CONFERENCE PROCEEDINGS

Volume 6, May 2010

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

May 6-8, 2010
The Joseph B. Martin Conference Center
Boston, Massachusetts, USA

Akif Ündar, PhD, Editor

Conference Founder
Akif Ündar, PhD

Local Conference Chair
Elizabeth D. Blume, MD

Honorary Co-Chairs
John A. Waldhausen, MD
William S. Pierce, MD

Organizing Committee
Elizabeth D. Blume, MD
John L. Myers, MD
Akif Ündar, PhD

Scientific Co-Chairs
Elizabeth D. Blume, MD
Pedro J. del Nido, MD
John L. Myers, MD
Giovanni Battista Luciani, MD
Ulrich Steinseifer, PhD
Akif Ündar, PhD

Penn State Hershey Children’s Hospital
Children’s Hospital Boston

Penn State Hershey Pediatric Cardiovascular Research Center
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

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Welcome to the Sixth Annual Event

Akif Ündar, PhD, Conference Founder

Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

On behalf of the Organizing Committee, I am pleased to welcome you to the Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion at the Joseph B. Martin Conference Center at Harvard Medical School in Boston, MA, USA. Elizabeth D. Blume, MD, Medical Director, Heart Failure/Transplant Program of the Children's Hospital Boston, will be the local conference chair. The scientific co-chairs of the pediatric event will be Elizabeth D. Blume, MD, Boston, MA, USA; Pedro del Nido, MD, Boston, MA, USA; Giovanni Battista Luciani, MD, Verona, Italy; John L. Myers, MD, Hershey, PA, USA; Ulrich Steinseifer, PhD, Aachen, Germany; and Akif Ündar, PhD, Hershey, PA, USA.

This year's meeting will commence on Wednesday, May 5, 2010 with registration. Formal presentations including a Key Note Lecture, Invited Lectures and regular slide and poster presentations will begin on Thursday morning (May 6, 2010) and continue through Saturday evening (May 8, 2010). 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 6, 2010). This year, conference participants had the distinct pleasure of hearing Dr. Pedro J. del Nido speak as the key note lecturer. In his lecture, Dr. del Nido addresses the FDA's initiative on Pediatric Cardiac Device Consortium.

Plenary sessions will be held throughout the conference structured the event by focusing on key topics including Neurological Outcomes (led by Co-Chairs John L. Myers, MD and Tom Spray, MD), Neuromonitoring Techniques (led by Co-Chairs Jane W. Newburger and Shunji Sano, MD), Pediatric Heart Valves (led by John E. Mayer), Pediatric Cardiac ECMO (led by Peter C. Laussen, MD, Elizabeth D. Blume, Francis Fynn-Thompson and Ravi Thiagarajan, MD). Two additional special sessions on Friday afternoon at the Children's Hospital Boston are an added bonus to this year's program.

1) ECLS Simulator Training: This session is for ICU physicians, CT surgeons, nurses and perfusionists involved in ECMO cannulation and management. The ECMO simulator will use to provide hands on training in ECPR. In addition, this program focuses on techniques to train residents/fellows and nurses for a successful ECMO program as well as techniques to build a simulator program.

2) Cardiac ICU Rounds and Case Presentations: These sessions will be held in the CICU at Children's Hospital Boston and led by CICU staff. Each session will be interactive during which active discussion from attendees is encouraged regarding all aspects of management and outcomes. The session will be suitable for all staff involved in the management of critically ill children with heart disease and will include a tour of the unit and
discussion regarding resources and staffing requirements.

The final plenary session, Bioengineering Approaches in Pediatric Cardiovascular Medicine (led by Co-Chairs Herbert H. Lipowsky, PhD, and Ulrich Steinseifer, PhD) will be discussing new pediatric cardiac pumps and microfluidic devices. This year’s meeting will conclude with a “hands-on” perfusion wet-labs session (led by Co-Chairs Larry Baer, CCP, W. Richard Owens, MT, CCP, and Bonnie L. Weaver, RN, MSN) on Saturday afternoon, May 8, 2010.

One hundred and one presentations, including invited lectures, slides, and posters will be presented at the Sixth Event. Once again, we have the opportunity to publish all of the conference abstracts in the April 2010 issue of artificial Organs, a peer-reviewed journal. In addition, the November 2010 issue of Artificial Organs is a Special Issue dedicated to manuscripts collected and peer-reviewed from presenters at the Sixth Conference. Our special thanks go to Angela T. Hadsell, Executive Editor, and Paul S. Malchesky, DEng, Editor-in-Chief, for making this possible.

Conference awards

This event continues to recognize young investigators, residents and students for their contributions to the advancement of cardiopulmonary bypass and mechanical circulatory support systems for pediatric patients. Conference awardees will be considered for recognition based on full manuscripts that detail their work.

Financial Support

Penn State Hershey Pediatric Cardiovascular Research Center and Penn State Hershey Children’s Hospital financially support this event to the maximum extent. In addition to the National Heart, Lung, and Blood Institute R13 grant support, we received funds from companies including Berlin Heart, MAQUET Cardiovascular, Somanetics Corporation, Abiomed, Circulite, Impulse Monitoring, MEDOS, Sorin Group USA, Syncardia Systems, Inc., St. Jude Medical, Terumo Cardiovascular Systems, and Wiley-Blackwell. Several other companies may also be added later as exhibitors.

Special thanks: Every detail of this event, including the location, was organized under the leadership of Drs. Betsy Blume and John L. Myers. My special thanks go to Dr. Blume for putting together an excellent scientific program and hosting this event at the Joseph Martin Conference Center. I also thank all invited speakers, slide, and poster presenters as well as conference participants for helping to make this conference another outstanding scientific event.

In addition, I sincerely appreciate all the organizational support we received from Christian Panasuak and her staff at the conference center to manage this unique event. I also want to thank Heather Stokes, along with several pediatric research nurses from the Pediatric Clinical Research Office at Penn State, and Dr. Feng Qiu, who helped to organize this event from A to Z.

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 Sixth Conference was supported in part by NHLBI R13 grant (5 R13 HL093852-02) awarded to Dr. Ündar.

