CONFERENCE PROCEEDINGS

Volume 5, May 2009

The Proceedings of the Fifth International Conference on *Pediatric Mechanical Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion*

Akif Ündar, PhD, Editor

Honorary Chairs

William S. Pierce, MD · John A. Waldhausen, MD

Program Co-Chairs

Elizabeth Blume, MD ·Sabine Daebritz, MD · Brian W. Duncan, MD · John L. Myers, MD
Gerson Rosenberg, PhD · Shunji Sano, MD, PhD · Akif Ündar, PhD · Ross M. Ungerleider, MD, MBA

PENNSTATE HERSHEY Children's Hospital 1855

ASAIO

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

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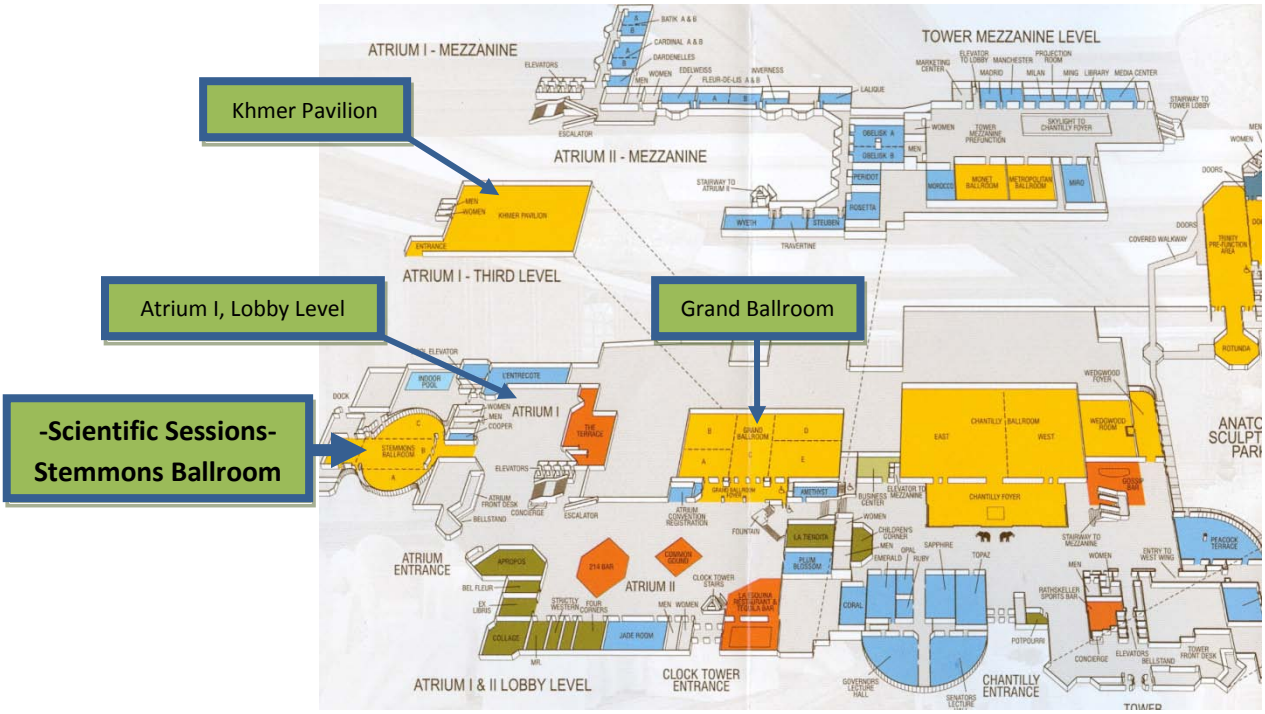

<u>Conference Event Locations</u>

Pediatrics Scientific Sessions – Stemmons Ballroom
Breakfasts & Lunches – Atrim I, Lobby Level
Poster Viewing & Breaks – Grand Ballroom, Atrium II, Lobby Level
Pediatrics Gala Dinner – Khmer Pavilion, Atrim I, Third Level

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Welcome to the Fifth Annual Event

Akif Ündar, PhD, Conference Founder
Pediatric Cardiac Research Laboratories, Departments of Pediatrics, Surgery, and Bioengineering, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

On behalf of the organizers of the ***Fifth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion***, I am honored to welcome each of you to this unique event.

This year's event is held ***in conjunction with the Joint Congress of the American Society for Artificial Internal Organs (ASAIO) 55th Annual Conference & the International Federation for Artificial Organs (IFAO).***

Our main focus and objectives have never changed during the past five years. **The overall objective of the proposed meeting is to bring together internationally know clinicians, bioengineers, and basic scientists involved in research on pediatric mechanical cardiac support systems and pediatric cardiopulmonary bypass procedures. The primary focus will be to *explicitly describe the problems with current pediatric mechanical circulatory support systems, methods, and techniques during acute and chronic support.***

The organizers believe that bringing together respected international scholars from 27 different countries at past four conferences has already made a significant impact on the treatment of pediatric cardiac patients during the past three years. Over 1,100 participants (250-300 participants each year) from many countries, including Argentina, Australia, Austria, Belgium, Brazil, Canada, China, Finland, France, Germany, Greece, Ireland, Italy, Japan, Kuwait, Netherlands, New Zealand, Poland, South Korea, Saudi Arabia, Scotland, Spain, Switzerland, Taiwan, Turkey, the United Kingdom, and the United States, have participated in the 2005, 2006, 2007, and 2008 events.

This year's meeting will include a "hands-on" perfusion workshop and a surgical video session on Wednesday, May 27, 2009. The meeting will commence on Wednesday evening, May 27, 2009 with registration. Formal presentations including a Key Note Lecture, Invited Lectures and regular slide and poster presentations will begin on Thursday morning (May 28, 2009) and continue through Saturday noon (May 30, 2009). Platform presentations will take place in two-hour blocks during the morning and afternoon sessions on Thursday, Friday, and Saturday. Additional slide and poster presentations will be chosen from submitted abstracts. A banquet for all participants is planned for Thursday night (May 28, 2009). All of the details including an updated scientific program can be found at the conference web site http://www.hmc.psu.edu/childrens/pedscpb/.

Over 100 presentations, including invited lectures, slides, and posters will be presented at the 5th Conference. For the first time, we have an opportunity to publish all of the

conference abstracts in a peer-review journal, ***Artificial Organs***. In addition, the November 2009 issue of ***Artificial Organs*** is dedicated to manuscripts that will be collected and peer-reviewed during the Fifth Conference. Our special thanks goes to Angela T. Hadsell, *Executive Editor*, and Paul S. Malchesky, DEng, *Editor-in-Chief*, for making this possible.

Financial Support

In addition to the ***National Heart, Lung, and Blood Institute*** and the ***Office of Rare Diseases at the National Institutes of Health R13 grant support***, we received funds from companies including Baxter Healthcare Corporation, Berlin Heart, Jarvik Heart, Impulse Monitoring, Levitronix, LLC, MAQUET Cardiovascular, Medos Medizintechnik AG, Somanetics Corporation, Sorin Group USA, and St. Jude Medical (as of April 1, 2009). As always, Penn State Hershey Children's Hospital and Penn State Hershey College of Medicine financially support this event to the maximum extent.

In concluding this welcoming letter, we thank the many dedicated individuals, in particular scientific co-chairs, John L. Myers, MD, Hershey, PA, USA, Elizabeth D. Blume, MD, Boston, MA, USA, Gerson Rosenberg, PhD, USA, Shunji Sano, MD, PhD, Okayama, Japan, Brian Duncan, MD, Cleveland, OH, USA, Sabine H. Daebritz, MD, Germany, and Ross Ungerleider, MD, MBA, Cleveland, OH.

Our motto continues to be: ***If the course of just one child's life is improved as a result of this event, we have reached our goal.***

Acknowledgements

The author personally thanks Julie Graham for her assistance in all aspects of managing this event. Specials thanks to Karen Burke and Jessica Kirk from ASAIO for their assistance in preparing for this joint event.

Funding for this conference was made possible (in part) by 1R13 HL 096358-01 from the ***National Institutes of Health, National Heart Lung and Blood Institute and The Office of Rare Diseases.*** The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Note: This letter was extracted from Dr. Ündar's invited editorial from the May 2009 issue of the Artificial Organs.

Scientific Committee

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Professor Emeritus
Evan Pugh Professor of Surgery
Penn State College of Medicine
Hershey, PA, USA

John A. Waldhausen, MD
Professor Emeritus
Founding Chairman of Surgery
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Elizabeth Blume, MD
Heart Failure/Transplant Program
Children's Hospital Boston
Boston, MA, USA

Gerson Rosenberg, PhD
Departments of Surgery and Bioengineering
Penn State College of Medicine
Hershey, PA, USA

Sabine Daebritz, MD
Medical Director, Thoracic & Cardiovascular Surgery
Evangelisches Krankenhaus Duisburg-Nord
Duisburg, Germany

Shunji Sano, MD, PhD
Department of Cardiovascular Surgery
Okayama University Graduate School of Medicine and dentistry
Okayama, Japan

Brian W. Duncan, MD
Department of Cardiac Surgery
Children's Hospital
Cleveland Clinic Foundation
Cleveland, OH, USA

Akif Ündar, PhD
Departments of Pediatrics, Surgery, and Bioengineering
Penn State College of Medicine
Penn State Children's Hospital
Hershey, PA, USA

John L. Myers, MD
Departments of Surgery and Pediatrics
Penn State College of Medicine
Penn State Children's Hospital
Hershey, PA, USA

Ross M. Ungerleider, MD, MBA
Department of Cardiothoracic Surgery
Rainbow Babies and Children's Hospital
Vice Chair for Education, Department of Surgery
Case Western Reserve University
Cleveland, OH, USA

Conference Supporters

Educational Grants

National Heart, Lung, and Blood Institute*
National Institutes of Health - Office of Rare Diseases*
Levitronix, LLC
Terumo

Conference Exhibitors

GOLD
Somanetics

BRONZE
Baxter Healthcare Corporation
Berlin Heart
Impulse Monitoring
Jarvik Heart
Luna Innovations
Maquet
MEDOS Medizintechnik AG
Sorin Group USA, Inc.
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*Funding for this conference was made possible (in part) by 1R13 HL 096358-01 from the ***National Institutes of Health, National Heart Lung and Blood Institute and The Office of Rare Diseases.*** The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Final Scientific Program

Wednesday, May 27, 2009

2:00pm – 5:00pm

PEDS Conference Wet Labs
Co-Chairs:, Tami Rosenthal, CCP, MBA (Philadelphia, PA), Karl Woitas, CCP (Hershey, PA) and Akif Ündar, PhD, (Hershey, PA)
Mast Mounted S5 with Neonatal Circuit
Tami Rosenthal, CCP, MBA (Philadelphia, PA)
Intraoperative Neuromonitoring
Stephen J. Kimatian, MD (Cleveland, OH)
Pulsatile vs. Non-Pulsatile Perfusion & **Microemboli Detection and Classification (EDAC) system**
Karl Woitas, CCP (Hershey, PA),
MEDOS Deltastream Blood Pump and Console
Shigang Wang, MD (Beijing, China)
New ECLS Circuit with a Levitronix Centrifugal Pump for Pediatric and Adult Patients
Aly El-Banayosy, MD (Hershey, PA)

6:00pm – 7:30pm

PEDS Conference Surgical Videos (up to 8 videos)
Co-Chairs: John L. Myers, MD (Hershey, PA) and V. Mohan Reddy, MD (Stanford, CA)

Thursday, May 28, 2009

7:00am – 8:00am	**PEDS Conference Registration/Speaker Ready Room Open/Breakfast**
8:00am	**Posters Placed ~ Posters will remain in place from 8am – 7pm**

Combined General Session of ASAIO, IFAO, and Pediatrics

7:45am – 8:00am	**Welcome** *Wayne Richenbacher, MD - President ASAIO* *Michael Lysaght, PhD – Chairman IFAO* *Akif Ündar, PhD - PEDS Conference Founder*
8:00am – 8:20am	**IFAO Osborne Award**
8:20am – 8:50am	**LECTURE - In Vitro Organ Models** *Linda Griffith, PhD – Professor of Chemical Engineering, MIT*
8:50am – 9:40am	**SYMPOSIUM - Artificial Organ Technologies for Women** ***Dialysis in Women*** *- Thomas Depner, MD – Professor of Internal Medicine, University of California at Davis* ***Ob/Gyn Tissue Engineering*** *- James Yoo, MD, PhD - Assistant Director, Associate Professor & Head Clinical Translation, Wake Forest University* ***Breast Implant Update*** *- Andrea Pozez, MD - Chair Plastic Surgery, Virginia Commonwealth University*
9:40am – 10:00am	***A TRIBUTE TO DRS. WILLEM KOLFF, ADRIAN KANTROWITZ, PEER PORTNER, & MICHAEL DEBAKEY***

All Pediatrics Scientific Sessions will be held in the *Stemmons Ballroom*

10:00am – 10:45am	**Exhibits, Posters & Refreshments**
11:00am – 12:00pm	**Key Note Lecture** ***Historical Perspectives and Personal Experiences*** *William I. Norwood, Jr., MD (Greenville, DE)* *Introduction: John L. Myers, MD (Hershey, PA)*
12:00pm – 1:00pm	**PEDS Conference Registrant Lunch**
1:00pm – 3:00pm	**Plenary Session #1:** **Clinical Heart Failure and Mechanical Support in Children** *Co-Chairs: Elizabeth D. Blume, MD (Boston, MA); Anne Dipchand, MD (Toronto, Canada)* **Epidemiology of Pediatric Heart Failure (10 min)** *Elizabeth D. Blume, MD (Boston, MA)* **Molecular Aspects of Childhood Heart Failure and Targeted Therapies (20 min)** *Jeffrey Towbin, MD (Cincinnati, OH)* **Patient Selection for Mechanical Support (20 min)** *Christopher Almond, MD (Boston, MA)* **How the Echocardiographer Can Aid in the Management of the Heart Failure Patient on Mechanical Support (20 min)** *Anne Dipchand, MD (Toronto, Canada)*

Clinical Trials in Pediatric Cardiology: The Pediatric Heart Network Experience (20 min)
Lynn Mahony, MD (Dallas, TX)
Discussion (30 min)

3:00pm – 3:45pm **Exhibits, Posters & Refreshments**

3:45pm – 5:00pm **Mini-Symposium: Anticoagulation in Pediatric Ventricular Support: Clinical Lessons**
Co-Chairs: M. Patricia Massicotte, MSc, MD, FRCPC, MHSc (Edmonton, Alberta, Canada) and Sabine H. Daebritz, MD (Germany)
Developmental Hemostasis: The Changing Coagulation System in Neonates, Infants, Teenagers and Adults (15 min)
Lisa Bomgaars, MD (Houston, TX)
Anticoagulation Medications: How Can We Monitor Their Effect? (15 min)
Holger Buchholz, MD (Edmonton, Alberta, Canada)
Is a Standardized Anticoagulation Protocol for Pediatric Ventricular Assist Devices Possible? (15 min)
M. Patricia Massicotte, MSc, MD, FRCPC, MHSc (Edmonton, Alberta, Canada)
Pediatric VAD Anticoagulation: Three Clinical Case Presentations (15 min)
Christopher Almond, MD (Boston, MA)
Discussion (15 min)

5:00pm – 7:10pm **Regular Slide Presentations #1 – MCS-ECLS-Bioengineering**
Co-Chairs: Aly El-Banayosy, MD (Hershey, PA), Kristine J. Guleserian, MD (Dallas, TX), and Adolfo A. Leirner, MD (Sao Paulo, Brazil)
12 presentations – 10 minutes each (7 min. presentation and 3 min. discussion)
Moderator: Aly El-Banayosy, MD (Hershey, PA)

s.1 **The Berlin Heart EXCOR Pediatrics – The SickKids experience 2004-2008**
Tilman Humpl, MD, Sarah Furness, RN, Colleen Gruenwald, RN, CCP, CPC, Cecilia Hyslop St. George, RN, Glen van Arsdell, MD
SickKids, Toronto, Canada

s.2 **Pediatric Application of the CircuLite Synergy Micro-Pump Technology**
Gail G. Farnan, RN[1], Oliver Marsille, PhD[1], Wolfgang Kerkhoffs[1], Robert C. Farnan[1], Changfu Wu[2], Zhongjun J Wu, PhD[2], Bartley P Griffith, MD[2]
[1]CircuLite, Inc., Saddle Brook, NJ and [2]Unversity of MD, Baltimore, MD.

s.3 **Bridge-to-bridge-to-Transplantation in Berlin Heart Era**
Michiaki Imamura, MD, PhD, Stephanie Rockett, APN, MNSc, Janet Bryant, RN, BSN, Parthak Prodhan, MD, Michael Schmitz, MD, W. Robert Morrow, MD, Elizabeth Frazier, Robert D.B. Jaquiss, MD
Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Pediatric Cardiac Surgery, Cardiology, and Cardiac Anesthesiology, Little Rock, Arkansas, USA

s.4 **Exchange Transfusion during Heart Transplantation for Children on Warfarin Therapy**
Kim-Chi Tran, Osman O. Al-Radi, Osami Honjo, Jian Wang, Colleen Gruenwald, Glen S. Van Arsdell
SickKids, Toronto, Canada

Moderator: Kristine J. Guleserian, MD (Dallas, TX)

s.5 **Better Outcomes with Ventricular Assist Device (VAD) vs ECMO as a Bridge to Pediatric Heart Transplantation**

Anne I. Dipchand MD, Cedric Manlhiot BSc, Brian W McCrindle MD, Glen Van Arsdell MD, Tilman Humpl MD
Labatt Family Heart Centre, Hospital for Sick Children, Toronto, Canada

s.6 **Extracorporeal Life Support in Pediatric Patients - Outcome of a Single Centre**
Coskun ST[*1], Coskun KO[2], Popov AF[2], Hinz J[3], Özpeker CU[1], Blanz U[1], Weitkemper HH[1], Schmitto JD[2], Morshuis M[1], Kececioglu D[0], Sandica E[1], Körfer R[1]*
[0]Department of Pediatric Cardiology, [1]Department of Cardiovascular Surgery, Heart and Diabetes Centre North-Rhine Westphalia, Ruhr-University of Bochum, Bad Oeynhausen Germany; [2]Department of Thoracic and Cardiovascular surgery, [3]Department of Anaesthesiology, Emergency and Intensive Care Medicine, University of Göttingen, Germany

s.7 **Extracorporeal Membrane Oxygenation Following Norwood Stage 1 Procedures**
Shinya Ugaki, Mahito Nakakura, Takuma Doguchi, Eiji Ito, Hironori Ebishima, Yasuhiro Fujii, Shingo Kasahara, Sadahiko Arai, and Shunji Sano
Department of Cardiovascular Surgery, Okayama University Hospital, Okayama, Japan

s.8 **Comparison of Two Types of ECLS Membrane Oxygenators with Pulsatile and Nonpulsatile Perfusion**
Nikkole Haines, BS, Shigang Wang, MD, John L. Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Moderator: Adolfo A. Leirner, MD (Sao Paulo, Brazil)

s.9 **Evaluation of an Ultra-Compact Extracorporeal Membrane Oxygenation (ECMO) System for Pediatric Use in an Acute Animal Study**
Teruyuki Hayashi[1], MS, Eisuke Tatsumi[2], MD, Nobumasa Katagiri[2], MS, Toshihide Mizuno[2], DVM, Toshikatsu Yagihara[3], MD
[1]Department of Clinical Engineering, [2]Department of Artificial Organs, [3]Department of Cardiovascular Surgery, National Cardiovascular Center, Suita, Osaka, Japan

s.10 **Application of Computer Modeling of Systemic VAD Support in Failing Fontan Physiology**
Lucian A. Durham, III, MD, PhD, Harold M. Burkhart, MD, Joseph A. Dearani, MD, Frank Cetta, Jr., MD, Sabrina D. Phillips, MD, Kartik Sundareswaran, PhD, Soon J. Park, MD
Divisions of Cardiovascular Surgery and Pediatric Cardiology, The Mayo Clinic, Rochester, MN and Thoratec Corp., Pleasanton, CA. USA

s.11 **Pediatric Mechanical Support with Artificial Myocardium System with Baroreflex Function**
Tomoyuki Yambe, MD, Yasuyuki Shiraishi, PhD, Hidekazu Miura, PhD, Kou Imachi, PhD
Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan.

s.12 **Development of a Computer-aided 3 D Bioprinting System for Bioartificial Organ**
Seung Joon Song[1,2], Jaesoon Choi[2], Yong Doo Park[1], Kyung Sun[1,3]
[1]Korea Artificial Organ Center, Korea University, Korea, [2]Departnent of Biomedical Engineering, Brain Korea 21 Project for Biomedical Science, College of Medicine, Korea University, Korea, [3]Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea

Poster Presentations - MCS-ECLS-Bioengineering

Posters will be available for viewing from 8:00am – 7:00pm

p.1 **Left Ventricular Assist for Pediatric Patients with Dilated Cardiomyopathy Using Medos VAD Cannula and Centrifugal Pump**
Shu-Chien Huang, MD, Nai-Hsin Chi, MD, Yih-Sharng Chen, MD, Nai-Kuan Chou, MD, Wen-Je Ko, MD, Shoei-Shen Wang, MD, PhD
Departments of Surgery, National Taiwan University Hospital, Taipei, Taiwan

p.2 **Management of Deep Wound Complications with Vacuum-Assisted Therapy after Berlin Heart EXCOR® Placement in the Pediatric Population**
Peter C. Kouretas, MD, PhD, Philip T. Burch, MD, Aditya K. Kaza, MD, Linda M. Lambert, MSN, CFNP, Madolin K. Witte, MD, Melanie D. Everitt, MD, Faizi A. Siddiqi, MD
Departments of Surgery, Pediatrics and Critical Care, The University of Utah, Primary Children's Medical Center, Salt Lake City, Utah.

p.3 **Experience with the Levitronix CentriMag® in the Pediatric Population as a Bridge to Decision and Recovery**
Peter C. Kouretas, MD, PhD, Aditya K. Kaza, MD, Philip T. Burch, MD, Stephen E. Clayson, MD, Melanie D. Everitt, MD, Craig H. Selzman, MD
Department of Surgery and Pediatrics The University of Utah, Primary Children's Medical Center, Intermountain Medical Center, Salt Lake City, Utah

p.4 **Initial Clinical Experience with the HeartMate® II Ventricular Assist System in a Pediatric Institution**
William R. Owens[1], Roosevelt Bryant, III[2], William J Dreyer[3], Jack F. Price[3], David L. S. Morales[2]
[1]Division of Congenital Heart Surgery, Texas Children's Hospital, Houston, Texas, U.S.A.[2]Michael E DeBakey Department of Surgery, Division of Congenital Heart Surgery, Baylor College of Medicine, Houston, Texas, U.S.A. [3]Department of Pediatric Cardiology, Baylor College of Medicine, Houston, Texas, U.S.A.

p.5 **Hemorrhagic Stroke in a Child with a Low Total Serum Cholesterol and New Support with a Berlin Heart Excor® Left Ventricular Assist Device**
Wesley A. McKamie, C.C.P.,[a] Michael L. Schmitz, M.D.,[a,b] Charles E. Johnson, R.N., C.C.P.,[a,b] Michiaki Imamura, M.D., Ph.D.,[a,b] Robert D. B. Jaquiss, M.D.[a,b]
[a]Arkansas Children's Hospital and [b]The University of Arkansas for Medical Sciences

p.6 **Orthotopic Heart Transplantation in a Child with Hereditary Spherocytosis**
Charles E. Johnson, R.N.,[a] C.C.P., Michael L. Schmitz, M.D.,[a,b] Wesley A. McKamie, C.C.P.,[a] R. Erik Edens, M.D. Ph.D.,[c] Michiaki Imamura, M.D., Ph.D.,[a,b] Robert D.B. Jaquiss, M.D.[a,b]
[a]Arkansas Children's Hospital, [b]The University of Arkansas for Medical Sciences, College of Medicine, [c]University of Iowa Children's Hospital

p.7 **A Novel Implantable Mechanical Circulatory Support System: The Artificial Ventricle**
Hisham M.F. Sherif, MD, Newark, DE, USA

p.8 **Initial in Vivo Evaluation of the 'TinyPump™' for LVAD application**
Mariko Kobayashi[1], MD, Masaharu Yoshikawa[2], MD, PhD, Takashi Kitao[1], DVM Satoshi Shoji[1], Shinya Machida[1], Hideyuki Osawa[1], Taisuke Ishii[1], Satoshi Waguri[1], MS, Tomohiro Konno[3], PhD, Kazuhiko Ishihara[3], PhD, Setsuo Takatani[1], PhD, DMed
[1]Department of Artificial Organs, Tokyo Medical and Dental University, [2]Department of Cardiovascular Surgery, Toyota Kousei Hospital, and [3]Department of Material Science, School of Engineering, The University of Tokyo

p.9 **The Effect of Pumpless Extracorporeal Lung Assist in Experimental Lung Injury**
Feilong Hei, MD,Yulin Tian , MD, Yongli Cui, MD,Kun Yu, MD, Cun Long, MD

Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany

p.18 **A Hemodynamic Evaluation of the Levitronix PediVAS Centrifugal Pump and Jostra HL-20 Roller Pump under Pulsatile and Non-Pulsatile Perfusion in an Infant CPB Model**

Noel Ressler, MPH, Alan R. Rider, Allen R. Kunselman, MA, J. Scott Richardson, Kurt A. Dasse, Ph.D, Shigang Wang, MD, Akif Ündar, PhD

Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, Bioengineering, and Health Evaluation Sciences, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA, Levitronix LLC, Waltham, MA, USA

p.19 **The Aachen MiniHLM – in vitro test results of the new design**

Jutta Arens, Dipl.-Ing.[1]; Heike Schnoering, MD[2]; Michael Pfennig, Dipl.-Ing[1]; Ilona Mager[1]; Jaime F. Vazquez-Jimenez, MD[2]; Thomas Schmitz-Rode, MD[1]; Ulrich Steinseifer, Dr. Ing[1]

[1]Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany, [2]Pediatric Cardiac Surgery, Medical Faculty, RWTH Aachen University, Germany

7:30pm – 10 pm **PEDS Registrants' Gala Dinner & Awards Recognition**

Moderators: Elizabeth D. Blume, MD, John L. Myers, MD, Akif Ündar, PhD

Friday, May 29, 2009

7:00am – 8:00am	**Speaker Ready Room Open/Breakfast**
8:00am	**Posters Placed ~ Posters will remain in place from 8am – 7pm**
8:00am – 10:00am	**PLENARY SESSION #2: Minimizing Adverse Effects of CPB: A Multi-Disciplinary International Approach** *Co-Chairs: J. William Gaynor, MD (Philadelphia, PA) and Shunji Sano, MD (Okayama, Japan)* **Open Heart Surgery and Cardiopulmonary Support/Bypass in the Premature Infant (15 min)** *V. Mohan Reddy, MD (Stanford, CA)* **Aortic Arch Reconstruction without Circulatory Arrest Using Moderate Hypothermia (15 min)** *Kristine J. Guleserian, MD (Dallas, TX)* **Warm Perfusion in Pediatric Cardiac Surgery: The European Experience with 8,000 Patients (15 min)** *Yves Durandy, MD (Massy, France)* **Myocardial Protection in Congenital Heart Surgery (15 min)** *Joanne P. Starr, MD (Newark, NJ)* **Pulsatile vs. Non-pulsatile Perfusion in Neonates and Infants (15 min)** *Atif Akcevin, MD (Istanbul, Turkey)* **Neuromonitoring During CPB Procedures (15 min)** *Stephen J. Kimatian, MD (Cleveland, OH)* **Valve Surgery in Congenital Heart Disease (15 min)** *Giovanni Battista Luciani, MD (Verona, Italy)* **A Dual-platform Proteomics Study of Plasma Biomarkers in Pediatric Patients Undergoing Cardiopulmonary Bypass** *Todd M. Umstead, BS (Hershey, PA)*
10:00am – 10:45am	**Exhibits, Posters & Refreshments**
10:45am – 12:00pm	**Invited Lectures** *Moderator: John L. Myers, MD (Hershey, PA)* **Recent Advances of Brain Protection During Cardiac Surgery – From Deep Hypothermia And Circulatory Arrest to Cerebral Perfusion (20 min)** *Shunji Sano, MD, PhD (Okayama, Japan)* **Determinants of Neurodevelopmental Outcome for Children with Congenital Heart Defects (20 min)** *J. William Gaynor, MD (Philadelphia, PA)* **An Update on Tissue Engineering in Heart Valves (20 min)** *Sabine H. Daebritz, MD (Germany)*
12:00pm – 1:00pm	**PEDS Conference Registrants Lunch**
1:00pm – 3:00pm	**PLENARY SESSION #3: Engineering Applications in the Pediatric Cardiac Surgery: An International Approach** *Co-Chairs: Gerson Rosenberg, PhD, (Hershey, PA) and Ulrich Steinseifer, PhD (Aachen, Germany)*

Penn State Hershey - International Center for Pediatric Cardiovascular Research (15 min)
Akif Ündar, PhD (Hershey, PA)
Miniaturization of ECMO Systems: Engineering challenges and Methods (15 min)
Ulrich Steinseifer, PhD (Aachen, Germany)
Pediatric Assist Device Development in Brazil (15 min)
Adolfo A. Leirner, MD (San Paulo, Brazil)
Microdevices for Measuring Systemic Inflammation (15 min)
Jeffrey D. Zahn, PhD (Pistacaway, NJ)
Towards Quantitative Hemodynamic Prediction in Challenging Single-ventricle Circuits: Surgical Pathway Designs, pVADs and Adult Fontans (15 min)
Kerem Pekkan, PhD (Pittsburgh, PA)
Quantitative Monitoring of Gaseous Microemboli with the EDAC(R) Quantifier (15 min)
Ted Lynch, PhD (Hampton, VA)
Optimizing the circuit design of a pulsatile ECLS in terms of EEP and SHE (15 min)
Kyung Sun, MD, PhD, MBA (Seoul, Korea); Choon Hak Lim, MD (Seoul, Korea)

3:00pm – 3:45pm **Exhibits, Posters & Refreshments**

3:45pm – 6:15pm **Regular Slide Presentations #2 – CPB and Bioengineering**
Co-Chairs: *Giovanni Battista Luciani, MD, (Verona, Italy), Amy Throckmorton, PhD (Richmond, VA, USA), and Elizabeth L. Carney, DVM (Hershey, PA, USA)*
14 presentations – 10 minutes each (7 min. presentation and 3 min. discussion)

Moderator: Giovanni Battista Luciani, MD, (Verona, Italy)

s. 13 The Benefits of High-flow Management in Children with Pulmonary Atresia with/without Major Atriopulmonary Collateral Arteries
Yasuhiro Fujii, MD, Yasuhiro Kotani, MD, Takuya Kawabata, MD, Shinya Ugaki, MD, Shigeru Sakurai, MD, Hironori Ebishima, MD, Hideshi Itoh, CCP, Mahito Nakakura, Sadahiko Arai, MD, Shingo Kasahara, MD, Shunji Sano, MD, Tatsuo Iwasaki, MD, and Yuichiro Toda, MD**
Department of Cardiovascular Surgery and Department of Anesthesiology and Resuscitology, Okayama University Hospital, Okayama, JAPAN*

s.14 The Re-warming Index Formula for Pediatric Cardiopulmonary Perfusion
Hideshi Itoh, CCP, Shingo Kashahara, MD, YasuhiroFujii, MD, YasuhiroKotani, MD, Sadahiko Arai, MD, Shunji Sano, MD
Departments of Cardiovascular Surgery, Okayama University Hospital, Okayama, JAPAN

s.15 Segmental Differences of Impaired Diastolic Relaxation Following Cardiopulmonary Bypass Surgery in Children – A Tissue Doppler Study
Linda B. Pauliks, MD, Akif Ündar, PhD, J. Brian Clark, MD, John L. Myers, MD,
Departments of Pediatrics, Surgery, and Bioengineering, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

s.16 Transcranial Doppler Ultrasonography: a Reliable Method of Monitoring Pulsatile Flow During Cardiopulmonary Bypass in Infants and Young Children
Ashley Rogerson, BS, Yulong Guan, MD, Stephen J Kimatian, MD, Allen Kunselman, MA, J. Brian Clark, MD, John L Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratories, Departments of Pediatrics, Surgery, Bioengineering, and Health Evaluation Sciences, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

s.17 Comparison of Bidirectional Glenn Procedure with and without CPB
Hironori Ebishima, Yasuhiro Kotani, Shinya Ugaki, Yasuhiro Fujii, Shigeru Sakurai, Hideshi Ito, Mahito Nakakura, Shingo Kasahara, Sadahiko Arai, Shingo Kasahara, Shunji Sano
Department of cardiopulmonary surgery, Okayama University, Okayama, Japan

s.18 Mechanical Aortic Valve Replacement in Children and Adolescents after Previous Repair of Congenital Heart Disease
Popov AF, Coskun KO, Tirilomis T, Schmitto JD, Ruschewski W
Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany

Moderator: Amy Throckmorton, PhD (Richmond, VA, USA)

s.19 Intravascular Mechanical Cavopulmonary Assistance for Patients with Failing Fontan Physiology
Sonya Bhavsar BS[1], Jugal Kapadia BS[1], Steven Chopski BS[1], and Amy Throckmorton PhD[1]
Mechanical Engineering[1], Virginia Commonwealth University, Richmond, VA, USA

s.20 A Microfluidic Immunosensor to Monitor Systemic Inflammation During CPB
Lawrence A. Sasso[1], Akif Ündar[2], Jeffrey D. Zahn[1]
[1]Department of Biomedical Engineering, Rutgers University, Piscataway, NJ
[2]Departments of Pediatrics, Surgery, and Bioengineering, Penn State Hershey College of Medicine, Penn State Children's Hospital, Hershey, PA

s.21 Comparative Finite-element Model Analysis of Ascending Aortic Flow in Bicuspid and Tricuspid Aortic Valve
Francesca Viscardi, Christian Vergara[1], Luca Antiga[2], Sabrina Merelli[2], Alessandro Veneziani[3], Giovanni Puppini, Giuseppe Faggian, Alessandro Mazzucco, Giovanni Battista Luciani
Div. of Cardiac Surgery Univ. of Verona, Italy; [1]Mario Negri Institute Ranica (BG) Italy, [2]Dept. of Information Technology, Univ. of Bergamo, Italy, [3]Dept. of Mathematics, Emory Univ., USA

s.22 Performance Validation in Arterial Cannula Representation - A special focus on Three Pediatric Cannulae
Kimberly A. Griffith, Branka Lukic, MS, Shigang Wang, MD, William J. Weiss, PhD, Gerson Rosenberg, PhD, John L. Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

s.23 Effects of the Pulsatile Flow Settings on Pulsatile Waveforms and Hemodynamic Energy in a PediVAS™ Centrifugal Pump
Shigang Wang, MD, Alan R. Rider, Allen R. Kunselman, MA, J. Scott Richardson, Kurt A. Dasse, PhD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Moderator: Elizabeth L. Carney, DVM (Hershey, PA, USA)

s.24 The Aachen MiniHLM– First Results in a Small Animal Model
Heike Schnoering, MD[1]ǂ, Jutta Arens, Dipl.-Ing.[2]ǂ, Joerg S. Sachweh, MD[1], Melanie Veerman[1], Rene Tolba, MD[3], Thomas Schmitz-Rode, MD[2], Ulrich Steinseifer, Dr. Ing.[2] and Jaime F. Vazquez-Jimenez, MD[1]
[1]Pediatric Cardiac Surgery, Medical Faculty, RWTH Aachen University, Germany,

[2]*Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany,* [3]*Institute for Laboratory Animal Science and Experimental Surgery, RWTH Aachen University, Germany ǂ Both Authors contributed equally to the manuscript*

s.25 Effect of the Miniaturized Cardiopulmonary Bypass System on the Inflammatory Response and Cardiac Function in Neonatal Piglets

Ko Yoshizumi[1], MD, Kozo Ishino[2], MD, Hironori Ebishima[1], MD, Shinya Ugaki[1], MD, Yasuhiro Kotani[1], MD, Shingo Kasahara[1], MD, Shunji Sano[1], MD
[1]*Department of Cardiovascular Surgery, Okayama University, Okayama, Japan*
[2]*Department of Cardiovascular Surgery, Showa University Northern Yokohama Hospital, Kanagawa, Japan*

s.26 Hemodynamic Changes in a Model of Chronic Heart Failure Induced by Multiple Sequential Coronary Microembolization in Sheep

Schmitto JD[1], Coskun KO[1], Coskun ST[2], Ortmann P[1], Sossalla S[3], Vorkamp T[1], Heidrich F[1], Popov AF[1], Heuer J[4], Hinz J[4], Quintel M[4], Schöndube FA[1]
[1]Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany, [2]Department of Cardiac Surgery, Heart and Diabetes Centre, Bad Oeynhausen, [3]Department of Cardiology, University of Goettingen, [4]Department of Anesthesiology, University of Goettingen

Poster Presentations - CPB/CFD/Bioengineering
Posters will be available for viewing from 8:00am – 7:00pm

p.20 Clinical study of artificial colloid in cardiopulmonary bypass

Jinxiao Hu, Long Cun
Department of Extracorporeal Circulation, Fuwai Hospital ,CAMS & PUMC, Beijing, China

p.21 Perioperative Monitoring of TEG on Haemostatic Function for Cyanotic Infants Undergoing Complexed Cardiac Surgery

Yongli Cui[1], M.D, Cun Long[1], M.D, Zhengyi Feng[1], M.D, Ju Zhao[1], M.D , Fuxia Yan[2], M.D, Yuhong Wang[2], M.D , Jinping Liu[1], M.D E-mail : cuiyongli@hotmail.com
[1]*Department of Cardiopulmonary Bypass,* [2]*Department of Anesthesiology, Cardiovascular Institute and Fuwai Hospital,CAMS and PUMS,Beijing ,China*

p.22 Continuous Hemodiafiltration in Children after Cardiac Surgery

Kenichi Watanabe,MD, Yasuyuki Suzuki,MD, Takeshi Goto,CE, Sanae Yamauchi,MD, Kazuyuki Daitoku,MD , Kozo Fukui, MD, Ikou Fukuda,MD
Department of Thoracic and Cardiovascular Surgery, Hirosaki University School of Medicine. Hirosaki, Aomori, Japan

p.23 Use of ECMO, surfactant, and HFOV for the management of intra-operative acute pulmonary hemorrhage post palliation of Tetralogy of Fallot with hypoplastic branch pulmonary arteries and anomalous coronary crossing RVOT

Meena Nathan MD, Meena Kalyanaraman MD, Jonathan Blank MD, Joel Hardin MD, Joanne Starr MD
Children's Heart Center, Children's Hospital of New Jersey, NBIMC, Newark.

p.24 Coronary Arterio-Venous Fistula: Surgical Indication in Childhood, Treatment and Results

Alkan T., Akcevin A., Türkoğlu H, Paker T, Aytaç A.
V.K.V. American Hospital, Dept. of Cardiovascular Surgery, Istanbul, TURKEY

p.25 Left Ventricular Contractility after Cardiac Procedures in Neonatal Piglets

Theodor Tirilomis, Oliver J. Liakopoulos, Lars Nolte, K. Oguz Coskun, Aron-Frederik Popov, Friedrich A. Schoendube

Department for Thoracic, Cardiac, and Vascular Surgery, University of Goettingen, Goettingen, Germany

p.26 The Impact of Pump Settings on the Quality of Pulsatility

Alan R. Rider, Noel M. Ressler, MPH, Allen R. Kunselman MA, Shigang Wang, MD, Akif Ündar, PhD

Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, Bioengineering, and Health Evaluation Sciences, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

p.27 Comparison of Pumps and Oxygenators with Pulsatile and Nonpulsatile Modes in an Infant Cardiopulmonary Bypass Model

Nikkole Haines, BS, Shigang Wang, MD, John L. Myers, MD, Akif Ündar, PhD

Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

p.28 Impact of the Post-Pump Resistance on Pressure-Flow Waveform and Hemodynamic Energy Level in a Neonatal Pulsatile Centrifugal Pump

Shigang Wang, MD, Nikkole Haines, BS, J. Scott Richardson, Kurt A. Dasse, Ph.D, Akif Ündar, PhD Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

p.29 Endothelium NO release during cardiac surgery: comparison between continuous and pulsatile flow cardiopulmonary bypass.

