Construction and Evaluation of a Bio-Engineered Pump to Enable Subpulmonary Support of the Fontan Circulation: A Proof-of-Concept Study

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DISCLOSURES/SOURCES OF FUNDING

• Dr. Taylor has financial interests in Miromatrix Medical, Inc. Dr. Adachi is a consultant and proctor for Berlin Heart Inc, Medtronic Inc, Jarvik Inc, BiVACOR Inc, and Sony-Olympus Medical Solutions Inc. None of the other authors has anything to disclose.

• Jack Carter, Jr. Technology Catalyst Fund, Baylor College of Medicine, Houston, TX.
SINGLE VENTRICLE HEART DISEASE

• ~2.0-2.5k children per year are born with single ventricle congenital heart disease in US

• Common palliative pathway with the Fontan circulation which has enabled >90-95% of patients to survive childhood

• Patients with Fontan circulation endure a range of complications related to increased central venous pressure/congestion and decreased cardiac output
  • Multi-organ dysfunction develops over time and continues to worsen, resulting in a “failing Fontan” physiology
  • A subpulmonary bio-engineered pump (BEP) is needed to relieve chronic central venous congestion and improve hemodynamics
Fontan Circulation:
- Elevated CVP
- Phasic, non-pulsatile Qp
- Decreased cardiac preload

Subpulmonary pump to provide:
- **lower CVP**
- augmented, pulsatile Qp
- increased cardiac preload
DEVICE FOR CHRONIC SUBPULMONARY FONTAN ASSISTANCE: BIO-ENGINEERED PUMP

- Long-term, biocompatible, non-thrombogenic, infection-resistant with growth potential
- Tissue engineering (TE) has been applied to patients with Fontan circulation
  - Demonstration of clinical efficacy for use as extracardiac conduits in patients with Fontan circulation\textsuperscript{1,2}.
  - Potential to leverage TE to create a “contractile extracardiac Fontan-tunnel” for subpulmonary support\textsuperscript{3,4}
- Aimed to create a functional BEP prototype by combining established tissue engineering techniques and commercially available components and evaluation of the device an \textit{in vitro} hemodynamic model
  A. Creation of a \textbf{biological reservoir} prepared from decellularized tissue
  B. Utilize a biological reservoir in the construction of a BEP
  C. Evaluation of the BEP in a simple flow loop representative of subpulmonary Fontan circulation

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ADULT CONGENITAL HEART

1 – Bockeria et al. 2017; 2 – Hibino et al. 2010
A) CREATION OF A BIOLOGICAL RESERVOIR PREPARED FROM DECELLULARIZED TISSUE

- Matrix decellularization
  - Porcine urinary bladders
  - Bladder submucosa was surgically delaminated from the smooth muscle and connective tissue layers
  - The tissue underwent serial hypertonic, hypotonic and detergent washes

- Biological reservoir preparation
  - Bilayer decell matrix base was created with a lamination process
  - Suture to create a tubular designed reservoir
B) UTILIZE A BIOLOGICAL RESERVOIR IN THE CONSTRUCTION OF A BIO-ENGINEERED PUMP
C) EVALUATING THE BIO-ENGINEERED PUMP IN A SIMPLE FLOW LOOP

- Construction of a simple flow loop
  - 2 compliance chambers
  - Device placed between the inferior vena cava (IVC) and pulmonary artery (PA)
  - Axial flow pump
  - 40% weight glycerin-water solution
  - Pressure transducers and a flow meter

- Baseline “subpulmonary circulation” conditions:
  - “filling pressure” ~ 6 mmHg
  - Flow of ~ 4.0 LPM
RESULTS – PULSATILE FLOW AND CREATION OF PRESSURE GRADIENT

- Non-active BEP
  - Decrease in flow from ~4.0 LPM to ~3.9 LPM
  - Pressure drop < 1 mmHg between the IVC and PA

- Activated BEP at 60 cycles per minute
  - Maintenance of flow at ~ 4.0 LPM
  - Maintained IVC at ~6 mmHg and increased PA to ~13 mmHg
CONCLUSIONS OF THIS PROOF-OF-CONCEPT STUDY

1. A biological reservoir can be created from a bilayered matrix. A bio-engineered pump (BEP) can be constructed by combining a biological reservoir of relevant volume with valves and an external compression device.

2. In a low-pressure circuit representative of a modified subpulmonary Fontan circulation, the BEP can produce pulsatile downstream flows and create a favorable pressure gradient across the device while maintaining low upstream pressure.

3. Next steps include further refinement and evaluation including but not limited to: mechanical properties, biomaterial degradation and remodeling/neotissue formation, long-term durability testing, advanced testing in a sophisticated mock circulation loop as well as in vivo performance.

4. This proof-of-concept study lays the groundwork for further investigation of the use of a BEP as a long-term support device to relieve venous hypertension, provide pulsatile pulmonary blood flow and maintain cardiac preload for the subpulmonary Fontan circulation.
ACKNOWLEDGEMENTS AND THANKS

• Dr. Doris Taylor
• Dr. Iki Adachi
• Dr. P. Alex Smith, Dr. Yaxin Wang, Hamsini Sriraman, Dr. Luiz C. Sampaio
• Eric Chau, Eric Guevara, CHF solutions (formerly Sunshine Heart Inc.), Dr. Anita Chandler
• Dr. Gary Dhillon

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