Note: This letter was extracted from Dr. Ündar’s invited editorial from the April 2010 issue of the Artificial Organs.
## International Faculty, Moderators & Wet lab Instructors

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

**Conference Supporters**

*Educational Grants:*

Penn State Hershey Pediatric Cardiovascular Research Center, Hershey, PA
Penn State Hershey Children’s Hospital, Hershey, PA
National Heart, Lung, and Blood Institute* [R13 grant (5 R13 HL096358-02)]

*Conference Exhibitors:*

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*Funding for this conference was made possible (in part) by 5 R13 HL096358-02 from the National Institutes of Health, National Heart Lung and Blood Institute. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official polices 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.*
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Final Scientific Program

Wednesday, May 5, 2010

1:00pm – 5:00pm Registration and Exhibition set-up

Thursday, May 6, 2010

7:00am – 8:00am Registration/Breakfast

8:00am – 8:15am Opening Remarks
Elizabeth D. Blume, MD, John L. Myers, MD, Akif Ündar, PhD

8:15am – 10:15am PLENARY SESSION #1 – NEUROLOGICAL OUTCOMES
Co-Chairs: John L. Myers, MD, Hershey, PA and Tom Spray, MD, Philadelphia, PA

Gil Wernovsky, MD, Philadelphia, PA (20 min)
Neurodevelopmental outcomes: scope of the problem and current challenges

Jane W. Newburger, MD, MPH Boston, MA (20 min)
Randomized trials of neuroprotective strategies in congenital heart surgery

Shunji Sano, MD, PhD, Okayama, Japan (20 min)
Recent advances of brain protection during cardiac surgery-from deep hypothermia and circulatory arrest to cerebral perfusion

Erle H. Austin, III, MD, Louisville, KY (20 min)
Multi-modality neuromonitoring for pediatric cardiovascular surgery: 2010 Discussion (20 min)

10:15am – 11:00am Break/Exhibits and Posters

11:00 am – 12:00pm KEY NOTE LECTURE
Pedro J. del Nido, MD, Boston, MA
Pediatric Cardiac Device Consortium: An FDA Initiative
Introduced by John L. Myers, MD, Hershey, PA

12:00pm – 1:00pm LUNCH

1:00pm -3:00pm PLENARY SESSION #2 – NEUROMONITORING TECHNIQUES
Co-Chairs: Jane W. Newburger, MD, Boston, MA and Shunji Sano, MD, PhD, Okayama, Japan
Frank A. Pigula, MD – Boston, MA (20 min)
Scientific evidence for the clinical application of regional perfusion
Tom Spray, MD, Philadelphia, PA (20 min)
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The Use of DHCA in Contemporary Congenital Heart Surgery – Is it safe?  
Richard Jonas, MD, Washington, DC (20 min)
Cardiopulmonary bypass and white matter injury in the young  
George M. Hoffman, MD, Milwaukee, WI (20 min)
Goal-Directed Cerebral Therapy to Prevent Peri-operative Ischemic Injury  
Brian Clark, MD, Hershey, PA (20 min)
Microemboli detection and classification during pediatric cardiopulmonary bypass

Discussion (20 min)

3:00pm – 3:45pm  
Break/Exhibits and Posters

3:45pm – 5:00pm  
Mini-Symposium #1 – Pediatric Heart Valves
Moderator: John E. Mayer, Jr., MD, Boston, MA

Giovanni Battista Luciani, MD, Verona, Italy (20 min)
The challenge of congenital valve disease
Ulrich Steinseifer, PhD, Aachen, Germany (20 min)
Systematic engineering of an expandable polymeric heart valve for neonates with congenital right ventricular outflow tract defects
John E. Mayer, Jr., MD, Boston, MA (20 min)
Tissue engineered pediatric heart valves
Discussion (15 min)

5:00pm – 5:30pm  
Invited Lecture
Tim Baldwin, PhD, NHLBI, National Institutes of Health, Bethesda, MD
The Launch and Plans for the NHLBI PumpKIN Contract Program

5:30pm – 5:45pm  
Invited Lecture
Mehmet Agirbasli, MD, Istanbul, Turkey
Inflammatory and hemostatic response to cardiopulmonary bypass in the pediatric population: feasibility of serological testing of multiple markers

5:45pm – 6:45pm  
Regular Slide Presentations #1 – Pediatric Cardiopulmonary Bypass
Co-Chairs: Giovanni Battista Luciani, MD, Verona, Italy and Linda Pauliks, MD, Hershey, PA, USA
(15 min each -- 10 min. presentation and 5 min. discussion)

S1. Mechanical Support and Medical Therapy Reverse Heart Failure in Infants and Children
Hannah Zimmerman, MD, Diane Covington, RN, Richard G Smith, MSEE, and Jack G. Copeland, MD.
University of Arizona Department of Surgery, Section of Cardiothoracic Surgery, AZ, USA

S2. Extracorporeal Membrane Oxygenation in Infants After Stage One Palliation: the Impact of Shunt Type and ECMO Indication on Mid-term Survival
Mark A Scheurer MD1,3, Joshua W Salvin MD1,3, Peter C Laussen MBBS1,3, Elizabeth Sherwin MD1,3, Francis Fynn-Thompson MD2,4, Sitaram Emani MD2,4, Ravi T Thiagarajan MBBS1,3
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

The Departments of Cardiology$^1$ and Cardiac Surgery$^2$, Children’s Hospital Boston; and the Departments of Pediatrics$^3$ and Surgery$^4$, Harvard Medical School, Boston MA

**S3. Improved Cerebral Oxygen Saturation and Blood Flow Pulsatility with Pulsatile Perfusion during Pediatric Cardiopulmonary Bypass**

Xiaowei W. Su, BS, Yulong Guan, MD, Mollie Barnes, CNIM, J. Brian Clark, MD, John L. Myers, MD, Akif Ündar, PhD.

*Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA*

**S4. Impact of oxygen delivery rich perfusion on regional brain perfusion during pediatric cardiopulmonary perfusion**

Hideshi Itoh, CCP, Sadahiko Ari, MD, Shinya Ugaki, MD, Ko Yoshizumi, MD, Shingo Kasahara, MD Shinji Sano, MD.

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

**S5. A Microfiltration Microdevice for Real-Time, Continuous Blood Filtration to Analyze Proteins Involved in Immune Activation during Cardiopulmonary Bypass**

Kiana Aran, BS, Yulong Guan, MD, Qi Sun, MD, Akif Ündar, PhD and Jeffrey D. Zahn, PhD.

*Rutgers University, Department of Biomedical Engineering, Piscataway, New Jersey, USA; Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA*

7:00pm – 9:30pm

**GALA DINNER & AWARDS RECOGNITION**

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

**Poster Presentations #1 8am-7pm**

**P1. Penn State Hershey Pediatric Cardiovascular Research Center: 2010 Update**

Akif Ündar, PhD, Linda Pauliks, MD, J. Brian Clark, MD, Jeffrey Zahn, PhD, Allen R. Kunselman, MA, Feng Qiu, MD, Qi Sun, MD, PhD, Kerem Pekkan, PhD, Elizabeth Carney, DVM, Timothy K Cooper DVM, Neal Thomas, MD, MSc, Dennis Chang, MD, Willard Freeman, PhD, Kent Vrana, PhD, Aly El-Banayosy, MD, Serdar H. Ural, MD, Ronald Wilson, VMD, MS, Sung Yang, PhD, Sarah Sturgis, MSN, Jennifer Stokes, RN, Jessica Beiler, MPH, Heidi Watts, RN, Amyee McMonagle, RN, Julie Vallati, RN, Larry D. Baer, CCP, David Palanzo, CCP, Robert Wise, CCP, Karl Woitas, CCP, Robert McCoach, CCP, Stephen E. Cyran, MD, Vernon M. Chinchilli, PhD, Deborah Reed-Thurston, MD, Nikkole Haines, BS, Ashley Rogerson, BS, Bonnie L. Weaver, RN, MSN, CCRN Mollie Barnes, CNIM, Lawrence Sasso, BS, Kiana Aran, BS, Xiaowei Su, BS, Jonathan Talor, BSE, Mehmet Uluer, MS, Sophia Peng, BS, Chiajung Karen Lu, MS, Tijen Alkan-Bozkaya, MD, Atif Akçevin, MD, Mehmet Agirbasli, MD, Kyung Sun, MD, PhD, MBA, Shigang Wang, MD, Yulong Guan, MD, Long Cun, MD, John L. Myers, MD

*Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, Public Health Sciences, Pharmacology, Comparative Medicine, Obstetrics &*
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Gynecology, and Anesthesiology, Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA.