G. Faggian[1], E. Lanzarone[2-3], F. Gelmini[4], A.C. De Prati[5], M. Tessari[1], T. Menon[1], H. Suzuki[5], M. Carini[4], R. Fumero[2], G.B. Luciani[1], M.L. Costantino[2]

Div. of Cardiac Surgery, Univ. of Verona[1]; Dept. Structural Engineering[2] and Bioengineering[3], Politecnico Milan; Chemical-Pharmaceutical Institute, Univ. of Milan[4]; Dept. Morphological and Biomedical Sciences, Univ. of Verona[5]; Italy.

p.30 Challenges in International Heart Surgery: Massive Air Embolism of Unusual Origin and Requirement for Modification of Standard Algorithms and Procedural Checks

Joseph Borondy, Peter Allen, Qasim Simmons, Carmen Giacomuzzi, Victor Carcioppolo, Scott Snider, Tom Pezzella, Dan Woodward, Karl Welke, A.Marath, St. Francis Heart Hospital, Indianapolis, IN

P.31 Force Reflecting Teleoperation for a Robotized Laparoscopic Gripper System

[1]Jaesoon Choi, PhD, [2]Jun Woo Park, PhD, [2]Du Jin Bach, MS, [2]Duck Hee Lee, MS, [1]Jung Joo Lee, PhD, [1]Kyung Sun, MD, PhD, MBA

[1]Korea Artificial Organ Center, College of Medicine, Korea University, Seoul, Korea

[2]Biomedical Engineering Branch, Research Institute, National Cancer Center, Gyeonggi, Korea

p.32 Hemodynamics of Sequential Coronary Bypass Grafting Configurations via Sketch-Based Surgical Planning Tool

Onur Dur[1], Sinan Tolga Coskun[2], Kasim Oguz Coskun[3], Levent B. Kara[1], Kerem Pekkan[1]

[1]Departments of Biomedical and Mechanical Engineering, Carnegie Mellon University, Pittsburgh, PA, [2]Department of Thoracic Cardiovascular Surgery, University of Bochum, Bad Oeynhausen, Germany, [3]Department of Thoracic Cardiovascular Surgery, University of Göttingen, Göttingen, Germany

Saturday, May 30, 2009

7:00am – 8:00am **Speaker Ready Room Open/Breakfast**

8:00am – 10:00am **PLENARY SESSION #4: National Heart, Lung, and Blood Institute**
Pediatric Grants Awardees
Co-Chairs: Tim Baldwin, PhD (Bethesda, MD); Elizabeth D. Blume MD (Boston, MA); William Pierce, MD (Hershey, PA)
The Penn State Pediatric VAD: Five Year Development Status (15 min)
William J. Weiss, PhD (Hershey, PA)
***In vivo* Evaluation of the PediaFlow™ Pediatric Ventricular Assist Device**
Harvey S. Borovetz, PhD (Pittsburgh,PA) **(15 min)**
Development progress of the Ension pediatric cardiopulmonary assist system (pCAS) (15 min)
Mark Gartner, PhD (Pittsburgh,PA)
Summary at Completion of the Jarvik 2000 NIH Pediatric Development Program (15 min)
Robert Jarvik, MD (New York, NY)
The PediPump: A Versatile, Implantable Pediatric Ventricular Assist Device—Update IV (15 min)
Brian Duncan, MD (Cleveland, OH)
Animal Models for Pediatric Circulatory Support Device Pre-Clinical Testing (15 min)
Elizabeth L. Carney, DVM (Hershey, PA)
FDA's Current Thinking on Clinical Trial Design and Patient Evaluation for Pediatric MCSDs (15 min)
Eric Chen, MS (FDA, Rockville, MD)
Discussion (15 min)

10:00am – 10:45am **Exhibits, Posters & Refreshments**

10:45am – 12:45pm **Mini-Symposium: Pediatric Perfusion**
Invited Lectures (Five 15-minute talks)
Co-Chairs: Tami Rosenthal, CCP, MBA (Philadelphia, PA); Richard Gates, MD (Orange, CA)
Improvements to ECMO (15 min)
Tami Rosenthal, CCP, MBA (Philadelphia, PA)
The Use of Bivalirudin/Angiomax for Pediatric Anticoagulation in HIT patients (15 min)
Richard Gates, MD (Orange, CA)
Clinical real-time monitoring of gaseous microemboli in pediatric cardiopulmonary bypass (15 min)
J. Brian Clark, MD (Hershey, PA)
Pediatric Myocardial Protection and Single Dose Cardioplegia (15 min)
Richard Ginther, Jr., CCP (Dallas, TX)
Myocardial recovery and retraining of the ventricular with ECMO after arterial switch operation (15 min)
Long Cun, MD, (Beijing, China)
Ecuador Hearts: The Penn State Hershey Medical Center Experience (15 min)
Robert Wise, CCP (Hershey, PA)

Development of Mechanical Circulatory Support Devices in China (15 min)
Wei Wang, MD, PhD, Deming Zhu, MD, Wenxiang Ding, MD
Shanghai Children's Medical Center, Affiliated by Shanghai Jiaotong University, School of Medicine

12:45pm **Meeting Adjourns**

International Scientific Committee

Feilong Hei, MD, China
F. Heidrich, Germany
J. Heuer, Germany
A. Craig Hillemeier, MD, USA
J. Hinz, Germany
Osami Honjo, Canada
Jinxiao Hu, China
Shu-Chien Huang, MD, Taiwan
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Kazuhiko Ishihara, PhD, Japan
Taisuke Ishii, Japan
Kozo Ishino, MD, Japan
Eiji Ito, Japan
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Meena Kalyanaraman, MD, USA
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Levent B. Kara, USA
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Shinya Machida, Japan
Ilona Mager, Germany
Lynn Mahony, MD, USA
Cedric Manlhiot, BSc, Canada
Oliver Marsille, PhD, USA
M. Patricia Massicotte, MSc, MD, FRCPC, MHSc, Canada
Daniel Mazur, BSE, USA
Alessandro Mazucco, Italy
Brian W. McCrindle, MD, Canada
Wesley A. McKamie, CCP, USA
T. Menon, Italy
Sabrina Merelli, Italy
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Kyoung Won Nam, PhD, Korea
Meena Nathan, MD, USA
Lars Notle, Germany
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Yukihiko Nose, MD, PhD, USA
P. Ortmann, Germany
Hideyuki Osawa, Japan
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William R. Owens, USA
CU.C. Özpeker, Germany
Walter E. Pae, Jr., MD, USA
T Paker, Turkey
George Pantalos, PhD, USA
Jun Woo Park, PhD, Korea
Soon J. Park, MD, USA
Yong Doo Park, Korea
Sonna Patel, PhD, USA
Linda Pauliks, MD, USA
Kerem Pekkan, PhD, USA
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Michael Pfenning, Germany

Sabrina D. Phillips, MD, USA
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Parthak Prodhan, MD, USA
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Scott Richardson, USA
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Alan R. Rider, USA
Stephanie Rockett, APN, MNSc, USA
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Gerson Rosenberg, MD, USA
Tami Rosenthal, CPP, MBA, USA
W. Ruschewski, Germany
Joerg S. Sachweh, MD, Germany
Shigeru Sakurai, MD, Japan
E. Sandica, Germany
Shunji Sano, MD, PhD, Japan
Lawrence A. Sasso, USA
J.D. Schmitto, Germany
Michael Schmitz, MD, USA
Thomas Schmitz-Rode, MD, Germany
Heike Schnoering, MD, Germany
Friedrich A. Schöndube, Germany
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Craig H. Selzman, MD, USA
Stuart Sheppard, PhD, UK
Hisham M.F. Sherif, MD, USA
Yasuyuki Shiraishi, PhD, Japan
Satoshi Shoji, Japan
Faizi A. Siddiqi, MD, USA
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Alan J. Snyder, PhD, USA
Ho Sung Son, MD, Korea
Seung Joon Song, Korea
S. Sossalla, Germany
Scott Snider, USA
Tom Spray, MD, USA
Cecilia Hyslop St. George, RN, Canada
Joanne Starr, MD, USA
Ulrich Steinseifer, PhD, Germany
Brigitte Stiller, MD, PhD, Germany
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Robert G. Svitek, PhD, USA
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Eisuke Tatsumi, MD, Japan
M. Tessari, Italy
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Theodor Tirilomis, MD, Germany
Yuichiro Toda, MD, Japan
Rene Tolba, MD, Germany
Jeffrey Towbin, MD, USA
Kim-Chi Tran, Canada
H Türkoğlu, Turkey
Shinya Ugaki, MD, Japan
Todd Umstead, BS, USA
Akif Ündar, PhD, USA
Ross Ungerleider, MD, USA
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Jaime F. Vazquez-Jimenez, MD, Germany
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Madolin K. Witte, MD, USA
Karl R. Woitas, CCP, USA
Dan Woodward, USA
Changfu Wu, USA
Zhongjun J. Wu, PhD, USA
Toshikatsu Yagihara, MD, Japan
Sanae Yamauchi, MD, Japan
Tomoyuki Yambe, MD, Japan
Fuxia Yan, MD, China
Masaharu Yoshikawa, MD, PhD, Japan
Ko Yoshizumi, MD, Japan
Kun Yu, MD, China

Jeffrey D. Zahn, PhD, USA
Ju Zhao, MD, China
Deming Zhu, MD, China

Historical Perspectives and Personal Experiences

William I. Norwood, Jr., MD

Epidemiology of Pediatric Heart Failure

Elizabeth D. Blume, MD
Associate Professor of Pediatrics, Harvard Medical School. Medical Director, Heart Failure/Transplant Program, Children's Hospital Boston. Boston, MA USA

The clinical syndrome of heart failure is the final common pathway of a complex combination of biologic, functional, and structural pathophysiologic mechanisms. The spectrum of etiologies in children are markedly different then in adults, as are cardiac physiology, clinical presentations, and compensatory mechanisms. The incidence and etiology of pediatric heart failure will be reviewed.

Epidemiology. The incidence of heart failure in children is difficult to estimate. The incidence data for cardiomyopathy will be reviewed, although only a minority of these patients have heart failure. The incidence of heart failure in young children with congenital heart disease has fallen in conjunction with improved surgical options for these patients including routine neonatal repairs that are undertaken prior to the onset of symptoms of HF. In contrast, the incidence of heart failure in patients following palliative surgery continues to rise as the life expectancy improves. The incidence of the various forms of cardiomyopathy in children has been recently published. In contrast, data concerning incidence and prevalence of heart failure in children are difficult to compile because the symptom complex is relatively nonspecific and often transient, and patients tend to be categorized according to the underlying disorder rather than the presence or absence of congestive heart failure.
The complexities of estimating heart failure incidence and prevelance, and the etiologies of pediatric heart failure population will be reviewed.

References

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Molecular Aspects of Childhood Heart Failure and Targeted Therapies

Jeffrey A. Towbin, M.D.
Pediatric Cardiology and The Heart Institute, Cincinnati Children's Hospital, Cincinnati, Ohio, USA

Purpose:
Heart failure in childhood occurs due to a myriad of genetic and acquired etiologies. The basic underlying mechanisms for heart failure, however, appear to follow a final common pathway. These basic mechanisms trigger the clinical phenotype, its clinical expression, and disease outcome. Understanding these etiologies and mechanisms should enable the development of targeted treatment strategies.

Methods:
Patients with cardiomyopathies were enrolled in molecular genetic screening studies and viral analysis to determine the etiologies of disease. Once disease-causing genes were identified, animal models were generated in an attempt to recapitulate the human condition and, when achieved, to study the pathophysiology of disease. Humans with these disorders and animals in whom the disease was created were treated with pharmacologic approaches while humans were also treated with VADs in some cases. The structure and function of the diseased hearts and the response to therapy and outcomes were studied.

Results:
A variety of genes have been identified in final common pathways that define phenotype. These genes encode proteins such as cytoskeletal and sarcomeric proteins and ion channels, as well as cell-cell junction proteins. In addition, acquired forms of disease, such as viral myocarditis, appear to result from disruption of similar pathways. Treatments focused on the abnormal proteins in these genetic-based patients appear to be effective in a subgroup of patients. Similarly, therapies now exist that alter the course of viral-induced disease.

Conclusions:
There are final common pathways that, when disturbed, result in clinical heart failure in children. Knowledge regarding the etiologies and mechanisms responsible for heart failure in children enables diagnosis, therapies, and risk stratification.

Patient Selection for Mechanical Support

Christopher Almond, MD[1], Ravi Thiagarajan, MD[1], Elizabeth Blume, MD[1], James Dinardo, MD[2], Dorothy Beke, BSN, MSN[1], Francis Fynn-Thompson, MD[3]
Departments of Cardiology – Division of Cardiac Critical Care[1], Cardiac Anesthesia[2], and Cardiac Surgery[3], Children's Hospital Boston; the Departments of Pediatrics, Surgery, and Anesthesia, Harvard Medical School—Boston, MA

Purpose:

Indications for ventricular assist device (VAD) therapy in children are not well defined. Nevertheless, clinicians are being asked to determine which patients merit VAD support even before the risk-benefit profile of emerging pediatric VADs is fully known. This talk summarizes our institution's approach to patient selection in the current era as we await the results of the first pediatric VAD trials already underway.

Methods:

Representatives from cardiac surgery, cardiac critical care, cardiac anesthesia and heart failure/transplant medicine at Children's Hospital Boston convened in 2007-8 to review current data on pediatric mechanical support and transplant waiting list mortality. The purpose was to devise a systematic approach to VAD support in children recognizing the lack of data presently available. Recommendations for support were classified according to level of committee consensus (i.e. consensus favoring support, consensus not favoring support, and no consensus at the present time).

Results:

Pediatric heart failure patients for whom there was general consensus that the perceived benefits of VAD therapy outweigh the suspected risks include children requiring ECMO support (Intermacs profile status 1/1a) who are actively listed for heart transplant without irreversible end-organ dysfunction. Patients in whom there was general consensus that the perceived benefits of VAD therapy do not outweigh the risks include patients who are stable (i.e. well-compensated) on inotropic therapy alone (INTERMACS profile status 3), and patients who meet criteria for higher INTERMACS status but have irreversible end-organ dysfunction and/or are not candidates for heart transplantation. There was no consensus regarding patients meeting criteria for Intermacs profile 2 (progressive decline); however the majority believed that VAD therapy should be considered for patients requiring extended or increasing mechanical ventilatory support or demonstrating compelling signs of progressive low-cardiac output syndrome despite optimal medical therapy if confirmed by invasive hemodynamic data. LVAD support is generally preferred over biventricular support; RVAD insertion should be strongly considered when overt signs of right heart failure persist despite adequate left heart decompression.

Conclusions:

Despite the lack of detailed risk-benefit data on emerging pediatric mechanical support technologies, we found reasonable consensus regarding specific subgroups of pediatric heart failure patients in whom VAD support is warranted and not warranted. Efforts to refine patient selection for pediatric VAD therapy should be considered a priority for pediatric device trials.

How the Echocardiographer Can Aid in the Management of the Heart Failure Patient on Mechanical Support

Anne I. Dipchand, MD, Labatt Family Heart Centre, Hospital for Sick Children, Toronto, Canada

In this session, the utility of echocardiography in the management of the heart failure patient on mechanical support will be explored. Management can be broadly separated into short term, acute care management needs and intermediate term follow up focusing on bridge to recovery.

In the acute care management phase, echocardiography plays a role in assessing ventricular filling and emptying and helps to guide parameters for pump settings. Other information with clinical implications includes presence and size of pericardial effusion, intracardiac thrombus formation, and vegetations.

With the increasing experience with mechanical support as a bridge to recovery, there is a need for objective means to assess the feasibility, timing and likelihood of success of device explantation. Echocardiography is a non-invasive modality that can be used to aid in the decision-making around myocardial recovery and device explantation. Literature and experience will be reviewed looking at the role of echocardiography in the assessment of ventricular remodeling and functional recovery.

Reference

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Clinical Trials in Pediatric Cardiology: The Pediatric Heart Network Experience

Lynn Mahony, Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX

Most current diagnostic and treatment plans for infants and children with cardiovascular disease are not supported by evidence from clinical trials, but instead are based on expert opinion, single-institution observational studies, or extrapolated from adult cardiovascular medicine. In response to this concern, the National Heart, Lung, and Blood Institute established the Pediatric Heart Disease Clinical Research Network (PHN) in 2001. Design and conduct of complex, multi-center studies in children with congenital and acquired heart disease must address numerous obstacles, including identification of an suitable clinically-relevant primary endpoint, lack of preliminary data on which to base sample size calculations, and recruitment of a sufficient number of subjects. To date, the PHN has initiated five randomized clinical trials and three observational studies. This presentation will describe the structure and function of the PHN, review ongoing studies, and discuss current and future challenges. Despite numerous challenges, the infrastructure is now well-developed and capable of implementing complex, multicenter protocols efficiently and recruiting subjects effectively.

Developmental Hemostasis: The Changing Coagulation System in Neonates, Infants, Teenagers, and Adults

Lisa Bomgaars M.D.
Departments of Pediatrics, Section of Hematology-Oncology,
Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA

Development changes in the hemostatic system occur throughout childhood. The greatest change in both pro-coagulant and anti-coagulant factors occurs during infancy. An understanding of the developmental changes is essential to properly assess coagulation data and anticoagulation therapy in children. This discussion will provide a brief overview of coagulation physiology and will review the developmental changes of the pro- and anticoagulant systems throughout childhood.

Is a standardized anticoagulation protocol for Pediatric Ventricular Assist Devices possible?

M. Patricia Massicotte, MSc, MD, MHSc
Pediatric Thrombosis/VAD program, Depts of Pediatric Cardiology/Hematology, Stollery Childrens Hospital, Mazankowski Heart Institute, University of Alberta, Edmonton, Alberta Canada

Background/Introduction:

Following ventricular assist device (VAD) surgical placement the most critical part of management is anticoagulation to maintain the normal balance of hemostasis ie. prevent thromboembolic events (pump, neurologic, peripheral) while minimizing bleeding events . Children have a number of differences in hemostasis compared to adults negating the use of adult guidelines for anticoagulation of VADs. Minimal data exists on the safety and efficacy of anticoagulant and antiplatelet therapies currently used in children with VADs are unknown.

Purpose/Methods/ Results:

Results from a review of the pediatric literature determining the anticoagulant and antiplatelet agents used in children with VADS, their estimated safety and efficacy and monitoring methods will be discussed. The presence or absence of a common anticoagulation protocol will be discussed.

Future:

Discussion of the attributes and challenges associated with the development and implementation and quality control of a standardized anticoagulation protocol will be carried out .

Pediatric VAD Anticoagulation: Three Clinical Case Presentations

Christopher Almond
Children's Hospital Boston, MA

The Berlin Heart EXCOR Pediatrics – The SickKids experience 2004-2008

Tilman Humpl MD, Sarah Furness RN, Colleen Gruenwald RN, CCP, CPC, Cecilia Hyslop St. George RN, Glen van Arsdell MD
The Hospital for Sick Children, Toronto, Canada

Purpose:
The ventricular assist device (VAD) Berlin Heart EXCOR Pediatrics has been available at our institution since 2004 for bridging pediatric patients to cardiac transplantation or recovery. The present study reviewed our results following VAD implantation.

Methods:
We retrospectively reviewed patients that underwent implantation of a VAD between 10/2004 and 10/2008. Demographic data collected included: age at implantation, gender, weight, underlying disease and previous extracorporeal membrane oxygenation (ECMO) support. Complications and outcome were also reviewed.

Results:
A total of 15 patients were identified, 9 female and 6 male, with an average age of 8.8 y (range 0.3-14.8) and average weight 31.1 kg (range 5.2-86.4) Indications for VAD support were dilated cardiomyopathy in 14 patients and progressing heart failure with a single ventricle physiology (bidirectional Glenn shunt) in 1 patient. Three patients (20%) were bridged from ECMO to VAD. Average support was 29 (1-108) days. Fourteen patients were on a bi-VAD, 1 patient (single ventricle) had single VAD support. Three patients developed mediastinal/pericardial fluid collections, requiring surgical exploration in 2, and drain insertion in 1. Three patients presented with neurological symptoms. Seizures occurred in 2 patients. One patient had a left occipital hemorrhage and posterior reversible encephalopathy syndrome and one had no findings on neuroimaging. Both recovered without sequealae. The third patient had hemiparesis (thalamic infarcts) concurrent with multiple systemic thromboembolic events. In 2 patients blood pumps were exchanged due to thrombus formation. No patient was weaned off the VAD, 2 patients (13%) died on the VAD, 1 patient died post transplant giving an overall survival after cardiac transplantation to hospital discharge of 80%. All surviving patients are neurologically intact at follow-up.

Conclusions:
In our experience, VAD support provides an effective means of bridging children with advanced dilated cardiomyopathy or heart failure to transplantation with a relatively small number of complications and deaths given the complexity of the patient population.

Pediatric Application of the CircuLite Synergy Micro-Pump Technology

Gail G. Farnan, RN[1], Oliver Marsille, PhD[1], Wolfgang Kerkhoffs[1], Robert C. Farnan[1], Changfu Wu[2], Zhongjun J Wu, PhD[2], Bartley P Griffith, MD[2], [1]CircuLite, Inc., Saddle Brook, NJ and [2]Unversity of MD, Baltimore, MD

Introduction:

In the past decade, implantable ventricular assist devices have emerged as a safe and effective treatment to improve survival and quality of life for adult heart failure patients. However, such options remain limited for pediatric patients requiring circulatory support.

CircuLite, Inc. (Saddle Brook, NJ) has developed a unique proprietary and patented miniature circulatory assist device, the *Synergy*™ Pocket Micro-pump System. The *Synergy* system features a mixed flow micro-blood pump that is designed to provide up to 3 liters/minute of blood flow and is intended for use as partial left ventricular support in chronic heart failure patients. The *Synergy* system is currently being studied under a European CE Mark trial. To date, sixteen patients have been enrolled, with an average support duration of 83 days (27-213 days).

CircuLite® *Synergy* Micro-pump

Encouraged by these successful results, CircuLite, in collaboration with University of Maryland, plans to develop a pediatric circulatory support system through tailoring the current *Synergy* system for infant and child applications.

Method:

The project consists of two phases. In Phase I, the micro-pump will be refined for a child application (5~35kg). The major work will be to modify the inlet tip of the current device for apical insertion. In Phase II, the micro-pump will be refined to reduce the flow so that it suitable for infant application (< 5kg). Phase II major tasks include a potential redesign of the rotor and further reducing the pump size, with adaption to the controller software and the cannulae system.

Concluding Remarks:

Both the CircuLite child and infant micro-pumps will be built upon the proprietary core blood pump technologies of the *Synergy* system, such as the rotor design and the motor technology. These new pediatric pumps will be designed to retain the key hemodynamic, hydraulic, and biocompatible characteristics of the *Synergy* system.

Bridge-to-bridge-to-Transplantation in Berlin Heart Era

Michiaki Imamura, MD, PhD, Stephanie Rockett, APN, MNSc, Janet Bryant, RN, BSN, Parthak Prodhan, MD, Michael Schmitz, MD, W. Robert Morrow, MD, Elizabeth Frazier, Robert D.B. Jaquiss, MD
Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Pediatric Cardiac Surgery, Cardiology, and Cardiac Anesthesiology, Little Rock, Arkansas, USA

Background
There has recently been increasing use of ventricular assist devices (VAD) to instead of extracorporeal membrane oxygenation (ECMO) to bridge small children to cardiac transplantation. Currently available VAD technology cannot be rapidly deployed. Some patients, therefore, may need extracorporeal membrane oxygenation (ECMO), and later transition to VAD support. We sought to compare outcomes for patients supported with bridge-to-bridge (ECMO to VAD) to a contemporary group of patients supported with VAD alone.

Methods
We conducted a retrospective review of all patients supported with intent to transplant with the Berlin Heart VAD system between 2007 and 2008 (n=17). Specific variables collected included the underlying cardiac diagnosis, size, duration of ECMO support, need for RVAD, occurrence of neurologic event, and ultimate outcome. Patients were divided into two groups for the purposes of analysis: ECMO-VAD (n=8) were patients supported with ECMO (duration; 2-14; mean 6.7 $\pm$ 4.1 day) and transitioned to VAD and VAD-ONLY (n=9) were placed on VAD directly.

Results
Etiologies of heart failure were markedly different. All patients in VAD-ONLY had dilated cardiomyopathy. In ECMO-VAD, three had congenital heart disease and 5 had myocarditis. Age, weight, and duration of VAD were not different. All patients in both groups survived to transplant or VAD explantation. One patient in each group was weaned from VAD, and all others were transplanted. In ECMO-VAD, there was one hospital death due to sepsis after weaning from VAD. There was one death after transplantation in the ECMO-VAD group due to rejection. ECMO-VAD had higher rate of RVAD placement ($p<0.05$). There were no early or late deaths in the VAD-ONLY group.

Conclusion
Outcomes for children who require emergent mechanical cardiac support with ECMO prior to the implantation of VAD are good and are similar to outcomes in children who do not require ECMO as a bridge to VAD.

	VAD-ONLY (n=9)	ECMO-VAD (n=8)
Age (year)	4.0 $\pm$ 3.3	2.6 $\pm$ 2.9
Weight (kg)	16.5 $\pm$ 12.1	11.7 $\pm$ 5.8
Duration VAD (day)	46.9 $\pm$ 44.6	43.4 $\pm$ 48.9
RVAD (n)	1	3
CVA (n)	4	2

Exchange transfusion during heart transplantation for children on warfarin therapy

Kim-Chi Tran, Osman O. Al-Radi, Osami Honjo, Jian Wang, Colleen Gruenwald, Glen S. Van Arsdell
The Hospital for Sick Children, Toronto, Canada

Patients on warfarin awaiting heart transplantation have increased risk of bleeding, prolonged operative time, and increased blood transfusion. Patients who had previous heart surgery, especially complex cyanotic congenital heart surgeries, and those on ventricular assist devices (VAD) are at greater risk. We sought to study the use of exchange transfusion to remove the patient's plasma and replace it with fresh frozen plasma augmented with coagulation factors to reduce the postoperative bleeding, shorten operative time, and reduce total blood exposure.

In this pilot study, nineteen children (3 to 18 years) who were on warfarin until heart transplantation were analyzed. Nine out of 19 underwent exchange transfusion in the first few minutes of cardiopulmonary bypass (CPB). Of patients in the exchange group 5 had previous congenital heart surgery (CHS), and 1 was on ventricular assist device (VAD). In the control group, 2 had previous CHS and 1 was on VAD.

Independent predictors of prolonged hemostasis time were VAD ($p=0.004$), previous CHS ($p=0.013$), and failure to undergo exchange transfusion if the preoperative INR was > 3 ($p=0.002$). Independent predictors of increased postoperative blood loss at 4 and 24 hours were preoperative INR > 3 ($p=0.003$ and $p<0.001$, at 4 and 24 hrs respectively) and failure to undergo exchange transfusion ($p=0.08$ and $p=0.008$, at 4 and 24 hrs respectively). The independent predictors of total blood product exposures were, female gender ($p=0.002$), larger BSA ($p<0.0001$), prolonged CPB time ($p<0.0001$), VAD ($p=0.01$), INR>3 ($p=0.06$), and receiving an exchange transfusion ($p<0.0001$).

Exchange transfusion in this setting may reduce operative homeostasis time, postoperative blood loss especially in patients on VAD support, who have undergone previous heart surgery and if the preoperative INR was grater than 3. Exchange transfusion did not reduce the overall exposure to blood products. A randomized study is warranted.

Better Outcomes with Ventricular Assist Device (VAD) vs ECMO as a Bridge to Pediatric Heart Transplantation

Anne I Dipchand MD, Cedric Manlhiot BSc, Brian W McCrindle MD, Glen Van Arsdell MD, Tilman Humpl MD
Labatt Family Heart Centre, Hospital for Sick Children, Toronto, Canada

Purpose:
ECMO has long been the sole means of mechanical support for pediatric patients with endstage cardiac failure, but has high waitlist mortality and a survival to hospital discharge of less than 50%. The purpose of this study was to compare waitlist mortality and survival in pediatric patients supported by ECMO to those supported by a ventricular assist device (VAD).

Methods:
Review of all patients listed for HTx since 2002 and requiring mechanical support. VAD support available from 2004 (Excor®). Competing risks analysis used to model survival to one of 4 outcomes (HTx, death on waitlist, delisting, improvement).

Results:
Thirty-eight patients were on mechanical support while awaiting HTx (24 ECMO, 15 VAD). Median age at listing was 1.2 years (birth-16.6) for ECMO and 11.3 years (0.3-14.6) for VAD. Diagnosis was cardiomyopathy in 33% for ECMO and 93% for VAD. Figure 1 shows the time course to the 4 outcomes. In the entire institutional cohort, patients on mechanical support had the shortest wait times but the highest waitlist mortality. Median time to HTx was 37 days (1-930) overall; 20 days (1-85) for ECMO and 39 days (5-161) for VAD. Mechanical support was associated with increased odds of HTx [HR 2.4 (1.7-3.3), p<0.0001] but also delisting or death waiting [HR 3.0 (1.1-7.8), p=0.03]. Waitlist mortality of 38% on ECMO was reduced to 13% following introduction of VAD. Survival post-HTx was improved with VAD support (92% vs. 80%).

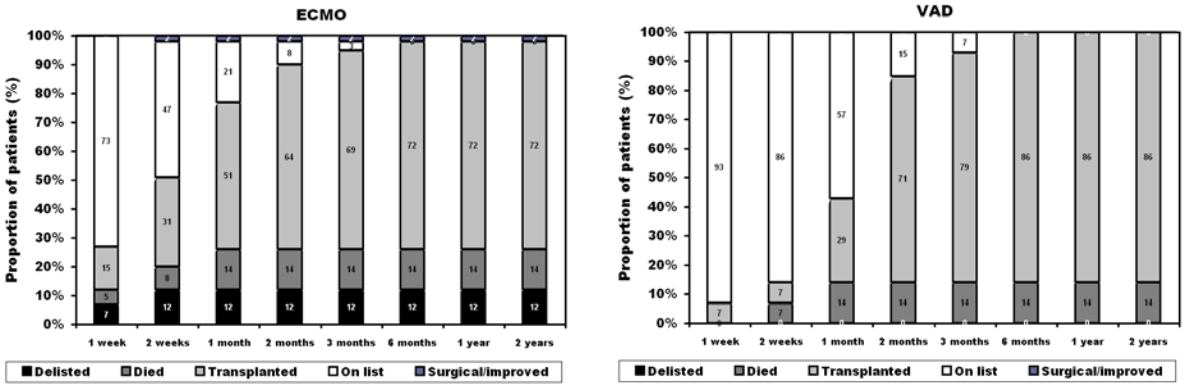


Figure 1: Time course to outcomes post-listing in ECMO and VAD patients

Conclusions:
Pediatric patients requiring mechanical support as a bridge to heart transplantation have short wait times but high waitlist mortality. Introduction of VAD support reduced waitlist mortality by more than half with improved post-HTx survival.

Extracorporeal Life Support in pediatric patients -outcome of a single centre-

Coskun ST*[1], Coskun KO[2], Popov AF[2], Hinz J[3], Özpeker CU[1], Blanz U[1], Weitkemper HH[1] , Schmitto JD[2], Morshuis M[1], Kececioglu D[o], Sandica E[1], Körfer R[1]
[o] Department of Pediatric Cardiology, [1]Department of Cardiovascular Surgery, Heart and Diabetes Centre North-Rhine Westphalia, Ruhr-University of Bochum, Bad Oeynhausen Germany; [2]Department of Thoracic and Cardiovascular surgery, [3]Department of Anaesthesiology, Emergency and Intensive Care Medicine, University of Göttingen, Germany

Background
In pediatric heart surgery low cardiac output (LCO) is the principal complication after corrective heart surgery. In LCO refractory to all therapeutic options mechanical circulatory support is the final method to keep these patients alive. In this present study we reviewed the outcome of pediatric patients who required mechanical circulatory support after corrective surgery and patients who became dilatative cardiomyopathie after myocarditis with extra corporeal membrane oxygenation (ECMO) or ventricle assisted devices (VAD).

Methods

A retrospective single centre consecutive cohort study was conducted in children who required different mechanical circulatory supports between 1991 and 2008. A total of 52 patients received extracorporeal life support, 27 male and 25 female. The indications for surgery were congenital heart disease (CHD) in 34 and dilatative cardiomyopathies (DCM) in 18 patients.
Results

Mean age was 10 years. 29 patients received ECMO and 23 patients received VAD. 16 patients out of 52 survived, 11 could be discharged after myocardial recovery from LCO and 5 could be discharged after successful heart transplantation. The all over mortality in patients with extracorporeal life support was 60.9%. The causes of death were multi organ failure and in 3 patients acute rejection after heart transplantation.

Conclusion

The use of extra corporeal life support (ECLS) shows a high mortality rate. However, ECLS can still help to keep some of those patients alive. Mechanical support devices are the ultimate chance to save time, to increase survival and to bridge the time until heart transplantation.

Extracorporeal Membrane Oxygenation Following Norwood Stage 1 Procedures

Shinya Ugaki, Mahito Nakakura, Takuma Doguchi, Eiji Ito, Hironori Ebishima, Yasuhiro Fujii, Shingo Kasahara, Sadahiko Arai, and Shunji Sano

Department of Cardiovascular Surgery, Okayama University Hospital, Okayama, Japan

Purpose:
Extracorporeal membrane oxygenation (ECMO) is one of the important circulatory assists for children with refractory cardiopulmonary dysfunction, but its role and indication after stage 1 Norwood procedure are controversial. We assessed outcomes and risk factors of patients who underwent stage 1 Norwood palliation and ECMO.

Methods:
We reviewed all patients who underwent stage 1 Norwood procedure and were supported with ECMO from Jun 2003 to Jan 2009 retrospectively.

Results:
Of the 57 children who went through stage 1 Norwood procedure during the study period, there were 15 runs of ECMO in 12 patients postoperatively. Operative diagnoses were 5 hypoplastic left heart syndrome, 5 hypoplastic left heart syndrome variant, and 2 critical aortic stenosis. There were 4 patients who had undergone bilateral pulmonary artery banding and 2 patients who had undergone aortic valvuloplasty before the stage 1 Norwood. Mean age was 27.5±29.5 days (3-99) and body weight was 2.6±0.5 kg (1.9-3.6) at the induction of ECMO. There were 5 of 12 children under 2.5 kg. The indications of ECMO were low cardiac output in 6, circulatory collapse needing cardiopulmonary resuscitation in 6 and hypoxia in 3. Five of 12 patients were successfully weaning from ECMO. The significant risk factors of inability of weaning from ECMO were the experience of circulatory collapse needing cardiopulmonary resuscitation and the induction of ECMO in the intensive care unit.

