A future without re-operations?

New horizons in pulmonary heart valve therapy

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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

**What to expect**

- Average duration: 2-4 hours
- Recovery time and discharge: up to a week
- Life at home: a life as normal as possible

**Methods**

- Reconstruction
  - Valve replacement (valved conduit)
  - Valve insertion (transcatheter)
- Repairs
  - Monoscusp patch
  - Transannular patch
Pulmonary heart valve options

- 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
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Life after surgery is progressing

Artificial heart valves are life-savers

# Children with CHD = # Adults with CHD

Surgery 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
Ideal valve?

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

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

 NB: investigational devices only
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Xeltis’ Restorative Heart Valve technology

Unique absorbable matrices

Restorative Valves
## Restorative technology in trials

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<thead>
<tr>
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<th>In-vitro</th>
<th>Pre-clinical</th>
<th>Clinical</th>
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<td><strong>Pediatric conduit (Fontan)</strong>&lt;br&gt;Positive 31-month clinical data presented WCPCCS 2017</td>
<td><img src="pediatric_conduit.png" alt="Image" /></td>
<td><img src="preclinical_conduit.png" alt="Image" /></td>
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<td><strong>Pulmonary Valve</strong>&lt;br&gt;Positive 2-year preclinical data&lt;br&gt;Published in <em>Eurointervention</em> 2017&lt;br&gt;First clinical experience ongoing</td>
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<td><strong>Aortic Heart Valve</strong>&lt;br&gt;Extending pipeline to high pressure circuit&lt;br&gt;Published in <em>Eurointervention</em> 2017</td>
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<td><strong>Vascular Applications</strong>&lt;br&gt;Further pipeline expansion underway</td>
<td><img src="vascular.png" alt="Image" /></td>
<td><img src="preclinical.png" alt="Image" /></td>
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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 aneurism seen in any case (most important for this indication)
Histopathology details
⇒ balanced scaffold absorption and tissue restoration

Replace with drawing

- Conduits is covered by neointimal tissue
- Resorption of the conduit
- Extension of neointima covered 2/3 of the leaflet
- Inflammation and ingrowth of neointimal tissue at resorption site
- Neointimal coverage of leaflet
- Partial breakdown of the leaflet with inflammation

2m, 6m, 12m
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
  - Including Ross procedure
Summary/Trial Status
Pulmonary valve in patients

Enrollment Started     07.07.16
Enrollment Completed   14.12.16

- Patients enrolled: 12 (6 boys)
- Age range: 2–12 years
- Clinical sites: Budapest (4)
                 Krakow (3)
                 Kuala Lumpur (5)
- Follow-up reached: 12 months – 12
                    18 months – [add]
- All patients are doing well
- No deaths, no reintervention or reoperation
- No device-related serious adverse events
- Information on:   - surgical techniques
                  - patients’ anatomy
                  - product efficiencies
# US Restorative pulmonary valve trial

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<tr>
<th>Trial Center</th>
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<tr>
<td>Children’s Healthcare of Atlanta</td>
<td>Kirk Kanter, MD</td>
<td>Janet Fernandez</td>
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<td></td>
<td></td>
<td><a href="mailto:Janet.Fernandez@choa.org">Janet.Fernandez@choa.org</a></td>
</tr>
<tr>
<td>Boston Children’s Hospital</td>
<td>Christopher Baird, MD</td>
<td>Michele Borisuk</td>
</tr>
<tr>
<td></td>
<td></td>
<td><a href="mailto:Michele.Borisuk@cardio.chboston.org">Michele.Borisuk@cardio.chboston.org</a></td>
</tr>
<tr>
<td>New York Presbyterian Hospital - Columbia University</td>
<td>Emile Bacha, MD</td>
<td>Kydanis Clase</td>
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<td></td>
<td></td>
<td><a href="mailto:kc3020@cumc.columbia.edu">kc3020@cumc.columbia.edu</a></td>
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<td>cumbiasurgery.org/clinical-trials/xplore-ii</td>
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<td>Children’s Hospital of Philadelphia</td>
<td>J William Gaynor, MD</td>
<td>Nancy Burnham</td>
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<td><a href="mailto:BURNHAMN@email.chop.edu">BURNHAMN@email.chop.edu</a></td>
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[www.xplore2trial.com](http://www.xplore2trial.com)
Ideal valve technology?

✓ Readily available
✓ All sizes
✓ Promising results
✓ Potentially durable solution
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Thank you!

Prof. Ger Bennink