P2. A µ-Hemocytometer for Hematocrit Level Measurement During Cardiopulmonary Bypass Procedures

1Myoung Gon Kim, MS, 2Sang Youl Yoon, PhD, 2Sung Yang, PhD  
1Department of Nanobio Materials and Electronics, 2School of Information and Mechatronics, 2Graduate Program of Medical System Engineering, GIST, Republic of Korea

P3. PH-stat versus alpha-stat perfusion strategy during antegrade cerebral perfusion

Takashi Sasaki, Lorenzo Boni, John T. Yeung, R. Kirk Riemer, Chandra Ramamoorthy, Frank L. Hanley, V. Mohan Reddy,  
Stanford University

P4. Perioperative Monitoring of Thromboelastograph on Blood Protection and Recovery for Severe Cyanotic Infants Undergoing Complex Cardiac surgery

1Yongli Cui, M.D, Fei Long Hei, M.D, Cun Long, M.D, Zhengyi Feng, M.D, Ju Zhao, M.D, Fuxia Yan, M.D, Yuhong Wang, M.D, Jiping Liu, M.D.  
1Department of Cardiopulmonary Bypass, 2Department of Anesthesiology, Cardiovascular Institute and Fuwai Hospital, CAMS and PUMS, Beijing, China

P5. A dynamic study on the hemolytic effect of negative pressure on blood

Jutta Arens, Dipl.-Ing.1‡, Petra De Brouwer, B.Sc.1; Ilona Mager; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, Dr. Ing.  
Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany

P6. Differential Immune Activation During Simulated Cardiopulmonary Bypass Procedure Using Freshly Drawn and Week Old Blood - A Pilot Study

Kiana Aran, BS, Yulong Guan, MD, Qi Sun, MD, Jeffrey D. Zahn, PhD and Akif Ündar, PhD.  
Rutgers University, Department of Biomedical Engineering, Piscataway, New Jersey, USA; Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA

P7. A new, innovative model of chronic ischemic cardiomyopathy induced by multiple coronary ligations in sheep

Schmitto JD1, Mokashi SA1, Lee LS2, Laurence R3, Schotola H2, Quintel M2, Coelho O3, Kwong R3, Bolman RM III1, Cohn LH2, Chen FY2  
1 Division of Cardiac Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA, 2Department of Anesthesiology, Emergency and Intensive Care Medicine, University of Goettingen, Germany, 3Department of Cardiac Imaging, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

P8. Myocardial contractility and relaxation after deep hypothermic circulatory arrest in neonatal piglets

Theodor Tirilomis, Aron-Frederik Popov, Oliver J. Liakopoulos, Marc Bensch, Jan D. Schmitto, Katja Steinke, K. Oguz Coskun, Friedrich A. Schoendube
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**P9. Air Handling Capabilities of Blood Cardioplegia Systems in a Simulated Pediatric Model**
David Palanzo, CCP*, Yulong Guan, MD, Caihong Wan, MD, Larry Baer, CCP*, Allen Kunselman, MA, Akif Undar, PhD
*Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, *Heart & Vascular Institute, Hershey, Pennsylvania, USA

**P10. Surgical Correction with single approach to the combination of Aorticopulmonary window and Interrupted Aortic Arch in Neonatal period**
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Depts. of Neonatology, Pediatric Cardiology, Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Children’s Hospital, Hershey, PA, USA

**P11. Cardiac Surgery of Prematures and Low birth weight newborns: Is it possible to change of fate?**
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Depts. of Neonatology, Pediatric Cardiology, Anesthesiology, Istanbul, TURKEY and Penn State University, Children’s Hospital, Hershey, PA, USA

**P12. Effects of pulsatile and nonpulsatile perfusion on cerebral oxygen saturation and endothelin-1 in Tetralogy of Fallot infants undergoing correcting heart surgery**
Ju Zhao MD#, Jiuguang Yang MD#, Jinping Liu MD#, Shoujun Li MD&, Jun Yan MD&, Ying Meng MD*, Xu Wang MD*, Cun Long MD#
# Department of Cardiopulmonary Bypass; & Surgery department of Pediatric Heart Center, * ICU of pediatric heart center, Fuwai Cardiovascular Hospital
Peking Union Medical College & Chinese Association of Medical Science, Beijing, P.R. China

**P13. Therapeutic value of Somatotropin in treatment of postoperative recurrent serous / chylous drainage in patients with Fontan circulation**
Alkan-Bozkaya T, Türkoğlu H, Akçevin A, Duman U*, Paker T, Ersoy C*, Ayda Aytaç*
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Dept. of Cardiovascular Surgery*, Istanbul, TURKEY

**P14. Innovative safety valve for prevention of total massive air embolism**
Dr. Vishwas K. Paul, Dr. Kishore Yadav, Dr. Sanjay Gaikwad, Dr. Vidyanand Chavan
Ashwini Co-op. Hospital & Research Centre, N.S. Bazar, N. Maharashtra, India

**P15. Relation between renal dysfunction requiring renal replacement therapy and Promoter polymorphism of the erythropoietin gene in cardiac surgery**
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Aron F. Popov¹, PhD, Jan D. Schmitto², PhD, Egbert G. Schulz¹, PhD, Kasim O. Coskun¹, PhD, Mladen Tzvetkov⁴, PhD, Stephan Kazmaier⁵, PhD, Janna Zimmermann⁵, MD, Friedrich A. Schoendube¹, PhD, Michael Quintel⁵, PhD, Jose Hinz⁵, PhD
¹Department of Thoracic Cardiovascular Surgery, University of Göttingen, Germany
²Division of Cardiac Surgery, Department of Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA,
³Center of Nephrology and dialysis Bovenden - Göttingen, Germany,
⁴Department of Clinical Pharmacology, University Medical Center, University of Göttingen, Germany,
⁵Department of Anaesthesiology, Emergency and Intensive Care Medicine, University of Göttingen, Germany