Conclusions:
Adequate induction of ECMO before irreversible fatal conditions can improve the outcome in impaired patients requiring support of ECMO following stage 1 Norwood procedure.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Comparison of Two Types of ECLS Membrane Oxygenators with Pulsatile and Nonpulsatile Perfusion

Nikkole Haines, BS, Shigang Wang, MD, John L. Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering,
Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The Medtronics Silicone Membrane Oxygenator for ECMO is commonly used in clinical practice for pediatric Extracorporeal Life Support (ECLS) in the US. A new hollow-fiber oxygenator, the MEDOS HILITE 800LT, is used for ECLS in Europe. We compared the effects of these two oxygenators on membrane pressure drops, circuit pressures and surplus hemodynamic energy (SHE) levels in a simulated ECLS model.

Methods:
The clinical set-up included the Jostra HL-20 heart-lung machine, either the Medtronics ECMO or the MEDOS 800LT with the company provided circuit components, a 10 Fr arterial cannula, and a pseudo-patient. We tested the system in nonpulsatile and pulsatile flow modes at two flow rates using a 40/60 glycerin/water blood analog, for a total of 48 trials, with n = 6 for each unique set-up. Pre- and post-oxygenator and arterial cannula pressures were recorded and pressure and flow waveforms provided hemodynamic energy data.

Results:
The pressure drops over the Medtronics ECMO were significantly higher than those over the MEDOS 800LT regardless of the flow rate or perfusion mode ($p<0.001$). At 500 ml/min in nonpulsatile mode the pressure drop over the Medtronics ECMO was 144.8 ± 0.2 mmHg, compared with 35.7 ± 0.2 mmHg over the MEDOS 800 LT, a 75.3% reduction with the MEDOS 800LT ($p<0.001$). The pre-oxygenator mean arterial pressures were also significantly increased with the Medtronics ECMO (245.3 ± 0.4 mmHg in pulsatile mode at 500 ml/min) compared the MEDOS 800LT (126.2 ± 0.2 mmHg in pulsatile mode at 500 ml/min) at the same settings ($p<0.001$). Pre-cannula SHE values with the Medtronics ECMO were consistently lower than those with the MEDOS 800 LT. See Table 1. Results were similar for other perfusion modes and higher flow rates

Table 1. Hemodynamic Energy and Pressure Data with the Jostra Roller Pump at 500 ml/min

Location	Parameter	Nonpulsatile		Pulsatile	
		MEDOS 800LT	Medtronics ECMO	MEDOS 800LT	Medtronics ECMO
Pre-Oxygenator	MAP	†118 ± 0.1	*245 ± 0.3	126 ± 0.2	*245 ± 0.4
	SHE	†6468 ± 94	*,†3489 ± 54	51126 ± 7	*18192 ±65
Pre-Cannula	MAP	†71 ± 0.1	*65 ± 3	77 ± 0.2	*65 ± 2
	SHE	†2845 ± 44	*-10 ± 0.4	23264 ± 3	*-166 ± 13

MAP (mmHg) = Mean Arterial Pressure, SHE (ergs/cm^3) = Surplus Hemodynamic Energy, *$p<0.001$ for MEDOS vs. Medtronics for all trials, † $p<0.001$ for Nonpulsatile vs. Pulsatile modes within each group

Conclusions:
These results suggest that the MEDOS HILITE 800 LT hollow-fiber membrane oxygenator better transmits hemodynamic energy to the patient, keeps mean circuit pressures lower and has lower pressure drops than the Medtronics Silicone membrane oxygenator.

Evaluation of an Ultra-Compact Extracorporeal Membrane Oxygenation (ECMO) System for Pediatric Use in an Acute Animal Study

Teruyuki Hayashi[1], MS, Eisuke Tatsumi[2], MD, Nobumasa Katagiri[2], MS, Toshihide Mizuno[2], DVM, Toshikatsu Yagihara[3], MD
[1]Department of Clinical Engineer, [2]Department of Artificial Organs
[3]Department of Cardiovascular Surgery
National Cardiovascular Center, Suita, Osaka, Japan

Introduction:
We have developed an ultra-compact ECMO system for quick resuscitation of neonates and infants with cardiopulmonary collapse. In the present study, we evaluated the basic performance of this system in 24 hours animal experiments.

Materials and methods:
The system consists of a newly-released membrane oxygenator for pediatric use (Oxia-IC, JMS, Japan) and a compact centrifugal pump (Mixflow3, JMS, Japan). The oxygenator is composed of polypropylene-made hollow-fiber membrane (surface area: 0.39m^2). The priming volumes of the oxygenator, the centrifugal pump, and the whole system are 37, 18, and 110 mL, respectively. The entire blood-contacting surface is coated with COAFREE® and COAFREE®II heparin-coating (JMS, Japan).

Under general anesthesia, two adult goats weighting 17 kg (Experiment-1) and 21 kg (Experiment-2) underwent 24 hours continuous Veno-Arterial ECMO with this system. Bypass flow rate was controlled at 1.5 ± 0.5 L/min, and the oxygen/blood flow ratio was set at 1.0. Heparin was intravenously injected at cannulation (100 I.U/kg), and then continuously administrated to control ACT between 150-200 seconds. Gas-exchange performances were evaluated in oxygen transfer and carbon dioxide removal rates. Hematological and coagulatory condition was assessed by measuring the levels of hemoglobin, serum free hemoglobin, platelet counts, ACT, APTT periodically.

Results:
In both experiments, 24 hours ECMO was successfully conducted without any adverse event. Device failure including serum leakage did not occur in any case. Gas-exchange performance was stably maintained. Average oxygen transfer rates of Expriment-1 and Experiment-2 were 55.2 and 61.6 mL/min, respectively. Average carbon dioxide removal rates of these experiments were 59.7 and 61.4 mL/min. Levels of hematological and coagulation-related factors were kept in physiological ranges. No clotting formation was found at inspection of the circuit after disassembly.

Conclusions:
The results of this study indicate that our ultra-compact ECMO system with 110 ml total priming volume can be safely applied to pediatric patients.

Application of computer modeling of systemic VAD support in failing Fontan physiology

Lucian A. Durham, III, M.D., Ph.D., Harold M. Burkhart, M.D., Joseph A. Dearani, M.D., Frank Cetta, Jr., M.D., Sabrina D. Phillips, M.D., Kartik Sundareswaran, Ph.D. and Soon J. Park, M.D. Divisions of Cardiovascular Surgery and Pediatric Cardiology, The Mayo Clinic, Rochester, MN and Thoratec Corp., Pleasanton, CA. USA.

Purpose:
Though the Fontan procedure has been enormously successful in palliation of single ventricle patients, many seem to progressively fail over time. LVADs have developed into stable platforms for long-term support of adult heart failure patients and with the success of axial flow devices, we hypothesized that the technology could provide clinical benefit to failing Fontan patient. The aim of this study was to use a computer model to evaluate VAD support in failing Fontan physiology.

Methods:
A computer model of Fontan circulation with heart failure was developed and the HeartMate II (HM II) (Thoratec Corp.) was connected to this model in a systemic configuration to examine its impact. Cardiac Catheterization data from seven patients with failing Fontan physiology were applied to this model to determine the clinical benefit of using the HM II in this manner.

Results:
Utilizing the HM II in a systemic configuration at 8,000 RPM, there was a 35% decrease in the systemic venous pressure in the Fontan circuit (22.6 ± 2.1 to 16.7 ± 2.2 mm Hg) and a 63% decrease in LA pressure (13.6 ± 1.2 to 4.9 ± 0.7 mm Hg) with a resultant 47% increase in cardiac index (2.3 ± 0.2 to 3.4 ± 0.2 L/min/M^2). The model also predicted patient specific issues where the VAD may not benefit the patient, such as fixed, elevated PVR (> 7 WU/m^2), EDP < 10 mm Hg, and high SVR.

Conclusions:
The data support the use of axial flow VAD technology in the management of failing Fontan physiology. Clinical correlation will allow for refinement of this model as a predictive tool in discerning which patients will benefit from placement of a VAD and what issues must be addressed prior to implanting the device.

Pediatric Mechanical Support with Artificial Myocardium System with Baroreflex Function

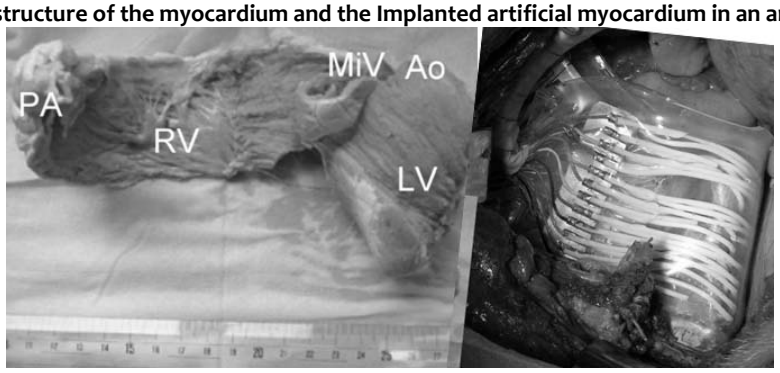
Tomoyuki Yambe, MD, Yasuyuki Shiraishi, PhD, Hidekazu Miura, Ph.D., Kou Imachi, PhD
Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan

Purpose:
For the pediatric mechanical support system, smaller is better, of course. So, we have developed the artificial myocardium system with shape memory alloy (SMA)actuator with nano technology with automatic control system.
In the patients with congestive heart failure, several investigators suggested that baroreflex sensitivity was reduced. So, we added the automatic baroreflex control system for the artificial myocardium system for the patients whose circulation was totally depending on the mechanical support system.

Methods:
For the precise assist of the failing heart, anatomical structure and pathological damage of the myocardium are very important issue. So, we have developed artificial myocardium which can implant into the chest cavity according to the damaged myocardium by the use of SMA. actuator covered with silicone material. Furthermore, baroreflex function was added to the artificial myocardium control system by the use of hemodynamic information.
Animal experimental series were carried out to determine the anatomical fitting of the artificial myocardium system, according to the myocardial anatomical structure as we shown in fig.1. And development of the Artificial baroreflex system was carried out with the information of the blood pressure, peripheral resistance, and pulse wave velocity and animal experiments were performed.

Results:
Fitting study of our artificial myocardium system were shown below and excellent fitting was observed and pump performance of the ventricle was improved. Information of the blood pressure, vascular resistance and PWV was useful for the Artificial baroreflex control system.

Fig 1. Anatomical structure of the myocardium and the Implanted artificial myocardium in an animal experiment



Conclusions:
These results suggest that the artificial myocardium system may be good candidates for the pediatric mechanical circulatory support system in future..

Development of a Computer-aided 3 D Bioprinting System for Bioartificial Organ

Seung Joon Song[1,2], Jaesoon Choi[2], Yong Doo Park[1], Kyung Sun[1,3]
[1]Korea Artificial Organ Center, Korea University, Korea, [2]Departnent of Biomedical Engineering, Brain Korea 21 Project for Biomedical Science, College of Medicine, Korea University, Korea, [3]Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea

Purpose:
Tissue engineering integrating biomaterials with cell and developmental biology is an applied science with the goal of generating implantable tissues and organ structures to improve human health. Especially, the development of a bio-printing technique has been a big issue. This paper attempts to develop a bio-printing as a rapid prototyping computer-aided 3D printing technology. This technology is based on using layer by layer deposition of cell and/or cell aggregates into a 3D gel with sequential maturation of the printed construct into perfused and vascularized living tissue or organ.

Methods:
Proposed bioprinting system consists of three axis of x-y-z motion control stage and one axis of nozzle control. The resolution in the x and y axis can be provided 0.05 μm, available not only micro-scaled resolution but also nano-scaled resolution. The size of single dot printed by a nozzle was 20 to 30 μm in diameter, which is close to the size of 1 or 2 living cells. We prepared some image data for printing biological tissue or organ structures and then numerical image data were extracted. CAD/CAM data were obtained from those image data and input to the system. System control and motion control algorithms were developed in Labview^{TM} software (National Instruments Co. U.S.A.). The specification of the developed system was compared with other research group's biopriting system.

Results:
A series of experiments to fabricate cell aggregates using cells embedded in alginate hydrogel with the bioprinting system prototype was performed. Through the experiments, we confirmed the feasibility of our system. Present systems under development mostly have micro-scale resolution, but our system has nano-scale resolution. We believe that the system can be applied to not only micro-scaled cell aggregates but also nano-scale single cell manipulation based applications.

Table 1. Comparison specification with other research group's system.

	Designed system	Kanagawa Academy	Carnegie Mellon Univ.	Tsinghua Univ.	iv. of Missouri-Columbia
Nozzle(sysringe)	RN microliter syringe niton, USA, 100 μm, inner diameter)	:A-JetTM(Epson, Japan)	MJ-AB inkjet(Microfab hnologies, Inc. Plano, TX)	stainless steel syringe nozzle(200μm, inner diameter)	cropipette(500μm, inner diameter)
Maximum operating frequency	100Hz	3kHz	100Hz(max: 20kHz)	79Hz	50Hz
Positioning resolution	.05μm(x-y), 0.125μm(z)	0.2μm	1.0μm(x-y), 0.1μm(z)	0.5μm	6.25μm
Maximum operating distance(X, Y, Z)	100*100*100(mm)	100*100*100(mm)	100*100*100(mm)	200*200*200(mm)	203*152*60(mm)
Hardware	Custom designed and ricated 4-axis bioprinting system	printing: PM-950C(Seiko on, Suwa, Japran), Z axis: ST-PRO-II(Cony Precision chnology, Tokyo, Japan)	mm miniature jack-stage (Edmund Optics Inc., arrington, NJ), Aerotech ATS150 X-Y linear motor slides, ATS300 Z stage Aerotech, Inc., Pgh. PA)	:M-300-II(CLRF, Tsinghua Univ., China)	Roland MDX-20 milling machine (Roland DGA orporation, Irvine, CA),

Left ventricular assist for pediatric patients with dilated cardiomyopathy using Medos VAD cannula and centrifugal pump

Shu-Chien Huang, MD, Nai-Hsin Chi, MD, Yih-Sharng Chen, MD, Nai-Kuan Chou, MD, Wen-Je Ko, MD, Shoei-Shen Wang, MD, PhD.
Departments of Surgery, National Taiwan University Hospital, Taipei, Taiwan,

Purpose:
The ventricular assist devices(VAD) for small pediatric patients were not commercially available in our country. Pneumatic pump such as Thoratec VAD is expansive, and not suitable for small-sized children. We try to use Medos VAD cannula and centrifugal pump to support pediatric patients with dilated cardiomyopathy with decompensated heart failure.

Methods:
From Janurary 2007 to December 2008, four pediatric patients with dilated cardiomyopathy received LVAD support. One patient received Thoratec LVAD, the other three patients were supported with centrifugal pump as LVAD. The operation was performed with cardiopulmonary bypass. The Medos arterial cannula was sutured to the ascending aorta, and the Apex cannula was inserted into left ventricular apex, and fixed with pledget sutures. Then the cardiopulmonary bypass was weaned-off and LVAD start to pump. The pump flow was gradually titrated to the filling status of left ventricle. The extracorporeal membrane oxygenation (ECMO) , if needed, was left as temporary support for right ventricular failure. The sternum was closed after hemostasis.

Results:
The age and body weight were summarized in Table 1. All the LVADs were successfully implanted and functioned well. Two patients with ECMO had severe lung edema before LVAD implantation. Both patients require ECMO for the post-operative period, and the ECMO were removed one day later with the pulmonary edema resolved. Among the three patients, two had successfully bridged to heart transplantation after support for 6 and 11 days, respectively. The first patient (10Kg) expired due to systemic emboli 30 days after LVAD support.

Table 1. Demographic data and outcome for pediatric patients with LVAD support

No	Age/Sex	Body weight(Kg)	Pre-Op ECMO duration(day)	LV apex cannula	Aorta cannula	Pump	LVAD flow/rpm	Outcome
1	**1y/M**	10	10	9mm	6mm	Biopump	1.0L/2000rpm	expired
2	**9y/M**	24	-	9mm	8mm	Biopump	3.0L/2000rpm	HTX
3	**15y/M**	70	1	15mm	10mm	CentriMag	4.5L/2600rpm	HTX

Conclusions:
These results suggest that the MEDOS VAD cannula and a centrifugal pump is a choice for temporary LVAD support in patients with intractable heart failure. The device is cheaper and bridge to heart transplantation successfully.

Management of Deep Wound Complications with Vacuum-Assisted Therapy after Berlin Heart EXCOR® Placement in the Pediatric Population

Peter C. Kouretas, MD, PhD, Philip T. Burch, MD, Aditya K. Kaza, MD, Linda M. Lambert, MSN, CFNP, Madolin K. Witte, MD, Melanie D. Everitt, MD, Faizi A. Siddiqi, MD
Departments of Surgery, Pediatrics and Critical Care, The University of Utah, Primary Children's Medical Center, Salt Lake City, Utah

Purpose:
Wound complications remain a significant cause of morbidity and mortality after implantation of a ventricular assist device (VAD). The Berlin Heart EXCOR® VAD is a versatile pulsatile system that has been successful in pediatric patients of all ages and sizes. We present our experience in the management of deep wound complications of the cannula-site using vacuum-assisted (VAC) therapy.

Methods and Results:
Our first patient is an 8 month with dilated cardiomyopathy. Despite optimum medical management, the patient underwent placement of a Berlin Heart EXCOR® VAD for left ventricular support. The post-operative course was significant for deep wound complications of both the inflow and outflow cannula sites. After surgical debridement, a vacuum-assisted closure (VAC) system was implemented. A polyurethane granufoam sponge was packed in each wound. An occlusive drape and suction were applied with continuous negative pressure of 125 mmHg. VAC dressings were changed every 48 hours. Both wounds were completely healed after 14 days of VAC therapy without growth of any microorganisms. The patient underwent successful heart transplantation without any infectious complications.

Our second patient is a 5 year old with dilated cardiomyopathy. This patient presented in cardiac failure, was emergently placed on extracorporeal membrane oxygenation and successfully bridged to a Berlin Heart EXCOR® VAD for biventricular support. The patient subsequently developed deep wound complications around each cannula site. Similar protocols were implemented with complete wound healing after 10 days of therapy without growth of any microorganisms.

Conclusions:
Cannula-site wound complications remain a significant challenge in patients after placement of a VAD. We present a novel strategy for the management of deep cannula-site wounds using VAC therapy in pediatric patients after placement of the Berlin Heart EXCOR® VAD. Implementation of the VAC system proved to be an efficient strategy to achieve complete wound healing without any infectious complications.

Experience with the Levitronix CentriMag® in the Pediatric Population as a Bridge to Decision and Recovery

Peter C. Kouretas, MD, PhD, Aditya K. Kaza, MD, Philip T. Burch, MD, Stephen E. Clayson, MD, Melanie D. Everitt, MD, Craig H. Selzman, MD.
Department of Surgery and Pediatrics The University of Utah, Primary Children's Medical Center, Intermountain Medical Center, Salt Lake City, Utah.

Purpose:
Application of short-term mechanical circulatory support (MCS) in the pediatric population with acute cardiac failure has traditionally been limited to ECMO, given the limited availability of pediatric-size pumps. The Levitronix CentriMag® system offers expanded options for short-term MCS for this population. We report two successful applications of the Levitronix CentriMag® as a bridge to decision after post-cardiotomy ventricular failure and as a bridge to recovery post heart transplantation.

Methods and Results:
Our first patient is a 13 year old male who presented with severe aortic valve insufficiency, cardiac failure and an ejection fraction of 20%. He underwent aortic valve replacement and was placed on a Levitronix LVAD secondary to post-cardiotomy failure. Inadequate ventricular recovery and the presence of a left ventricular thrombus directed the decision to place a Thoratec HeartMate II® after six days of support. The thrombus was removed thru the apex of the ventricle prior to placement of the Thoratec. Endomyocardial biopsy revealed myocarditis. The patient is doing well after 3 months, discharged to home, with the potential for myocardial recovery.

Our second patient is a 13 year old female with dilated cardiomyopathy who underwent heart transplantation. Her post-operative course was complicated by severe graft failure. Levitronix CentriMag® pumps were implanted for short-term biventricular support. After three days, weaning trials were initiated with complete recovery of the donor heart. The Levitronix support system was successfully explanted with an uneventful recovery after heart transplantation.

Conclusions:
The Levitronix CentriMag® has proven to be a versatile, short-term circulatory support system for our pediatric patients. We present two unique successful applications of emergency short-term support for bridge to decision in complex pediatric patients. The first patient was bridged to a long-term Thoratec LVAD with the potential for recovery and the second patient was supported after heart transplantation with a full recovery.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Initial Clinical Experience with the HeartMate® II Ventricular Assist System in a Pediatric Institution

William R. Owens[1], Roosevelt Bryant, III[2], William J Dreyer[3], Jack F. Price[3], David L. S. Morales[2]

[1]Division of Congenital Heart Surgery, Texas Children's Hospital, Houston, Texas, U.S.A.
[2]Michael E DeBakey Department of Surgery, Division of Congenital Heart Surgery, Baylor College of Medicine, Houston, Texas, U.S.A.
[3]Department of Pediatric Cardiology, Baylor College of Medicine, Houston, Texas, U.S.A.

In many adult cardiac programs, intracorporeal mechanical circulatory support has become a routine treatment for end-stage cardiac failure. For the pediatric population, options are often limited by a small body habitus. Even when an adolescent's weight may suggest adequate space for device implant, most intracorporeal adult devices remain too large for adolescents.

The Thoratec HeartMate® II (HMII) (approved by the FDA in April of 2008) is a small, noiseless device that is easily operated and monitored. By having an uncomplicated operating system and small percutaneous drive line, the HMII provides an opportunity for these patients to aggressively rehabilitate to become a better transplant candidate and also provides the potential to be discharged home.

The two youngest patients ever to utilize the HMII are also the first two cases of using the HMII at a free standing pediatric hospital. A 12yo, 53kg, girl with dilated cardiomyopathy was supported for 85 days before receiving her heart transplant. The second patient, a thirteen year old, 149kg, Hispanic male suffering from morbid obesity and dilated cardiomyopathy, was supported for 128 days. The HMII allowed for rehabilitation and nutritional education, resulting in this patient losing 50 kg before heart transplant. Despite both of these patients' size, their thoracic cavities were that of a pre-adolescent and thus techniques were developed to avoid morbidities like chest wall abrasion and bleeding.

Because of differences between adult and pediatric patients and institutions, these cases provided unique challenges. However, as pediatric device therapy is now maturing, pediatric programs such as Texas Children's Hospital have begun to develop strategies for mechanical support that factor in patient's size and need for long-term or temporary support, utilizing the growing number of devices (i.e. Jostra Rotoflow®, Tandem Heart PTVA®, Thoratec CentriMag®, Berlin Heart EXCOR®, etc.) that are now available to children.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Hemorrhagic Stroke in a Child with a Low Total Serus Cholesterol and New Support With a Berlin Heart Excor® Left Ventricular Assist Device

Wesley A. McKamie, C.C.P.,[a] Michael L. Schmitz, M.D.,[a,b] Charles E. Johnson, R.N., C.C.P.,[a,b] Michiaki Imamura, M.D., Ph.D.,[a,b] Robert D. B. Jaquiss, M.D.[a,b] [a]Arkansas Children's Hospital and [b]The University of Arkansas for Medical Sciences

Introduction:

Low serum cholesterol has long been associated with hemorrhagic stroke. Most of these observations have come from adult studies.[1] There have been no reports of this association in children.

Case Report:

A 6 yo Japanese female with an idiopathic dilated cardiomyopathy, and severe congestive heart failure was listed for a cardiac transplant. Her condition was chronic and she appeared severely cachectic. She required escalating inotropic support. As a bridge to transplantation, a Berlin Heart® left ventricular assist device (LVAD) was placed without incident. She was weaned from cardiopulmonary bypass and the LVAD rate was increased to facilitate a cardiac index of 2.8 l/min/m^2. Her inotropes were weaned until she was supported with low dose epinephrine by POD#2. Later that day, sodium nitroprusside was added to control her blood pressure (BP). On POD#2 and #4, she had a couple occasions of BPs of 130-134/75-80 mm Hg (baseline pre-LVAD BPs were in the range of 75-110/40-70). The child had a seizure on POD#5 and appeared lethargic. A CT scan of the head showed an intracerebral hemorrhage of approximately 3.28 x 0.56 cm in size in the anterior superior falx. She ultimately received a successful orthotopic heart transplant and did well with no residual neurological deficit.

Discussion:

The relationship between intracranial hemorrhage and low serum cholesterol levels is unclear, but it is theorized that hypertension (HTN), especially diastolic HTN, in the presence of hypocholesrolemia weakens the endothelium of cerebral arteries. It has long been known that poor nutritional status as well as severe alcoholism and previous severe illness is related to decreased serum cholesterol and decreased survival from stroke.[1] Risk factors for intracerebral hemorrhage in adults include low serum cholesterol, hypertension, smoking, coagulopathy, and intracerebral vascular anomalies.[2] Our patient was severely cachectic with hypocholesterolemia pre-LVAD placement. Post-LVAD placement, she was briefly hypertensive but was also subjected to enhanced cardiac output and pulsatile flow. Hypocholesterolemic adult patients have a higher risk for hemorrhagic transformation of an ischemic stroke after pulsatile blood flow is returned after thrombolysis.[3]

Conclusions:

Severely debilitated children with hypocholesterolemia may be at risk for hemorrhagic stroke after pulsatile LVAD placement, especially in the presence of HTN.

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Orthotopic Heart Transplantation in a Child with Hereditary Spherocytosis

Charles E. Johnson, R.N.,[a] C.C.P., Michael L. Schmitz, M.D.,[a,b] Wesley A. McKamie, C.C.P.,[a] R. Erik Edens, M.D. Ph.D.,[c] Michiaki Imamura, M.D., Ph.D.,[a,b] Robert D.B. Jaquiss, M.D.[a,b] [a]Arkansas Children's Hospital, [b]The University of Arkansas for Medical Sciences, College of Medicine, [c]University of Iowa Children's Hospital

Introduction:
Hereditary spherocytosis (HS) is a genetic, and frequently familial hemolytic blood disease with variable clinical effects. Most commonly, patients present with anemia, splenomegaly, and possibly jaundice. The disease arises as a result of defects in any of a number of proteins responsible for maintaining the shape and flexibility of the red blood cell (RBC), resulting in an osmotically fragile and characteristically spherical red blood cell.[1] Theoretically, cardiopulmonary bypass (CPB) can post additional risks to patients with HS because of higher hemolysis and subsequent renal dysfunction. There area only a few reports of management of open heart surgery for children with HS. There are no reports of an orthotopic heart transplantation in a child with HS.

Case Report:
A 6 yo Japanese boy with HS, idiopathic dilated cardiomyopathy, and severe congestive heart failure was listed for a cardiac transplant. His prior history included a cholecystectomy and frequent RBC transfusions. His preop blood smear showed 1+ spherocytes. A suitable donor heart became available, and the patient was taken to the OR. His starting hematocrit was 24.8%. After induction of anesthesia with standard monitoring including NIRS, we placed central venous and arterial monitoring catheters, and surgery began. CPB began after an uneventful arteriovenous cannulation. We performed a 1.5X patient blood volume exchange transfusion by draining blood via the venous cannula and simultaneously transfusing packed RBCs and fresh frozen plasma through the arterial cannula. Surgical transplantation and separation from CPB were uneventful. The transplanted heart functioned well. There was no macrohematuria. The postoperative Hct was 46% and there were 1+ spherocytes by POD#2. He was discharged home 1 mo later.

Discussion:
The actual risk for hemolysis during CPB in patients with HS is unknown. Previous case reports have advocated using poloxamer 188, a non-ionic antihemolytic detergent that protects RBC membranes during CPB, haptoglobin to reduce plasma free hemoglobin that could damage kidneys, or both.[2] Others have reported CPB-assisted heart surgery without exchange transfusion, polaxamer 188, or haptoblobin that still showed no significant hemolysis.[3] We chose to reduce circulating spherocytes by means of an exchange transfusion in an attempt to reduce the risk of renal failure from plasma free hemoglobin and possibly pulmonary hypertension. However, without controlled trials of these therapeutic interventions, the effectiveness of these treatments is entirely unclear, and controlled treatment is unlikely for this uncommon use.

Conclusions:
For this report of an orthotopic heart transplant in a pediatric patient with HS, a 1.5X exchange transfusion at the start of CPB was used to reduce circulating spherocytes. This 6 yo did not have significant hemolysis with CPB.

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A Novel Implantable Mechanical Circulatory Support System: The Artificial Ventricle

Hisham M.F. Sherif, MD, Cardiovascular Surgery, 7 Vinca Drive, Newark, DE 19702, USA

Purpose:
We introduce a novel design for a new totally internal mechanical circulatory support pump for replacement of one or both ventricles. The device has a long projected service life, a totally implantable, readily available and off-the-shelf energy source

Methods:
The proposed device is a pulsatile, positive-displacement blood pump composed of a compliance chamber, constructed of a biocompatible, non-thrombogenic material. At its base, this chamber incorporates two bioprosthetic valves in opposite orientation- an inlet valve and an outlet valve. The two valves are each connected to a vascular graft. The chamber is surrounded by radially-arranged contractile elements, made of an electro-active polymer and connected to a common stimulating electrode. The entire assembly is housed in a hermetically sealed biologically inert shell. The electrode is connected to the output of a conventional implantable permanent pacemaker. The energy output from the pacemaker will cause the deformation of the contractile elements and thus compression of the compliance chamber, effecting ejection of the blood through the outlet valve.

Results and Conclusions:
Based on a design emulating the natural anatomic configuration and utilizing a new class of materials, the device shall provide mechanical assistance or replacement of the native heart function for an extended period of time. The proposed design is completely implantable; composed of readily available materials; has minimal energy requirements and an extended service life on internal power supply.

Initial in Vivo Evaluation of the 'TinyPump™' for LVAD Application

Mariko Kobayashi[1], MD, Masaharu Yoshikawa[2], MD, PhD, Takashi Kitao[1], DVM
Satoshi Shoji[1], Shinya Machida[1], Hideyuki Osawa[1], Taisuke Ishii[1], Satoshi Waguri[1], MS,
Tomohiro Konno[3], PhD, Kazuhiko Ishihara[3], PhD, Setsuo Takatani[1], PhD, DMed
[1]Department of Artificial Organs, Tokyo Medical and Dental University, [2]Department of Cardiovascular Surgery, Toyota Kousei Hospital, and [3]Department of Material Science, School of Engineering, The University of Tokyo

Purpose:
To meet requirements in small patients, an ultra-miniature rotary centrifugal blood pump 'TinyPump™' with 5ml prime has been designed showing feasibility for low flow control in acute CPB and lung support. In this study, biocompatibility and hemodynamic performance of the TinyPump™ were evaluated in Shiba goats for LVAD application.

Methods:
Seven one-year old female Shiba goats (weight 11.9-14.9 kg) were used for this study. Through left lateral thoracotomy, inflow cannula (20Fr) was inserted to the LV apex and the 6-mm Dacron outflow graft was anastomosed to the descending aorta, connecting the TinyPump treated with 2-methacryloyloxyethyl phosphoryl choline (MPC) and placed extracorporeally via 50cm long 1/4" tubings. Postoperatively, pump flow in all animals was kept at 50% of the native pulmonary artery flow (1.8±0.3L/min) and anti-coagulation was controlled by keeping ACT over 200 seconds. The animals were grouped into acute (n=3, 6-hour), transient (n=3, 9-, 21- and 24-hour), and sub-chronic (n=1, 6-day) to analyze the effects of the TinyPump™ on hemodynamics, hemolysis and organ function.

Results:
In the acute group, mean aortic and central venous pressures were maintained normal. Mean hematocrit remained higher than 20% with lactic acid peaking out at one hour post-operatively. There was no organ failure in any animals. In the transient group, the TinyPump™ provided from partial to full circulatory support enabling stable hemodynamics. In the sub-chronic 6-day animal, plasma free hemoglobin peaked out at 3 post-operative days. Thrombus formation was observed in the acute and transient groups around bearing area, whereas subsequent design change has brought thrombus-free performance in the 6-day animal.

Conclusions:
Our initial animal experience has shown that the MPC treated TinyPump™ can maintain hemodynamics with minimum adverse effects to the blood components and organ function. Additional longer-term animal studies are required to confirm feasibility of the TinyPump™ for chronic circulatory support in small patients.

The effect of pumpless extracorporeal lung assist in experimental lung injury

Feilong Hei, MD,Yulin Tian , MD, Yongli Cui, MD,Kun Yu, MD, Cun Long, MD,
Department Extracorporeal Circulation, Cardiovascular Institute and Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100037. China

Purpose:

Pumpless extracorporeal lung assist（pECLA）technique was developed to support pulmonary function in cases with severe respiratory insufficiency. The aim of this experimental study was to test the effectiveness of pECLA in the canine model with acute respiratory distress syndrome（ARDS）.

Methods:

Six healthy hybrid canines of either gender were used, weighed 22.66±1.21kg（mean±SD）. Dogs **were anesthetized with pentobarbital** sodium 30 mg/kg i.v，and then 0.08-0.10 ml/kg oleic acid was injected intravenously. When the PaO2/FIO2 ratio (P/F) ≤26.7kPa (200mmHg), the ARDS model was successfully established. pECLA was established by an arterio-venous shunt including a low-resistance membrane oxygenator which was placed between unilateral carotid artery and venae femoralis.The Changes of homodynamic and artery blood gas were recorded before and after pECLA support.

Results:

SaO2 and PaO2 were significantly higher after pECLA than before pECLA. ($p<0.01$)
PaCO2 was significantly lower after pECLA than before pECLA. ($p<0.01$). See Table 1.However, **there** were no **significant differences in hemodynamic variables between** before and after pECLA. See Table 2.

Table 1. Changes of artery blood gas before and after pECLA support

Time	SaO2	PaO2	PaCO2
before pECLA	80.47±3.70	6.17±0.45	126 ± 0.2
after pECLA	94.65±1.48*	8.47±0.47*	77 ± 0.2*

pECLA = Pumpless Extracorporeal Lung Assist, SaO2 (%) =Arterial Oxygen Saturation, PaO2 (kPa) = partial pressure of oxygen in artery, PaCO2 (kPa) = partial pressure of carbon dioxide in artery, *$p<0.01$ after pECLA vs. before pECLA

Table 2. Changes of homodynamic before and after pECLA support

Time	HR	MAP	CVP	PAP
before pECLA	151.8±13.8	126.2±12.43	1.3 ± 0.5	18.5 ± 3.2
after pECLA	169.0±19. 8	117.5±13.4	1.1 ± 0.4	19.0 ± 2.5

HR (beats/min) =heart rate, MAP (mmHg) = Mean Arterial Pressure, CVP (mmHg) = central venous Pressure, PAP (mmHg) = **Pulmonary** Arterial Pressure.

Conclusions:

The pECLA is feasible and effective in patients with acute respiratory distress syndrome. It is very important to **keep homodynamic stability** during pECLA support.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

In vitro Thrombogenicity Evaluation of the TandemTot Pediatric Centrifugal Pump

Amber N. Loree, BS, Robert G. Svitek, PhD

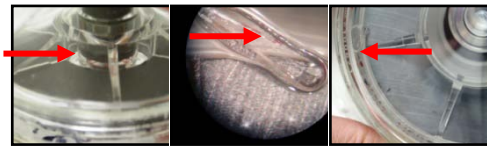
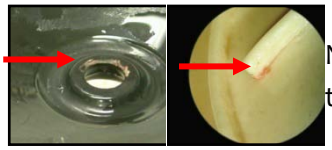
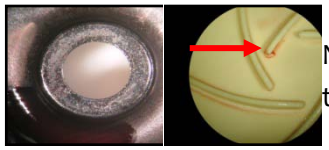
CardiacAssist, Inc. Pittsburgh, Pennsylvania, USA

Purpose:
CardiacAssist, Inc. is developing the TandemTot, an extracorporeal, circulatory assist system that can be placed percutaneously (for up to 30 days). The system consists of a transseptal venous cannula inserted into the left atrium, a pump, an arterial cannula, and a controller. Patients from 2-40 kg can be supported by custom cannulae ranging in size from 8-14 Fr. A new centrifugal pump was prototyped using cast urethane. The objective of this study was to compare the thrombogencity of the TandemTot pump to the Medtronic BP-50.

Methods:
Identical test loops were constructed using a reservoir, 1/4" tubing, and the pumps. Porcine blood was anticoagulated with citrate dextrose at the slaughterhouse, and recalcified before the test. Heparin was added to each loop to achieve an ACT of 200s. The flowrate was set to 0.4 LPM. After three hours, the pumps were rinsed with saline, disassembled, and visually evaluated for thrombus formation. The first test compared thrombogencity between the Medtronic BP-50 and the TandemTot. A second test investigated the effect temperature had on thrombus formation by placing the TandemTot pump motor on ice.

Results:
The BP-50 had significant thrombus at the shaft/seal interface, the impeller, and housing. The TandemTot had thrombus at the shaft/seal interface and on a surface defect on the impeller. When tested on ice, the TandemTot only had thrombus on the impeller defect.

Table 1. Locations of Thrombus Formation after Three Hours

	Location		
Pump	Shaft/Seal	Impeller	Housing
BP-50			
TandemTot			No thrombus
TandemTot on Ice			No thrombus

Conclusions:
The new TandemTot centrifugal pump design produced thrombus at the shaft-seal interface, but less overall thrombus than the BP-50 pump. The thrombus in the TandemTot can be eliminated by increasing the heat dissipation of the pump motor.

