Native Outflow Tract Transcatheter Pulmonary Valve Replacement in the US

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Disclosures

• As a faculty member of SCAI, I have the following disclosures:
  – Medtronic
    • Consultant, P.I., Proctor
  – NuMED, Inc
    • Consultant, P.I., Proctor
  – Beijing Med-Zenith Medical Scientific Co.

• Off label use of FDA approved devices will be discussed
Acknowledgements

• Professor Philipp Bonhoeffer
  – A great friend
  – A creative genius
  – The TPV “brains”

• Medtronic TPV Team
  – Tremendous hard work
  – A scientific approach

• Drs. Evan Zahn & Alistair Phillips at CSMC, Matt Gillespie at CHOP, and Kanishka Ratnayaka at NHLBI/Rady

• The Tissue Engineering team at NCH
Study Design and Implant
Bilateral Melody TPV: CHOP (Matt Gillespie)

- **10 sheep**
- **Surgical trans-annular patch** 10
- **Melody placed distal to RUL** 5
Challenging Patient

- 33 y/o p/o TOF
  - R & L BT shunts
  - Total repair with large transannular RVOT patch
  - AF: s/p ablation
  - Severe biventricular dysfunction
    - RVEF 17% & LVEF 21%
  - BiV pacing with AICD
  - Morbid obesity: 142 Kg, BSA 2.5 m2
  - Severe restrictive lung disease...smoker
  - Severe PR and poor surgical candidate for S-PVR
  - Turned down for cardiac transplant...severe obesity
MPA: 3.1cm by 3.0cm
RPA: proximal narrowing to 1.5cm x 1.2cm
LPA: proximal narrowing to 1.2cm x 1.3cm
Post RPA Melody TPV After P-5010XL Stent
Post LPA Melody TPV After P-3110XL Stent
Study Population

Anomalies of the RVOT

- Tetralogy of Fallot
  - With Pulm Stenosis
    - Surgical correction of RVOT (non-conduit) = ~77% of RVOT Patients
  - With Pulm Stenosis/Atresia
    - Right Ventricle to Pulmonary Artery (RV – PA) Conduit

- Truncus Arteriosus
  - RV – PA Conduit

- Transposition Great Arteries
  - RV – PA Conduit

- Others
  - RV – PA Conduit

*est. 22% of all CHD patients*
Dilated RVOT: A Problem To Solve
Infundibular Reducer Excitement
From Infundibular Reducer to Native Outflow Tract TPV
Prototype Native Outflow Tract TPV
Custom Patient Experience

- Custom Patient Experience
  - Dr. Philipp Bonhoeffer approached Medtronic to create a custom device
  - 42 y/o male
    - RVOT patch-repaired patient with severe pulmonary regurgitation
    - Mechanical MVR
    - Multiple complicated surgeries
    - Very stormy post op course
    - High surgical risk
    - Ethics committee & Medtronic agreed on custom-made device
  - Implanted January, 2009
Pre Implant CT Evaluation
First in Man: Philipp Bonhoeffer
Jan 2009, GOSH
The Native Outflow Tract TPV Team
GOSH January, 2009
Medtronic Native Outflow Tract Transcatheter Pulmonary Valve (TPV) Research Clinical Study “Early Feasibility Trial”
Study Overview

- Non-randomized, prospective, competitive enrollment, early feasibility study

- Three study sites
  - The Hospital for Sick Children, Toronto
    - PI: Dr. Lee Benson (3 implants)
  - Nationwide Children’s Hospital, Columbus
    - PI: Dr. John P. Cheatham (10 implants)
  - Boston Children’s Hospital, Boston
    - PI: Drs. James E. Lock & Lisa Bergersen (7 implants)

- Up to 20 study subjects to be implanted
  - Consented for 5 year follow-up
  - 20 subjects implanted and trial closed (May 2013 – May 2015)
Inclusion Criteria

• **Pulmonary regurgitation with:**
  o Severe PR as measured by Doppler echo, OR
  o PRF ≥ 30% as measured by cardiac magnetic resonance

• **Clinical indication for surgical placement of RVOT conduit or bioprosthetic pulmonary valve with:**
  o Symptoms secondary to pulmonary regurgitation as classified by Investigator, OR
  o RVEDVi ≥ 150 ml/m²

• **Subject is willing to consent to participate and will commit to completion of all follow-up requirements**
Product Overview
Native Outflow Tract TPV Delivery System

- Porcine pericardial tissue valve, AOA treated
- Tissue valve mounted on self expandable frame
- Coil loading catheter
- 1 size: 25 Fr
- Loading funnel to collapse valve prior to sheathing