P15a. The prototype of Polish extracorporeal pulsatile pediatric heart assist device – POLVAD-PED

(1)Foundation for Cardiac Surgery Development, Artificial Heart Laboratory, Zabrze, Poland;
(2)Foundation for Cardiac Surgery Development, Biocybernetics Laboratory.
Friday, May 7, 2010

7:00am – 8:00am  Registration/Breakfast

PLENARY SESSION #3 – Pediatric Cardiac ECMO - Where are we going?
Co-Chairs: Peter C. Laussen, MD and Elizabeth D. Blume, MD

8:00am -8:10am  Introduction and Welcome  
Peter C. Laussen, MD, Boston, MA

8:10am – 8:40am  ECMO past to present: Review value and results  
Robert H. Bartlett, MD, Ann Arbor, MI

8:40am - 9:10am  ECMO current realities: Complications, neurodevelopment outcomes and what we don’t know  
Francis Fynn-Thompson, MD, Boston, MA

9:10am – 9:30am  ECMO research in the current regulatory environment  
Pearl O’Rourke, MD, Boston, MA

9:30am - 10:00am  Break/ Exhibits and Posters

10:00am – 12:30pm  NEW Clinical strategies: Decision making, outcomes, and future direction for ECMO  
Co-Chairs: Francis Fynn-Thompson, MD and Ravi Thiagarajan, MD

- ECMO to support Cardiopulmonary Resuscitation  
  Ravi Thiagarajan, MD
- Transport of ECMO patients  
  Robert D.B. Jaquiss, MD
- Anticoagulation of ECMO patients  
  M. Patricia Massicotte, MD
- Adult ECMO issues & outcomes  
  Aly El-Banayosy, MD
- When to Transition ECMO patients to VAD  
  Christopher Almond, MD
- Constructing the Ideal ECMO Circuit: Analysis of Each Component Using In Vitro and In Vivo Testing  
  John L. Myers, MD
- ECMO equipment on the horizon  
  Peter Betit, RRT
- How to build and train an ECMO team  
  Catherine Allan, MD

Discussion with full panel (30 minutes)

12:30 – 1:30pm  LUNCH

Parallel Sessions:

1:30pm – 3:05pm  Regular Slide Presentations #2  
Moderator: Olaf Reinhartz, MD, Stanford, CA, USA
Invited Lecture: Non-invasive assessment of ventricular function on mechanical circulatory support
Linda Pauliks, MD, Hershey, PA (20 min)

5 presentations from selected abstracts (15 min each -- 10 min. presentation and 5 min. discussion)

S6. Pneumatic Pulsatile Ventricular Assist Device as a Bridge to Heart Transplantation in Pediatric Patients
Antonio Amodeo, MD; Gianluca Brancaccio, MD, PhD; Sergio Filippelli, MD; Zaccaria Ricci, MD; Stefano Morelli, MD; Maria Giulia Gagliardi, MD; Roberta Iacobelli, MD; Guido Michielon, MD; Sergio Picardo, MD; Giacomo Pongiglione, MD and Roberto M. Di Donato, MD.
Department of Cardiac Surgery and Pediatric Cardiology, Ospedale Pediatrico Bambino Gesù, Rome, Italy

S7. Extracorporeal Membrane Oxygenation Following Norwood Stage 1 Procedures
Department of Cardiovascular Surgery, Okayama University Hospital, Okayama, Japan

S8. Extracorporeal membrane oxygenation for pediatric cardiopulmonary resuscitation
Shu-Chien Huang, En-Ting Wu, Yih-Sharng Chen, Wen-Je Ko, Chung-I Chang, Ing-Sh Chiu, Shoel-Shen Wang.
Departments of Surgery, and Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

S9. COMPARISON OF PERFUSION QUALITY IN HOLLOW-FIBER MEMBRANE OXYGENATORS FOR NEONATAL EXTRACORPOREAL LIFE SUPPORT
Jonathan Talor, BSE, Stella Yee, BS, Alan Rider, Allen R. Kunselman, MA, Yulong Guan, MD, Akif Ündar, PhD
*Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics, †Department of Surgery, ‡Department of Bioengineering, §Department of Public Health Sciences, Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

S10. Comparison of Retrograde Flow between Three Centrifugal Blood Pumps in a Pediatric ECLS Model
Yulong Guan, MD, Robert McCoach, CCP, Allen Kunselman, MA, J. Brian Clark, MD, John L. Myers, MD, Akif Ündar, PhD
Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery & Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, PA, USA

3:00 pm – 3:45 pm  Break/ Exhibits and Posters
3:45 pm – 5:45 pm  Regular Slide Presentations #3
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Co-Chairs: Atif Akcevin, MD, Istanbul, Turkey and Robert D.B. Jaquiss, MD, Little Rock, Arkansas, USA

8 presentations from selected abstracts (15 min each -- 10 min. presentation and 5 min. discussion)

S11. ADVANTAGES OF PULSATILE PERFUSION MODE ON VITAL ORGAN RECOVERY IN PEDIATRIC PATIENTS
Atif Akçevin, MD, Tijen Alkan-Bozkaya, MD, Akif Ündar, PhD
Istanbul Bilim University, Dept. of Cardiovascular Surgery, Istanbul, TURKEY and *Penn State Milton S. Medical Center, Penn State Hershey Children’s Hospital, Hershey, PA, USA

S12. Pulsatile Flow Improves Cerebral Blood Flow in Pediatric Cardiac Surgery
Wei Wang, MD. PhD., Shuying Bai, MD., Shujing Zhang, MD., Deming Zhu, MD.
Department of Pediatric Thoracic and Cardiovascular Surgery, Shanghai Children’s Medical Center, Shanghai Jiaotong University, School of Medicine

S13. Blood transfusion in pediatric surgery
Yves Durandy, M.D.
Department of Intensive Care and Perfusion, Institute Hospitalier Jacques Cartier, Massy, France

S14. Cerebral oxygen metabolism during total body flow and antegrade cerebral perfusion at deep and moderate hypothermia
Stanford University, CA, USA

S15. A Newly Developed Miniaturized Heart Lung Machine – Expression of Systemic Inflammation in a Small Animal Model
Heike Schnoering, MD¹‡, Jutta Arens, Dipl.-Ing.²‡, Estela Terrada, PhD¹ Joerg S. Sachweh, MD², Maximilian W. Runge¹, Thomas Schmitz-Rode, MD², Ulrich Steinseifer, Dr. Ing.² and Jaime F. Vazquez-Jimenez, MD³.
¹Pediatric Cardiac Surgery, Medical Faculty, RWTH Aachen University, Germany
²Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany

S16. Comparison of a Miniature Centrifugal Rotary Pump (TinyPump) and Roller Pump in Neonatal Piglets
Ko Yoshizumi¹, Setsuo Takatani², PhD, DMed, MD, Hiroshi Ohtake³, MD, Go Watanabe⁴, MD.
¹Departments of General & Cardiothoracic Surgery, Kanazawa University, Kanazawa, Japan
²Department of Artificial Organs, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Tokyo, Japan