Optimal pressure regulation of the pneumatic VAD with bellows-type driver

Jung Joo Lee, PhD, Bum Soo Kim, MS, Jaesoon Choi, PhD, Hyuk Choi, PhD, Chi Bum Ahn, MS, Kyoung Won Nam, PhD, Gi Seok Jeong, PhD, Choon Hak Lim, MD, PhD, Ho Sung Son, MD, PhD, Kyung Sun, MD, PhD

Korea Artificial Organ Center, Korea University
Biomedical Science of Brain Korea 21, College of Medicine, Korea University
Department of Anesthesiology and Pain Medicine, Korea University Medical College
Department of Thoracic and Cardiovascular Surgery, Korea University Medical College, Seoul, Korea

Purpose:
The bellows-type pneumatic VAD generates pneumatic pressure with compression of bellows instead of using an air compressor. This VAD driver has a small volume that is suitable for portable device. But improper pneumatic pressure set up can not only fail adequate flow generation but also cause durability problem. In this study, a pneumatic pressure regulation system for optimal operation of the bellows-type VAD has been developed.

Methods:
The optimal pneumatic pressure conditions according to various afterload conditions aiming optimal flow rate were investigated and an afterload estimation algorithm was developed. The developed regulation system which consists of a pressure sensor and a two-way solenoid valve estimates the current afterload and regulates the pneumatic pressure to the optimal point for the current afterload condition. Experiments were performed in a mock circulation system.

Results:
The afterload estimation algorithm showed sufficient performance with the standard deviation of error, 8.8mmHg. The flow rate could be stably regulated with developed system under various afterload conditions.

Conclusions:
The shortcoming of a bellows-type VAD could be handled with this simple pressure regulation system.

Estimation of Native Cardiac Output of Patients Under Ventricular Assist Device Support Using Frequency Analysis of Arterial Pressure Waveform

[2]Jun Woo Park, PhD, [1]Jaesoon Choi, PhD, [1]Jung Joo Lee, PhD, [1]Hyuk Choi, PhD, [3]Byoung Goo Min, PhD, [1]Kyung Sun, MD, PhD, MBA

[1]Korea Artificial Organ Center, College of Medicine, Korea University, Seoul, Korea, [2]Biomedical Engineering Branch, Research Institute, National Cancer Center, Gyeonggi, Korea. [3]Dept. of Biomedical Engineering, College of Medicine, Seoul National University, Seoul, Korea

Purpose:

Native cardiac output (CO) of patients under ventricular assist devices (VADs) is one of the important indices representing the activity of the patients' heart. Arterial pressure waveforms can be acquired using non-invasive methods and have the information about native and VAD's blood flow. The objective of this paper is to estimate the native CO of these patients by separating two pressure components, native heart and VAD, using frequency analysis of arterial pressure waveforms.

Methods:

Using the Fast Fourier Transform (FFT) method, frequency components of native heart and VAD were found. Utilizing bandpass filterbank that includes base frequency and its harmonics, arterial pressure waveforms were separated into two pressure components. Using a simplified cardiovascular model,the relationship between mean arterial pressure and mean CO was derived. The ratio of CO and pump output (PO), ρ, can be estimated as a ratio of mean pressures produced by native heart and VADseparately. This ratio is not related to parameters of physiological model. We can estimate native CO as a product of ρ and PO of VAD. In vitro mock circulation experiments and in vivo animal experiments were performed to verify the proposed methods.

Results:

Fig. 1 shows ρ from in vitro experiments. Theoretically, ρ must equal 1. From experiments, we obtained ρ of 1.038 (R^2 = 0.9399) from in vitro cases and ρ of 0.9758 (R^2 = 0.9768) from in vivo cases. Fig. 2 shows estimated CO of native heart using ρ and measured PO of VAD. We obtained Y = 0.995X (R^2 = 0.5778, RMSE = 0.241) from in vitro cases and Y = 0.9035X (R^2 = 0.7230, RMSE = 0.217) from in vivo cases.

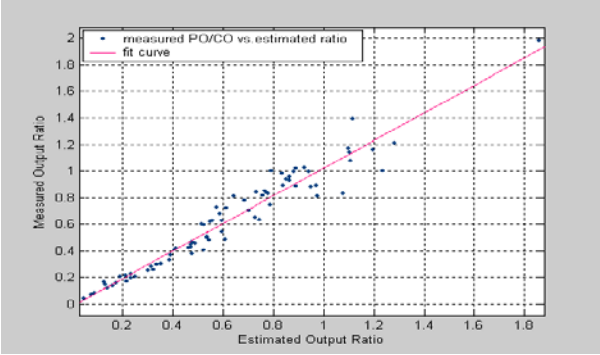


Fig. 1. Finding ρ: in vitro test results

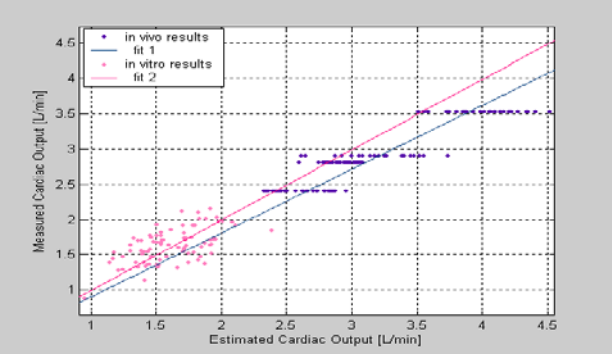


Fig. 2. Results of native cardiac output estimation

Conclusions:

With bandpass filterbank, we could separate two pressure components from arterial pressure waveform. The ratio of mean pressures reflected the ratio of mean cardiac outputs well in vitro and in vivo experiments. And, using this ratio, we could estimate native cardiac output with high accuracy.

Cuff-less and Non-invasive Estimation of Continuous Blood Pressure Based on PTT

Youngsung Kim, Jaesoon Choi, PhD, Kyung Sun, MD, PhD, MBA
Korea Artificial Organ Center, College of Medicine, Korea University, Seoul, Korea,

Purpose:
This study suggests a method for continuous monitoring of BP(blood pressure), an important fundamental vital sign of human body, with a cuff-less and non-invasive estimation using PTT (Pulse Transit Time). The monitoring methods for BP generally use physical sensors which directly or indirectly contacts with the blood vessel, but this kind of method may hardly be available in emergency situation requiring rapid treatment. In that kind of situation, to take BP reading, devices measuring BP by inflating a cuff around the arm are mostly used. However, that provides only the instantaneous BP value. This paper introduces a wrist type device developed for non-invasive continuous BP measurement and an estimation algorithm based on PTT

Methods:
The developed device is easy-to-use and small-size wrist type apparatus for measuring ECG, PPG, temperature and etc. With the ECG signal and pulse wave velocity through blood vessel measured by the device, BP can be estimated using an algorithm that uses a regression model. In order to evaluate the efficacy of the device and the estimation algorithm, a series of measurement tests was performed in 100 people. In each test, the conventional NIBP measurement based on sphygmomanometery or oscillometry was first performed two times and the measurements using our wrist type device that requires 40 seconds measurement and processing time followed. And lastly BP from BM2Pluse with cuff that is a commercial product was measured.

Fig. 1. Wrist Type device

Results:
Table.1 shows the results of the experiment and the statistical comparison.

Table. 1. Subject taking part in comparison reference and wrist device

Subject condition	Oscilometry	BM2Pluse		Wrist Device	
	mean (mmHg)	mean (mmHg)	p-value	mean (mmHg)	p-value
Hypertension	131 ± 2	129 ± 4	0.09	121 ± 9	0.312
Hypotension	108 ± 2	106 ± 3	<0.06	110 ± 5	0.302
Over sixty years old	128 ± 1	127 ± 4	0.08	122 ± 7	0.286
Under sixty years old	106 ± 1	105 ± 3	0.07	110 ± 6	0.293
The others	112 ± 2	114 ± 2	<0.06	109 ± 3	0.193

Conclusions:
As shown in the results, we could confirm that the estimation of BP by PTT comes close to BP provided by the conventional method and the commercial product although the statistical comparison showed relatively weak correlation. It is expected that better precision and correctness could be achieved through estimation algorithm refinements based on the promising results of this study.

Development of a Control Algorithm to Maintain Full-Filling State of the Blood Pump for a Bellow-type Pneumatic Ventricular Assist Device

C.B. Ahn, MS, J.J. Lee, PhD, J. Choi, PhD, and K. Sun, MD, PhD
Korea Artificial Organ Center, Department of Biomedical Engineering, Brain Korea 21 Project for Medical Science, College of Medicine, and Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea.

Purpose:
In the bellows-type pneumatic ventricular assist device, filling status of blood sac is affected by various conditions as preload and inflow resistance. In order to maintain full-filling status of the blood sac independently of conditions change, there is needed a control algorithm that copes with such changes. In this study, we developed a control algorithm that estimates current filling status and control some variables to maintain full-filling status.

Methods:
The developed algorithm consists of two parts; filling status estimation and full-filling control. The algorithm uses two variables as input parameters (pneumatic pressure of the blood pump assembly and pump rate) and two variables as control parameters (the time ratio of systole-diastole and pump rate). The algorithm controls S/D ratio and PR to get full-filling status. Experiments were performed in an assumption that the afterload pressure is fixed to 100 mmHg.

Results:
At in vitro performance test, the developed algorithm could estimate the inflow status at an accuracy of 10% and could adjust the control parameters automatically to maintain full-filling state of the blood pump. The full-filling status could be acquired with developed algorithm with an accuracy of 10%.

Conclusions:
This study showed the full-filling status could be maintained with an automatic control algorithm although it is performed at confined conditions. If it could perform at all conditions, it is thought to contribute to enhance the operation stability. For this sake, it would be needed more study on various afterload conditions and operations in *in vivo* conditions.

Reliability Study of Extracorporeal Electro-mechanical Pneumatic Biventricular Assist Device

[1,2]Hyuk CHOI, Ph.D., [2]Jaesoon Choi, Ph.D., [4]Kyung Won Nam, Ph.D.,[2]Gi Seok Jeong, Ph.D., [2]Jung Joo Lee, Ph.D., [2]Ho Chul Kim, Ph.D, [2]Chi Bum Ahn, M.A., [3]Ho Sung Son, MD, Ph.D., [3]Kuk Hui Son, MD,Ph.D., [5]Choon Hak Lim, MD,Ph.D., [1,2]Yong Doo Park, Ph.D., [2]Chang Mo Hwang, Ph.D., and [2,3]Kyung Sun MD,Ph.D.

Department of Medical Science, College of Medicine, Korea University, Korea., [2]Korea Artificial Organ Center, Korea University, Korea.,[3]Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea., [4]National Cancer Center, Korea., [5]Anesthesiology and Pain Medicine, Korea University, Seoul, Korea.

Purpose:
Since 2002, extracorporeal electro-mechanical pneumatic ventricular assist device (VAD) has been developed by Korea Artificial Organ Center, Korea University under a Health & Medical Technology R& D program (2002-2008). *In vivo* and *In vitro* tests are required to check for reliability of our system.

Methods:
In vitro durability testing was conducted on the pneumatic VAD to determine device durability and to evaluate device failures. A total of 6 separate tests were conducted for the cumulative test. Failures were analyzed using failure mode and effects analysis (FMEA) and fault tree analysis (FTA) principles, and customized software continuously acquired data during the test period. Over this period, 21 *In-vivo* animal tests were done. (14 cases were LA to LV cannulation, and LV apex cannulation was applied at 7 cases.)

Results:
The 1 and 2 year reliability of the pneumatic VAD was shown to be 91.2 % and 54.9%, respectively, at 80% confidence. The longest post operation day (182 days) in Korea was newly recorded at *In vivo* animal testing (bovine, 90 kg, male, 3.5-4.0 l/min of flow rate, and 55 bpm).

Conclusions:
In vitro and *In vitro* tests were conducted on the pneumatic VAD. Failures that were observed during testing were analyzed. Korea Food and Drug Administration (KFDA) approval will be obtained in the near future.

Eulerian Method for Numerical Prediction of Hemolysis in PediaFlow VAD

*Jeongho Kim, MS, *Samuel J. Hund, MS, **Amanda Daly, MS,
**Marina V. Kameneva, PhD, *James F. Antaki, PhD
*Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania, USA
**Department of Bioengineering, Department of Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Purpose:
An Eulerian approach was adopted to investigate hemolysis generation in the PediaFlow™ ventricular assist device (VAD), a miniature magnetically levitated blood pump for infants and small children (3-20 kg). The objective of this study was to validate hemolysis prediction by CFD with experiment results.

Methods:
The fluid dynamics within the PediaFlow (PF2) VAD was simulated computationally using CFX (Ansys, Inc.) employing an SST turbulence model and assuming an asymptotic viscosity for blood (3.5 cP) and a density of 1080 kg/m^3. An additional species transport model was used to estimate hemolysis based on the work of Garon et al. 2004. Experimental data were obtained by placing the PF2 into a flow loop and recirculating bovine blood (0.43 L at a 29% Hct) for 2 hours. The pump was operated at 13,200 rpm and generated a flow of 1.2 L/min. The computational results were compared to experimental results. A prediction was then made for hemolysis generation in the future generation (PF3) currently under development.

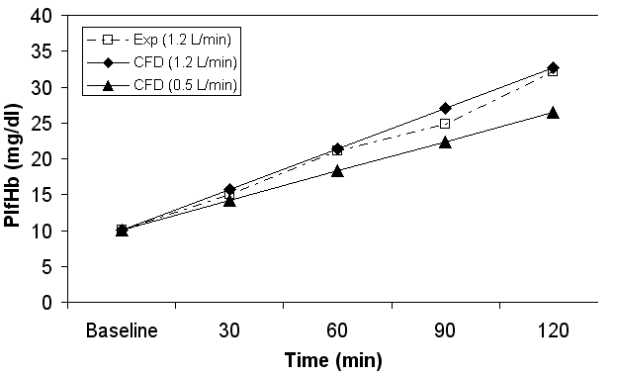


Figure 1: Comparison of numerically predicted plasma free hemoglobin (CFD) with in-vitro experiment (Exp.) (0.43 L,

Results:
Both experimental and numerically predicted CFD plasma free Hemoglobin (plfHb) were found to increase linearly with time over the two-hour duration considered. (See Figure 1.) There was a strong agreement between the CFD prediction and experiments: NIH of 0.0477 vs. 0.0467 respectively. The model was then used to simulate the hemolysis generated by the PF2 at a lower flow rate of 0.5 L/min, resulting in a predicted decrease of plfHb generation by 19%. Subsequent simulation of hemolysis in the PF3 pump resulted in a predicted normalized index of hemolysis (NIH) of 0.07 for a flow rate of 1.2 L/min and 11,000 rpm.

Conclusions:
This study showed that hemolysis estimation with an Eulerian approach yielded comparable results to in-vitro experiments and can be an effective and efficient tool for hemodynamic optimization of the PediaFlow™ VAD.

Aortic valve surgery in congenital heart disease: A single centre experience

Coskun KO, Popov AF, Tirilomis T, Schmitto JD, Ruschewski W
Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany

Background:
The optimal treatment of congenital aortic valve lesions is discussed controversially. This study was performed to evaluate outcome after surgical treatment of aortic valve lesions in congenital aortic valve disease.

Methods:
Between 2000 and 2008 sixty-one patients (mean age 12.5±9.4 years, range 1 day-40 years) underwent aortic valve surgery due to congential heart disease. Previous related procedures included ballon valvuloplasty (n=23) and open commissurotomy (n=10). Furthermore, 39.3% (n=24) had undergone 1-3 previous cardiovascular operations. Indication for surgery were aortic insufficiency in 15% (n=9), aortic stenosis in 24% (n=15), and mixed disease in 61% (n=36).

Results:
The Ross procedure was perfomed in 37.7% (n=23). Aortic valve repair was done in 18% (n=11), commissurotomy in 14.8% (n=9), and aortic valve replacement with biological or mechanical protheses in 29.5% (n=18). Concomitant procedures were performed in 91.8% (n=56) due to associated congenital cardiac defects. The overall hospital mortality rate was 5% (3 of 60). Four patients needed reoperation, and two patients underwent catheter ablation postoperatively. Implantation of permanent pacemaker occurred in six patients for total

AV-block. At the latest clinical evaluation all survivors are in NYHA class I-II and are living normal lives.

Conclusion:
Aortic valve surgery in patients with congenital heart disease has had a low mortality and morbidity in our series. Aortic valve repalcement should be delayed until the implantation of an adult-sized protheses is possible. Ross procedure is an excellent alternative to mechanical valve replacement in cases with suitable aortic and pulmonary valve morphology. Surgical technique as well as timing should be tailored for each patient individually.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

A Hemodynamic Evaluation of the Levitronix PediVAS Centrifugal Pump and Jostra HL-20 Roller Pump under Pulsatile and Non-Pulsatile Perfusion in an Infant CPB Model

Noel Ressler, MPH, Alan R. Rider, Allen R. Kunselman, MA, J. Scott Richardson, Kurt A. Dasse, Ph.D,
Shigang Wang, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, Bioengineering, and Health Evaluation Sciences, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA
Levitronix LLC, Waltham, MA, USA

Purpose:
The objective of this investigation was to test the Levitronix PediVAS pump alongside the Jostra HL-20 roller pump to ascertain and compare their hemodynamic outputs during non-pulsatile and pulsatile perfusion modes in a simulated pediatric cardiopulmonary bypass circuit.

Methods:
The pediatric bypass circuit used in this study is identical to that used in the clinical setting. The system was driven by either the Jostra HL-20 roller pump or the Levitronix PediVAS centrifugal pump. The Levitronix continuous flow pump utilized a customized controller to engage in pulsatile perfusion with equivalent pulse settings to the Jostra HL-20.

The pseudo pediatric patient was perfused with flow rates between 500 and 900 ml/min (100 ml/min increments) under pulsatile and non-pulsatile mode. Hemodynamic measurements and waveforms were recorded at the pre-cannula location, while the mean arterial pressure of the pseudo *patient* was maintained at 40 mmHg for each test. At each flow rate 24 trials were conducted yielding a total of 120 experiments (n=60 pulsatile and n=60 non-pulsatile).

Results:
The following table represents surplus and total hemodynamic energy values of the Jostra HL-20 roller pump and the Levitronix CentriMag centrifugal pump during pulsatile and non-pulsatile perfusion at several different flow rates.

Table 1. Pre-cannula surplus and total hemodynamic energy values for a flow rate of 1000ml/min

Flow & Pump	SHE (ergs/cm^3)		THE (ergs/cm^3)	
(ml/min)	NP	P	NP	P
500-J	†2241 ± 15	*14808 ± 128	†85275 ± 931	*102913 ± 590
500-L	1.2 ± 0.1	*#19912 ± 329	81828 ± 151	*#113031 ± 330
600-J	†2487 ± 37	*15548 ± 683	†94446 ± 232	*113233 ± 1261
600-L	1.0 ± 0.1	*#21139 ± 200	90986 ± 476	*#124240 ± 312
700-J	†2449 ± 42	*16457 ± 545	†105799 ± 783	*126769 ± 1171
700-L	1.0 ± 0.1	*#23119 ± 378	102880 ± 93	*#138705 ± 312
800-J	†2311 ± 23	*16377 ± 56	†117828 ± 264	*138408 ± 468
800-L	0.8 ± 0.1	*#24968 ± 334	114255 ± 93	*#152764 ± 269
900-J	†2182 ± 51	*16037 ± 357	†130184 ± 720	*150933 ± 841
900-L	0.5 ± 0.1	*#26358 ± 252	127306 ± 109	*#166984 ± 251

NP = Non-pulsatile, P = Pulsatile, SHE = Surplus Hemodynamic Energy, THE = Total Hemodynamic Energy
* p< 0.001 Pulsatile vs. Non-Pulsatile † p< 0.001 Jostra Non-Pulsatile vs. Levitronix Non Pulsatile
# p< 0.001 Jostra Pulsatile vs. Levitronix Pulsatile

Conclusions:
The results of this study provide evidence favoring the capabilities of the Levitronix pump under a customized pulsatile setting. During pulsatile CPB, the Levitronix PediVAS produced more surplus hemodynamic energy than the Jostra HL-20 roller pump at each flow rate.

The Aachen MiniHLM – in vitro test results of the new design

Jutta Arens, Dipl.-Ing.[1]‡; Heike Schnoering, MD[2]‡; Michael Pfennig, Dipl.-Ing.[1]; Ilona Mager[1]; Jaime F. Vazquez-Jimenez, MD[2]; Thomas Schmitz-Rode, MD[1]; Ulrich Steinseifer, Dr. Ing.[1]

[1] Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany
[2] Pediatric Cardiac Surgery, Medical Faculty, RWTH Aachen University, Germany
‡ Both Authors contributed equally to the manuscript

Purpose:
In 2008 we introduced a new concept for a miniaturized heart-lung machine (MiniHLM) for neonates with congenital heart defect. The MiniHLM is a highly integrated system with 102 ml priming volume (incl. arterial filter and a/v line) and reduced blood contact surface and thus may diminish known complications related to cardio-pulmonary bypass (e.g. inflammatory reaction and capillary leak syndrome). To validate the over all concept and some further design optimizations we conducted an in vitro test series.

Methods:
According to DIN EN 12022 / ISO 7199 following tests were conducted:

1. Oxygen and carbon dioxide transfer rates
2. Pressure drop on blood and gas side
3. Hemocompatibility (blood cell damage) tests comparing the Aachen MiniHLM to a Medos Hilite® 1000. Increase of plasma-free Hemoglobin and reduction of platelets and white blood cells were determined.
4. Heat exchanger performance tests

For all blood tests heparinized porcine blood was used.

Results:
Oxygen and carbon dioxide transfer rates were sufficient up to the aimed max. flow rate of 700 ml/min.
Max. pressure drop of the oxygenator stayed below 30 mmHg with blood and below 10 mmHg with saline solution.
The comparative hemocompatibility tests revealed no statistical significant differences concerning reduction of platelets between MiniHLM and Hilite® 1000, slightly less reduction of white blood cells in the Hilite® 1000. The increase of of the plasma-free hemoglobin was lower in the MiniHLM over the 6 hour test period.
The heat exchanger performance factor R was

$$R = \frac{T_{Blood,outlet} - T_{Blood,inlet}}{T_{Water,inlet} - T_{Blood,inlet}} = 60\%$$

Figure 1: The Aachen MiniHLM

Conclusions:
The in vitro tests revealed a sufficient performance and hemocompatibility of the MiniHLM. Together with the results of the animal test series and the low priming volume of the system this confirms the concept of the MiniHLM.

Acknowledgment
This project is funded by Fördergemeinschaft Deutsche Kinderherzzentren.

Open Heart Surgery and Cardiopulmonary Support/Bypass in the Premature Infant

V. Mohan Reddy, MD
Falk CV Research Center, Stanford University, Stanford, CA

Aortic Arch Reconstruction Using Cardiopulmonary Bypass and Moderate Hypothermia without Circulatory Arrest

KJ Guleserian, RM Ginther, RM Gorney, SR Leonard, JM Forbess
Children's Medical Center/UT Southwestern Medical Center, Dallas, TX

Background: Aortic arch reconstruction requiring cardiopulmonary bypass is usually performed with circulatory arrest (CA) or selective cerebral perfusion at profound hypothermia (H-SCP). We describe outcomes of patients who underwent aortic arch reconstruction using only moderate hypothermia with selective cerebral perfusion (M-SCP).

Methods: Retrospective review of all patients undergoing aortic arch reconstruction with MSCP (lowest rectal temperature 25°C degrees) from March 2005 to April 2008. All echocardiographic, angiographic, operative and perfusion data were reviewed including near infrared spectroscopy (NIRS) data.

Results: There were 54 patients (19 two-ventricle, 35 single-ventricle) identified. Single-ventricle (1V) diagnoses included: hypoplastic left heart syndrome (HLHS) or variant HLHS (N=24), unbalanced AV canal (N=5), double-inlet left ventricle with arch hypoplasia (N=3), and double-outlet right ventricle with mitral atresia and arch hypoplasia (N=3). Two-ventricle (2V) diagnoses included: coarctation of the aorta (CoA) with VSD (N=11), CoA with arch hypoplasia (N=4), interrupted aortic arch (IAA) (N=3) and recurrent CoA late s/p IAA repair (N=1). Median age at surgery was 5 days (range, 1 day-10yrs) and median weight was 3.2kg (2-32kg). There were 4 operative deaths in the 1V group (11.4%) including one neonate with HLHS/intact atrial septum/cor triatriatum, one with unbalanced AVC/CHARGE syndrome, one 2.1kg neonate with HLHS/mosaic Turner's syndrome, and one 2kg ex 34-week neonate with HLHS/large LV thrombus. There were no operative deaths in the 2V group. There were no instances of multi-organ failure referable to renal, hepatic, gastrointestinal, or spinal cord injury in either group. Delayed sternal closure was performed in all patients in the 1V group and 2/19 (10.5%) of the 2V group. Median intubation time was 4 days (range, 0.5-95 days), median ICU stay was 8 days (range, 1-110 days) and median hospital stay was 20 days (range, 3-177 days) for the entire cohort. Median follow-up was 18.1 months (range, 2 mos-3 yrs) with recurrent arch obstruction occurring in 2 patients (4%), both of whom were in the 1V group.

Conclusions: Aortic arch reconstruction with M-SCP is feasible and safe for both 1V and 2V patients, with a low incidence of recurrent arch obstruction. Avoidance of prolonged cooling and rewarming using this technique may also reduce overall cardiopulmonary bypass support time.

Warm Perfusion in Pediatric Cardiac Surgery: The European Experience with 8.000 cases

Yves Durandy M.D. Department of Intensive Care and Perfusion Institut Hospitalier Jacques Cartier Massy France

One fascinating challenge in cardiopulmonary bypass is to find the best compromise between risk and safety. Pediatric warm surgery was developed with this challenge in mind. The major benefit of hypothermia, a reduction of metabolic rate, is counterbalanced by its own negative effects. So, the rationale for normothermic perfusion is mainly to prevent the systemic adverse effects of hypothermia described in the literature, including:

- a higher incidence of surgical wound infection;
- coagulation disturbances with bleeding diathesis observed even during mild hypothermia;
- increased fluid extravasation; and
- altered oxygen and glucose uptake in the brain and inadequate brain perfusion during or after bypass ("no-reflow" phenomenon)

The rationale for warm blood cardioplegia is that a 90% decrease in myocardial oxygen consumption is due to the electromechanical arrest of the heart; oxygen consumption is only minimally reduced further by deep myocardial hypothermia. However, the safety of warm surgery remains a matter of concern for many pediatric surgeons.

The advantages of warm surgery in adults were demonstrated first in 1989, and later confirmed. We have shifted from pediatric hypothermic perfusion and cold blood cardioplegia to warm perfusion and intermittent warm blood cardioplegia in two stages. The first stage was from 1955 to 2001. During this 6-year period 1.900 patients were operated on with warm perfusion and intermittent cold blood cardioplegia. Since continuous warm blood cardioplegia was unrealistic for many pediatric procedures, we postponed the use of warm cardioplegia until the efficiency and safety of intermittent warm blood cardioplegia was demonstrated in adults. Our second stage in the development of warm perfusion and intermittent warm blood cardioplegia began in 2001. To date, we have experience in this technique with more than 3200 patients.

Following this 2001 trial several French and European pediatric centers adopted normothermia. Overall, approximately 10000 procedures have been performed in 6 pediatric centers.

It is noteworthy that all the different types of cardiac defect were treated using warm perfusion, including interruption of the aortic arch, total pulmonary anomalous venous return and hypoplastic left heart syndrome. There is no longer a need for deep hypothermia and circulatory arrest. We must also emphasize that prolonged cardiopulmonary bypass with a long aortic cross clamp time are safely performed with warm surgery.

The main advantages of normothermia compared to hypothermia are:

- shorter procedure;
- spontaneous defibrillation after aortic unclamping;
- lower levels of post-operative Troponin I;
- a more stable hemodynamic allowing a short time to extubation; and
- decreased length of stay in intensive care.

We did not experience any deleterious effects of normothermic perfusion on the brain or the kidney.
Normothermia is a more physioplogical approach to pediatric surgery than hypothermia. The large European trial proves that it is an efficient, safe and reproducible technique.
A demonstration of its superiority over hypothermia awaits randomized trials.

Myocardial Protection in Congenital Heart Surgery

Joanne P. Starr MD
Newark, New Jersey

Since the advent of cardiopulmonary bypass surgery, the ability to adequately protect the myocardium against injury has been a constant challenge. Several different methods and strategies for myocardial protection have been employed over the past 50 years. Traditionally, methods of myocardial protection in congenital heart surgery have been modeled from adult cardiac surgery. However, there are significant differences between adult and pediatric hearts (mature vs. immature) in terms of structure, function, and metabolism. Additionally, most pediatric repairs are intracardiac requiring long aortic cross clamp times and/or hypothermic circulatory arrest. During this time the myocardium is especially vulnerable to ischemia and subsequent reperfusion injury. In addition, those patients who require staged procedures (i.e. single ventricles) are repeatedly exposed to risk of ischemia.

There have been several advances in techniques for repair of congenital heart defects and in the postoperative management of these patients. However, perioperative myocardial damage with its resultant postoperative low cardiac output still accounts for significant morbidity and mortality following technically successful repairs. The full impact of poor myocardial protection with its resultant myocardial dysfunction may not become evident until months or even years later. Therefore, optimization of myocardial protection is as important as the performance of the surgical repair itself.

Myocardial protection strategies begin as early as the preoperative phase with the use of inotropes, afterload reduction and mechanical ventilation with sedation +/- muscle relaxant thus decreasing myocardial workload and stress. During the perioperative phase the strategies for myocardial protection described are numerous and can be broken down into cardioplegic and non-cardioplegic. Cardioplegic strategies include cardioplegia content, blood vs. crystalloid cardioplegia, cardioplegia delivery and temperature selection. Non-cardioplegic strategies include ischemic preconditioning, non circulatory arrest (standard aortic cross clamp), circulatory arrest, beating heart and ultra filtration during and post bypass. In addition, the use of steroids, complement C4a, heparin coated circuits etc. to mitigate against the generalized inflammatory response may also have a protective effect on myocardial function.

This talk will review current methods and new research in myocardial protection for congenital heart surgery.

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Pulsatile vs. Non-Pulsatile Perfusion in Neonates and Infants

Atif Akcevin, MD, Tijen Alkan-Bozkaya, MD, Akif Ündar, PhD
V.K.V. American Hospital, Dept. of Cardiovascular Surgery, Istanbul, TURKEY and *Penn State Hershey Children's Hospital, Penn State Hershey College of Medicine, Hershey, PA, USA

Purpose:
We have already completed several preliminary studies regarding the effects of perfusion modes on the recovery of vital organs and the outcomes of pediatric cardiac patients (1-3). The objective of this study is to investigate the impact of pulsatility during CPB procedure in neonates and infants.

Methods:
136 consecutive pediatric patients undergoing open heart surgery for repair of congenital heart disease were prospectively entered into the study and were assigned to either the pulsatile perfusion group (Group P, n = 89) or the nonpulsatile perfusion group (Group NP, n = 47). Identical components of the extracorporeal circuit (membrane oxygenator, arterial filters, and cannulae) were used. The same heart-lung machine (Stockert S3) was used for both pulsatile and non-pulsatile studies. Pulsatile flow is used only during X-Clamp duration.

Results:
There were no statistically significant differences seen in either preoperative or operative parameters between the two groups (age, BSA, weight, X-Clamp and CPB time, base flow, flow rates and hemofiltration).
The Group P, compared to Group NP, had significantly less inotropic support [number of agents 1.57±0.78 vs 2.38±0.84, p = 0.0012; dopamine 7.6±2.16 vs 8.04±3.07 µg/kg/min, p = 0.025; dobutamine 1.31±0.3 vs 1.45±0.4 µg/kg/min, p = 0.041), adrenalin 0.024±0.02 vs 0.041±0.02 µg/kg/min, p = 0.021], less intubation period (10.69±3.04 vs 16.69±4.99 hours, p = 0.032), less duration of ICU (1.67±0.88 vs 4.75±1.93 days, p = 0.015) and hospital stay (6.93±0.14 vs 9.25±2.32 days, p = 0.0028).

Lower lactate levels (14.94±9.11 vs 16.34±13.08 mg/dL, p = 0.03), higher albumine levels (3.31±0.3 vs 3.12±0.3 µg/kg/min, p = 0.047) and higher urine output (576.12 ± 25.4 vs 407.76 ± 25.2 ml/day, p = 0.012) during ICU period were observed in the pulsatile group.

Conclusions:

Based on our results, pulsatile flow significantly improved vital organ recovery and the outcomes of neonates and infants. Currently, we routinely use pulsatile flow in every pediatric case at our hospital.

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Intra Operative Neurologic Monitoring During CPB Procedures

STEPHEN J. KIMATIAN,† KENNETH J. SALIBA,* MOLLIE L. BARNES,‡§ J. BRIAN CLARK,¶ AND JOHN L. MYERS¶ From the Department of †Pediatric Anesthesiology, Cleveland Clinic Foundation, Cleveland, Ohio, the Department of *Anesthesiology and ‡Neuromonitoring, Penn State College of Medicine, Hershey, Pennsylvania;§Impulse Monitoring, Inc., Columbia, Maryland; and the ¶Department of Surgery, Penn State College of Medicine, Hershey, Pennsylvania.

Purpose:
Multi modal neurologic monitoring for pediatric patients undergoing surgery requiring the use of cardiopulmonary bypass (CPB) was first described by Austin et al. (Austin et al, Journal of Thoracic and Cardiovascular Surgery, Vol 114, No 5, 1997, pp707-715) . While initially used almost exclusively for research, continued experience with intra operative neurologic monitoring (INM) for this patient population has suggested a number of compelling arguments for considering the application of INM as part of a standard of care. This session will discuss one institutions experience with the application of INM for pediatric patients requiring CPB.

Background:
During the period of 2002 to 2004, (INM) was integrated into the standard management of pediatric cardiac patients requiring CPB at the Penn State Hershey Children's Hospital. INM was modeled on the process described by Austin et al (Austin 1997) and consisted of Near Infrared Spectroscopy (NIRS), Trans Cranial Doppler (TCD), and eight channel electroencephalography (EEG). The monitoring procedures were modified to include Somatosensory Evoked Potentials (SSEPs) for patients of appropriate age and size. During this time there were no other significant changes made to either the standard management of patients or the members of the surgical team (surgery, anesthesiology, nursing, or perfusion).

Results:
Initially the implementation of INM was part of a research protocol examining the effectiveness of pulsatile vs. non pulsatile perfusion. Subsequent retrospective chart review on blood utilization and patient hematocrit while on CPB showed significant changes that could not be readily be explained by influences other than that of having the addition of the immediate feedback from the INM. This was demonstrated by an increased use of donor blood in the CPB circuit prime and the maintenance of a higher hematocrit during the bypass period (Kimatian et al., ASAIO Journal. 54(5):467-469, September/October 2008), as well as a number of significant anecdotal findings that have convinced the team of the value of this mode of monitoring in optimizing patient outcomes.

Anecdotal case findings have included: retrograde middle cerebral artery flow in a patient status post modified Blalock-Taussig shunt that resolved after conversion to a right ventricular to pulmonary artery conduit (Sano) (Kimatian, et al, ASAIO Journal. 52(5):608-610, September/October 2006); seizure activity that would have gone unrecognized except for the presence of changes on EEG and NIRS; changes in anesthetic depth and increased risk of awareness as indicated by shifts in EEG frequency; and changes in sensory evoked potentials suggestive of potential neurologic injury at the spinal cord level or distal that resolved with changes in CPB management.

Discussion:
The addition of INM was associated with a significant change in the management of pediatric patients on CPB. These were both quantifiable, as seen with the analysis of blood utilization, and anecdotal, as seen with several cases of inter operative interventions stimulated by the INM data. However, given this operative team's already low incidence of significant neurologic injury in the peri operative period, it is difficult to quantify the overall benefit on outcomes. The fact that the interventions stimulated by the availability of INM data are consistent with those supported by studies examining post operative outcomes and function (Wypij et al, The Journal of Thoracic and Cardiovascular Surgery, Volume 135, Number 2 2008, pp 355 - 360) suggests that these interventions are appropriate. Rather than using protocols for neurologic protection that do not necessarily address the individual pathophyisiology of a specific patient, the use of INM data has provided real time feedback to the operative team with results that correlate with those of retrospective studies while at the same time allowing for individual patient variability.