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Patient Selection & Follow-up
20 Patients in 3 Sites Worldwide

Pre-Screening
- Echo
- CMR

→ Standard of Care

No

Informed Consent (if not already)
- Verify inclusion/exclusion criteria

→ Excluded

No

Yes

Screening
- CT angiography
- SLA created to assess device fit

→ Exited from study

No

Yes

Implant
- Angiography to confirm device function

Hospital Discharge
- Clinical Assessment
  - CT
  - Echo

1 Month
- Clinical Assessment
  - Echo
  - Fluoroscopy

3 Month
- Clinical Assessment
  - Echo

6 Month
- Clinical Assessment
  - Echo
  - Fluoroscopy

1 Year
- Clinical Assessment
  - Echo
  - CMR

2-5 Years: Clinical Assessment, Echo

In vivo loading condition analysis
(every 5 subjects)

- Screening Committee recommendation; Investigator has final decision

Yes
Imaging of the RVOT in TOF

Approach to analyzing the RVOT

Kan Hor, MD & Team

- 3D RVOT to 3D RVOT segmented images
Imaging of the RVOT in TOF

- Many faces of TOF: Various RVOT anatomy
  - Goal: Improve our ability to determine if this single device fits into the various RVOT
Imaging of the RVOT in TOF

Dynamic 3D Imaging

- WIP: 3D (dynamic) imaging (x-sectional images)?
- Color coded segmentation helps improve our ability to visualize the dynamic nature of the RVOT in TOF
Dual Source Flash CT
We take pictures & HD movies of the virtual SLA implant in systole & diastole
Perimeter Plots

Acceptable fit

Unacceptable fit

Possible Fit?
Simulating Implant in the SLA Model
NCH Team Performed the FIM Implant of the new Native Outflow Tract TPV on May 30\textsuperscript{th}, 2013
PA Angiogram Pre Implant
Pre & Post Implant: ICE
What Have We Learned?

• The 25 Fr delivery system is usually not too difficult to place the valve at the target site
  – The “flexibility” of the self expandable frame allows the delivery system to “bend” in the native RVOT
  – Since these patients do not have an RV-PA conduit, catheter course is favorable

• The frame composition is not as easy to visualize compared to the platinum composition of the Melody frame…less radiopaque

• Because the Native TPV frame is much longer than the Melody TPV, removing the long “carrot” through the frame is more challenging
  – Also, none of these patients have pulmonary stenosis so the Native TPV frame is not as “secure” as the Melody TPV

• While an arduous process of approval is in place, the intense scrutiny of a Screening Committee is very valuable in this trial
What Have We Learned?

- Patient selection and careful anatomic screening are critical parts of the process as anatomies vary widely.

- Dynamic nature of anatomy makes device design challenging; a single device design will not accommodate all anatomies.

- Thus far, no implanted patient has met ALL engineering criteria set forth...we are still learning!

- A larger valve with several frame dimensions may serve more patients.

- Collaboration with regulatory authorities is key.
For Larger Outflow RVOT: Edwards-Sapien XT
29mm Sapien XT Valve: New Opportunities

Edwards SAPIEN XT Transcatheter Heart Valve
29 Sapien XT For Larger Outflow RVOT: Perventricular
Courtesy of Evan Zahn and Alistair Phillips, CSMC
The Work of the Tissue Engineering and Surgical Research Team at NCH

Drs. Toshiharu Shinoka & Christopher K. Breuer

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The Work of the Tissue Engineering & Surgical Research Team at NCH

- This preliminary work in the mouse model, will be transferred to a larger animal model
- Initially, the TEHV will be surgically implanted
- Eventually, the TEHV will be adapted to a percutaneous, transcatheter delivery system with a bioresorbable frame
  - LeDucq Grant Proposal: $7M
  - Fetal delivery of TEHV in fetus with severe RVOTO
Interventional Cardiology MR Program

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Radiation Injury
No Radiation Required
CMR Image converted to a 3 Dimensional Image

iCMR = cardiac imaging core

Diagnostic
Interventional
MRI inspired
3D printing
Cardiac Mechanics

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Conclusions

• Transcatheter valve replacement began over a decade ago for pulmonary valve failure in CHD...the Melody story beginning in 2000

• Next, a Native TPV was implanted in 2009

• Currently, the Native TPV trial in the US is a highly engineered driven study

• However, with the work in the US and OUS, the Native TPV will become a reality

• New imaging and technology will be used
Thank You

Seth & Olivia  Hunter & Willa