S17. Evaluation of neonatal membrane oxygenators in terms of GME capturing and transmembrane pressure drop
Feng Qiu, MD, Yulong Guan, MD, Xiaowei Su, BS, Allen Kunselman, MA, Akif Ündar, PhD.
Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA

S18. The Role of Phospho-AMPK and VEGF in a Model of Chronic Heart Failure
Schmitto JD\textsuperscript{1,4}, Heidrich F\textsuperscript{1}, Schotola H\textsuperscript{2}, Vorkamp T\textsuperscript{3}, Ortmann P\textsuperscript{1}, Coskun KO\textsuperscript{3}, Coskun ST\textsuperscript{1}, Popov AF\textsuperscript{1}, Friedrich M\textsuperscript{1}, Sohns C\textsuperscript{1}, Sossalla S\textsuperscript{3}, Hinz J\textsuperscript{3}, Quintel M\textsuperscript{2}, Schöndube FA\textsuperscript{1},
\textsuperscript{1}Department of Thoracic, Cardiac and Vascular Surgery, University of Goettingen, Germany, \textsuperscript{2}Department of Anaesthesiology, Emergency and Intensive Care Medicine, University of Goettingen, Germany, \textsuperscript{3}Division of Cardiology and Pneumology, University of Goettingen, Germany, \textsuperscript{4}Division of Cardiac Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA.

Parallel Afternoon Session: (Advance Registration is required)

ECLS Simulator Training: This session is for ICU physicians, CT surgeons, nurses and perfusionists involved in ECMO cannulation and management. It will use the ECMO simulator to learn ECPR hands on training. In addition, this program focuses on techniques to train residents/fellows and nurses for a successful ECMO program as well as techniques to build a simulator program. This program will run twice in the afternoon, and each session will incorporate 25 people maximum.

Cardiac ICU Rounds and Case Presentations: These sessions will be held in the CICU at Children’s Hospital Boston and lead by CICU staff. Each session will be interactive during which active discussion from attendees is invited regarding all aspects of management and outcomes. There will be 2 sessions, each of 90 minutes duration, and space is restricted to 20 participants for each session. The session will be suitable for all staff involved in the management of critically ill children with heart disease and will include a tour of the unit and discussion regarding resources and staffing requirements.

1:30 - 3:00 pm

- ECLS Simulator Training #1
  Peter Weinstock, MD, PhD, Catherine Allan, MD, Ravi Thiagarajan, MD
  Group #1 (Max 25 people, registration required)

- CICU Rounds: Case presentations and open discussion
  Children’s Hospital Boston, Cardiac Intensive Care Unit
  Mel Almodovar, MD
  Group #2 (Max 20 people, registration required)

3:30 - 5:00 pm

- ECLS Simulator Training #2
  Group #3 (Max 25 people, registration required)

- CICU Rounds: Case presentations and open discussion
  Children’s Hospital Boston, Cardiac Intensive Care Unit
  Peter Laussen, MD
P16. Pediatric Extracorporeal Life Support (ECLS) Systems: Education and Training at Penn State's Milton S. Hershey Medical Center Children's Hospital
Robert McCaugh, RN, CCP, Bonnie Weaver, RN, MSN, CCRN, Elizabeth Carney, DVM, J. Brian Clark, MD, Linda Paulikis, MD, Yulong Guan, MD, Fen Qiu, MD, Dennis Chang, MD, Deborah Reed-Thurston, MD, John L. Myers, MD, Akif Ündar, PhD
Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, Comparative Medicine and Perfusion Services. Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

P17. Anti-human leukocyte antigen antibody sensitization in very young children undergoing ventricle assist device as a bridge to heart transplantation
Gioia Grutter, MD, Antonio Amodeo, MD, Gianluca Brancaccio, MD, Guido Michielon, MD, Sergio Filippelli, MD, Roberto M. Di Donato, MD, Giacomo Pongiglione, MD, and Francesco Parisi, MD.
Department of Pediatric Cardiology and Cardiac Surgery, Bambino Gesù Pediatric Hospital, Rome, Italy

P18. MECHANICALLY ASSISTED TOTAL CAVOPULMONARY CONNECTION WITH A NEW AXIAL FLOW PUMP
Antonio Amodeo, MD, Robert Jarvik MD, Guido Michielon MD, M. Giulia Gagliardi MD, Enrico Iannace MD, Gianluca Oricchio MD, Gianluca Brancaccio MD, Sergio Filippelli MD, Sergio Picardo MD, Giacomo Pongiglione MD, Roberto Di Donato MD.
Department of Cardiac Surgery and Pediatric Cardiology, Ospedale Pediatrico Bambino Gesù, Rome, Italy

P19. The Changes of Inflammatory Cytokines in the Support of Extracorporeal Membrane Oxygenation (ECMO)
Feilong Hei, MD, Hong Sun, MD, Shuyi Lu, MD, Kun Yu, MD, Liang Sun, MD, Cun Long, MD.
Department Extracorporeal Circulation, Cardiovascular Institute and Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100037, China.

P20. Extra Corporeal Circulation in Pediatric Accidental Hypothermia
Coskun KO,1 Popov AF,1 Schmitto JD,2 Hinz J,2 Schoendube FA,1 Tirilomis T1
1 Department of Thoracic Cardiovascular Surgery, University of Göttingen, Germany
2 Division of Cardiac Surgery, Department of Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA
3 Department of Anaesthesiology, Emergency and Intensive Care Medicine, University of Göttingen, Germany

P21. The Choice of ECMO and VAD in Children
Wei Wang, MD, PhD, Wei Zhang, MD, Lei Jiang, BS, Haibo Zhang, MD, PhD, Deming Zhu, MD, Zhiwei Xu, MD.
Department of Pediatric Thoracic and Cardiovascular Surgery, Shanghai Children's Medical Center, Shanghai Jiaotong University, School of Medicine, China
P22. Mechanical Performance Comparison between two Centrifugal Blood Pumps in an Adolescent-Adult ECLS Model
Yulong Guan, MD, Xiaowei W Su, BS, Robert McCoach, CCP, Allen Kunselman, MA, Aly El-Banayosy, MD, John L. Myers, MD, Akif Ündar, PhD
Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA.

P23. Implantable Cardioverter Defibrillator in familial Friedreich Ataxie
Coskun KO1, Popov AF1, Schmitto JD1,2, Schoendube FA1, Zenker D1
1 Department of Thoracic Cardiovascular Surgery, University of Göttingen, Germany
2 Division of Cardiac Surgery, Department of Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA.