Valve Surgery in Congenital Heart Disease

Giovanni Battista Luciani, MD, Pediatric Cardiac Surgery, University of Verona, Italy

Congenital valve disease (CVD) occurs as part of complex malformations, as well as in isolated form. Whereas CVD may affect children and adults, average age at operation is significantly younger than acquired valve disease and peaks in the 4th-5th decades of life. Semilunar valve disease, primarily aortic in isolated CVD and pulmonary in complex malformations, represents 80-90% of all CVD interventions. In addition, due to the presence of associated pathology, by definition in complex congenital malformations, but also highly prevalent in isolated forms of CVD, including aortic root or ascending aortic lesions (55-70%), acquired coronary heart disease (10-15%) and other miscellaneous conditions (5-10%), management of CVD is often palliative in that it portends multiple interventions during one's lifetime. Furthermore, given the onset during childhood or early adulthood, surgery for CVD introduces the concept of sustainable treatment in terms of quality of life. Indeed, both expected survival at the time of initial operation, which commonly exceeds 20 years, and need to accommodate for growth, exercise, education, employment, socialization and pregnancy directly influence surgical strategies in a way distinctly different from acquired valve disease. Therefore, valve repair is imperative in CVD and successful to a variable extent, ranging from 10-20% of overall cases, depending on the valve involved (semilunar versus atrioventricular) and the severity of valve pathology. Durability of repair is often the issue and highlights the palliative character of congenital valve surgery. A solid alternative in case of failure of repair or primarily irreparable lesions is stentless valve surgery (autograft, homograft, xenograft), almost exclusively confined to semilunar valve pathology. Stentless valve surgery may serve as many as 30-40% of patients with CVD and, similar to repair, it guarantees normal quality of life but at the same time introduces the need for reintervention (operative, transcatheter). Bioprosthetic valve replacement has the ability to serve both semilunar and atrioventricular irreparable CVD: compared with stentless solutions, it allows slightly worse quality of life (exercise, preganancy), and does not protect against risk of reoperation. Finally, mechanical valve replacement constitutes the more traditional and widely adopted strategy for irreparable valve disease in the young. Far from a definitive solution of CVD (endocarditis, pannus, perivalvar leak), in theory it does not imply secondary or multiple surgical interventions. In spite of considerable progress in terms of management of chronic anticoagulation, however, it is associated with the worse quality of life and the highest prevalence of thromboembolic and hemorrhagic complications. The latter represent perhaps the most invalidating and dreaded morbid events in a young, socially active patient population. In addition, mechanical valve replacement excludes secondary trans-catheter interventions, which are increasingly applied to patients with CVD. Operative risk of CVD surgery, both in terms of mortality and morbidity, is lower than the one for acquired, in spite of higher prevalence of associated procedures, reoperation and emergent indication, possibly due to younger age. possibly due to younger age at surgery. Mortality is primarily associated with urgent/emergent presentation (endocarditis, dissection) and preoperative ventricular dysfunction. Most common late untoward events are reintervention, surgical or percutanoeus, in patients having repair or stentless valve replacement and prosthetic-valve related complications (thrombosis, embolism, hemorrhage, endocarditis) in those having mechanical devices.

The mainstay of surgical strategy for CVD is, often palliative, repair. For irreparable valve lesions stentless valves are increasingly employed, as normal quality of life is traded for lower freedom from multiple interventions (operative, transcatheter).

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

A Dual-platform Proteomics Study of Plasma Biomarkers in Pediatric Patients Undergoing Cardiopulmonary Bypass

Todd M. Umstead BS[1], Chia-jung K. Lu BA[1], Willard M. Freeman PhD[2], John L. Myers MD[3], J. Brian Clark MD[3], Neal J. Thomas MD[1], Vernon M. Chinchilli PhD[4], Kent E. Vrana PhD[2], Akif Ündar PhD[1,3,5] and David S. Phelps PhD[1]
Penn State Center for Host defense, Inflammation, and Lung Disease (CHILD) Research and the Department of Pediatrics[1], and the Departments of Pharmacology[2], Surgery[3], Public Health Sciences[4] and Bioengineering[5], Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Systemic inflammatory response syndrome (SIRS) is a major problem in pediatric patients undergoing cardiopulmonary bypass (CPB) and can lead to multiple organ dysfunction syndrome. The current study employed a dual-platform proteomics approach which used two-dimensional difference gel electrophoresis (2D-DIGE) coupled with matrix-assisted laser desorption ionization time of flight tandem mass spectrometry (MALDI-ToF) and a multi-analyte profile (MAP) immunoassay to identify and quantify a total of more than 100 potential clinical biomarkers, including many known to be related to SIRS, in the plasma of pediatric CPB patients. Identifying these biomarkers and characterizing the changes they undergo in patients after CPB may aid in the identification of at-risk patients. This approach may also identify proteins that are associated with other pathways or processes that may be adversely affected by CPB.

Methods:
Blood samples from 10 patients were collected immediately before CPB and 24 hours after weaning from CPB. Plasma was isolated and an aliquot used for MAP multiplexed immunoassays. A second aliquot of plasma was depleted of the 14 most abundant plasma proteins (which account for 96% of the protein content of normal plasma) to allow for the detection of proteins of lesser abundance in the remaining 4% prior to analysis using 2D-DIGE and MALDI-ToF mass spectrometry.

Results:
A total of 556 spots were visualized in gels from all samples by 2D-DIGE. MALDI-ToF was used to identify 269 of these spots constituting isoforms of 44 distinct proteins and accounting for 88% of the protein resolved by the gel system. An additional 90 proteins were identified by MAP analysis, bringing the final protein total to 129, including 5 proteins that were detected by both platforms. Of the 129 identified proteins, 71 underwent significant changes in expression after CPB ($p<0.05$-compensating for multiple comparisons) with 34 increases and 37 decreases. Many of the proteins with significant changes were categorized using the PANTHER gene ontology database as being involved in immunity/defense, protein metabolism and modification, and as signaling molecules. Further analysis of the protein changes using Ingenuity Pathways Analysis software found many of these proteins to be associated with the "acute phase response signaling" pathway, such as C-reactive protein, ferritin, interleukin (IL)-6, lipopolysaccharide binding protein (LBP), serum amyloid P component, and von Willebrand factor (vWF), all of which were increased by more than 2-fold 24 hours after CPB.

Conclusions:
These results demonstrate the usefulness of this two-pronged proteomics approach in characterizing changes in circulating plasma proteins in children undergoing CPB. Some of these changes may have been anticipated based on the previous reporting of inflammation or SIRS following CPB, however the approach used in this study documented simultaneously the changes in many of the involved proteins.

Recent Advances of Brain Protection During Cardiac Surgery – From Deep Hypothermia And Circulatory Arrest to Cerebral Perfusion

Shunji Sano,MD
Department of Cardiovascular Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Deep hypothermia and circulatory arrest(DHCA) had been developed in Japan in 1960's and Kyoto technique was introduced to Green Lane Hospital in New Zealand. In 1970, Barrett-Boyes et al. published a paper of primary repair in neonates and infants using this technique. Since then, DHCA has been used as a golden standard in most of the cardiac surgery in neonates and small infants. The advantages of DHCA are enabling to perform a meticulous cardiac surgery in neonates and small infants under bloodless field and minimize the cardiopulmonary bypass time. On the other hand, most important disadvantage of DHCA is a limited circulatory arrest time. It is widely recognized that safe circulatory arrest time is less than 40-45 minutes, especially to the brain. In 1990's many paper were published neurodevelopmental damages in children who were used DHCA even less than 40 minutes.

Because of these, antegrade cerebral perfusion techniques were developed in Japan to the patients with arch reconstruction both in children and adults. Fukuoka Children's group has been used this technique since early 1990's and Asou et al first published cerebral perfusion to avoid DHCA in 1996. We started use this technique since 1995 to the patients mostly with CoA/IAA complex and HLHS. Our technique was to insert an arterial cannula into ascending aorta directly to most of the CoA/IAA complex and into the PTFE tube which is anastomosed to the innominate artery. Isolated cerebral and myocardial perfusion are established by clamping the aortic arch between the innominate artery and left carotid artery. By using this technique, we could minimize myocardial ischemic time. In early 2000's, we have developed lower body perfusion through duct to minimize lower body low flow time. Recently,Fukuoka children group also has developed whole body perfusion technique and we have developed non-working heart technique.

One of the most important projects of cardiac surgery in 21 century is brain protection. We still do not know optimal flow, pressure and temperature in this new technique, therefore further study and development are mandatory.

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Determinants of Neurodevelopmental Outcome for Children with Congenital Heart Defects

J. William Gaynor, MD
Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

There has been increasing recognition of adverse neurodevelopmental outcomes in some survivors of neonatal and infant cardiac surgery. Studies at our institution have shown that patient-specific factors such as birth weight, ethnicity, and the presence of a genetic syndrome are important determinants of neurodevelopmental outcome after neonatal and infant cardiac surgery. These patient-specific factors explain considerably more of the variability in outcomes at 1 year of age than do intraoperative management strategies, such as the use and duration of DHCA and hematocrit during CPB. In particular, neither the use nor the duration of DHCA was associated with a worse outcome at 1 year of age.

Many studies of neurodevelopmental outcome after cardiac surgery have focused on intraoperative management strategies. This focus is understandable inasmuch as these strategies can be modified and thus there is an opportunity to potentially improve outcomes. On the basis of these studies, many surgeons have modified their intraoperative support techniques. However, review of these studies suggests that the benefit of changing intraoperative support techniques may be less than hoped. Indeed, the findings of previous studies, as well as the current study, are consistent with the hypothesis that factors (recognized and unrecognized) other than intraoperative management strategies are more important determinants of outcome and explain more of the variability in outcomes. The neurologic status of children with CHD is often abnormal at birth, before surgical intervention. There is increasing evidence that in utero central nervous system development is often abnormal in children with CHD. Microcephaly and congenital central nervous system malformations are common. Recent studies from our institution have demonstrated that cerebral blood flow is very low in some neonates with uncorrected CHD, often with evidence of cerebral ischemia and preoperative white matter injury characterized by periventricular leukomalacia. Newborn infants with CHD are also exposed to the potential risks of hypoxia, acidosis, and hypotension. Low birth weight is an important predictor of worse outcome. Many factors may contribute to low birth weight, including prematurity, associated genetic syndromes, placental insufficiency, and intrauterine growth restriction, all of which may increase the risk of neurodevelopmental delay.

In addition, genetic factors are a major determinant of neurologic outcome in children with CHD. Many defects are part of well-described syndromes with associated developmental dysfunction, independent of the cardiac defect or cardiac surgery. APOE is an important regulator of cholesterol metabolism. APOE-containing lipoproteins are the primary lipid transport vehicles in the central nervous system. There is increasing evidence that APOE is important for neuronal repair. There are three common isoforms of APOE (E2, E3, and E4), which are encoded by three alleles (ε2, ε3, and ε4, respectively) and vary by single amino acid substitutions. A strong association has been validated between the *APOE* ε4 allele and Alzheimer disease. *APOE* genotype has been shown to have an important role as a determinant of neurologic recovery after central nervous system ischemia, intracerebral hemorrhage, and traumatic brain injury. There is evidence of an association of *APOE* genotype with neurocognitive decline after cardiac surgery in adults and children. The finding that the *APOE* ε2 allele is associated with a worse outcome is consistent with the hypothesis that genetic variants that do not cause CHD may alter the response to environmental factors and thus increase susceptibility to neurologic injury.

We evaluated neurodevelopmental outcomes at 1-year of age in a large, heterogeneous cohort of patients undergoing repair of 2-ventricle CHD, patient-specific factors are important determinants of neurodevelopmental outcomes at 1-year of age and contribute more substantially to the risk of adverse neurodevelopmental outcomes than do intraoperative management strategies. Consistent with previous studies, intraoperative management strategies explain only a small portion of the variability in outcomes. Previously described risk factors (both patient-specific and intraoperative variables) explain only part (<30%) of the variability in neurodevelopmental outcomes, suggesting that unrecognized factors are important determinants of outcome.

Genetic factors are a major determinant of neurologic outcome in children with CHD. Future studies of neurologic outcome and neuroprotective strategies must include risk-stratification for genetic and other patient factors that may alter the risk of central nervous system injury and adverse neurologic outcomes. These factors may be more important determinants of outcome than are intraoperative management strategies. To improve neurodevelopmental outcomes for children with CHD, we must identify and understand the biologic pathways underlying interindividual variation in outcomes and develop individualized, targeted therapeutic strategies.

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An Update on Tissue Engineering in Heart Valves

Sabine Daebritz, MD
Cardiac Centre of Duisburg is part of the Evangelisches und Johanniter Klinikum Niederrhein gGmbH, Germany

Tissue engineering is the generation of functional living tissue of cells – either autologous, allogenic or xenogenic.
Clinical applications are in plastic surgery (skin), general surgery (liver), endocrinology (pancreas), urology (bladder), orthopaedics (bone, cartilage, ligaments) and cardiovascular surgery (patches, conduits and heart valves).

The general principle in tissue engineering of heart valves consist of

1. harvesting cells (`mature´ fibroblasts or endothelial cells from vascular structures or omnipotential cells as progenitor cells from immature sources (umbilical cord, chorionic villi)
2. Culturing the cell suspension
3. Seeding the cells on scaffolds, which can be resorbable or non-resorbable of various materials
4. Conditioning the constructs in a `bio-reactor´ under different pressure conditions
5. Implantation into the same individual

Various concepts have so far been applied (s. table 1). Shinoka et al. were the first to perform a valve leaflet replacement study in a lamb model in 1995. Sodian et al. were successful in tissue-engineering a tri-leaflet heart valve in 2000. Hoerstrup et al. generated a tri-leaflet heart valve from human marrow stromal cells and autologous pulmonary artery conduits from human umbilical cord cells in 2000 and 2002, respectively. Schmidt et al. reported the use of umbilical cord blood derived progenitor cells for tissue engineering of vascular grafts. Sodian et al. generated heart valves using cryopreserved vascular umbilical cord cells in 2006.

There has been human implantation of tissue engineered valves, but not all were successful. Simon published early failure of tissue engineered porcine heart valves in 2003. On the other hand, Cebotari et al. implanted decellularised homografts seeded with autologous progenitor cells in children in pulmonary position and recognized an increase in diameter and thus potential growth. Dohmen et al. implanted decellularised homo- or xenografts seeded with autologous endothelial cells in the pulmonary position in adults.

The role of biomaterials is to generate functional tissue by being interactive, integrative, degradable (if desired) and to stimulate specific cell response on the molecular level (extracellular matrix formation). Degradation is mainly desired for the potential of growth in the context of congenital heart disease. One example of a biodegradable matrix is poly-4-hydroxybutyrat = P4HB, which has a porosity of 80% and a pore size of 200-400µm. In heart valve tissue engineering, the design of the valves is of major importance. Recently, rapid prototyping techniques have been applied for fabrication of heart valve scaffolds with physiologic sinus of Valsalva (Sodian et al 2009). Bioreactor conditioning has been widely applied for increasing the durability of the seeded constructs. According to recent investigations (Sodian 2006), cryopreserved and recultivated cells keep the characteristics of living cells shown by staining, electron microscopy, analysis of extracellular matrix, increase of intracellular Ca++ concentration after histamine stimulation and by biomechanical testing (Instron). Storage is in liquid nitrogen in 10%DMSO in `cryotubes´ in a computerized process of freezing. This concept has the ultimate goal of using umbilical cell sources for heart valve `replacement´ in patients who have prenatal diagnosis of heart disease.

Tissue engineering products are designed as pharmaceutics. Thus, the requirements of potential human application include a manufacturing permit and GMP (Good Manufacturing Practice) accreditation.

Reference	Cell source	Scaffold material	Conditioning	Constructs
Shinoka 1995	Vascular	Polymer(PGA)	No	Leaflet in post position of PV
Steinhoff 2000	Vascular	Decell. Matrix	No	`valved conduit´ in pulm. position
Sodian 2000	Vascular	Polymer (PHA)	No	`valved conduit´in pulm. position
Hoerstrup 2000	Vascular	Polymer (PGA/P4HB)	Bio-reactor	`valved conduit´in pulm. position
Jockenho-vel 2001	Vascular	Autol. fibrin	No	In-vitro
Shinoka 2001	Vascular	Polymer	No	Conduit in pulmonary position
Hoerstrup 2002	Bone marrow	Polymer (PGA/P4HB)	Bio-reactor	In-vitro
Sodian 2006	Cryo. vasc. umb. cord. Cells	Polymer (P4HB)	Bio-reactor	In-vitro
Cebotari 2006	Autol. proge-nitor cells	Decell. homo-Grafts	Bio-reactor	In-vivo (human) in pulmonary position
Schmidt 2007	Amnion fluid progenitors cells	Polymer	Bio-reactor	In-vitro
Dohmen 2007	Vascular (vein)	Decell. homo- or xenografts	Bio-reactor	In-vivo (human)
Ouyang 2008	Bone marrow	Decell. xeno-grafts	No	In-vivo monocusp in abdom. aorta

PENN STATE HERSHEY - INTERNATIONAL CENTER FOR PEDIATRIC CARDIOVASCULAR RESEARCH

Akif Ündar, PhD, Linda Pauliks, MD, J. Brian Clark, MD, Jeffrey Zahn, PhD[1], Allen R. Kunselman, MA, Qi Sun, MD, PhD, Kerem Pekkan, PhD[2], Kenneth Saliba, DO, Elizabeth Carney, DVM, Gerson Rosenberg, PhD, Neal Thomas, MD, MSc, Willard Freeman, PhD, Kent Vrana, PhD, Aly El-Banayosy, MD, Serdar H. Ural, MD, Ronald Wilson, VMD, MS, Todd M. Umstead, BS, Joanna Floros, PhD, David S. Phelps, PhD, William Weiss, PhD, Alan Sung Yang, PhD[3], Stephen Kimatian, MD, Stephen E. Cyran, MD, Vernon M. Chinchilli, PhD, Tijen Alkan, MD[4], Atif Akcevin, MD[4], Kyung Sun, MD, PhD, MBA[5], Shigang Wang, MD[6], Long Cun, MD[6], John L. Myers, MD

Pediatric Cardiac Research Laboratories, Departments of Pediatrics, Surgery, Bioengineering, Health and Evaluation Sciences, Pharmacology, Comparative Medicine, Obstetrics & Gynecology, and Anesthesiology, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA;
[1]Dept. of Bioengineering, Rutgers, The State University of New Jersey, Piscataway, NJ, USA;
[2]Dept.of Bioengineering, Carnegie Mellon University, Pittsburgh, Pennsylvania, USA;
[3]School of Information and Mechatronics, School of Medical System Engineering, Gwangju Institute of Science and Technology, Gwangju, South Korea
[4] Dept. of Cardiovascular Surgery, American Hospital, Istanbul, Turkey;
[5] Dept. of Surgery, Korea University, Seoul, South Korea;
[6]Dept. of Cardiopulmonary Bypass, The Fuwai Hospital, Beijing, China

Over the past five years at Penn State Hershey we have established a multi-disciplinary research team with the goal to improve the outcomes for children undergoing cardiac surgery with cardiopulmonary bypass.

The Penn State Hershey - International Center for Pediatric Cardiovascular Research has been established with the collaboration of teams from multiple academic departments and representing multiple disciplines. This center will combine basic science, engineering, and clinical applications under the unified mission of pediatric cardiovascular research. Scientists and clinicians in the center will represent the departments of Pediatrics, Surgery, Bioengineering, Anesthesiology, Comparative Medicine, Public Health Sciences, Pharmacology, and Obstetrics & Gynecology.

Our major objective is the development of novel technologies and methodologies to be used in minimizing the adverse effects of cardiovascular operations and cardiopulmonary bypass in neonates, infants, and children. Particular attention will be focused on the morbidities of cerebral, myocardial, pulmonary, and renal injury.

The rich history of research and development in mechanical circulatory support at Penn State Hershey should facilitate the recognition of this Center as an ideal proving ground for new devices in the field of pediatric cardiopulmonary bypass and mechanical circulatory support. In this environment, translational research can be conducted with absolute scientific objectivity and freedom from commercial bias.

Within the past five years, our pediatric cardiac research group has generated over 271 publications (98 articles and 173 abstracts), over 124 national and international presentations and invited lectures, as well as over $7.5 million in grants. Additionally, we have trained dozens of medical students, post-doctoral fellows, and undergraduate and graduate biomedical engineering students.

The Penn State Hershey Department of Pediatrics contributed over $600,000 in funds to support the creation of the new pediatric cardiac research laboratory. Many research components in the lab (e.g., heart-lung machines, heater and cooler units, advanced ultrasound devices) are identical to the clinical instruments used in our pediatric cardiac

operating room. In addition, we are testing several new European pumps and oxygenators for future clinical studies in pediatric patients in the US.

Since its creation in 2005, this *International Conference* has made significant contributions to the fields of pediatric mechanical circulatory support and pediatric cardiopulmonary perfusion. As a result of this conference, over 200 peer-reviewed articles have been published in the American Society for Artificial Internal Organs (ASAIO) Journal. Penn State Hershey provided financial support for the first two conferences in 2005 and 2006. Several conferences have now received NHLBI and NIH-ORD funding through R13 grant applications. Our new R13 NHLBI proposal for the next five years has received a promising score. In addition, we have received important financial support for the conference from private industry sources. With the creation of the ***Penn State Hershey - International Center for Pediatric Cardiovascular Research,*** we strive to become a leading center for the innovation and development of novel devices and treatments for congenital heart surgery. We also seek to educate more bioengineers, medical students, residents, post-doctoral fellows, and junior faculty members in pediatric cardiovascular research. Finally, we seek to continue the growth of this special conference, in order to provide a scientific venue for the pioneering research being performed in pediatric mechanical circulatory support and cardiopulmonary perfusion.

Our laboratories page, http://www.pennstatehershey.org/web/childrenshearteartgroup/research/overview, includes all of our current projects (clinical, basic science, and bioengineering) publications, presentations, as well as national and international collaborators within our center. Investigators interested in collaborating with us with on current or new projects should send an e-mail to aundar@psu.edu.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Miniaturization of ECMO Systems: Engineering challenges and Methods

Ulrich Steinseifer, Dr.-Ing.[1]; Ali Kashefi, Dr.-Ing.[1]; Marcus Hormes, Dipl.-Ing.[1]; Mark Schoberer, MD[2]; Thorsten Orlikowsky, MD[2], Mehdi Behbahani, Dipl.-Ing.[3]; Marek Behr, Ph.D.[3] and Thomas Schmitz-Rode, MD[1]

[1] Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany
[2] Paediatric and Adolescent Medicine, RWTH Aachen University, Germany
[3] Computational Analyses of Technical Systems, RWTH Aachen University, Germany

Purpose:
Miniaturization of organ support systems is a major trend that opens new options, particularly for paediatric therapies.
For extracorporeal lung assist, system miniaturization is mainly achieved by integration of system components such as pump, oxygenator and heat exchanger, by optimization of gas exchange efficiency, and by optimized blood flow in the system and its components.
In this study, we present the engineering methodology for ECMO system miniaturization on hand of a highly integrated ECMO system for treatment of respiratory failure in premature infants with extremely low birth weights (<800g).

Methods:
As a central component we developed a hollow fibre oxygenator with integrated silicone tubes (Fig 1.). Their dilatation and collapse under cyclic pressurizing generates a pulsatile blood flow within the oxygenator compartment and thus the entire circuit. Simultaneous control of the blood temperature may be achieved by tempering of the pressurizing medium.
Besides serving for blood transport, the pulsatile flow improves the gas exchange efficiency by reducing the plasma barrier as the main resistance for the gas transport to and from the red blood cells.
In addition, we developed a numerical model for the CFD simulation of gas exchange in hollow fibre modules and its optimization through optimum fibre arrangement. The numerical model is experimentally validated by in vitro oxygenation of porcine blood in a proprietary mini-oxygenator module (MicroMOx) with a reproducibly definable fibre arrangement.
The blood flow in the system and its components is mainly depending on the component design. In particular, the oxygenator inflow is critical for an optimum washout of the device and an even distribution of blood flow around all fibres. Thus, we currently apply a PDE-constraint numerical method for shape optimization of the oxygenator inflow and experimentally validate it by means of Particle Image Velocimetry (PIV).

Results:
In a first iteration we developed a prototype module of a ECMO system with total priming volume of 22 ml and a hollow fibre membrane surface of 0,15 m^2 for a gas exchange rate (O_2) of 6,1 ml/min at 100 ml/h blood flow, a Hb of 12g/dl and an initial saturation of 65%.

Conclusions: The systematic application of engineering tools and methods leads to significant system miniaturization and thus opens new options for paediatric therapies.

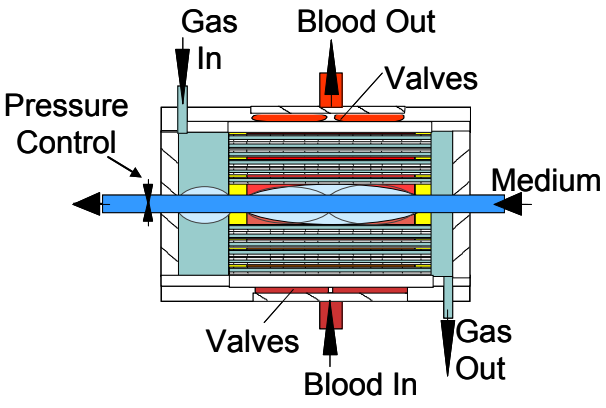


Fig. 1: Pulsatile Pump Oxygenator (schematic)

Pediatric Assist Device Development in Brazil

Cestari, IA*, Hayashida SA*, Ferrara E**, Bacht S*, Muramatsu M**, Christensen KT***, Leirner AA*
*Bioengineering Division, Heart Institute, Medical School, University of Sao Paulo, Brazil
** Institute of Physics, University of Sao Paulo, Brazil
*** Department of Theoretical and Applied Mechanics, Univ. of Illinois, Champaign-Urbana, USA

Purpose:
We present the development of a paracorporeal pediatric VAD. The pump is pneumatic with free-floating membrane and fabricated in 30 ml and 15 ml sizes. It is made of two rigid PU chambers divided by a flexible PU diaphragm defining the blood and pneumatic chambers. Two tri-leaflet bovine pericardium valves are used in the inflow and outflow ports. All the polymer blood-contacting surfaces are heparin coated. The driving console operates in ECG synchronized, asynchronous or full-to-empty modes. Maximum positive driving pressure is 250 mm Hg and suction can be applied to -50 mm Hg

Methods:
Except for item a all data relates to the 15 ml model.
a) Dynamic performance was evaluated using a mock circulatory loop in full-to-empty mode at 100 mmHg afterloads on both 15ml and 30 ml versions.
b) Particle image velocimetry was employed to study the flow within the device. The fluid was seeded with 10 μm particles and fields parallel to the membrane and perpendicular to the inflow tract were illuminated with laser sheets by means of a pair of pulsed Nd:YAG lasers. The images were acquired with a CCD camera and provided data for determination of flow velocity, kinetic energy and Reynold stress distributions.
c) *In vitro* hemolysis test was performed using fresh bovine blood at 37^{O}C, Ht > 40%
d) *In vivo* testing used anesthetized "Large White" pigs, (n=14; 10-12 Kg weight) which were studied acutely for 120 min after cannulation. LV assist was applied from apex to innominate artery and RV assist from right atrium to pulmonary artery. Biventricular assistance was applied in 7 animals (G_{VAD}) and the hemodynamic parameters were compared to those of 7 animals with cannulation alone with no assistance applied ($G_{Control}$). Cardiac rate, mean arterial pressure (MAP), mean pulmonary artery pressure, left atrium pressure, and thoracic aortic flow were recorded continuously. Cardiac output was measured with a Swan-Ganz catheter .The Cardiac Index (CI), systemic vascular resistance and pulmonary vascular resistance indexes were determined.

Results:
a) The dynamic performance measured is shown in Table 1

Table 1

Preload (mm Hg)	Suction (mm Hg)	$Flow_{30}$ (ml/min)	$Flow_{15}$ (ml/min)
0	0	1800	885
0	-25	3450	1200
18	0	3090	1166
18	-25	3880	1296

b) Velocity, kinetic energy and Reynold stress data were obtained and used to correct the device's contours.
c) Normalized index of hemolysis (NIH) found was 0.074 gr/100 L
d) All animals in $G_{Control}$ died within 60 minutes from cannulation while all animals in G_{VAD} survived for 120 minutes. Immediately after sternotomy and cannulation the CI decreased 23,3% in $G_{Control}$ and 17,3 % in $G_{VAD.}$ The CI and MAP in $G_{Control}$ progressively decreased until the animal died. In G_{VAD} with biventricular assistance the CI stayed between 3,1 $l.min^{-1}.m^{-2}$ and 4,1 $l.min^{-1}.m^{-2}$ during the 120 min duration of the experiment.

Conclusion:
Results obtained until now indicates the possibility of clinical application in the short term.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Development of a Microdialysis Monitor for Tracking Systemic Inflammation During Cardiopulmonary Bypass

Jeffrey D. Zahn, PhD[1], Kiana Aran, BS[1], Alex Fok, BS[2], Akif Ündar, PhD[2]
BioMEMS Laboratory, Department of Biomedical Enigneering, Rutgers University, Piscataway, NJ
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering,
Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
Continuous monitoring of systemic inflammatory responses in patients undergoing CPB procedures will aid physicians in developing clinical applications for the treatment and prevention of inflammation during cardiac surgery in pediatric patients. To accomplish this goal a microdiagnostic system is being developed consisting of a novel microdialysis device (Fig. 1) to continuously separate plasma proteins from blood components. This system is tested in-vitro by sampling blood, during a mock CPB model, from a sampling manifold connected to the arterial port of the membrane oxygenator on the heart-lung machine and comparing measured complement concentrations between the blood introduced into the device, the filtered dialysate and whole blood samples taken from the circulation loop.

Methods:
The set-up included a Jostra HL-20 heart-lung machine, a 10 Fr arterial cannula, and a pseudo-patient. The reservoir channel in the microdevice was perfused from the pressure generated by the CPB pumphead while the perfusion channel was perfused with lactated ringers using a syringe pump. The in-vitro normothermic CPB circulation loop was primed with 500 ml of heparinized blood hemodiluted to 26% Hct in lactated ringers and perfused at a rate of 500 ml/min at an arterial circuit pressure of 100 mmHg. The flow rates through the reservoir and perfusion channels were 40 and 4 µl/min respectively. The fluid from both the outlet of the reservoir and perfusion channels was continuously collected over a two hour circulation time. A 1 ml discrete blood sample was also collected every 15 minutes directly from the arterial port of the membrane oxygenator. Each sample was snap frozen at -80°C and subsequently analyzed for complement C3a, C4a and C5a concentrations a commercially available anaphylatoxin cytometric bead kit (BD Biosciences, San Jose, CA, USA).

Results:
The results show a good correlation between the measured C3a, C4a and C5a concentrations taken from the three sources (dialysate, reservoir or direct draw) (Fig. 2). The results confirmed the ability of the microdialysis device to track complement concentrations of the circulating blood in CPB circuit.

Conclusions:
These results suggest that the further development of the microdiagnostic system, with the inclusion of a microimmunoassay will allow realtime monitoring of inflammation during CPB procedures.

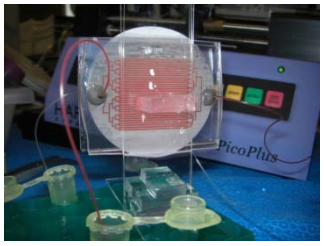


Figure 1: Microdialysis device being Perfused with blood from heart lung machine

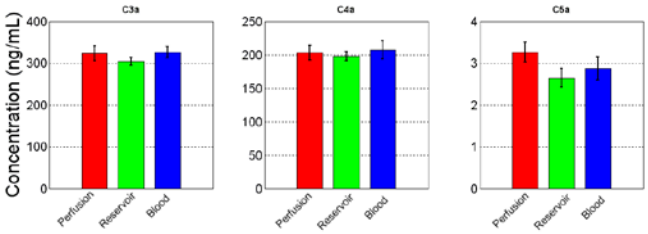


Figure 2: Comparison of complement concentrations between dialysate (perfusion) reservoir and direct draw (blood) samples.

Towards Quantitative Hemodynamic Prediction in Challenging Single-ventricle Circuits: Surgical pathway designs, pVADs and adult Fontans

Kerem Pekkan, PhD
Pediatric Cardiovascular Fluid Mechanics Laboratory, Biomedical Engineering Department, Carnegie Mellon University, Pittsburgh, Pennsylvania, USA

Purpose:
A recent lumped-parameter investigation illustrated the significance of total cavopulmonary connection (TCPC) pathway flow resistance on cardiac output (CO) in single ventricle circuits (Sundareswaran, Pekkan, et.al. AJP 295(6): H2427-35, 2008). This study prompted further emphasis on the precise effects of respiratory dependent caval flow augmentation and its pulsatile hemodynamic energetics. To elucidate hemodynamic differences, a study using patient-specific caval flow waveforms obtained from "functional" and "healthy" adult Fontan patients are conducted. Synthetic optimal caval flow waveforms predicted from this study can be realized by a number of mechanical assist options.

Methods:
Pulsatile hemodynamics in TCPC pathways are quantified using experimentally validated computational fluid dynamics (CFD). Outflow CFD boundary conditions at pulmonary arteries are improved in order to incorporate the "failed" Fontan caval waveforms having characteristic backflow. An *in vitro* pulsatile Fontan flow loop is developed for pVADs implementation.

Results:
Our findings quantified the effect of respiration and pulsatility on the internal energy dissipation of the TCPC pathway and identified that optimization of phase-shift between caval flows leads to lower energy dissipation up to 30%. For physiological patient-specific caval waveforms the power loss can be reduced significantly (up to 20%) by the optimization of all the three major harmonics (Fig. 1). Mean power loss calculated over one respiratory cycle of a "failed" Fontan patient is 15% higher than the power loss calculated for "functional" Fontan patient (9.82 vs. 11.3 mW). Having higher power loss values at this critical condition can cause reduced CO.

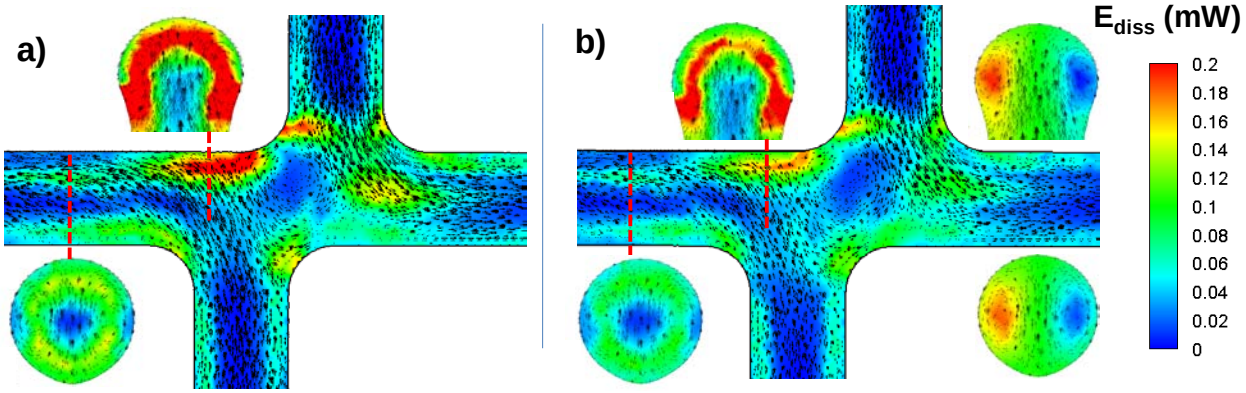


Figure 1. Comparison of time-averaged energy dissipation within the 1DO TCPC model with healthy (a) and (b) optimal caval waveforms at 3LPM CO. Cross-section variation of energy dissipation are also plotted.

Conclusions:
To achieve higher cardiac output in single-ventricle circuits a novel physiological pathway utilizing the respiratory dependent power loss modulation is suggested. This new mode of modulation would be severely reduced for patients with paralyzed diaphragms and can explain their suboptimal hemodynamic characteristics. Proposed patient-specific waveform optimization protocol can be implemented in Fontan mechanical assist therapies.

Quantitative Monitoring of Gaseous Microemboli with the EDAC® Quantifier

Ted Lynch, PhD
Luna Innovations Incorporated, Roanoke, VA USA

Purpose:
Numerous studies have suggested that microemboli passed to the brain during cardiopulmonary bypass results in neurological deficits. The recent introduction to the market of the EDAC® Quantifier provides a new capability for monitoring microemboli as small as 10 microns in diameter at three sites within the bypass circuit. The purpose of this presentation is to provide an overview of the monitoring capabilities of the EDAC® and to provide recent clinical results of studies conducted with the EDAC®.

Methods:
A combination of in vitro closed loop studies and clinical data will be presented to provide an overview of EDAC® capabilities. Statistical analysis of the data and case studies will be presented to provide examples of the type of data the EDAC® provides and how clinicians might use this data to help protect patients from the neurological damage caused by microemboli.

Results:
The results presented here are consistent with earlier findings that gaseous emboli may be introduced into the bypass circuit both from the surgical field, and during perfusionist interventions such as drug injections or transfusion through the venous reservoir. While the venous reservoir, oxygenator and arterial line filter effectively protect the patient against massive air embolism, several studies have shown that the components do not completely remove gaseous microemboli (GME) from the bypass circuit, and GME returning to the patient can contribute to neurological damage via cerebral ischemia and systemic inflammation.

Conclusions:
The detection and sizing capabilities of the EDAC™ QUANTIFIER can provide perfusionists with an early warning signal of elevated embolic loads in a CPB circuit, so that operating parameters may be adjusted to minimize loads delivered to a patient.

Optimizing the circuit design of a pulsatile ECLS in terms of EEP and SHE

Kyung Sun, MD, PhD, MBA, Choon Hak Lim, MD
Departments of Thoracic and Cardiovascular Surgery, and Anesthesiology and Pain Medicine, Korea Artificial Organ Center, Korea University, Seoul, Korea

The controversy over the benefits of pulsatile and nonpulsatile flow during cardiopulmonary bypass procedures continues. Clinical investigations, as well as animal experiments, have produced overwhelming evidence that pulsatile perfusion is more beneficial to patients than nonpulsatile flow. Many investigations have been reported that there were no difference between the two perfusion modes. Recently, evaluating pulsatility with precise quantification of pressure-flow waveforms, well-designed experimental method, selection of components of the pump, membrane oxygenators, and aortic cannulae preventing pulsatile energy loss are needed to compare the effect of perfusion type.

It is suggested that pulsatility can be evaluated with Energy Equivalent Pressure Formula (EEP) and Surplus Hemodynamic Energy (SHE).

