic data of established transcatheter and surgical pulmonary valve prostheses as well as the Hancock 22 mm conduit used in this study, the XPV has a favourable hemodynamic data. These data are to be confirmed in a human clinical study, which is currently underway.

Limitations

Interpretation of this study is limited by the relatively small number of echocardiographic evaluations available. Echocardiograms at the immediate postoperative visit (t=0) were not available. Absence of a clear electrocardiographic signal on echocardiographic images was another limitation, particularly for PR assessment. Ideally, the conduit dimensions should be quantified on a three-dimensional imaging modality.

To accommodate the 21 mm conduit tested in the present study, we used an adult ovine model (2-4 years). One important advantage of ETR is the potential for growth (already confirmed in the present study), a characteristic that is especially relevant to growing children. Therefore, a younger ovine model could have been theoretically more suitable. We do not see, however, a reason to assume that the pattern of conduit growth seen in the adult model would be different if younger sheep were used.
Conclusion. The XPV shows encouraging results in an adult sheep model up to 24-months after implantation without luminal narrowing or hemodynamic deterioration.
Impact on daily practice:

Clinical application of the biodegradable pulmonary valved-conduit is currently underway and results are awaited soon. The results of the present pre-clinical study, after confirmation in the clinical study, should usher in a new era of constructive treatment for congenital heart diseases.

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Conflict of interest statement: Marieke Brugmans is employed by Xeltis. Martijn Cox is employed by Xeltis and has shares of Xeltis. All other authors have no relevant conflicts of interest to declare.
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Figure legends

Figure 1. Flow chart of the study and the key echocardiographic assessment time points.

Figure 2. Diagram displaying the locations of echocardiographic measurements of the pulmonary valved-conduit morphology and function.

Figure 3. Serial changes of peak pressure gradient of individual animals at the subvalvular (A) and valvular (B) levels of the biodegradable pulmonary valved-conduit.

Figure 4. Serial changes of the conduit patency index of individual animals at the subvalvular (A) and valvular (B) levels of the biodegradable pulmonary valved-conduit.

Figure 5. The severity of pulmonary regurgitation at different time points after implantation of the biodegradable pulmonary valved-conduit (A) and the Hancock valved-conduit (B).

*Animal #70215 images were non-analyzable

Figure 6. Serial changes of mean pressure gradient of individual animals at the subvalvular (A) and valvular (B) levels of the biodegradable pulmonary valved-conduit.

Figure 7. Serial changes of peak velocity of individual animals at the subvalvular (A) and valvular (B) levels of the biodegradable pulmonary valved-conduit.

Figure 8. Serial changes of conduit diameter of individual animals at the subvalvular (A) and valvular (B) levels of the biodegradable pulmonary valved-conduit.
Table 1. Jet width criteria of pulmonary regurgitation severity

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<th>Grade</th>
<th>Description</th>
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<tr>
<td>None</td>
<td>No diastolic colour flow jet</td>
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<td>Trace</td>
<td>Pinhole colour flow jet on ventricular side of the leaflets</td>
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<tr>
<td>Mild</td>
<td>Jet width &lt;20% of the valve/conduit width*</td>
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<tr>
<td>Moderate</td>
<td>Jet width 20% to 40% of the valve/conduit width</td>
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<tr>
<td>Severe</td>
<td>Jet width &gt;40% of the valve/conduit width</td>
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*As measured at the valvular (leaflet) level.
Table 2. Flow reversal criteria of pulmonary regurgitation severity

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<td>No diastolic colour flow reversal at level of the valve leaflets</td>
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<td>Diastolic colour flow reversal extending above the valve leaflets but confined to proximal half of main PA</td>
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<td>Moderate</td>
<td>Diastolic colour flow reversal extending into distal main PA</td>
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<td>Severe</td>
<td>Diastolic colour flow reversal extending into PA branches</td>
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PA, pulmonary artery
Table 3. Summary of quantitative assessment of echocardiogram assessment

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<th>Visit</th>
<th>3 months</th>
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<td><strong>Maximal conduit dimensions (mm)</strong></td>
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<td><strong>Pulmonary regurgitation (Jet width to RVOT ratio, %)</strong></td>
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<td><strong>Peak systolic pressure gradient (mmHg)</strong></td>
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</table>

Abbreviations, HPV, Hancock pulmonary valved conduit XPV, NA, Not available or not applicable; Xeltis biodegradable pulmonary valved conduit. For other abbreviations, see the supplementary table 1.

* n=6; # n=5; § n=2
Table 4. The severity of pulmonary regurgitation for sheep in the two study groups.

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<th>Animal ID</th>
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<th>3-months</th>
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</tbody>
</table>

XPV, Xeltis pulmonary valved-conduit; HPV, Hancock valved-conduit.
Figure 1

23 animals in the study population

No images were available (n=9)
Died right after surgery (n=1)
Died 11 days after surgery (n=1)

20 animals received XPV

Procedure

3 animals received Hancock

9 animals were assessed by TTE

3 months

3 animals were assessed by TTE

8 animals were assessed by TTE

6 months

3 animals were assessed by TTE

7 animals were assessed by TTE

9 months

Scheduled sacrifice (n=5)

7 animals were assessed by TTE

12 months

Scheduled sacrifice (n=2)

2 animals were assessed by TTE

18 months

2 animals were assessed by TTE

24 months

Sacrificed due to endocarditis (n=1)
Figure 2

Echocardiographic measurements

- At 5-10 mm proximal to the leaflets (subvalvular)
- At the conduit leaflets (valvular)
- At <10 mm distal to the leaflets (distal)

Figure 2
Figure 3

A  

B
Figure 4

A

Conduit patency index (subvalvular) XPV

% 70

-20 -10 0 20 30 40 50 60 80

Months after the procedure

B

Conduit patency index (valvular) XPV

% 70

-20 -10 0 20 30 40 50 60 80

Months after the procedure
Figure 5

A and B: Graphs showing PR severity control over months after implantation for different patient groups. The graphs display the percentage of patients in each severity group (trace, mild, moderate) across various time points post-implantation.

- **A**: Shows a comparison of PR severity control for two different patient groups (n=9 and n=7) with varying time points (7, 6, 3, 4, 2, 1) post-implantation.
- **B**: Demonstrates PR severity control for another patient group (n=3) with months post-implantation ranging from 2 to 3.

The data highlights the effectiveness of the procedure in controlling PR severity over time.
Figure 7
Figure 8

A

Months after the procedure

Conduit diameter (valvular) HPV

mm

40 35 30 25 20 15 10 5 0

B

Conduit diameter (subvalvular) HPV

mm

40 35 30 25 20 15 10 5 0

Months after the procedure

Diagnosis: As a public service to our readership, this article – peer reviewed by the editors of EuroIntervention – has been published immediately upon acceptance as it was received. The content of this article is the sole responsibility of the authors, and not that of the journal.