P24. Biocompatibility Evaluation of the ‘TinyPump’™ for Pediatric Left Ventricular Assist Device Application
Takashi Kitao1, Yusuke Ando3, Masaharu Yoshikawa3, Tarou Kimura3, Hideyuki Ohsawa4, Shinya Machida5, Tomohiro Konno5, Kazuhiro Ishihara5, Setsuo Takatani5
1 Department of Artificial Organs, Tokyo Medical and Dental University, Tokyo, Japan
3 Department of Cardiovascular Surgery, Kyushu University Graduate School of Medicine, Fukuoka, Japan
5 Department of Mechanical Engineering, Shibaura Institute of Technology, Tokyo, Japan
5 Department of Material Science, Graduate School of Engineering, University of Tokyo, Tokyo, Japan.

P25. Evaluation of Capiox FX05 Oxygenator with an integrated arterial filter on trapping gaseous micro-emboli and pressure drop with open and closed purge line
Feng Qiu, MD, Sophia Peng, BS, Allen Kunselman, MA, Brian J. Clark, MD, John L. Myers, MD, Akif Ündar, PhD.
Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA.

P26. Unilateral absence of pulmonary artery with Tetralogy of Fallot: Rare Cardiac Pathology
Istanbul Bilim University, Dept. of Cardiovascular Surgery, V.K.V. American Hospital, Dept. of Cardiovascular Surgery*, Istanbul, Turkey.

P27. SURGICAL APPROACH TO “SWISS CHEESE” VSDs
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Depts. of Pediatric Cardiology and Cardiovascular Surgery, Istanbul, Turkey

P28. Ventricular Assist Device Implantation With A Prior Mechanical/Prosthetic Valve: A Retrospective Review Of A Single-Center Experience
Suyog A. Mokashi, MD, Jan D. Schmitto, MD, PhD, Lawrence S. Lee, MD, R. Morton Bolman, MD, Prem Shekar, MD, Gregory S. Couper, MD, Frederick Y. Chen, MD, PhD.
Division of Cardiac Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

P29. Surgical Approach to Aortic Coarctation in the Neonatal-Infant Population
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Dept. of Cardiovascular Surgery, Istanbul, TURKEY.

P30. Pattern Width Variation by Printer Control Parameters in a Hydrogel-based Bioprinting System
Seung Joon Song, MS, Jaesoon Choi, PhD, Yong Doo Park, PhD, So Young Hong, MS, Kyung Sun, MD, PhD, MBA.
Korea Artificial Organ Center, Brain Korea 21 Project for Biomedical Science, Department of Biomedical Engineering, Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea.

P31. Evaluation of HL-20 Roller Pump and Rotaflow Centrifugal Pump on Perfusion Quality and Gaseous Microemboli Handling
Stella Yee, BS,* Feng Qiu, MD,* Alan Rider,* Xiaowei Su, BS, * Allen R. Kunselman, MA, Yulong Guan, MD,* Akif Ündar, PhD*, †,‡
*Pediatric Cardiovascular Research Center, Department of Pediatrics, †Department of Surgery, ‡Department of Bioengineering, §Department of Public Health Sciences, Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Saturday, May 8, 2010

7:00am – 8:00am  Breakfast/Exhibits

8:00am – 10:00am  PLENARY SESSION #4 – Bioengineering Approaches in Pediatric Cardiovascular Medicine

Co-Chairs: Herbert H. Lipowsky, PhD, University Park, PA and Ulrich Steinseifer, PhD, Aachen, Germany

Bartley P. Griffith, MD, Baltimore, MD (15 min)
Feasibility of CircuLite’s Circulatory Support System in Children

Andreas Spilker, Dipl.-Ing, Stolberg, Germany (15 min)
DP3 pump for acute and chronic pediatric cardiopulmonary support

Peter Nüsser, PhD (15 min) Germany
Pediatric Berlin Heart

Herbert H. Lipowsky, PhD, University Park, PA (15 min)
Pulsatile flow in the Microcirculation

Jeffrey D. Zahn, PhD, Piscataway, NJ (15 min)
Autonomous Continuous Flow Microimmunofluorocytometry Assay for Real Time Tracking of Biomarkers during CPB

Sung Yang, PhD, Gwangju, Korea (15 min)
Microfluidic devices for a fully integrated blood test system

Akif Ündar, PhD, Hershey, PA (15 min)
Translational Research for Pediatric CPB and MCS

Thorsten Siess, PhD, Aachen, Germany (15 min)
Continuum of cardiac support ranging from neonates to teenagers

10:00am – 10:45am  Break/Exhibits and Posters

10:45am – 12:00pm  Mini-Symposium #2: Pediatric Oxygenators
Moderator: Larry Baer, CCP, Hershey, PA and Akif Ündar, PhD, Hershey, PA

Eisuke Tatsumi, MD, PhD, Osaka, Japan (15 min)
Development of an Ultra-Durable Heparin-Free ECMO System and Its Clinical Application to Pediatric and Adult Patients in Japan

Ulrich Haag – Hechingen, Germany (15 min)
QUADROX-i oxygenators for neonatal & pediatric CPB and ECLS

Andreas Becker, PhD - Terumo (15 min)
Capiox FX: A New Generation of Pediatric Oxygenators with Fully Integrated Arterial Filter

Adriano Mazzoli – Sorin (15 min)
Impact of CPB System Architecture on Dynamic Prime Volume in Neonatal CPB

Discussion (15 min)

12:00pm – 1:00pm  LUNCH
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

**Parallel Sessions:**

**1:00pm – 3:00pm**

**Regular Slide Presentations #4**

8 presentations from selected abstracts (15 min each -- 10 min. presentation and 5 min. discussion)

**Microdevices – Moderator: Jeffrey D. Zahn, PhD, Piscataway, New Jersey, USA**

**S19. A Microfluidic Device For Continuous WBC Separation And Lysis From Whole Blood**

1Seung Mo Jung, MS, 2Myoung Gon Kim, MS, 3Sang Youl Yoon, PhD, 1,2,3Sung Yang, PhD

1Department of Nanobio Materials and Electronics, 2Graduate Program of Medical System Engineering, 3School of Information and Mechatronics, GIST, Republic of Korea, *Email: syang@gist.ac.kr

**S20. Highly Accurate and Consistent Microfluidic Viscometer for Continuous Viscosity Measurement**

1Yang Jun Kang, MS, 3Sang Youl Yoon, PhD, 1,2,3Sung Yang, PhD

1Department of Nanobio Materials and Electronics, 2School of Information and Mechatronics, 3Graduate Program of Medical System Engineering, GIST, Republic of Korea,

**S21. A Microdevice for Immunological Synapse Formation of T Cells Utilizing Protein Patterning on The PDMS Structure by Hydrophilic Surface Treatment**

1Donghee Lee, MS, 2Sangyoung Lee, BS, 3Sang Youl Yoon, PhD, 1,2,3Sung Yang, PhD

1Department of Nanobio Materials and Electronics, 2School of Information and Mechatronics, 3Graduate Program of Medical System Engineering, GIST, Republic of Korea,