EEP is based on the ratio between the area beneath the hemodynamic power curve ($\int fpdt$) and the area beneath the pump flow curve ($\int fdt$) during each pulse cycle. SHE is calculated by multiplying the difference between the EEP and the mean arterial pressure by 1332.

We tried to revise pulsatile extracorporeal life support system (the Twin-Pulse Life Support, T-PLS) by changing the circuit design to get more pump output and effective pulsatility. EEP and SHE were used for evaluating pulsatility. Serial circuit configuration and parrallel circuit configuration were compared (Fig. 1).

We found that both circuit design generate effective pulsatility and the parallel circuit configuration provides higher flow than the serial circuit configuration and also, EEP and SHE was very useful in evaluating pulsatility and optimizing the circuit design of pulsatile ECLS.

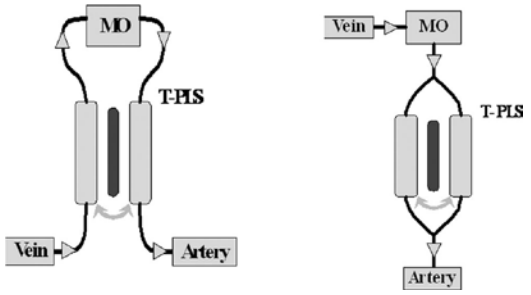


Fig. 1. Circuit configurations of the T-PLS (MO, membrane oxygenator). (a) The serial circuit configuration. A conventional membrane oxygenator (Capiox SX10, Terumo Co.) is placed between the twin blood sacs serially. (b) The parallel circuit configuration.The twin blood sacs of the T-PLS are placed parallel and downstream of a gravity-flow membrane oxygenator (Capiox CX230, Terumo Co)

The Benefits of High-flow Management in Children with Pulmonary Atresia with/without Major Aortopulmonary Collateral Arteries

Yasuhiro Fujii, MD, Yasuhiro Kotani, MD, Takuya Kawabata, MD, Shinya Ugaki, MD, Shigeru Sakurai, MD, Hironori Ebishima, MD, Hideshi Itoh, CCP, Mahito Nakakura, Sadahiko Arai, MD, Shingo Kasahara, MD, Shunji Sano, MD, Tatsuo Iwasaki, MD*, and Yuichiro Toda, MD*.
Department of Cardiovascular Surgery and Department of Anesthesiology and Resuscitology*, Okayama University Hospital, Okayama, JAPAN

Purpose:
The high-flow management of cardiopulmonary bypass (≥2.4 L/min/m^2) is a standard strategy used at this institute for children with pulmonary atresia (PA) due to a fear that the blood flow may be diverted by the major/minor aortopulmonary-collateral-arteries and hypervascularization due to long-term hypoxia. There is no evidence concerning the optimal cardiopulmonary bypass flow (CPBF) in this patient's population. The purpose of this study was to describe the validity of high-flow management in children with PA.

Methods:
The CPB records of 23 children with PA who underwent a definitive biventricular repair between Feb 2006 and Nov 2008 were retrospectively reviewed. The mean age at the operation was 33 ± 22 months. The mean body-surface-area was 0.49 ± 0.10 m^2. Patients who required flow-down of less than 2.0 L/min/m^2 were excluded. The blood-pressure during CPB was controlled with the same protocol.

Results:
The mean cooling-temperature was 28.4 ± 3.7 °C. The mean minimum hematocrit was 25.0 ± 3.4 %. The mean maximum CPBF at the initiation of CPB, the mean maximum CPBF during aortic cross-clamping (ACC), the mean minimum CPBF during ACC, and the mean maximum CPBF after rewarming were 3.1 ± 0.5, 3.1 ± 0.5, 2.6 ± 0.4, and 3.2 ± 0.4 L/min/m^2, respectively. The higher CPBFs were significantly correlated with the lower serum lactate levels (Table). The lowest oxygen-delivery during CPB had significant influences on the urine-output during CPB (R=0.547, P=0.007), the serum lactate levels at the end of CPB (R=-0.442, P=0.035) and the postoperative thoracic effusion (R=-0.459, P=0.028).

Table 1. Correlations between CPB flows and serum lactate levels.

	Initiation Flow		Max Flow During ACC		Min Flow during ACC		Rewarming Flow	
	R	P	R	P	R	P	R	P
Max Lac during ACC 2.3 ± 1.3 (0.8-5.5) mmol/L	-0.061	0.782	-0.437	0.037	-0.617	0.002		
Max Lac at the end of CPB 2.3 ± 1.1 (0.7-5.3) mmol/L	-0.416	0.048	-0.695	<0.001	-0.682	<0.001	-0.486	0.019
Max Lac during CPB 2.7 ± 1.3 (1.0-5.5) mmol/L	-0.263	0.226	-0.547	0.007	-0.708	<0.001		

ACC; Aortic cross-clamping, CPB; cardiopulmonary bypass, Lac; serum lactate level, P; P value, R; correlation coefficient.

Conclusions:
A CPBF of 2.4 L/min/m^2 may not be sufficient and the maximum requirement of CPBF may be 3.2 L/min/m^2 or more in this patient population. The high-flow management may contribute to a better urine-output, a less activated anaerobic metabolism, and a shorter duration of thoracic drainage.

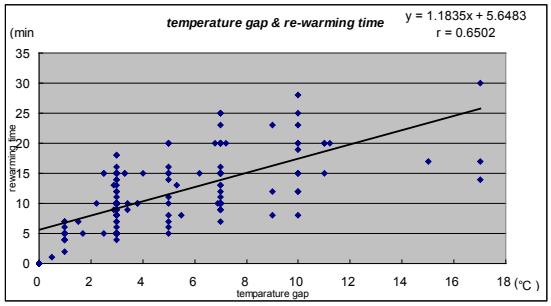
THE RE-WARMING INDEX FORMULA FOR PEDIATRIC CARDIOPULMONARY PERFUSION

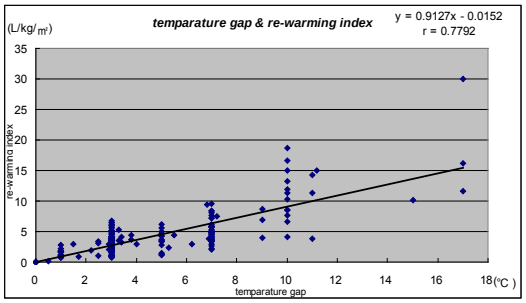
Hideshi ITOH CCP, Shingo KASAHARA, MD, Yasuhiro FUJII, MD, Yasuhiro KOTANI, MD, Sadahiko ARAI, MD, Shunji SANO, MD
Departments of Cardiovascular Surgery, Okayama University Hospital, Okayama, JAPAN

Purpose:
The purpose of this study is to find the re-warming index formula for estimation of ideal re-warming technique for pediatric cardiopulmonary perfusion.

Methods:
We investigate re-warming time, perfusion flow, perfusion temperature, body weights and body surface areas to calculate the re-warming index in 220 pediatric cardiopulmonary perfusion cases retrospectively.
We defined the re-warming index means that re-warming time multiplies perfusion flow divided by body weight and body surface area.
A perfusion circuit consists of Terumo baby-RX5 and hard shell reservoir, Capiox pediatric arterial filter and 3/16-inch tubing throughout.

Results:
There was a significant correlation between temperature gap and re-warming time (n=220, y=1.1835x+5.6483, r=0.6502).
There was a significant correlation between re-warming index and temperature gap (n-220, y=0.9127x-0.0152, r=0.7793).
Temperature gap: (target temperature) - (perfusion temperature)





Conclusions:
The following re-warming index formula gives us the novel information of re-warming techniques for pediatric cardiopulmonary perfusion.

$$\Phi = (T \cdot Q)/(R \cdot S) = 0.9127P - 0.0152$$

Φ: re-warming index(L/kg/㎡), T: re-warming time(min), Q: perfusion flow(L), R: body weight(kg), S: body surface are(㎡), P: temperature gap(℃)

We can estimate ideal perfusion flow and re-warming time by using this re-warming index formula as a re-warming technique for pediatric cardiopulmonary perfusion.

Segmental Differences of Impaired Diastolic Relaxation Following Cardiopulmonary Bypass Surgery in Children – A Tissue Doppler Study

Linda B. Pauliks, MD, Akif Ündar, PhD, J. Brian Clark, MD, John L. Myers, MD,
Departments of Pediatrics, Surgery, and Bioengineering, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

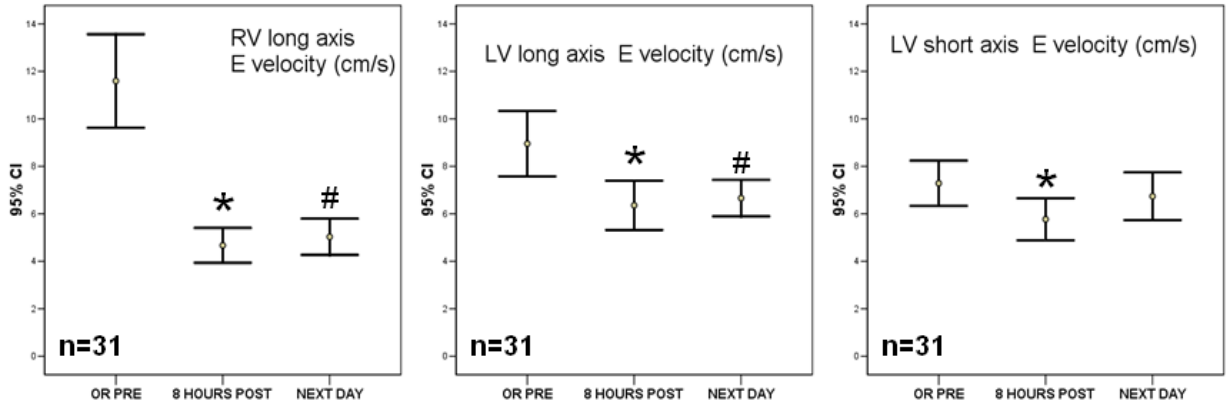
Purpose: Impaired myocardial relaxation is an important after effect of cardiopulmonary bypass (CPB). Infants with their immature calcium metabolism may be particularly vulnerable. However, it has been difficult to quantitate diastolic dysfunction clinically. This study used tissue Doppler to measure regional diastolic myocardial velocities in 31 pediatric patients undergoing open heart surgery.
Methods: Color tissue Doppler images were acquired in the OR just before, 8 and 24 hours post CPB surgery. Early (E) and atrial (A) diastolic velocities were determined. Long axis motion was assessed from apical views near the mitral and tricuspid ring and radial wall motion from parasternal.
Results: The study included 31 children aged 3.6±4.4y (6d to 16y) with a mean weight of 14.7±13.7kg and BSA of 0.59±0.35m^2. All children were in sinus rhythm. Results are summarized in Table 1 and Figure 1.

Table 1: Diastolic Tissue Velocities in 31 Children Before and After CPB Surgery

	RV Long axis		LV long axis		LV short axis	
	E (cm/s)	A (cm/s)	E (cm/s)	A (cm/s)	E (cm/s)	A(cm/s)
OR PRE	-11.3±5.3	-13.4±7.3	-9.2±3.9	-5.6±3.0	-7.3±2.5	-5.6±3.0
POST	-4.7±1.9 *	-10.1±4.3	-6.4±2.7*	-4.4±2.6	-5.8±2.3 *	-4.4±2.4
NEXT DAY	-5.0±2.0 #	-9.4±3.6#	-6.7±2.1#	-4.1±1.7	-6.8±2.6	-3.7±2.0#

* p<0.05 pre vs. post. # pre vs. next day. E early. A atrial wave.

Figure 1: Segmental Differences of Diastolic Velocity Changes



Conclusions: Tissue Doppler analysis of regional wall motion revealed significant impairment of LV and RV diastolic relaxation in the early postoperative phase after CPB. Initially, all segments were significantly altered but by 24 hours regional differences became apparent: LV radial wall motion was recovered while longitudinal fibers in LV and RV appeared to be less resilient. RV myocardial mechanics were most abnormal.
Tissue Doppler analysis may deepen our understanding of myocardial recovery and offers a sensitive tool to compare different cardioprotective strategies.

Transcranial Doppler Ultrasonography: a reliable method of monitoring pulsatile flow during cardiopulmonary bypass in infants and young children

Ashley Rogerson, BS, Yulong Guan, MD, Stephen J Kimatian, MD, Allen Kunselman, MA, J. Brian Clark, MD, John L Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratories, Departments of Pediatrics, Surgery, Bioengineering, and Health Evaluation Sciences, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

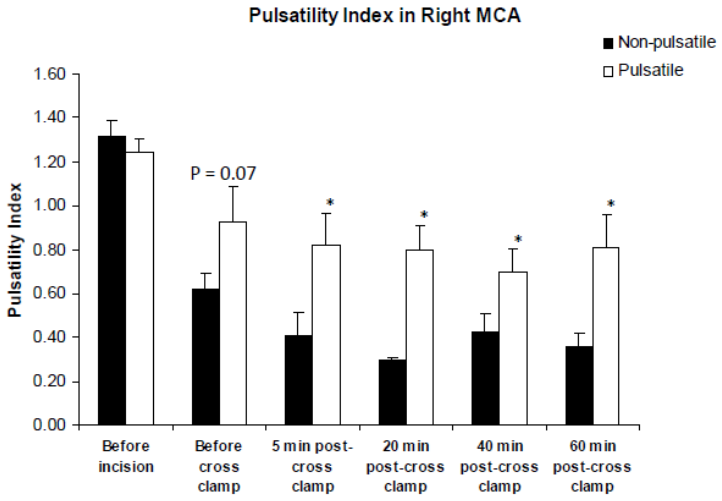
Purpose:
In order to prevent adverse neurologic outcome following pediatric cardiopulmonary bypass (CPB), optimal cerebral hemodynamics must be maintained during the procedure. The objective of this study was to demonstrate that transcranial Doppler (TCD) is a feasible method of measuring pulsatility in cerebral vasculature and can be utilized in future research exploring the neurologic benefits of pulsatile flow in pediatric CPB.

Methods:
Focusing on *Gosling's Pulsatility index* (PI), we compared perioperative TCD measurements in pediatric patients on pulsatile (N=13) and non-pulsatile flow (N=13) settings on CPB. PI was recorded from each patient's right middle cerebral artery (MCA) prior to the first incision, on CPB for 3-5 minutes but before the aortic cross clamp was applied. PI measurements were then taken at 5, 20, 40, and 60 minutes post-cardioplegia. All components of the circuit were FDA approved and selected based on previous studies demonstrating high quality pulsatile perfusion.

Results:
Patients in each group were similar in age, weight, and body surface area. Pulsatile and non-pulsatile groups had similar CPB and cross-clamp times, and received similar inotropic support. Prior to the first incision and 3-5 minutes on CPB, both groups had similar levels of MCA pulsatility. PI was significantly greater in the MCA throughout the duration of cross clamp time in the pulsatile group (Figure 1).

Conclusions:
Under the assumption that pulsatility in the patient's MCA prior to the first incision is a representation of optimal cerebral perfusion, it is clear the pulsatile group achieved cerebral perfusion that closely approximates this physiologic environment. TCD monitoring provides real-time information regarding cerebral perfusion during pediatric cardiac surgery. PI is a valid parameter for monitoring cerebral perfusion and these methods utilizing TCD will be employed in further research investigating the neurologic benefits of pulsatile flow in pediatric CPB.

Figure 1



Comparison of Bidirectional Glenn Procedure with and without CPB

Hironori Ebishima, Yasuhiro Kotani, Shinya Ugaki, Yasuhiro Fujii, Shigeru Sakurai, Hideshi Ito, Mahito Nakakura, Shingo Kasahara, Sadahiko Arai, Shunji Sano
Department of cardiopulmonary surgery, Okayama University, Okayama, Japan

Purpose:
The bidirectional Glenn shunt procedure (BDG) is performed for cyanotic single ventricle heart disease, usually with CPB, even though off pump BDG is possible to perform as sufficient saturation of arterial blood oxygen or anatomical features. We compared the results of BDG with and without CPB at our institute.

Methods:
From December 2005 to November 2008, 80 patients underwent BDG at our hospital. Both emergency cases and the cases with additional intracardiac operations were excluded. Seven cases without CPB, including 3 cases with centrifugal pump support, (with a mean age ; 1.3±0.3 years, and a mean weight ; 8.6±0.8 kg) and 9 with CPB (with a mean age ; 1.7±0.9 years, and a mean weight ; 9.0±1.4 kg) were compared in regard to the operation time, the volume of bleeding and blood transfusion, the lab data regarding the pre- and post-operative hematocrit levels, the duration of intubation and the CCU stay.

Results:
All patients survived and no patients demonstrated any neurological complications. Four in 7 cases without CPB had bilateral SVC or anatomical V-V shunt, and Glenn procedure was performed under direct ligation of the SVC. Three were supported with a centrifugal pump from SVC to RA during BDG anastomosis. In 9 cases with CPB, the mean time of pump and MUF was 57.1±8.1 min and 9.8±0.6 min, respectively. Regarding all factors, no significant difference between each group was observed. See Table 1.

Table 1.

	Ope time (min)	bleeding/BW	post Ht (%)	intubation (h)	CCU stay (d)
BDG without CPB	163.6±17.5	8.0±3.6	40.3±1.8	6.7±3.4	4.0±0.8
BDG with CPB	190.3±16.5	9.6±2.0	38.2±1.2	3.0±0.8	3.3±0.9

Conclusions:
These results suggest that off pump BDG is safe to perform and CPB is not necessarily required in simple BDG procedure. This not only avoids problems related to CPB, it is also economical.

Mechanical aortic valve replacement in children and adolescents after previous repair of congenital heart disease

Popov AF, Coskun KO, Tirilomis T, Schmitto JD, Ruschewski W
Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany

Background:
Due to improved outcome after surgery for congential heart defects, grown ups with congenital heart defects (GUCH) become an increasing population. In order to evaluate operative risk and early outcome after mechanical aortic valve replacement (AVR) in this population, we reviewed patients who underwent previous repair of congenital heart defects.

Methods:
Between 07/2002 and 11/2008 fifteen (10 male and 5 female) consecutive patients (mean age 14.5 ± 10.5 years) underwent mechanical AVR. Hemodynamic indications for AVR were aortic stenosis in four (27%), aortic insufficiency in eight (53%), and mixed disease in three (20%) after previous repair of congenital heart defects. All patients had undergone one or more previous cardiovascular operations due to congenital heart disease. Concomitant cardiac procedures were performed in all of them. In addition to AVR, in two patients a mitral valve replacement was performed. One patient recieved a right ventricle-pulmonary artery conduit replacement as concomitant procedure. The mean size of implanted valves was 23 mm (range 17-29mm).

Results:
There were neither early deaths, nor late mortality till 12/2008. Two patients developed postoperative complete heart block requiring permanent pacing. Two patients showed a mild mitral regurgitation without hemodynamic significance. At the latest clinical evaluation all patients were in good clinical condition without a pathological increased gradient across the aortic valve prothesis or paravalvular leakage in echocardiography.

Conclusion:
Mechanical AVR has excellent results in patients after previous repair of congenital heart defects in childhood, even in combination with complex concomitant procedures. Previous operations do not significantly affect postoperative outcome.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Intravascular Mechanical Cavopulmonary Assistance for Patients with Failing Fontan Physiology

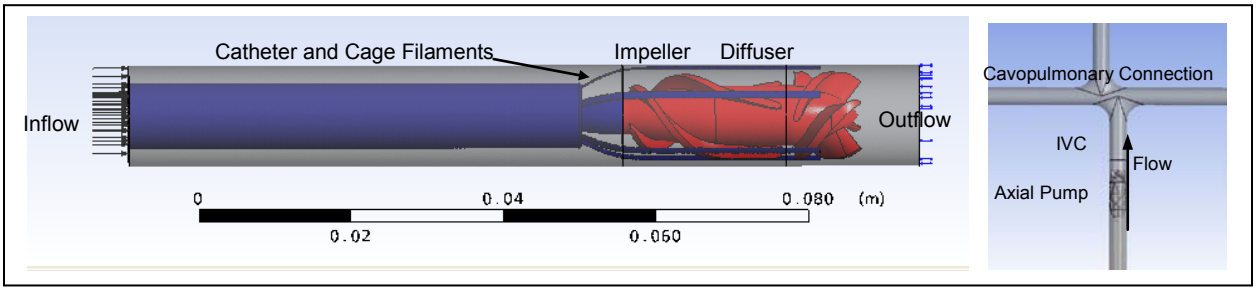
Sonya Bhavsar BS[1], Jugal Kapadia BS[1], Steven Chopski BS[1], and Amy Throckmorton PhD[1].
Mechanical Engineering[1], Virginia Commonwealth University, Richmond, VA, USA.

Purpose:
Approximately 40,000 live births each year with congenital heart disease require surgical intervention. In severe cases, babies are born with significant and multiple malformations of their heart chambers and vasculature such that they are categorized to have a single ventricle physiology. The incidence of children born with a single ventricle heart is about 2 per 1000 births.
To provide a viable bridge-to-transplant, bridge-to-recovery, or bridge-to-surgical reconstruction for these patients, we are developing a collapsible, percutaneously-inserted, magnetically levitated axial flow blood pump to support the cavopulmonary circulation in adolescent and adult patients. This blood pump will augment pressure and thus flow in the inferior vena cava through the lungs and ameliorate the poor physiology of the univentricular circulation.

Methods: Computational fluid dynamics analyses were performed to create a design of the impeller, protective cage of filaments, and set of diffuser blades for this axial flow blood pump. The grid consisted of approximately 2 million elements with high quality construction. These analyses included the generation of pressure-flow characteristics, scalar stress estimations, and blood damage indices. A quasi-steady analysis of the diffuser rotation was also completed.

Results:
The numerical predictions of the pump performance demonstrated a pressure generation of 2 to 25 *mmHg* for 1 to 7 LPM over 3000 RPM to 8000 RPM. Scalar stress values were less than 200 Pascal and fluid residences times were within acceptable ranges.

Conclusions:
These results support the continued design and development of this device, building upon previous numerical work and experimental prototype testing. Development of the motor-magnetic bearing suspension system is also underway. This research project will produce a new therapeutic tool that will provide mechanical assistance to patients with failing single ventricle physiology.



A Microfluidic Immunosensor to Monitor Systemic Inflammation During CPB

Lawrence A. Sasso[1], Akif Ündar[2], Jeffrey D. Zahn[1]
[1]Department of Biomedical Engineering, Rutgers University, Piscataway, NJ; [2]Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, PA

Purpose:
It is evident that cardiac surgeries involving cardiopulmonary bypass (CPB) induce complex inflammatory responses, which can lead to many postoperative complications. The study of this response has been hindered by the lack of timely measurements of inflammation markers. Current technologies generally provide measurements with sample periods of over an hour, and there are strict limitations on the volume of blood which can be drawn from a patient while undergoing CPB procedures. A microfluidic immunosensor is presented which monitors the concentration of inflammation markers from a continuous sample stream with real-time data at a high sample rate.

Methods:
The microdevice assay is based on combining sample preparation and flow cytometry analysis within a microdevice, allowing immuno-fluorocytometry of antibody conjugated beads. In this setup the primary antibody is immobilized on a paramagnetic bead and the secondary antibody is conjugated with a fluorescent marker to create an antigen sandwich immunoassay. Magnets on opposite sides of a microchannel allow autonomous serial bead processing by directing the beads into a sample antigen stream and subsequently into a wash stream. In a second stage, a similar process occurs where the beads are incubated with the fluorescent secondary antibody. A focused laser and photomultiplier tube (PMT) measure the fluorescent intensity of each bead, which is proportional to the concentration of antigen in the sample.

Results:
The device was benchmarked by measuring the relative concentration of complement C3a in a sample stream. Samples containing C3a at concentrations of 1.25 µg/ml, 2.5 µg/ml, 3.75 µg/ml and 5.0 µg/ml were run for 5 minute intervals. The incubation time for each stage was measured to be approximately 45 seconds. The mean fluorescence intensity of the beads was determined as a function of C3a concentration. Figure 2 shows these results.

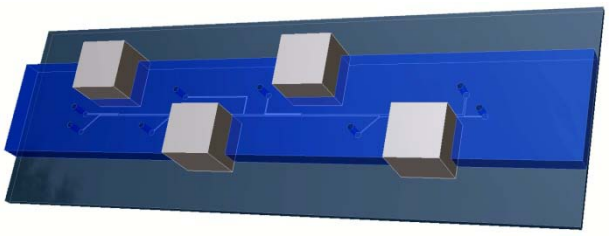


Figure 1. Conceptual rendering of microdevice

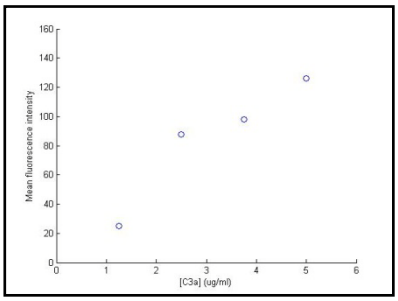


Figure 2. Mean bead fluorescence intensity versus C3a sample concentration

Conclusions:
The success of the first iteration continuous inflammation sensor is a promising step toward the development of a complete clinical systemic inflammation monitoring system. Future work will include direct measurement of human blood as well as the inclusion of more inflammation markers in parallel assays. Ultimately, the continuous inflammation monitoring system will allow a more thorough understanding of the systemic inflammatory response during CPB, which could lead to better treatments to mitigate the complications from cardiac surgery.

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Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Comparative finite-element model analysis of ascending aortic flow in bicuspid and tricuspid aortic valve

Francesca Viscardi, Christian Vergara°, Luca Antiga^, Sabrina Merelli^, Alessandro Veneziani*, Giovanni Puppini, Giuseppe Faggian, Alessandro Mazzucco, Giovanni Battista Luciani

Div. of Cardiac Surgery Univ. of Verona, Italy; ° Mario Negri Institute Ranica (BG) Italy,
^Dept. of Information Technology, Univ. of Bergamo, Italy, *Dept. of Mathematics, Emory Univ., USA

Purpose:
Role of genetic versus haemodynamic factors influencing ascending aortic pathology is controversial. In order to test the effect of bicuspid aortic valve geometry on ascending aortic flow, a finite element analysis model was undertaken.

Methods:
A surface model of aortic root and ascending aorta was obtained from MR images of patients with bicuspid and tricuspid aortic valve using the segmentation capabilities of Vascular Modeling Toolkit. Analytical models of bicuspid (antero-posterior commissures) and tricuspid orifices were mathematically defined. Final models were turned into a volumetric mesh of linear tetrahedra for computational fluid dynamics simulations. Numerical simulations were performed with the Finite Element Code LifeV (MOX-Milan, INRIA-Paris, EPFL-Lausanne).

Physiological inflow boundary conditions at inlet were imposed by introduction of a Lagrange multiplier. Parameters of different aortic flow velocity were assessed for four levels: aortic annulus, sinus of Valsalva, sinotubular junction, ascending aorta.

Results:
Comparison of finite-element analysis models of bicuspid and tricuspid aortic valve shows different blood flow velocity. Bicuspid flow shows an asymmetrical distribution of velocity field towards the convexity of the mid-ascending aorta, between sinus of Valsalva and ascending aorta, across the sinotubular junction, returning symmetrical in distal ascending aorta (Fig.1). On the contrary, tricuspid flow is symmetrical in each aortic segment (Fig.2). Moreover, aortic flow in bicuspid model gains a maximum velocity of 5,5 m/s at the systole, while in the tricuspid maximum velocity is 2,6 m/s.

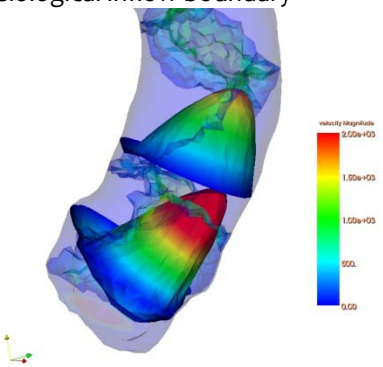

Fig. 1.

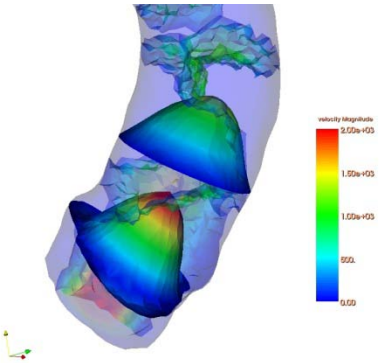

Fig. 2.

Conclusions:
Comparison between models shows an asymmetrical and higher flow velocity in the bicuspid model. The asymmetry is more pronounced at the aortic level known to be more exposed to aneurysm formation in bicuspid patients. This supports the hypothesis that haemodynamic factor may contribute to ascending aortic pathology in this subset of patients.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Performance Validation in Arterial Cannula Representation

-A special focus on three pediatric cannulae

Kimberly A. Griffith, Branka Lukic, MS, Shigang Wang, MD, William J. Weiss, PhD, Gerson Rosenberg, PhD, John L. Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering,
Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The performance of the arterial cannula has the potential to greatly impact the overall outcome of the cardiopulmonary bypass procedure. In pediatric cannulae, subtle differences more than simply scaling, must be recognized in order to maximize the efficiency. Three top-performing pediatric cannulae were compared and evaluated, including the Terumo TenderFlow, DLP 770xx Pediatric One Piece, and RMI Fem-Flex II Femoral arterial cannulae.

Methods:
Data was collected from an extracorporeal circuit, identical to that used in the clinical operating room. The pre- and post-cannula pressures were recorded, maintaining a post-cannula aortic pressure of 40 mmHg. The circuit contained a glycerin/water mixture blood analog to simulate the viscosity of blood. Data acquisition was accomplished using computer software, to collect pump flow rates and pressure waveforms.

Results:
The results of each cannula exhibited significant differences, despite two of the (10 Fr) cannulae having identical tip diameters. While all three 10 French cannulae remained inside clinical ranges of allowable pressure drop and maximum flowrate, Terumo and DLP 8 French cannulae exceeded the pressure limit between a flow range of 460-560 ml/min. The 8 Fr RMI cannula remained just under 100 mmHg at 600 ml/min.

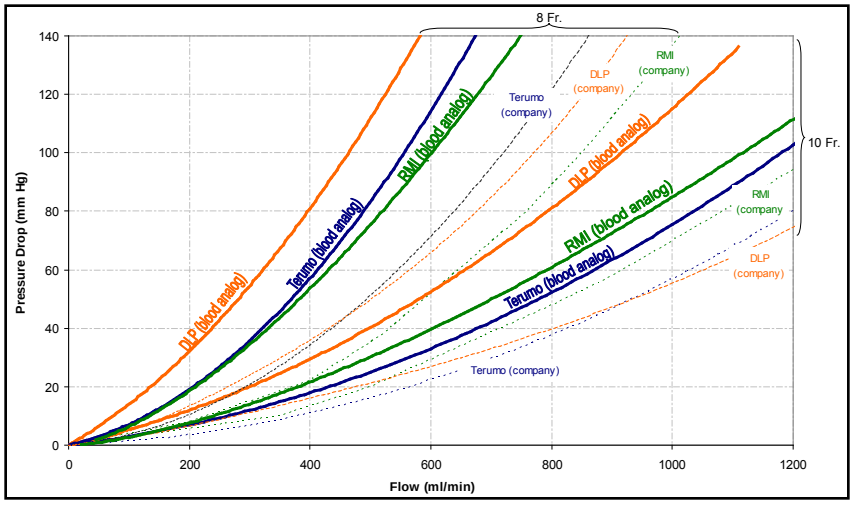

Figure 1. Pressure-flow curves show variation according to cannula properties and testing conditions. The dotted lines represent company data, with water used to collect performance data.

Conclusions:
Despite very little research having been conducted in pediatric arterial cannulae design, previous studies have attempted to signify the importance of the tip inner diameter, due to variation among same size designations. Past and current research and clinical guidelines focus on the importance of a pressure limit threshold. The general standard may suffice for the adult population, but stricter guidelines must be investigated to minimize risk to the pediatric population in particular. The strict limitations of the pediatric field validate the need to identify further performance factors and validate performance representation.

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Effects of the Pulsatile Flow Settings on Pulsatile Waveforms and Hemodynamic Energy in a PediVAS™ Centrifugal Pump

Shigang Wang, MD, Alan R. Rider, Allen R. Kunselman, MA, J. Scott Richardson, Kurt A. Dasse, PhD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study was to test different pulsatile flow settings of the PediVAS™ centrifugal pump to seek an optimum setting for pulsatile flow to achieve better pulsatile energy and minimal backflow.

Methods:
The PediVAS™ centrifugal pump and the conventional pediatric clinical circuit, including a pediatric membrane oxygenator, arterial filter, arterial cannula, and ¼ inch circuit tubing were used. The circuit was primed with 40% glycerin water mixture. The post-cannula pressure was maintained at 40 mmHg by a Hoffman clamp. The experiment was conducted at 800 ml/min of pump flow with a modified pulsatile flow setting at room temperature. The pump flow and pressure readings at pre-oxygenator and pre-cannula sites were simultaneously recorded by a data acquisition system.

Results:
The results showed that backflows appeared at flow rates of 200 - 800 ml/min (200 ml/min increments) with the default pulsatile flow setting and only at 200 ml/min with the modified pulsatile flow setting. With an increased rotational speed difference ratio (see Table 1) and a decreased pulsatile width, the pulsatility increased in terms of surplus hemodynamic energy and total hemodynamic energy at pre-oxygenator and pre-cannula sites. Backflows appeared at pre-oxygenator and pre-cannula sites at a 70% of rotational speed difference ratio. The modified pulsatile flow setting was better than the default pulsatile flow setting in respect to pulsatile energy and backflow. The pulsatile width and the rotational speed difference ratio significantly affected pulsatility.

Table 1. Hemodynamic energy (ergs/cm3) at pre-oxygenator and pre-cannula sites during non-pulsatile mode (NP) and pulsatile mode (P) with different rotational speed difference ratios (Diff).

Groups	Flow rate (ml/min)	Pre-oxygenator site		Pre-cannula site	
		SHE	THE	SHE	THE
NP	811.6±5.7	2.7±0.5	316933.7±3343.6	0.7±0.1	106882.8±2895.2
P-Diff-10	812.2±5.5	*2788.2±51.5	320736.6±3355.7	*1029.4±28.8	108448.1±2874.7
P-Diff-30	818.7±5.5	*†23580.4±402.7	*†349329.0±3429.9	*†8752.6±206.1	*†121051.2±2916.0
P-Diff-50	823.9±6.6	*†63641.2±1050.2	*†402364.0±3733.1	*†23824.5±453.8	*†144588.2±3046.4
P-Diff-70	823.7±6.5	*†117722.3±1452.1	*†471048.7±4158.2	*†44487.6±710.0	*†174708.5±3330.0

SHE: surplus hemodynamic energy; THE: total hemodynamic energy
* $p < 0.001$ NP vs. P; † $p < 0.01$ P-Diff-10 vs all other pulsatile settings (P-Diff-30-40-50)

Conclusions:
These results suggest that the parameter of the rotational speed difference ratio can automatically increase pulsatility with increased rotational speeds. Further studies will be conducted to optimize the pulsatile flow setting of the centrifugal pump.

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The Aachen MiniHLM–first results in a small animal model

Heike Schnoering, MD[1]‡, Jutta Arens, Dipl.-Ing.[2]‡, Joerg S. Sachweh, MD[1], Melanie Veerman[1], Rene Tolba, MD[3], Thomas Schmitz-Rode, MD[2], Ulrich Steinseifer, Dr. Ing.[2] and Jaime F. Vazquez-Jimenez, MD[1]

[1] Pediatric Cardiac Surgery, Medical Faculty, RWTH Aachen University, Germany
[2] Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany
[3] Institute for Laboratory Animal Science and Experimental Surgery, RWTH Aachen University, Germany
‡ Both Authors contributed equally to the manuscript

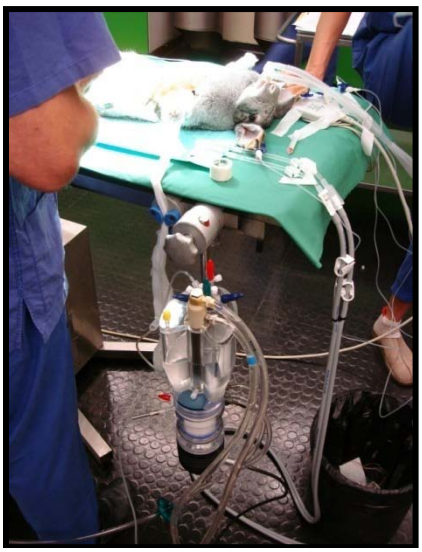
Purpose:
Surgical operations for cardiac anomalies often require the use of heart-lung machines (HLM), ensuring adequate blood circulation and oxygenation in an external circuit. Due to the large extrinsic surface contact area and the essential addition of foreign blood, this procedure is associated with numerous risks for the patient such as severe inflammatory reactions and haemolysis. The risk is very high in low birth weight newborns and specially on premature. On this account we developed a new miniaturized heart lung machine for neonates with a total static priming volume of 102 ml (including arterial/venous line) and tested it in a small animal model.

