A FUTURE WITHOUT RE-OPERATIONS?

New horizons in pulmonary heart valve therapy

January 29, 2018

Prof. Dr. Gerardus Bennink

Chief and head of pediatric cardio-thoracic congenital surgery
Heart Center of the University of Cologne
Congenital heart defects

CHDs:
- Most common birth defect (1%)
- Around 40,000 U.S. babies each year

CHD of RVOT
15-20% of all CHDs:
- Tetralogy of Fallot
- Truncus Arteriosus
- Pulmonary Atresia
- TGA+VSD+LVOTO

Procedure
RVOT reconstruction
- Pulmonary heart valve replacement
## RVOT Surgery

<table>
<thead>
<tr>
<th>What to expect</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average duration: 2-4 hours</td>
<td>Reconstruction</td>
</tr>
<tr>
<td>Recovery time and discharge: up</td>
<td>- Valve replacement (valved conduit)</td>
</tr>
<tr>
<td>to a week</td>
<td>- Valve insertion (transcatheter)</td>
</tr>
<tr>
<td>Life at home: a life as normal</td>
<td>Repairs</td>
</tr>
<tr>
<td>possible</td>
<td>- Monosusp patch</td>
</tr>
<tr>
<td></td>
<td>- Transannular patch</td>
</tr>
</tbody>
</table>
Pulmonary heart valve options

Homograft
- Homograft with pericardial hood

Valved conduits with biological/mechanical valve

Xenograft

Mechanical valve alone
Transcatheter pulmonary heart valves - TPVs

Less invasive:
No open-heart surgery

- Not for babies/smaller children
- Not first heart valve replacement option
Life after surgery is progressing

Artificial heart valves are life savers

# Children with CHD = # Adults with CHD

Surgery is often not a definitive cure

Most patients require additional operation(s)/medications
Heart valve replacement is currently unavoidable

Calcification  Patient growth  Stenosis
Reduced blood flow

Reduced oxygen in the blood
Breathlessness  Tiredness  Fatigue
Re-intervention

Figure 2: Freedom from the second redo pulmonary valve replacement. Numbers above the x-axis represent patients remaining at risk.

Ideal valve?

- Readily available
- Non-thrombogenic
- All sizes
- Excellent flow dynamic
- Life-long guarantee
On the horizon

- Fully synthetic restorative heart valves
- De-celluralized homografts
- Stem-cells (very early stages)

! NB: investigational devices only
Xeltis’ Restorative Heart Valve technology
Xeltis’ Restorative Heart Valve technology

Unique absorbable matrices

Restorative Valves
## Restorative technology in trials

<table>
<thead>
<tr>
<th>Technology</th>
<th>In-vitro</th>
<th>Pre-clinical</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric conduit (Fontan)</td>
<td><img src="pediatric_conduit.png" alt="Image" /></td>
<td>Positive 31-month clinical data</td>
<td>Presented WCPCCS 2017</td>
</tr>
<tr>
<td>Pulmonary Valve</td>
<td><img src="pulmonary_valve.png" alt="Image" /></td>
<td>Positive 2-year preclinical data</td>
<td>Published in Eurointervention 2017</td>
</tr>
<tr>
<td>Aortic Heart Valve</td>
<td><img src="aortic_valve.png" alt="Image" /></td>
<td>Extending pipeline to high pressure circuit</td>
<td>Published in Eurointervention 2017</td>
</tr>
<tr>
<td>Vascular Applications</td>
<td><img src="vascular.png" alt="Image" /></td>
<td>Further pipeline expansion underway</td>
<td></td>
</tr>
</tbody>
</table>
Pulmonary Valve

Pre-Clinical Animal Data

- Over 50 sheep implanted
- Juvenile and adult sheep
- Up to 24 months implantation

- Key findings
  - Better survival than controls (Hancock)
  - After 24 months significant degradation, small fragments remaining
  - Stable healing and tissue restoration
  - Positive functionality overtime
  - Limited calcification compared to controls
  - No aneurysms seen in any case (most important for this indication)
Histopathology details

Balanced scaffold absorption and tissue restoration

Conduit is covered by new tissue.

New tissue thickening at the base.

2m

Resorption of the conduit.

2mm

New tissue covered 2/3 of the leaflet.

Partial breakdown of the leaflet with inflammation.

6m

Inflammation and ingrowth of new tissue at resorption site.

New tissue coverage of leaflet.

12m

Dr. Renu Virmani

New tissue

Conduit

Leaflet
Pulmonary valve in patients

First trial in EU/Asia

**Target indication**
- RVOT correction or reconstruction
- Patients younger than 22 years
- Patients with the following CHDs
  - Tetralogy of Fallot
  - Truncus Arteriosus
  - Pulmonary Atresia
  - Transposition of Great Arteries with Ventricular Septum Defect (VSD)
  - Pulmonary Stenosis in combination with other defects in CHD syndromes

**Additional indication**
- Replacement of previously implanted, but dysfunctional, pulmonary heart valves
## Summary/Trial Status

### Pulmonary valve in patients

<table>
<thead>
<tr>
<th>Enrollment Started: 07.07.16</th>
<th>Enrollment Completed: 14.12.16</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients enrolled: 12 (6 boys)</td>
<td>• All patients are doing well</td>
</tr>
<tr>
<td>• Age range: 2–12 years</td>
<td>• No deaths, no reintervention or reoperation</td>
</tr>
<tr>
<td>• Clinical sites:</td>
<td>• No device-related serious adverse events</td>
</tr>
<tr>
<td>– Budapest (4)</td>
<td>• Information on:</td>
</tr>
<tr>
<td>– Krakow (3)</td>
<td>– Surgical techniques</td>
</tr>
<tr>
<td>– Kuala Lumpur (5)</td>
<td>– Patients’ anatomy</td>
</tr>
<tr>
<td>• Follow-up reached:</td>
<td>– Product efficiencies</td>
</tr>
<tr>
<td>– 12 months – 12</td>
<td></td>
</tr>
</tbody>
</table>
US Restorative pulmonary valve trial

Trial Centers

Children’s Healthcare of Atlanta
Investigator: Kirk Kanter, MD
Contact: Janet Fernandez
Janet.Fernandez@choa.org

Boston Children’s Hospital
Investigator: Christopher Baird, MD
Contact: Michele Borisuk
Michele.Borisuk@cardio.chboston.org

New York Presbyterian Hospital – Columbia University
Investigator: Emile Bacha, MD
Contact: Kydanis Clase
kc3020@cums.columbia.edu
columbiasurgery.org/clinical-trials/xplore-ii

Children’s Hospital of Philadelphia
Investigator: J William Gaynor, MD
Contact: Brenna Klepczynski
klepczynski@email.chop.edu

Visit: www.xplore2trial.com
Ideal valve technology?

Readily available

All sizes

Promising results

Potentially longer lasting

A future not to be missed!
A FUTURE WITHOUT RE-OPERATIONS?

New horizons in pulmonary heart valve therapy

Thank you!

Prof. Gerardus Bennink