**Engineering – Moderator: Amy L. Throckmorton, PhD, Richmond, Virginia, USA**

**S22. In vitro flow dynamics of pediatric right ventricular outflow tract reconstruction with bicuspid valved PTFE conduit**

Onur Dur (1), Masahiro Yoshida (2), Philip Manor (1), Alice Mayfield (1), Peter Wearden (2), Victor Morell (2), Kerem Pekkan (1)

1) Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA
2) Department of Cardiothoracic Surgery, Children's Hospital of Pittsburgh, Pittsburgh, PA


1,2Jaesoon Choi, PhD, 1,2Jun Woo Park, PhD, 1,2Seung Joon Song, MS, 1Jung Chan Lee, PhD, 1,4Kyung Sun, MD, PhD, MBA

1Korea Artificial Organ Center, 2Brain Korea 21 Project for Biomedical Science, 3Department of Biomedical Engineering, 4Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, 5Institute of Medical and Biological Engineering, Medical Research Center, Seoul National University, Seoul, Korea

**S24. Filament Support Spindle for an Intravascular Cavopulmonary Assist Device**

Amy L. Throckmorton PhD, Jugal Y. Kapadia MS, Thomas M. Wittenschlaeger BS MA, Tanisha J. Medina BS, Hien Q. Hoang BS, and Sonya S. Bhavsar BS.
S25. Description of a flow optimized oxygenator with integrated pulsatile pump
Ralf Borchardt\textsuperscript{1}, Dipl.-Ing.; Peter Schlanstein\textsuperscript{2}, Dipl.-Ing.; Jutta Arens\textsuperscript{1}, Dipl.-Ing.; Roland Graefe\textsuperscript{1}, Dipl.-Ing.; Fabian Schreiber\textsuperscript{2}, Dipl.-Ing.; Thomas Schmitz-Rode\textsuperscript{1}, MD; Ulrich Steinseifer\textsuperscript{1}, PhD, \textsuperscript{1}Department of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany, \textsuperscript{2}Institut für Textiltechnik, RWTH Aachen University, Aachen, Germany

S26. Improving oxygenator performance using computational simulation and flow field based parameters
Roland Graefe, Dipl.-Ing.; Ralf Borchardt, Dipl.-Ing.; Peter Schlanstein, Dipl.-Ing.; Jutta Arens, Dipl.-Ing.; Johannes Dieter, Dipl.-Ing.; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD, Department of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

3:00 pm – 3:45 pm
Break/ Exhibits and Posters

3:45 pm – 5:00 pm
Regular Slide Presentations #5
Moderator: Akif Ündar, PhD, Hershey, PA

5 presentations from selected abstracts (15 min each -- 10 min. presentation and 5 min. discussion)

S27. Particle Image Velocimetry Measurements of an Idealized Total Cavopulmonary Connection with Mechanical Circulatory Assistance in the Inferior Vena Cava
Steven G. Chopski, BS\textsuperscript{1}, Emily Downs, BS\textsuperscript{1}, Sonya S. Bhavsar, BS\textsuperscript{1}, Jugal K. Kapadia, MS\textsuperscript{1}, Chris Haggerty, MS\textsuperscript{1}, Ajit P. Yoganathan, PhD\textsuperscript{2}, Amy L. Throckmorton, PhD\textsuperscript{1}
\textsuperscript{1}Mechanical Engineering, Virginia Commonwealth University, Richmond, Virginia, USA; \textsuperscript{2}Wallace H. Coulter School of Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA, USA

S28. ECMO Support for Pediatric Patients with Acute Fulminant Myocarditis
Shye-Jao Wu, MD, Chun-Chi Peng, MD, Ming-Ren Chen, MD
Departments of Surgery, Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan

Joerg S. Sachweh, MD, Heike Schnoering, MD, Benita Hermanns-Sachweh, MD, Sabine Detering, MD, Nina Gronloh, MD, Rene Tolba, MD, Ulrich Steinseifer, Jaime Vazquez-Jimenez, MD
Pediatric Cardiac Surgery, Pathology, Laboratory Animal Science and Applied Medical Engineering, RWTH Aachen University, Aachen, Germany

S30. Impact of tubing length on hemodynamics in a simulated neonatal ECLS circuit
Feng Qiu, MD, Mehmet C. Uluer, ScM, Allen Kunselman, MA, Brian J. Clark, MD, John L. Myers, MD, Akif Undar, PhD, Pediatric Cardiovascular Research Center, Departments of Pediatrics,
S31. Utilization of discovery proteomics to identify plasma biomarkers in pediatric patients undergoing cardiopulmonary bypass – a clinical view
Chia-jung K. Lu BA, Todd M. Umstead BS, Willard M. Freeman PhD, John L. Myers MD, J. Brian Clark MD, Neal J. Thomas MD, Vernon M. Chinchilli PhD, Kent E. Vrana PhD, David S. Phelps PhD and Akif Ündar PhD
Penn State Center for Host defense, Inflammation, and Lung Disease (CHILD) Research and Penn State Hershey Pediatric Cardiovascular Research Center and the Department of Pediatrics, and the Departments of Pharmacology, Public Health Sciences and Bioengineering, Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA

Parallel Afternoon Session: (Advance Registration is required)
1:00pm – 4:45pm
Wet labs
(Maximum 15 participants for each lab)
Co-Chairs: Larry Baer, CCP, Hershey, PA, W. Richard Owens, MT, CCP, and Bonnie L. Weaver, RN, MSN, CCRN

ECLS with Rotaflow (pediatric and adult) Robert M. McCoach, RN, CCP & Bonnie L. Weaver, RN, MSN, CCRN

Berlin Heart
W. Richard Owens, MT, CCP & Tilman Humpl, MD

Medos DP3 Circuit (Pump and oxygenator) Andreas Spilker, Dipl.-Ing.

Pulsatile and Non Pulsatile CPB Circuits Robert Wise, CCP, Larry Baer, CCP

Intra-operative Neuromonitoring J. Brian Clark, MD, Mollie Barnes, CNIM

Terumo’s FX oxygenator and System 1 Deb Zarro

Sorin – Neonatal/Pediatric CPB circuits Bo Meier, BS, CP

3:00pm – 3:30pm Break/ Exhibits and Posters
3:30 pm – 5:00pm Wet Labs (continued)
5:00 pm Closing remarks (Bonnie L. Weaver, RN, MSN, CCRN)
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

**International Scientific Committee**

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Neurodevelopmental Outcomes: Scope of the Problem and Current Challenges

Gil Wernovsky, MD
The Cardiac Center at The Children's Hospital of Philadelphia and Divisions of Cardiology, Anesthesia and Critical Care Medicine, University of Pennsylvania School of Medicine, Philadelphia PA, US

Advances in prenatal detection, perioperative management and cardiothoracic surgical techniques have contributed to a significant increase in the number of children with complex congenital cardiac disease entering preschool and beyond. As initial survival has increased, and indeed is now expected for most forms of congenital cardiac disease, greater attention has been directed toward understanding the longer-term neurodevelopmental and functional outcomes of this growing patient population.