Methods:
14 female Chinchilla Bastard rabbits, 8 with Dideco Kids® and Stöckert roller pump (modified dynamic priming volume 175 ml), 6 with the MiniHLM (dynamic priming volume 120 ml), were operated. We compared these two systems concerning haemolysis and blood gas analysis. The rabbits were anesthetized and sternotomized, followed by cannulation of the aorta and the right atrium. The Aorta was clamped after starting the HLM, cardiac arrest was achieved by blood cardioplegia. Blood for examination of haemolysis (free haemoglobin and fibrinogen) and blood gas analysis was taken before skin incision, 15 minutes after opening the aorta and 30 minutes after cardiopulmonary bypass (CPB). After 1 hour aortic clamp time the HLM was gradually reduced, the heart was decannulated and the sternum was closed.

Results:
All rabbits could successfully be weaned off after 1 hour of aortic clamp time. No foreign blood was used in all cases. Blood gas analysis was excellent in all operations. The use of the MiniHLM resulted in statistically significant lower differences of fibrinogen compared to Dideco Kids®. Free haemoglobin (fHb) was reduced slightly, but not statistically significant.

	Dideco Kids®	MiniHLM	p-value
Diff. Fib1*	1.59 ± 0.60	0.77 ± 0.45	0.014
Diff. Fib2•	1.58 ± 0.63	0,73 ± 0.51	0.020
Diff. fHb1*	54.5 ± 41.3	28.5 ± 20.7	0.181
Diff. fHb2•	47.7 ± 30.8	24.6 ± 18.6	0.534

* Difference between skin incision/15 min after opening aorta
• Difference between 15 min after opening aorta/ 30 min after CBP



Conclusions: This new developed MiniHLM with low priming volume, less haemolysis and excellent gas transfer (O_2 and CO_2) may reduce complications during heart surgery in neonates.

Effect of the miniaturized cardiopulmonary bypass system on the inflammatory response and cardiac function in neonatal piglets

Ko Yoshizumi[1], MD, Kozo Ishino[2], MD, Hironori Ebishima[1], MD, Shinya Ugaki[1], MD, Yasuhiro Kotani[1], MD, Shingo Kasahara[1], MD, Shunji Sano[1], MD

[1]Department of Cardiovascular Surgery, Okayama University, Okayama, Japan

[2]Department of Cardiovascular Surgery, Showa University Northern Yokohama Hospital, Kanagawa, Japan

Purpose:

It was hypothesized that the cognitive impairment and the hemodynamic instability after the neonate cardiac surgeries with the cardiopulmonary bypass might be exacerbated by the hemodilution. Therefore to determine the impacts of miniaturization of CPB circuit on hemodynamics and the inflammatory response of the neonatal piglets, the followed method was applied.

Methods:

A bloodless miniaturized CPB circuit system including the followings, was used;

1. a Terumo Baby-RX oxygenator (43 ml priming volume),
2. a hard shell venous reservoir,
3. a remote roller pump head.

Twelve neonatal piglets (body weight 3.8±0.2kg) were divided into two groups based on prime volume; **Group I** (prime volume 75 ml), **Group II** (prime volume 175 ml)

These piglets were placed on the mild hypothermic CPB (30-32℃) for one-hundred twenty (120)minutes. The modified ultrahemofiltration(MUF) and blood transfusion was not performed. Inotropic and vasoactive drugs were not used in this study.

RESULTS:

After CPB, the points below had significant differences;

1. Group I had a dramatically higher hematocrit value than Group II. Furthermore the lowest hematocrit value during CPB was significantly higher than Group II.
2. The piglets in Group I had dramatically improved in terms of the cardiopulmonary function after CPB than Group II ,right ventricular cardiac index [l/kg/min].
3. The pulmonary vascular resistance index [dynes/cm^5/kg].
4. IL-6 [pg/ml] and the thrombin-antithrombin complex levels [ng/ml] were lower in Group I than in Group II.
5. The percent lung water content was also remarkably less in group I than in Group II.

Please refer to the table below.

	priming of CPB	Hematocrit (%)			Labo data	
	volume (ml)	Pre-CPB	Lowest during CPB	Post-CPB	IL-6	TAT
Group I	75	40±4	27±3	28±3	4370±2346	9.9±7.7
Group II	175	40±5	22±2*	23±1*	9058±2307†	25.1±8.8†

*p<0.05 for Group I vs. Group II, † p<0.01 for Group I vs. Group II

Conclusions:

The miniaturized bloodless prime circuit for the neonatal CPB has shown that the influence of the hemodilution can reduce the subsequent inflammation response, furthermore it can be suggested that the influence of the lower prime volume would be particularly effective to reduce the pulmonary vascular resistance and the right ventricular dysfunction in a neonate.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Hemodynamic changes in a model of chronic heart failure induced by multiple sequential coronary microembolization in sheep

Schmitto JD[1], Coskun KO[1], Coskun ST[2], Ortmann P[1], Sossalla S[3], Vorkamp T[1], Heidrich F[1], Popov AF[1], Heuer J[4], Hinz J[4], Quintel M[4], Schöndube FA[1]

[1]Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany
[2]Department of Cardiac Surgery, Heart and Diabetes Centre, Bad Oeynhausen
[3]Department of Cardiology, University of Goettingen,
[4]Department of Anesthesiology, University of Goettingen
schmitto@med.uni-goettingen.de

Objective:
Although a large variety of animal models for acute heart failure exist, valuable models for studies on the effect of ventricular assist devices in chronic heart failure are scarce. We established a stable and reproducible animal model of chronic heart failure in sheep and aimed to investigate the hemodynamic changes of this animal model of chronic heart failure in sheep.

Methods:
In 10 sheep (n=10,77±2 kg) chronic heart failure was induced under flouroscopic guidance by multiple sequential microembolization through bolus injection of polysterol microspheres (90µm,n=25.000) into the left main coronary artery. Microembolization(CME) was repeated up to three times in three week intervals until animals developed stable signs of heart failure. During each operation hemodynamic monitoring was performed through implantation of central-venous-catheter, arterial-pressure-line and right-heart-catheter, as well as pre- and postoperative clinical investigations. All animals were followed for 3 months and then sacrificed for histological examination.

Results:
All animals developed clinical signs of heart failure as indicated by increased heart rate at rest (68±4 bpm to 93±5 bpm (3mo) ($p<0,05$)), increased respiratory rate at rest (28±5 to 38±7 ($p<0,05$)) and increased body weight 77±2 kg to 81±2 kg ($p<0,05$) due to pleural effusion, peripheral edema and ascites. Hemodynamic signs of heart failure were revealed as indicated by increase of CVP, PAP and PCWP as well as a decrease of CO, SV and MAP three months after first CME.

Conclusions:
Multiple sequential intracoronary microembolization can effectively induce myocardial dysfunction with clinical and hemodynamic signs of chronic ischemic cardiomyopathy. The present model may be suitable in experimental work on heart failure and left ventricular assist devices, e.g. for studying the impact of mechanical unloading, mechanisms of recovery and reverse remodeling.

Clinical study of artificial colloid in cardiopulmonary bypass

Jinxiao Hu , Long Cun
Department of Extracorporeal Circulation,Fu Wai Hospital ,CAMS & PUMC,Beijing,100037 CHINA

Purpose:

The purpose of this prospective randomized study was to compare clinical effects of two different artificial colloids on coagulation function,colloid osmotic pressure and volume regulation.

Methods:

59 adult patients with valve disease or congenital heart disease were involved and divided into two groups randomly: Voluven group(n=29) and Gelofusin(n=30). All of the CPB machines were primed with lactate ringer's and discharge all solution in the reservoir. After that, we primed voluven and gelofusion respectively in two different groups and compared the effects on coagulation function,colloid pressure and volume management. We compared coagulation function by sonoclot and volume of thoracic drainage in 24hours after operation. We tested sonoclot with some parameters (such as ACT, CR, PF) at pre-CPB, after protamine administration and after 6hour in ICU. We also evaluate colloid osmotic pressure at five time points: pre-CPB, during CPB after weaning from CPB, after 2hours in ICU, after 6hours in ICU. We recorded artifice colloids volume per kilogram that administrated in 24hours after operation.

Results:

There was significant difference in PF between the two groups at after protamine administration and after 6hour in ICU time points. There were no difference in colloid osmotic pressure, volume of thoracic drainage and artificial colloids volume per kilogram that administration in 24hours after operation.

Conclusions:

The platelet function was preserved better in volume group ($p < 0.05$). There was no difference in other parameters.

Perioperative monitoring of TEG on haemostatic function for cyanotic infants undergoing complexed cardiac surgery

Yongli Cui[1], M.D, Cun Long[1], M.D, Zhengyi Feng[1], M.D, Ju Zhao[1], M.D , Fuxia Yan[2], M.D, Yuhong Wang[2], M.D , Jinping Liu[1], M.D E-mail：cuiyongli@hotmail.com
([1]Department of Cardiopulmonary Bypass, [2]Department of Anesthesiology, Cardiovascular Institute and Fuwai Hospital,CAMS and PUMS,Beijing,100037,China)

Purpose: Complex congenital heart disease (CCHD) operations usually lead to a profound coagulation disturbance especially for those severe cyanotic infants (HCT>54%). So we investigated the perioperational haemostatic feature of those patients and transfusion therapy effect under the help of thromboelastograph (TEG).

Methods: Twenty cyanotic CCHD children (HCT=69.0±6.2%) who will receive Double root translocation(DRT) or Artery switch operation(ASO) were involved. 2ml venous blood samples were respectively taken at anesthesia induction(T1), rewarming to 36℃(T2), after heparin neutralization(T3), and 4 hours after operation(T4). The basic haemostatic function and changes were evaluated by different TEG parameters (MA, MAp, MAf). All patients underwent transfusion therapy based on their TEG results at T3, and then were observed the effect at T4.

Results: The whole haemostatic function (MA1=44.1±6.8mm) of these patients was obviously lower than normal values at T1, especially for the functional fibrinogen level (Ffg) (MAf1=3.9±1.5mm), but the platelet function was relatively intact (MAp1=40.6±5.1mm). The MA1 and MAf1 were negatively correlated with HCT (r=-0.671, P=0.034; r=-0.849, P=0.002), but MAp1 did not show the same relationship with it (P=0.162). The MA2 was decreased to the lowest at T2 compared with T1 (P=0.021) with the significant decrease of platelet function (MAp2=33.7±3.6, P=0.001) and little change of Ffg (MAf2=4.13±1.9, P=0.877). At T3, compared with T2, there was obviously improvement in MA3 and MAf3 (P=0.010, P=0.00 respectively) without obviously increase of MAp3 (P=0.138). Every parameter reached healthy level at T4 after therapy. MA4 was much better than MA1 and was normalized (P=0.02, MA4=56.7±4.3mm）. MAp4 recovered to the level before operation, and MAf4 was significantly better than MAf1 and reach normal level (P=0.00，MAf=14.4±2.2).

Conclusion: Severe cyanotic pediatric patients usually combined with worse haemostatic function and very low functional fibrinogen level. The preoperative whole haemostatic function and Ffg had negative correlation with HCT but not platelet function did. During cardiopulmonary bypass (CPB), the platelet suffered from much more depletion than the fibrinogen. So the transfusion therapy including two parts: remedying the fibrinogenopenia and recovering the loss of platelet in CPB seemed more effective.

Continuous hemodiafiltration in children after cardiac surgery

Kenichi Watanabe,MD, Yasuyuki Suzuki,MD, Takeshi Goto,CE, Sanae Yamauchi,MD, Kazuyuki Daitoku,MD , Kozo Fukui, MD, Ikou Fukuda,MD

Department of Thoracic and Cardiovascular Surgery, Hirosaki University School of Medicine.
5 Zaifucho, Hirosaki, Aomori, 036-8562, Japan

Purpose:
The incidence of acute renal failure (ARF) in postoperative period after congenital cardiac surgery with cardiopulmonary bypass (CPB) was assessed by several authors to range between 2.7 and 9%, with survival rate ranging from 21 to 70%.Although peritoneal dialysis is commonly used for children with ARF, recently continuous hemodiafiltration (CHDF) has been widely accepted due to improvements in the vascular access and machines with volumetric control for accurate ultrafiltration. We retrospectively evaluated the efficacy of CHDF for ARF after congenital cardiac surgery in our hospital.

Methods:
From April 2002 to January 2009, 7 patients aged 23 days to 9 years (median 7 months) , body weight from 1.7 to 22.4kg, who underwent surgical procedures for congenital heart disease required dialysis therapy using CHDF. The patients' files were reviewed for cardiac malformation type and surgical procedures, duration of CPB and aorta cross clumping, need for inotropic support, preoperative renal function assessment (serum creatinine, urea), CHDF (indications, equipment, anticoagulation, duration of treatment, metabolic efficacy described by serum creatinine and urea concentration) and the final outcome: renal function recovery and overall survival rate.

Results:
Three patients required ECMO support and CHDF after the operation. One of them did not wean from ECMO support and another died because of multiple organ failure due to peritonitis by the duodenal perforation. Five patients (71%) were recovered renal function to normal. Duration of treatment by CHDF was from 14 to 680 hours, and net ultrafiltration was 3.5±1.4 ml/kg/hr. Serum creatinine and urea concentration of these patients 2.3±1.6mg/dl, 43.7±17.0 before CHDF and 0.5±0.2, 13.5±8.1 after CHDF ($p<0.05$). Thorombocytopenia (platelets count below 10 $\times 10^4$/ul) was observed in all patients, and platelet concentrates (0.76±0.7 ml/kg/hr) were infused during CHDF. There was one complication during CHDF, that was hypotension after the changing the set of CHDF because of clotting.

Conclusions:
We suggest that the CHDF is an effective treatment alternative in renal dysfunction after congenital cardiac surgery.

Use of ECMO, surfactant, and HFOV for the management of intra-operative acute pulmonary hemorrhage post palliation of Tetralogy of Fallot with hypoplastic branch pulmonary arteries and anomalous coronary crossing RVOT

Meena Nathan MD, Meena Kalyanaraman MD, Jonathan Blank MD, Joel Hardin MD, Joanne Starr MD
Children's Heart Center, Children's Hospital of New Jersey, NBIMC, Newark

Introduction:
Acute pulmonary hemorrhage occurring intraoperatively during repair of complex congenital lesions is rare and often fatal entity. To date there have been few case reports. We describe our experience with managing this rare complication using a combination of ECMO, surfactant therapy and high frequency oscillatory ventilation.

Methods:
A 7 week, 2.6 kg female ex 33 week preemie, birth weight of 1.6 kg with Tetralogy of Fallot-subpulmonic and pulmonic stenosis with main and branch pulmonary artery hypoplasia, supravalvular aortic stenosis was admitted to our CICU with severe cyanosis and low cardiac output. She was intubated, sedated and paralyzed, resuscitated and taken emergently to the operating room. Intraoperative findings confirmed echo findings of hypoplastic main and branch pulmonary arteries and single left coronary artery with a large right coronary branch crossing the RVOT. Based on this we performed a 3.5 mm central shunt on cardiopulmonary bypass. On attempting to wean off cardiopulmonary bypass she developed massive pulmonary hemorrhage. She was placed back on cardiopulmonary bypass. Surfactant was administered and the shunt occluded. There was a massive amount of blood from the ETT that backed up into the ventilator circuit on attempting to re-open the shunt. The shunt was re-occluded and the blood suctioned from the ETT and a Mapleson bag was set at 25 cm pressure and hooked up to the ETT to tamponade the bleeding. She was transitioned on to ECMO. She was subsequently placed on high frequency oscillatory ventilator. A second dose of surfactant was administered 24 hours later and she was successfully weaned off ECMO initially to HFOV, then onto conventional ventilation after 72 hours of ECMO. She did require shunt thrombectomy prior to weaning off ECMO.

Discussion:
Severe pulmonary hemorrhage is a rare often lethal phenomenon and has been reported to occur in the sick premature neonates, in association with collagen vascular disease, in sepsis, or in older infants and adolescents with chronic cardiopulmonary disease. In addition, there have been few idiopathic cases reported. There have been several reports of use of ECMO, plasmapharesis, surfactant therapy, or high frequency ventilator for successful management of pulmonary hemorrhage in these settings. Massive pulmonary hemorrhage occurring after cardiopulmonary bypass is extremely rare and usually fatal. There have been a few case reports of successful therapy. This is the first report of successful use of combination therapy to treat this condition. ECMO by ensuring adequate cardiopulmonary support, allowed the use of high mean airway pressure to tamponade the bleeding. Surfactant therapy and high frequency oscillatory ventilation then allowed for recruitment of alveoli.

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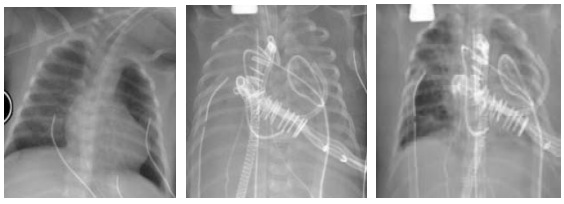

Coronary Arterio-Venous Fistual: surgical Indication in Childhoos, Treatment and Results

Alkan T., Akcevin A., Türkoğlu H, Paker T, Aytaç A.
V.K.V. American Hospital, Dept. of Cardiovascular Surgery, Istanbul, TURKEY

Coronary artery - venous fistula cases (a-v fistula) are 0,4% of cardiac anomalies. Its prognosis is asymptomatic in childhood and it may also cause cardiac insufficiency findings. Spontaneous healing is possible. In the course of years, angina pectoris and cardiac insufficiency may appear more evidently. In our clinic, eight patients have been operated due to a-v coronary fistula starting from June ,1988. Patient ages were from 14 months to 11 years (average age is 5,5). 3 of the patients were female children and 5 of them were male children. 3 of the fistulas were originated from LAD, 3 of them from RCA , and 2 of them were originated from Cx artery. 6 of them were drained into right ventricle and 2 of the fistulas were drained into right atrium. Accompanied pathologies were ASD in one patient and mitral cleft in another patient. Both accompanied pathology were recovered by operation. Extracorporeal circulation was applied during surgical operation in all cases. Primary closure of the fistula was applied in 3 cases, pericardial patch repair was used in 3 cases and in 2 cases ligation was applied. In all cases, any postoperative complication was not observed. Tracing terms in patients, under regular control, were from 8 months to 13 years (average term 92,2 months). Functional capacity of all patients were NYHA I, and they had not any problem. If obvious clinical complains is not existing in child patients with a-v coronary fistula, they may be followed for a period. If spontaneous healing does not occur, early repair operations provide successful results and absolute recovery.

Left Ventricular Contractility after Cardiac Procedures in Neonatal Piglets

Theodor Tirilomis, Oliver J. Liakopoulos, Lars Nolte, K. Oguz Coskun, Aron-Frederik Popov, Friedrich A. Schoendube
Department for Thoracic, Cardiac, and Vascular Surgery, University of Goettingen, Goettingen, Germany

Purpose: Extracorporeal perfusion and myocardial reperfusion after heart arrest for cardiac surgery may depress postoperative hemodynamics. In a previous study on newborn piglets we found hemodynamic depression even in animals without cardiopulmonary bypass. The aim of present study was re-analysis of data regarding myocardial contractility of left ventricle.

Methods: Newborn piglets were examined. After median sternotomy and exposure of the heart a Millar pressure transducer-tip catheter was placed in left ventricle. A sonomicrometric piezoelectric crystal was implanted in left ventricular wall. Animals were placed on mild hypothermic cardiopulmonary bypass for 180 minutes, including 90 minutes of cardioplegic arrest (CPB group) or were examined for the same time interval without cardiopulmonary perfusion (non-CPB group).
Left ventricular contractility in meaning of max dP/dt, contractility index (max dP/dt/P), and changes in regional myocardial wall thickness were calculated and analyzed.

Results: Left ventricular max dP/dt decreased during time in non-CPB group (1760 $\pm$ 205 mmHg/s vs. 1170 $\pm$ 205 mmHg; $p<0.05$), while remained stable in CPB group. There was no difference between non-CPB and CPB group. Contractility index was higher in non-CPB group, but without significant difference to the CPB group. The amplitude of left ventricular wall thickness decreased in both groups, but differences did not reach statistical significance between the groups.

Conclusions: Present data releave stable myocardial contractile function early after heart surgery in a neonatal piglet model.Cardiopulmonary bypass do not affect left ventricular myocardial contractility adversely.

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The Impact of Pump Settings on the Quality of Pulsatility

Alan R. Rider, Noel M. Ressler, MPH, Allen R. Kunselman MA, Shigang Wang, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, Bioengineering, and Public Health Sciences, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study was to evaluate the pulsatile performance of the Jostra HL-20 roller pump under several different base flow and pump head settings in a simulated pediatric bypass circuit.

Methods:
The circuit used in this study was identical to that used in pediatric open heart surgery. The pump flow rate was set at 800 ml/min for both pulsatile and non pulsatile perfusion modes and the mean arterial pressure of the pseudo patient was maintained at 40 mmHg for each experiment. At the beginning of each trial, a set of non pulsatile data were recorded. The roller pump was then switched to pulsatile perfusion.

The baseflow was set at 0% and data was recorded for 20, 30, and 40 percent pump start points. The baseflow was then increased to 10, 30, and 50 percent, where each pump head start point (20, 30, and 40 percent) was tested. Pressure and flow waveforms were recorded at pre-oxygenator, pre-cannula and post-cannula sites under each pump setting. A total of 91 experiments were performed (n=7 for non-pulsatile and n=84 for pulsatile).

Results:
The following table represents surplus and total hemodynamic energy values of the Jostra HL-20 roller pump during pulsatile and non-pulsatile perfusion under several baseflow and pump head percentage settings.

Table 1. Surplus and total hemodynamic energy values at the pre-cannula site for 800ml/min flow rate

		Pulsatility Start %	Base Flow 0	10	30	50	100
SHE	NP	-	-	-	-	-	3,720 ± 78
	P	20	27,780 ± 687*#	24,296 ± 641*†#	17,515 ± 264*†#	11,440 ± 86*†#	-
		30	42,207 ± 1,038*#	36,515 ± 601*†#	25,290 ± 572*†#	15,605 ± 285*†#	-
		40	58,595 ± 1,508*	50,204 ± 948*†	34,434 ± 310*†	20,944 ± 223*†	-
THE	NP	-	-	-	-	-	131,322 ± 7,229
	P	20	167,379 ± 6,283*#	160,878 ± 6,139*†#	151,627 ± 6,567*†#	143,283 ± 6,390†	-
		30	187,241 ± 6,364*#	178,989 ± 6,373*#	162,543 ± 6,442*†	148,885 ± 6,783*†#	-
		40	209,050 ± 5,012*	197,160 ± 6,605*	174,881 ± 6,713*†	156,166 ± 6,070*†	-

NP = Non-pulsatile, P = Pulsatile, SHE = Surplus Hemodynamic Energy, THE = Total Hemodynamic Energy
* p< 0.01 Non-Pulsatile vs. Pulsatile † p< 0.01 0% baseflow vs. other baseflows within respective pulsatility start % group
# p< 0.01 40% pulse start % vs. other pulse start % within respective baseflow group.

Conclusions:
Lower base flows and smaller durations between the pump start and stop times produce greater amounts of surplus and total hemodynamic energy. Pulsatile perfusion provides more hemodynamic energy than non-pulsatile perfusion under all test conditions. Minimizing base flow and shortening the pulsatile start-stop interval together, provides the greatest gain in hemodynamic energy. Ultimately, these concepts can be used in the clinical setting for creating quality pulsatile energy and improved patient outcomes.

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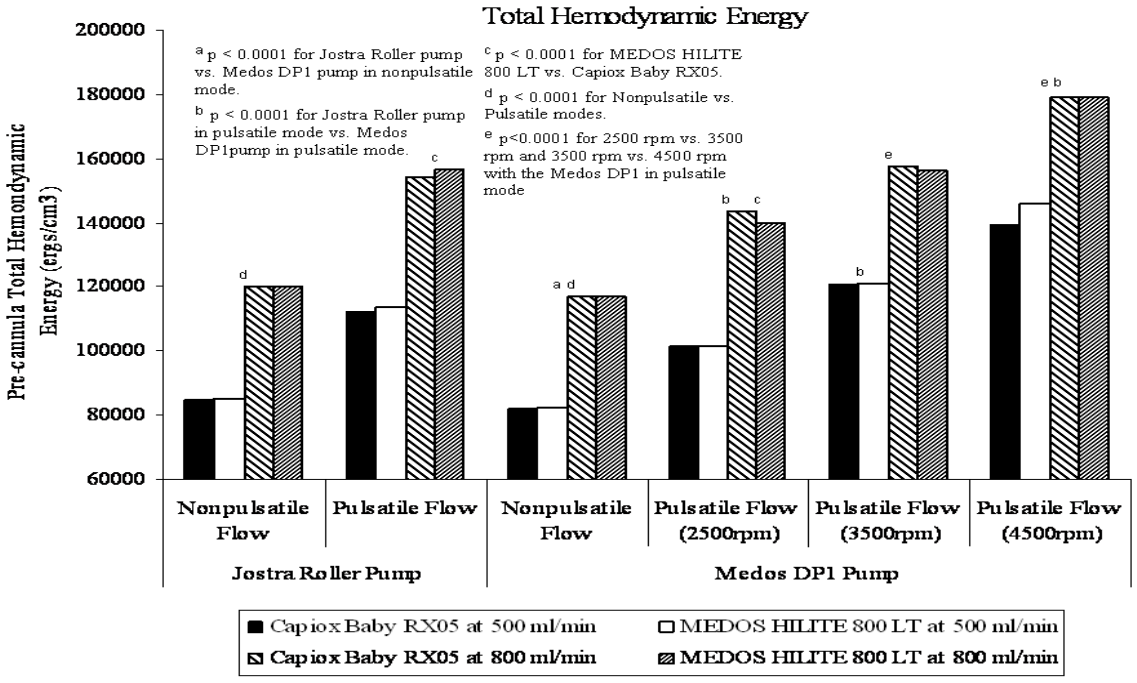
Comparison of Pumps and Oxygenators with Pulsatile and Nonpulsatile Modes in an Infant Cardiopulmonary Bypass Model

Nikkole Haines, BS, Shigang Wang, MD, John L. Myers, MD, Akif Ündar, PhD
Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering,
Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
We investigated the effect of circuit components on the quality of pulsatility delivered throughout an infant cardiopulmonary bypass model.

Methods:
We compared two bloodpumps, the Jostra HL-20 heart-lung machine and the MEDOS DELTASTREAM® DP1 Bloodpump, and two oxygenators, the Capiox Baby RX05 and the MEDOS HILITE® 800LT, in terms of mean arterial pressure, energy equivalent pressure, surplus hemodynamic energy, total hemodynamic energy, and pressure drop over the oxygenators using a blood analog. The components were combined in unique circuits and tested in nonpulsatile and pulsatile modes, at two flow rates (500 and 800 ml/min), and three rotational speed differentials when using the MEDOS DP1 for 144 trials in total.

Results:
The Jostra pump produced some pulsatility in nonpulsatile mode and better pulsatility in pulsatile mode than the MEDOS DP1 at a rotational speed differential of 2500 rpm, but not at 3500 or 4500 rpm. The MEDOS DP1 produced almost no pulsatility in nonpulsatile mode. Pressure drops over the Capiox RX05 were markedly higher, at 92.5 ± 0.4 mmHg with the MEDOS DP1 at 800 ml/min and 4500 rpm in pulsatile mode, than those over the MEDOS 800LT oxygenator, which was 67.0 ± 0.1 mmHg at the same settings. Total hemodynamic energy results at the pre-cannula site are shown below.



Conclusions: These results suggest that careful selection of each circuit component, based on the individual clinical case and component specifics, are necessary to achieve the best quality of pulsatility.

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Impact of the Post-Pump Resistance on Pressure-Flow Waveform and Hemodynamic Energy Level in a Neonatal Pulsatile Centrifugal Pump

Shigang Wang, MD, Nikkole Haines, BS, J. Scott Richardson, Kurt A. Dasse, Ph.D, Akif Ündar, PhD

Pediatric Cardiac Research Laboratory, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study was to test the impact of different post-pump resistances on pulsatile pressure-flow waveforms and hemodynamic energy output in a mock extracorporeal system.

Methods:
The circuit was primed with a 40% glycerin-water mixture and a PediVAS™ centrifugal pump (Levitronix LLC, Waltham, MA, USA) was used. The pre- and post-pump pressures and flow rates were monitored via a data acquisition system. The post-pump resistance was adjusted using a Hoffman clamp at the outlet of the pump. Five different post-pump resistances and five rotational speeds were tested with non-pulsatile (NP: 5000 RPM) and pulsatile (P: 4000 RPM) modes.

Results:
No backflow was found when using pulsatile flow. With isoresistance, increased arterial resistances decreased pump flow rates (NP: from 1,912 ml/min to 373 ml/min; P: from 1,485 ml/min to 288 ml/min), increased post-pump pressures (NP: from 333 mmHg to 402 mmHg; P: from 223 mmHg to 274 mmHg) and increased hemodynamic energy output with pulsatile mode (see Table 1). Pump flow rate correlated linearly with the rotational speed of the pump (RPMs), whereas post-pump pressures and hemo-dynamic energy outputs showed curvilinear relationships with RPMs. The maximal pump flow rate also increased from 618 ml/min to 4,293 ml/min with pulsatile mode and from 581 ml/min to 5,665 ml/min with non-pulsatile mode.

Table 1. The ranges of flow rates, outlet pressures and surplus hemodynamic energy values with pulsatile (P) and non-pulsatile (NP) modes at different resistances (R).

Groups	Flow rate (ml/min)		Pressure (mmHg)		SHE (ergs/cm^3)	
	NP	P	NP	P	NP	P
R1	201.3 - 1912.1	215.0 - 1485.4	14.6 - 333.3	15.7 - 223.9	0.0 - 0.4	853.2 - 30560.3
R2	207.3 - 1128.0	217.8 - 852.1	32.6 - 373.1	35.8 - 253.0	0.1 - 1.0	4089.0 - 41445.7
R3	206.3 - 716.5	214.0 - 539.5	59.5 - 389.6	65.6 - 265.1	0.3 - 1.1	9426.1 - 47663.2
R4	200.3 - 500.8	205.6 - 380.0	95.3 - 398.0	104.5 - 269.8	0.3 - 3.7	17604.0 - 53266.3
R5	199.4 - 373.1	203.4 - 288.4	139.5 - 402.2	152.1 - 274.0	1.6 - 3.9	29338.4 - 60430.4

Conclusions:
The results of this study showed that higher post-pump resistance reduced the pump flow range, and increased post-pump pressure and surplus hemodynamic energy output with pulsatile mode. Higher rotational speeds also generated higher pump flow rates, post-pump pressures and increased pulsatility.

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Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Endothelium NO release during cardiac surgery: comparison between continuous and pulsatile flow cardiopulmonary bypass.

G. Faggian[1], E. Lanzarone[2-3], F. Gelmini[4], A.C. De Prati[5], M. Tessari[1], T. Menon[1], H. Suzuki[5], M. Carini[4], R. Fumero[2], G.B. Luciani[1], M.L. Costantino[2].

Div. of Cardiac Surgery, University of Verona[1]; Dept. Structural Engineering[2] and Bioengineering[3], Politecnico Milan; Chemical-Pharmaceutical Institute, University of Milan[4]; Dept. Morphological and Biomedical Sciences, University of Verona[5]; Italy.

Purpose:

Reduced NO release has been associated with vasoconstriction and poor organ perfusion during CPB. Aim of the study was to compare endothelial NO release in patients undergoing continuous or pulsatile flow CPB.

Methods:

Eighteen patients having elective CABG were assigned to either continuous (Group 1) or pulsatile (Group 2) CPB. Exclusion criteria were: diabetes, peripheral vascular disease, redo, associate procedures, LVEF <50%, intra- and post-operative complications requiring vasoactive drugs. CPB was established using a roller pump and ½" silicon tubing. The non continuous flow of the pulsatile group was obtained by means of the S3 Pulsatile Flow Control (Stöckert, München, Germany) connected to the pump, by imposing three parameters: simulated frequency; pulse duration; basal flow. Blood samples were drawn after anesthesia induction (PRE), 10 min after start of CPB (INTRA) and 1 hour after operation (POST): plasma was used for detection of NO_2^- and NO_x (NO_2^- + NO_3^-) concentration, while cellular component for evaluation of NOS activity in erythrocytes (eNOS), using a high sensibility chemiluminometer.

Results:

There was no difference in age, gender, BSA, duration of surgery, supplied to nominal flow ratio. Mean systemic pressure during bypass was higher in Group 2 (68.8 ± 7.4 vs 59.4 ± 6.5, p=0.02). There was no difference between groups in eNOS at any of the time points. However, intraoperative NO_2^- and NO_x were significantly lower than preoperative in Group 1 patients (Table).

NO_2^-	PRE	INTRA	POST	p
Group 1	100.0±0.0	88.2±10.9	92.8±17.3	0.01
Group 2	100.0±0.0	105.7±16.7	104.9±10.8	0.36
NO_x				
Group 1	100.0±0.0	77.8±19.0	82.4±20.5	0.01
Group 2 CPB	100.0±0.0	90.8±12.5	88.6±16.1	0.05

Conclusions:

Pulsatile CPB is associated with preservation of NO release. Considering eNOS is unchanged, NO release seems to be of endothelial origin. These findings may have relevant clinical implications in terms of vascular tone regulation and end-organ perfusion during cardiac surgery.

Challenges in International Heart Surgery: Massive Air Embolism of Unusual Origin and Requirement for Modification of Standard Algorithms and Procedural Checks

Joseph Borondy, Peter Allen, Qasim Simmons, Carmen Giacomuzzi, Victor Carcioppolo, Scott Snider, Tom Pezzella, Dan Woodward, Karl Welke, A.Marath
St. Francis Heart Hospital, Indianapolis, IN

Objective:
The need to provide cardiac surgery in developing countries continues to grow. There are many organizations that have assisted countries in establishing programs for cardiac intervention. In conducting international cardiac surgery, an unanticipated intraoperative perfusion complication encouraged us to review procedure and equipment checks for perfusion management when standards of excellence are not available. We describe the index case, contrast it to a similar case in a mature program and detail our response: pediatric perfusion protocols, specific for developing programs.

Methods:
Case 1. occurred in an advanced cardiac center: blood-air foam penetrated the oxygenator's air/oxygen inflow line. During hypothermic arrest, oxygenator substitution permitted continuation of the surgical procedure without adverse outcome. An oxygenator design moulding fault was confirmed.

Case 2. occurred during an international start up program, using donated equipment that included a single air circuit alarm. Suddenly, massive air entered the oxygenator. Despite retrograde cerebral perfusion and satisfactory heart procedure, brain damage and death occurred. The oxygenator was faultless; a malfunctioning oxygen tank regulator valve was confirmed.

Results:
These experiences with divergent outcomes in contrasting settings motivated us to develop a modified algorithm for pediatric perfusion management which specifically addresses: numerical unit value differences, sterility, un-contaminated blood availability, room temperature and humidity, atmospheric pressure differences in various geographical locations, quality checks on donated equipment, safety protocols, documenting non-availability of equipment, and counter measures to prevent air/oxygen inflow disasters using modified circuitry to ensure controlled delivery when tank gas air/oxygen is used.

Conclusion:
Protocols assist compliance with international standards in developing programs. They also reduce ethical concerns about operating or withholding surgery, team dynamics, unfamiliar settings, language barriers and when procedural missteps are possible.

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Force Reflecting Teleoperation for a Robotized Laparoscopic Gripper System

[1]Jaesoon Choi, PhD, [2]Jun Woo Park, PhD, [2]Du Jin Bach, MS, [2]Duck Hee Lee, MS, [1]Jung Joo Lee, PhD, [1]Kyung Sun, MD, PhD, MBA
[1]Korea Artificial Organ Center, College of Medicine, Korea University, Seoul, Korea
[2]Biomedical Engineering Branch, Research Institute, National Cancer Center, Gyeonggi, Korea

Purpose:
Many types of cardiac surgeries including atrial septal defect repair, mitral valve repair, coronary artery bypass are performed with surgery robot system nowadays. Robot-assisted cardiac surgery enables hand tremor filtering, enhanced ergonomics and motion scaling, which were not available in conventional MIS (Minimally Invasive Surgery). However, robotic MIS is faced with a problem that tactile information of internal organs and surgical instruments can hardly be provided to the surgeon. To overcome such limitation, a modified position error-based force feedback (PEBFF) algorithm was devised and implemented in an experimental robotized laparoscopic gripper system.

Methods:
To estimate the gripping torque of the slave, we used a contact model between the slave and the external environment using position error and its derivatives. The structure of the modified PEBFF controller is as in Fig. 1. A robotized laparoscopic gripper with a master-slave configuration, composed of a master handle and a slave instrument actuation module, has been specially devised and implemented. We performed *in vitro* experiments of gripping an artificial tissue pad with the developed gripper system.

Results:
Fig. 2 shows the result of torque tracking control at master. Master torque followed slave torque well in magnitude and trend. With this torque fed back to the master, we could detect boundaries of any object that come in contact with the slave. When the slave contacted rigid objects, the position error and its derivatives were larger than those of an elastic tissue pad. We could also feel the difference between rigid and elastic objects. However, the sensitivity needs to be improved further.

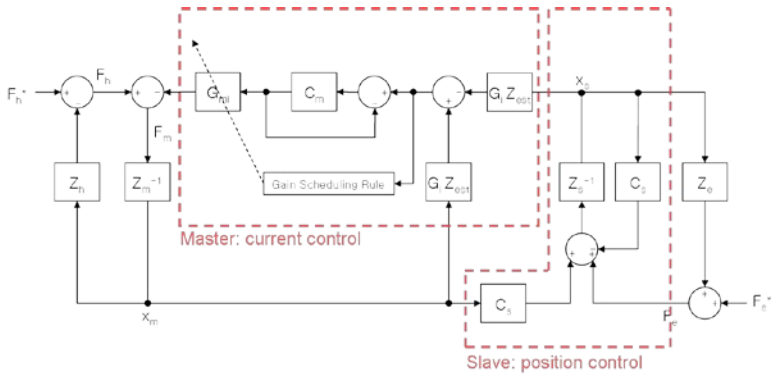

Fig. 1. Modified PEBFF control scheme

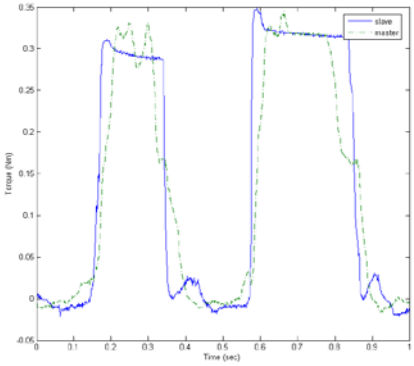

Fig. 2. Torque tracking performance

Conclusions:
A modified PEBFF algorithm was developed, implemented and evaluated with a robotized laparoscopic gripper system. Results from in vitro experiments showed acceptable performance in detecting boundaries of an object and softness discrimination.

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Hemodynamics of Sequential Coronary Bypass Grafting Configurations via Sketch-Based Surgical Planning Tool

Onur Dur (1), Sinan Tolga Coskun (2), Kasim Oguz Coskun (3), Levent B. Kara (1), Kerem Pekkan (1)
1) Departments of Biomedical and Mechanical Engineering, Carnegie Mellon University, Pittsburgh, PA
2) Department of Thoracic Cardiovascular Surgery, University of Bochum, Bad Oeynhausen, Germany
3) Department of Thoracic Cardiovascular Surgery, University of Göttingen, Göttingen, Germany

Purpose:
This study aims i) to analyze the hemodynamic efficiency of the sequential grafting from left anterior descending artery (LAD) to obtuse marginal (OM) i.e. raising a daughter parallel branch from the parent coronary artery bypass graft (CABG) beneath the occluded artery section, ii) to compare the efficiency of sequential grafting strategy to single coronary artery bypass grafts (CABG) i.e. end-to-side anastomosed to left anterior descending artery (LAD) and obtuse marginal (OM).

Methods:
The LAD CABG initiates from the ascending aorta and anastamosed to the native coronary artery distal to the stenosed region. The proximal and end anastomosis locations are selected according to the surgical settings of an actual proximal LAD grafting performed in bovine heart (Fig.1). The 3D sequential graft between the LAD and OM is created by mimicking the actions of the surgeon in the operating room using the first version of an in-house anatomical editing and surgical planning tool. Efficiency of each LAD, OM and sequential graft designs is evaluated using experimentally validated 2nd order computational fluid dynamics (CFD) solver of Fluent (ANSYS Inc, PA) incorporating impedance based outlet boundary conditions to simulate pulsatile coronary blood flow.

Results:
Preliminary results with single LAD grafting indicate that the energy dissipation and vorticity inside the graft decreases about 20% from arbitrary suboptimal to optimal configurations. In addition, LAD flow rate calculated through steady state 3D simulations of native coronary circulation agrees well with the previous ultrasound angiography measurements conforming the accuracy of the framework.

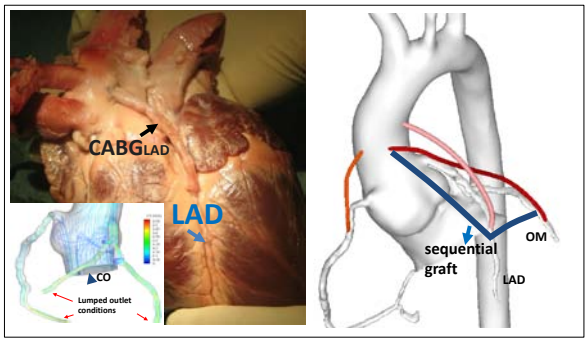

Fig. 1 Simulated LAD CABG operation [left], 3D CFD model (insert), 3D LAD CABGs and sequential grafting created by the anatomical editing tool [right]

Conclusions:
This study, for the first time, investigates the hemodynamic efficiency of sequential coronary bypass grafting strategies by coupling our *in-house* 3D sketch based surgical editing tool and CFD. Our preliminary results suggest that the bulk shape of the CABG design is critical for increased energy efficiency inside the CABG which enables better coronary perfusion due to the decreased vascular resistance of the graft geometry.

The Penn State Pediatric VAD: Five Year Development Status

William J. Weiss, Ph.D., Gerson Rosenberg, Ph.D., J. Brian Clark, M.D., Elizabeth Carney, D.V.M., Christopher A. Siedlecki, Ph.D., Dennis Hicks, John Reibson, Branka Lukic, M.S., Rebecca Peterson, Eric Yeager, Brad Doxtater, Timothy Cooper, D.V.M., Keefe B. Manning, Ph.D., Steven Deutsch, Ph.D., James P. Runt, Ph.D., John Myers, M.D., William S. Pierce, M.D.
Departments of Surgery, Bioengineering, Pediatrics, Comparative Medicine, and Materials Science and Engineering, The Pennsylvania State University, Hershey and University Park, Pennsylvania, USA

Purpose:
Penn State has developed a pulsatile pneumatic sac-type Pediatric Ventricular Assist Device based on the design of the adult-sized Pierce-Donachy (Thoratec®) VAD. The Pediatric VAD exists in two sizes: an Infant VAD with a dynamic stroke volume of 12-14 ml, and a Child VAD with a 25-30 ml stroke volume. At the completion of the five-year NHLBI Contract Program NHLBI-HV-04-01 "Pediatric Circulatory Support ", we have completed the design requirements, pump and cannula design, and initial process development.

Methods:
The primary design objective has been to produce a device with a low thrombogenic risk. This is especially challenging since the fluid mechanics in small-scale devices favor low wall shear rates and have a higher propensity for clot formation, relative to adult-sized devices. We have therefore invested significant efforts in understanding the spatial and temporal properties of blood flow in the pump and cannulae. Special attention has been focused on the valves, since thrombosis in pediatric VADs has often been associated with this region. We have also undertaken comparative studies of commercially available segmented polyurethanes with the goals of selecting the least thrombogenic blood contact material (through *in vitro* coagulation and platelet adhesion tests) and optimizing the fabrication process.

Results:
At the conclusion of the current contract, we have completed the design of the Infant VAD. The basic design has remained stable throughout 15 chronic *in vivo* studies. Improvements have included a new Björk-Shiley monostrut custom valve (manufactured in–house), a re-designed diaphragm, and improvements in the diaphragm and seals.

We have achieved a relevant and stable animal model in the 20-25 kg lamb, although early losses due to respiratory failure required more time and resources than originally anticipated. We have also added hematologic and platelet function assays that have contributed to a more stable anticoagulation protocol. The results of the 15 chronic studies, especially the 6 most recent studies, have demonstrated healthy survival to the desired duration of 4 weeks. Clinical evidence of thromboembolism (stroke) occurred in one early case which was likely due to a dislodged intraventricular thrombus related to the design and placement of the cannula. Excellent results have been maintained in the most recent animals in which we have reduced the level of heparin anticoagulation. The heparin dose has been reduced in the most recent animals, and antifactor-Xa assays have confirmed low levels of heparin activity. Platelet suppression has not been used.
A new portable pneumatic driver is currently under development.

Conclusions:
The Penn State Pediatric VAD has demonstrated low thrombogenic risk in animal studies. The research and development activities have been carried out under Quality System Regulation (QSR) guidelines, with special emphasis on developing the design history, and manufacturing processes and documentation, required for manufacturing scale-up and a future IDE submission.

Fifth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

In vivo Evaluation of the PediaFlow™ Pediatric Ventricular Assist Device

Peter D. Wearden, MD, PhD[1], Timothy M. Maul, PhD[1,2], Ergin Kocyildirim, MD[1], Amanda R. Daly, BS[2], Carl A. Johnson Jr., BS[2], Joshua Woolley, BS[2], Brad Paden, PhD[4], Dave Paden, BS[4], Shaun Snyder, BS[4], Josiah Verkaik, BS[4], James F. Antaki, PhD[3], Fangjun Shu, PhD[2], Gil Bearnson, PhD[5], John Kirk, MS[5], Pratap Khanwilkar, PhD[5], Marina Kameneva, PhD[2], William R. Wagner, PhD[2], Harvey S. Borovetz, PhD[2], and the PediaFlow Consortium[1-5]

Cardiothoracic Surgery, Children's Hospital of UPMC[1]; Bioengineering, University of Pittsburgh[2] and Carnegie Mellon[3]; LaunchPoint Technologies Inc.[4]; and WorldHeart Inc[5], USA

Purpose:
Our consortium is developing a miniaturized, fully implantable, magnetically levitated ventricular assist device (VAD) for neonatal and pediatric patients (3-20kg) in cardiac failure. We report here recent *in vivo* results for the PediaFlow VAD in a pre-clinical ovine model. The planned implantation times were 30 and 60 days to correspond with a 6 month anticipated patient use.

Methods:
Three pumps were implanted in juvenile lambs (30-40kg) via left, fourth interspace thoracotomy. The inlet conduit was a modified 18fr. Medtronic DLP cannula inserted into the left ventricle through a stab incision and secured with a sewing ring. The outflow graft was a modified 18fr. Medtronic EOPA cannula inserted into the descending thoracic aorta. The animals received IV Coumadin (INR >2.0) and daily monitoring for plasma free hemoglobin (pfHb), platelet activation (measured by flow cytometry), and serum chemistries. Pump parameters and flow estimation were recorded on a data acquisition system throughout the implants. At explant, a full post-mortem analysis was performed along with histologic analyses.

Results:
Post-operative fibrinogen and platelet activation demonstrated expected post surgical increases before returning to near baseline values. Hematocrit and pfHb remained at baseline values throughout the studies. Serum chemistries (including kidney and liver function) remained within normal limits. One implant was terminated at 17 days due to driveline failure. Two implants survived to planned experimental termination at 30 and 70 days. Post-mortem analysis: no thrombus within the pump and usual ring thrombus at connection sites. Gross and microscopic examination revealed no cardiac or pulmonary changes. A single kidney of each animal demonstrated minor cortical infarction.

Table 1. Biocompatibility results for the PediaFlow VAD. Values are presented as mean ± SD with baseline values in parenthesis

Implant Number (Flow Rate)	Study Length	Hematocrit (%)	pfHb (mg/dL)	Fibrinogen (mg/dL)
1 (1.5 L/min)	**17 days**	26.1 ± 2.8 (24.0)	6.5 ± 1.4 (10.7)	431 ± 139 (270)
2 (1.5 L/min)	**30 days**	24.5 ± 2.8 (24)	10.7 ± 4.0 (16.6)	303 ± 140 (230)
3 (0.5 L/min)	**70 days**	33.7 ± 4.3 (33)	11.0 ± 2.8 (14.4)	222 ± 89 (140)

Conclusions: Our *in vivo* results for the PediaFlow VAD demonstrate excellent blood biocompatibility over a range of pediatric flow rates for prolonged implant times. A third design evolution (approximately the size of an AA battery) is currently undergoing *in vivo* testing.

Development progress of the Ension pediatric cardiopulmonary assist system (pCAS)

Mark Gartner, Ph.D., Greg Johnson, Ph.D., Patrick Cahalan, B.S., *John Biggerstaff, Ph.D., **George Pantalos, Ph.D.
Ension, Inc., Pittsburgh, Pennsylvania, USA, *University of Tennessee, Knoxville, Tennessee, USA, **University of Louisville, Louisville, Kentucky, USA

Purpose:
Ension, Inc. is developing a cardiopulmonary assist system (pCAS) designed to support pediatric patients up to 25 kg requiring extracorporeal membrane oxygenation (ECMO). pCAS addresses shortcomings associated with current ECMO systems focusing particularly on improved blood compatibility, functionality, and reduced system complexity.

Methods:
The pCAS pump-oxygenator is comprised of a centrifugal blood pump integrated with a high-efficiency oxygenator driven by a controller console providing power and user interface functions. Computer aided modeling, finite element-based stress analyses, and computational fluid dynamics techniques were utilized in the design of the blood-contacting pump-oxygenator. The engineered bioactive surface incorporated in the pCAS is intended to mitigate adverse reactions to device surfaces and the need for high levels of anticoagulation. In vitro testing has included extensive mock circulatory loop evaluations for blood compatibility using both animal and human blood-based assays. In vivo testing has included piglets (acute) and calves (chronic) to evaluation hemodynamic functionality and long-term blood compatibility.

Results:
Data from a total of 24 animal experiments, as well as *in vitro* testing in mock circulatory loops, has demonstrated adequate blood flow and gas transfer. In vitro blood compatibility testing of Ension's bioactive surface using both animal and human blood has shown significant improvements in multiple bio-markers when compared to untreated controls. These *in vitro* results have been corroborated in 3 day *in vivo* calf studies.

Conclusions: The ability of the pCAS to provide the necessary cardiopulmonary support for the intended patient population has been demonstrated. In vitro and in vivo results strongly suggest that blood compatibility will be significantly enhanced.

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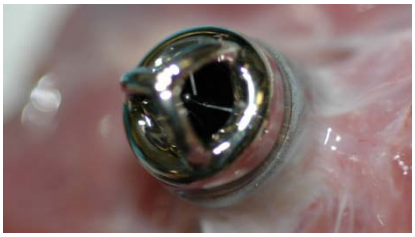
Summary at Completion of the Jarvik 2000 NIH Pediatric Development Program

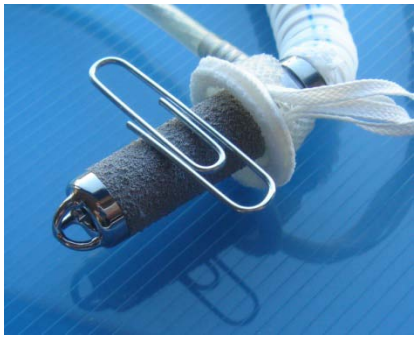
Robert Jarvik, MD, Zhongjun Wu, PhD., Craig Sherman, Latha Kavala, and Bartley Griffith, MD.
Jarvik Heart, Inc., New York, New York, and the University of Maryland, Baltimore, MD.

Program Objective:
The program developed small versions of the intra-ventricular Jarvik 2000 Heart for children and infants. The goal was to complete the child size model and demonstrate feasibility of the infant model.

Methods:
Scaled down versions of the adult model were developed and tested using pin in sleeve bearings. Numerous designs were analyzed and tested. Heat, wear, and power were measured. Tissue deposition on the bearings was analyzed. A special controller with higher motor torque was developed. All these efforts produced excellent *In Vitro* results but failed *In Vivo*. We then initiated a new type of bearings. Cone bearings support a tapered shaft on the tips of three streamlined posts using high precision ceramic components. Child and infant pumps were redesigned with cone bearings, and tested in sheep. Infant pump development work was increased to achieve a finished device design.

Results:
The pin bearing child models failed in sheep in about a month due to bearing thrombus and rotor seizure. The pin bearing infant pump failed sooner. The cone bearings remained clean at 60 days, when an inflow cage was used to prevent occluding the opening and infection was avoided. The longest pump on durability test has now exceeded 9 months. Computational bearing analysis predicts durability of decades. A new pediatric controller with integrated batteries, child lock features, and programmable speed settings operates up to 40,000 RPM.





The Infant Jarvik 2000

Specifications of the Adult and Pediatric Jarvik 2000 Blood Pumps

Jarvik 2000 Size	Diameter (mm)	Length (cm)	Volume (cc)	Weight (g)	Priming Vol (cc)	Aortic Graft (mm)	Speed (RPM)	Flow L/min
Adult	26	7.8	30	90	7	16	8-14,000	1-10
Child	18	5.9	12	35	4	10	10-18,000	½ - 5
Infant	10.5	5.2	4	11	1	6 or 8	20-40,000	¼ - 4

Conclusions:
Both the child and infant size pumps have been successfully developed. In the final year of the program we have emphasized the infant size pump and completed the system design. The infant model can be run over a very wide speed range to provide sufficient flow for tiny newborns on up to teenagers.

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The PediPump: A Versatile, Implantable Pediatric Ventricular Assist Device—Update IV

Brian W. Duncan, M.D., M.B.A., Kiyotaka Fukamachi, M.D., Ph.D., Lawrence D. Noble, Jr., M.S., David T. Dudzinski, B.S., Christine R. Flick, B.S., Hideyuki Fumoto, M.D., Akira Shiose, M.D., Ph.D., Yoko Arakawa, M.D., Tohru Takaseya, M.D., Ph.D., Fernando Casas, Ph.D., William A. Smith, D.Eng.
Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, USA

Introduction:
The PediPump™ is a ventricular assist device in development at the Cleveland Clinic designed for the support of pediatric patients. The development program currently is completing the fifth and final year of funding by the National Heart, Lung and Blood Institute's Pediatric Circulatory Support Program (PCSP).

Methods:
The basic design of the PediPump has remained unchanged throughout the funding period and is a mixed-flow ventricular assist device with a magnetically suspended impeller (Figure 1). The bulk of the testing of the program has been done with the third-generation or Mark III pump; however, the latest iteration is the Mark IV pump, which employs fewer magnet rings in the bearings. The pump measures 10.5mm at the outlet diameter by 67 mm in length; further size reductions are possible with new hardware providing a motor lead exit point closer to the impeller.

Results:
Progress and achievements for the PediPump program can be considered according to the three Specific Aims of the original PCSP proposal:

- Basic engineering: Along with size reductions, substantial design improvements have been incorporated in each iteration of the design, including the magnetic bearings, axial touch points, motor and heat transfer path. In addition, the overall assembly has been made easier and more reliable. Nine Mark III and five Mark IV pumps have been or will be produced to support current and planned in vivo and in vitro studies. Two Mark III pumps are running on endurance tests, which in mid-February 2009 have exceeded 3,400 and 2,300 hours without problems.
- Anatomic modeling and device fitting studies: We have developed CT and MRI based techniques for anatomic modeling and device fitting to facilitate device implantation. Using these techniques, we can perform on-screen virtual fitting and can create physical models (biomodels) for children of various sizes and anatomic subtypes to assist in preoperative planning. Currently, these techniques are being validated by intraoperative fitting studies using device mock-ups in pediatric cardiac surgical procedures.
- In vivo testing: To date, six acute (six-hour duration) and nine chronic (30-day target duration) implantations have been performed in sheep. All implantations have been performed as a left ventricular assist device with cannulation of the left ventricular apex and descending aorta. Based on our in vivo tests, implantation of the PediPump appears to be relatively easy; in addition, we have observed excellent hemodynamic performance, essentially no hemolysis and minimal thrombotic deposition during support.

Conclusions:
Cleveland Clinic's PediPump program under support of the PCSP has led to the development of a pediatric ventricular assist device that has satisfactory performance during our in vivo testing program and during in vitro assessment of long-term durability. With additional refinements, the current Mark IV version of the pump fundamentally appears to be ready to support a program of clinical testing.

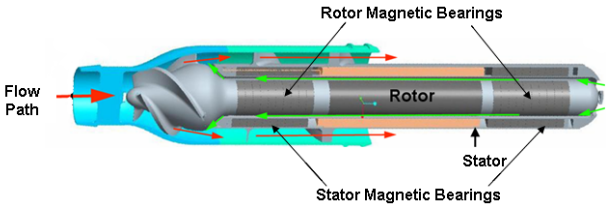

Figure 1. Mark IV PediPump demonstrating components and blood flow path.

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Animal Model Development for The Penn State Pediatric Ventricular Assist Device

Elizabeth L. Carney, DVM, John L. Myers, MD, J. Brian Clark, MD, Rebecca Peterson, BS, Ronald P. Wilson, VMD, MS, William J. Weiss, PhD
Departments of Comparative Medicine and Surgery, Penn State College of Medicine and Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
In March 2004, the National Heart, Lung, and Blood Institute (NHLBI) awarded five contracts to develop devices providing circulatory support for infants and small children with congenital and acquired cardiac disease. Since 2004, the team at Penn State College of Medicine has developed a pneumatically-actuated ventricular assist device (VAD) with mechanical tilting disk valves and 12 ml stroke volume. To date, hemodynamic performance, thrombogenesis, and hemolysis have been evaluated in 16 animals.

Methods:
Sheep (16-25 kg, Dorset-Finn, either sex) were obtained from a purpose-bred flock. Venous access was established 2 wk prior to surgery to allow for hematology and thromboelastography (TEG) studies, as well as fluid therapy. One hour prior to surgery, cefazolin was administered intravenously (IV). Anesthesia was induced using midazolam and ketamine IV, followed by intubation and mechanical ventilation using 1% isoflurane in 60-80% oxygen. A triple lumen, long-term intravenous catheter was placed in the left jugular vein, allowing intraoperative continuous rate infusion (CRI) of fentanyl, lidocaine, lactated ringers solution, and heparin. Intraoperative monitoring included arterial blood pressure and blood gas, body temperature, central venous pressure, ECG, end tidal CO_2, heart rate, O_2 saturation, tidal volume, and lung compliance. Periodic deep sighs were given manually to re-inflate collapsed lung and prevent atelectasis. Following VAD implantation, two large bore chest tubes were placed in the right and left thoracic cavity. During closure of the left thoracic wall, a wound diffusion catheter was incorporated into the deep muscle layer, and 5 ml of Bupivicaine was instilled into the catheter. Fentanyl CRI was discontinued during closure of the incision, and IV buprenorphine and flunixin meglumine were administered. Ventilator support was provided as needed until extubation. Arterial blood gas readings were used to assess oxygenation and acid-base status. Analgesia (buprenorphine and flunixin meglumine IV and bupivicaine instilled in the wound catheter) was given for 72 hr and then gradually discontinued. Antibiotic therapy (cefazolin or ciprofloxacin IV) was continued for a minimum of 7 days. Fluid therapy was gradually decreased from 2x to 0.5x maintenance, to promote oral water intake. Hay and grain were offered *ad lib.*, and oral probiotic was administered once daily to promote optimal rumen function. Unfractionated heparin CRI was administered to maintain a clotting time 2x normal, as measured by TEG, and a PTT of 1.5x normal. Twice weekly hematologic studies included CBC, serum chemistries, PTT, fibrinogen, anti-factor Xa, and platelet aggregation. Daily nursing care was applied to incision, catheter, and chest tube sites.

Results:
Time after implant has ranged from 0-40 days. Respiratory, renal, and hepatic failure; infection; and adverse pump events have been the main obstacles to success. Most recently, a male sheep implanted with Version 3 Infant VAD was electively terminated at 35 days post-implant, with no major adverse events.

Conclusions:
Establishing a reliable, reproducible animal model closely representing the human condition is critical to moving a medical device from the benchtop to clinical trials. We have chosen juvenile sheep < 25 kg in order to 1) match the cardiac output of the intended human recipients and 2) allow for management of a chronically instrumented animal. Development of the animal model has progressed alongside device development and refinement, leading to recent successes.

FDA's Current Thinking on Clinical Trial Design and Patient Evaluation for Pediatric MCSDs

Sonna Patel-Raman, Ph.D., Kathryn O'Callaghan, B.S., Eric Chen, M.S., Matthew Hillebrenner, M.S.E.
Division of Cardiovascular Devices, Center for Devices and Radiological Health, Food and Drug Administration, Rockville, MD 20850

Purpose:
In the pediatric heart failure arena, the United States Food and Drug Administration (FDA) recognizes that there are multiple challenges for developing clinical trial designs and patient evaluations for mechanical circulatory support device evaluation (MCSDs). Today, stakeholders including the FDA, National Institutes of Health (NIH), medical device industry and the clinical community are working together to develop reasonable pathways for the evaluation of pediatric MCSDs.

FDA's Current Thinking
The design of adequate pediatric clinical trials for MCSD remains a complicated issue due to several challenges, such as: 1) limited study population, 2) development of clinically meaningful endpoints, 3) tools for assessing quality of life and neurological outcomes, 4) ethical issues of investigational studies in the pediatric population, and 5) heterogeneity of disease etiology.

The FDA anticipates the initiation of clinical trials to meet the critical need of MCSDs for pediatric heart failure patients in the near future. As a result of the limited study population, FDA acknowledges the difficulty of conducting randomized trials to assess either safety and effectiveness for pre-market approval or safety and probable benefit for humanitarian device exemption. To address complexities related to clinical evaluation of these patients, FDA has initiated discussions with industry and the clinical community to determine consistency of present practices for evaluation of pediatric neurological and neurocognitive deficits. At this time, there does not appear to be a consistent evaluation method.

Conclusions
As the field of MCSD evolves to include multiple options for the treatment of pediatric heart failure, FDA is committed to working with industry and the clinical community to develop creative and innovative solutions for trial design and patient evaluations.

Improvements to ECMO

Tami Rosenthal CCP, MBA
Children's Hospital of Philadelphia

Purpose
To review evolving trends of ECMO equipment and management strategies and their effect on ECMO patient care at The Children's Hospital of Philadelphia.

Discussion
In 1975, just 3 years after the first successful ECMO, there were four membrane oxygenators available for use on ECMO. This was shortly before FDA approval was required for all medical devices. Thirty-four years later one of those same oxygenators is still used for ECMO. For many years ECMO equipment and management stayed largely constant with minimal changes. Medical management continued to improve and made ECMO unnecessary for many patients. As a result of those improvements, overall ECMO survival has decreased. Those patients still requiring ECMO support are sicker and as a result have worse outcomes.

In 2002, an increase in perfusionist involvement was noted and as a result ECMO began a slow transformation. The perfusionists started to bring some of the technology used on CPB to the ECMO field. Roller pumps, which have been used for ECMO since the beginning, were starting to be replaced by centrifugal pumps. The silicone membrane was being replaced in some situations by a hollow fiber oxygenator or the new PMP membrane. Additional safety devices were added that had not been used before. Anticoagulation status and monitoring stayed constant but heparin coatings allowed for a delay in starting heparin for post cardiotomy patients with bleeding. Many different issues prompted change in centers across the U.S. adding new techniques that continue to shape ECMO programs today.

The ECMO circuit used at CHOP was relatively unchanged for almost two decades. Ongoing venous drainage issues prompted the perfusion team to get involved. In coordination with the ECMO team, perfusion introduced the Better Bladder to the CHOP ECMO circuit. There was some resistance to change and a learning curve which provided obstacles to be overcome. The result was immediate improvement and hospital wide transition to the Better Bladder. Further changes to the ECMO circuit followed and prompted a positive attitude towards any future changes.

Conclusion
The coordinated effort of perfusionists and ECMO specialists can promote change to the current systems. Many of the techniques and equipment used for CPB are applicable to the ECMO field. The benefits seen for CPB can be attained by ECMO and result in improved care for ECMO patients.

The Use of Bivalirudin/Angiomax for Pediatric Anticoagulation in HIT Patients

Richard N Gates, MD, Paul Yost, MD, Beth Parker, CCCP
Divisions of Cardiothoracic Surgery and Anesthesia, CHOC Children's, Orange County, California, USA

Purpose: Infants with heparin induced thrombocytopenia (HIT) represent a challenging and high risk group of patients when they require cardiopulmonary bypass (CPB). Bivalirudin offers many potential pharmacologic advantages over other non-heparin anticoagulants for such patients. We describe our protocol for the use of bivalirudin in a five month old infant undergoing stage two Norwood for HLHS.

Methods: The patient was a five months, six kilogram infant who developed HIT after a bowel resection complicating initial Norwood stage one. After redo sternotomy and dissection the child received an initial dose of Bivalirudin of 1mg/kg and .5 mg/kg five minutes later. The cardiopulmonary bypass circuit was primed with 50mg bivalirudin/400cc volume. With initiation of CPB a continuous infusion of 2.5mg/kg/min of bivalirudin was begun. ACT was targeted for 400s with examination prior to bypass and each 15 minutes thereafter. Bivalirudin was discontinued with separation from bypass and during modified ultrafiltration (MUF).

Results: ACT was 286 after initial 1mg/kg bolus and 597 after the second .5mg/kg bolus and initiation of CPB. At a rate of 2.5mg/kg/min ACT ranged between 461 and 597. At the completion of MUF, the ACT was 316. Twenty minutes after MUF the ACT was 214. No clots were noted in the CPB circuit and good hemostasis was achieved within 10 minutes after MUF was completed. Operative time was 160 minutes; time from completion of MUF to sternal closure was 30 minutes. Post –MUF 60cc of processed cell saver blood was re-infused and no clotting factors were required. Chest tube output was 10, 10, 3, & 4 ccs respectively at hour's 1-4 post op.

Conclusions: Bivalirudin provides effective anticoagulation for infants requiring CPB in the presents of HIT. Bivalrudin's efficacy is effectively monitored by ACT and after CPB its short half-life facilitates the ability to achieve hemostasis in a timely fashion.

Clinical real-time monitoring of gaseous microemboli in pediatric cardiopulmonary bypass

Shigang Wang, MD,[*] Karl Woitas, CCP,[†] J. Brian Clark, MD, John L. Myers, MD,[*,†] Akif Ündar, PhD[*,†,‡]
[*] Pediatric Cardiac Research Laboratories, Department of Pediatrics, [†] Surgery, and [‡] Bioengineering, Penn State Milton S. Hershey Medical Center, Penn State College Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
Gaseous microembolism can cause postoperative neurologic morbidity in children undergoing cardiopulmonary bypass (CPB). Although the extracorporeal components can remove the majority of air bubbles from the circuit, a number of microemboli escape elimination and are transmitted to the patient. In clinical practice, gaseous microemboli may play a significant and underappreciated role in the development of postoperative neurological complications. The objective of this study is to monitor the occurrence of gaseous microemboli during pediatric CPB in real-time, to seek the sources of emboli in the CPB circuit, and to compare the results of conventional transcranial Doppler (TCD) and the recently approved Emboli Detection and Classification (EDAC) Quantifier system.

Methods:
After Institutional Review Board approval, patients were selected and underwent intracardiac repair using our routine CPB circuit and techniques. The circuit was primed, deaired, and CPB established with gravitational venous drainage. Vacuum-assisted venous drainage (VAVD) was used as needed to augment drainage. EDAC utilizes an advanced ultrasound technique to detect and classify gaseous microemboli as small as 10 microns in real-time. EDAC quantifiers were positioned on the venous line and on the post-filter arterial line, and a TCD probe was positioned on the right middle cerebral artery.

Results:
Four pediatric patients (weights 3.2-13.8 kg) were studied. VAVD was used in all patients. Three patients survived to hospital discharge, and no patient showed evidence of adverse neurological event. Before the initiation of CPB, gaseous microemboli were detected in two cases when giving volume through the arterial line. Within the first 5 min of CPB, air appeared in the venous line and gaseous microemboli were detected in the arterial line in all patients. Gaseous microemboli were also found during the aortic clamp interval. During post-CPB modified ultrafiltration, gaseous microemboli were detected when giving volume through the arterial line. Overall, there were 3,192-14,699 gaseous microemboli detected in the arterial line during CPB, more than 99% of which were smaller than 40 microns.

Conclusions:
Significant amounts of gaseous microemboli originate from the CPB circuit. Although EDAC and TCD both use ultrasound to detect microemboli, EDAC can provided increased detection of gaseous microemboli. EDAC detected a larger number of gaseous microemboli in the arterial line than were detected by in the middle cerebral artery by TCD, likely reflecting the different sensitivities of the two devices. Conventional TCD cannot detect emboli below 40 microns, and cannot classify emboli by size. A dual-modality monitoring approach with both EDAC and TCD should provide the best available technology for the detection of gaseous microemboli in the extracorporeal circuit and the cerebral circulation. Using EDAC and TCD together could strengthen the monitoring of gaseous microemboli, which could lead to better techniques to minimize embolism and improve neurologic outcomes.

Pediatric Myocardial Protection and Single Dose Cardioplegia

Richard M. Ginther, Jr., CCP
Division of Pediatric Cardiothoracic Surgery, UT Southwestern Medical Center
Children's Medical Center of Dallas, Dallas, Texas, USA

Myocardial protection strategies and cardioplegia solutions have been studied for over fifty years. Despite extensive experimental models supporting various techniques, myocardial protection remains dependent on clinician experience. The structural and physiologic differences between immature and mature myocardium further complicate the efforts to attenuate ischemic injury. The Children's Medical Center of Dallas uses a cold, 1:4 [Blood:Crystaloid], high potassium, single dose cardioplegia solution. Ischemic times up to three hours and normal heart function following the removal of the aortic cross clamp have been observed using our single dose technique. This simple and inexpensive cardioplegia solution is an effective pediatric myocardial protection routine.

Myocardial recovery and retraining of the ventricular with ECMO after arterial switch operation

FENG Zhengyi , LONG Cun, LIU Jingpin, ZHAO Ju
Department of Extracorporeal Circulation,Fu Wai Hospital ,CAMS & PUMC,Beijing,100037 CHINA

Purpose:

Extracorporeal membrane oxygenation (ECMO) has been successfully used for circulatory and respiratory support post-operative, we reviewed the experience of myocardial recovery and retraining of the ventricular with cardiac failure after arterial switch operation (ASO) in FUWAI hospital.

Methods:

From January 2005 to August 2007,nineteen consecutive congenital heart disease patients (age 3 days to 4 years)who underwent cardiopulmonary dysfunction were rescued with ECMO, Heparin coated tubing and oxygenator were employed (Minimax Ox+Biomedicus centrifugal pump 13 cases,Jostra Ox+ Rotaflow centrifugal pump 5cases and Lilliput Ox+ Rotaflow centrifugal pump 1 cases)all patients applied veno-artery(V-A) ECMO with drainge from right atrium and perfusion via ascending aorta by sterntomy .Blood flow rate was 20-150ml/kg and ACT maintained 130-210sec.

Results:

The duration of ECMO was 64-366hrs ,There were 12 cases weaning from ECMO successful (63.2% ,12/19), and 9 patients were survival to hospital discharge (47.4% ,9/19).Eight ASO cases of which could not wean from ECMO even if 'monitoring parameter', including myocardial enzyme ,stable hemodynamic ,Lac+, urine,and X-ray recovery to normal.ECMO ran more extra-assist time (96±56 hrs) to retrain LV until these patients separated from ECMO. During retraining, maintained the flow rate 20-50ml/kg , MAP 56-70mmHg,CVP 6-9cmH_2O and LAP 6-10cmH_2O.

Conclusions:

ECMO can offer the effective circulatory support for patients underwent the arterial switch operation with ventricular dysfunction to ensure a successful postoperative myocardial recovery.also ECMO play the role of LV retraining in 'unprepared' TGA after ASO.

Ecuador Hearts: The Penn State Milton S. Hershey Medical Center Experience

Robert K. Wise, CCP, Robert M. McCoach, CCP, Larry D. Baer, CCP, John L. Myers, MD, J. Brian Clark, MD
The Penn State Milton S. Hershey Medical Center, Penn State Children's Hospital, Hershey, PA 17033

For the past ten years the Children's Heart Group, Penn State Hershey Medical Center has traveled to the Roberto Gilbert Elizalde Hospital de Ninos, in Guayaquil, Ecuador providing cardiac surgery to children of the region. In conjunction with the surgeries, our aim is to provide additional training in the diagnosis and treatment of congenital heart disease to the local physicians and staff, so that they are better able to serve their community. The group is partnered with Variety International's Lifeline program, which provides monetary assistance for the mission.

The multi disciplinary team of surgeons, anesthesiologists, cardiologists, intensivists, perfusionists, and nurses (OR, ICU) has grown in both number and capabilities over the past decade. The most recent trip in November, 2008 was spread over 20 days and included 50 people. This trip included the first time use of intra operative neuro-monitoring and several cases were able to be performed in the electrophysiology lab.

Guayaquil is Ecuador's largest city, having an estimated population of just under 3 million people While the city is the country's financial hub and has many modern buildings and amenities, the majority of the population lives in poverty. Most do not have any form of insurance and cannot afford basic health care therefore the ability to get open heart surgery is nearly impossible. Over the past ten years we have been able to perform surgery on 200 children, at little or no cost to the families.

Despite our longevity in conducting the mission, several challenges arise each year. They range from the language barrier, increased difficulty in obtaining the required supplies, increased paperwork to transport the equipment, equipment failure, and unusual conditions of the children. It is hard to anticipate many of these challenges, however, you must be prepared for everything. Even with the difficulties that can arise, the trip continues to be a worthwhile and rewarding endeavor.

Development of Mechanical Circulatory Support Devices in China

Wei Wang, MD, PhD, Deming Zhu, MD, Wenxiang Ding, MD.
Shanghai Children's Medical Center, Affiliated by Shanghai Jiaotong University, School of Medicine

The failing myocardium producing low cardiac output syndrome is a common clinical pathophysiologic state. Currently, use of mechanical circulatory support is an essential aspect for treatment of the patients with cardiac failure. Several groups in China are engaged in the design and research of the MCS devices. The type of device is calssified as pulsatile, rotary, total artificial heart (TAH).

Two types of pulsatile pump were driven by air (pneumatic). The Luo-Ye pump, one of the pulsatiile pump, have been used clinically for more than ten years. The other is a push-plate left ventricular device, with variable rate mode.

Various rotary devices classified into axial and centrifugal pump, depending on the impeller geometry. The maglev technique is used in most of the rotary pump and some types have been used clinically and some were detected in lab or animal studies. Some kinds of total implantable pump, such as one axial pump, developed by Qian, was totally intraventricular and another is designed as aortic valvo-pump, were developed.

One kind TAH was developed in China. The main constituents were two axial pumps, two reservoir tanks mocking right and left atria, flow meters, two pressure gauges and the resistance adaptor.

Although much room to be improved, different kinds of MCS devices are being studied in China.

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