Multiple studies have shown that children with complex CHD requiring surgery in early infancy have an increased incidence of fine and gross motor delays, academic and behavioral difficulties, and inattention/hyperactivity; they are also more likely to have executive planning deficits, delays in expressive language, and lower than expected scores on standardized intelligence quotient (IQ) tests. In children with complex disease, these neurodevelopmental findings have been identified consistently in all follow-up studies, and seem to be independent of the underlying anatomic diagnosis, geographic location, language spoken and socioeconomic status. Equally concerning has been the recent identification that there has been little improvement on the frequency or severity of these findings in the past two decades.

The figure below (from ref 20) demonstrates some of the multiple factors that may impact upon mid-term neurological outcomes, including both modifiable and non-modifiable risk factors. There has been great interest of late to focus on the operating room as the most likely source of central nervous system injury that is modifiable, including the conduct of cardiopulmonary bypass in general and the use of deep hypothermic circulatory arrest in particular. Because of the changing neurodevelopmental challenges as children mature, it may take 10 years or longer to determine the benefits, or risks, of new perfusion, monitoring or postoperative techniques. All too often, well-meaning clinicians have made major changes in clinical practice – such as the widespread use of continuous cerebral perfusion during neonatal arch reconstruction - without adequate clinical trials or registry data to suggest improvement with the alternative strategies. New strategies touted using historical controls should be interpreted cautiously, before widespread adoption of new techniques.

Inadequate attention has been paid to the potential morbidities in the intensive care unit, both preoperatively and postoperatively, which may be modifiable and have a significant impact on longer term function. Well designed trials, including tracker trials and randomized clinical trials, as well as registry data which includes systematic long-term cardiac and neurodevelopmental follow-up, is a paradigm shift which should be adopted and endorsed by national and international societies.

During follow-up visits, the cardiologist and primary caregiver should inquire about school performance, behavior and other developmental issues, and partner with the child’s primary care provider and necessary consultants and therapists to formulate a plan for evaluation and management of possible behavior and academic difficulties. Parents should be made aware of the potential for academic and behavioral difficulties early in the follow-up process.
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

**Selected References:**

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.

References
Purpose:
Neuromonitoring during surgical repair of congenital heart defects strives to detect and correct potentially injurious physiologic imbalances. Our goal is to describe the benefit to be derived from integration of currently available modalities for peri-operative monitoring.

Methods:
1. Four-channel EEG continuously monitors cerebrocortical synaptic activity within the anterior and posterior circulations of both hemispheres.
2. Somatosensory-evoked potentials (SEP) assess integrity of afferent pathways from limbs, through the spinal cord to the cerebral cortex.
3. Transcranial Doppler (TCD) ultrasound bilaterally measures change in middle cerebral artery blood flow velocity.
4. Multi-channel non-invasive near-infrared spectroscopy monitors regional microcirculatory oxygen saturation (rSO₂) in the cerebral cortex bilaterally as well as the peri-vertebral, peri-renal and mesenteric vascular beds.
5. Commercially available signal analyzers now permit integration of all this information into a single, unified display.
6. Internet communication protocols permit remote on-line neurophysiologist consultation and supervision of operating room-based neuromonitoring technologists.

Results:
When used in concert, these modalities aid in the quick detection and correction of:
- malpositioned bypass cannulas or a transesophageal echocardiography (TEE) probe;
- systemic hypotension, hypoxia, hypovolemia, anemia or acid-base imbalance;
- hypnotic inadequacy or excess;
- cerebrocortical, subcortical, brainstem, peri-vertebral, peri-renal or mesenteric hypoperfusion;
- cerebral hyperperfusion;
- gaseous and particulate cerebral embolism;
- suboptimal cooling and rewarming;
- seizure activity.

The 1994 introduction of multi-modality neuromonitoring in our institution led to an initial reduction of the neurologic complication incidence from 26 to 10%. A decade later the incidence had fallen to 5% where it remains today. Recently, extension of neuromonitoring into the post-operative period appears to have resulted in reduction of non-neurologic morbidity and length of hospital stay.

Conclusions:
This experience suggests that the clinical and economic benefits of peri-operative multi-modality neuromonitoring more than justify the effort and expense of its application. Nevertheless, additional prospective studies are greatly needed to objectively quantify this apparent benefit.

References:
Regional Cerebral Perfusion; Clinical Practice and Scientific Justification

Frank A. Pigula MD
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Boston Children’s Hospital
Boston, Ma, USA

Purpose:
Regional cerebral perfusion (RCP) was introduced into the clinical arena nearly a decade ago. Since that time many centers have adopted this as the standard of care for surgical reconstruction of the aortic arch. We will review the current practice prevalence of RCP, techniques, and outcomes. Special attention will be given to the current state of knowledge of RCP, as it is integrated into clinical practice, and the scientific justifications that support its use.

Methods:
Primary data sets regarding the use of RCP will be presented, as there will be an evaluation of the current laboratory and clinical literature. Technical and practical considerations regarding the use of RCP will also be addressed.

Results:
There is a strong theoretical attraction to use RCP for arch reconstruction in neonatal cardiac surgery, and it has been adopted as “standard of care” by some. We will review the scientific studies that have supported RCP, and an evaluation of the results from clinical series.

Conclusions:
While there is laboratory and clinical evidence that RCP is beneficial, to date there are no large clinical trials which establish it as a superior technique. The goal of this presentation is to

1. Describe past work supporting the clinical use of RCP
2. Describe current utilization and practice variation in the use of RCP
3. Identify gaps in our knowledge regarding the use of RCP
Microemboli Detection and Classification during Pediatric Cardiopulmonary Bypass

J. Brian Clark, MD, Feng Qiu, MD, Yulong Guan, MD, Karl Woitas, CCP, John L. Myers, MD, Akif Ündar, PhD
Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

**Purpose:** Although emboli within the cardiopulmonary bypass (CPB) circuit are largely removed by standard components, some emboli escape elimination and are transmitted to the patient. Microemboli may be an underappreciated cause of postoperative neurologic morbidity. Improved detection of microemboli may lead to better strategies to minimize embolization and improve neurologic outcomes.

**Methods:** We have used transcranial Doppler (TCD) ultrasound for monitoring of cerebral blood velocity and embolic signals in pediatric patients undergoing CPB. TCD can alert the surgical team to potentially injurious situations such as cannula malposition or occult embolization, thus prompting corrective maneuvers. As part of multi-modality neuromonitoring, TCD has been demonstrated to reduce the incidence of acute adverse neurologic events. However, TCD has a limited sensitivity for smaller microemboli, with a threshold for detection of 40 microns. The Emboli Detection and Classification Quantifier has a lower threshold at just 10 microns, and may offer improved capability for microemboli monitoring. We have evaluated this device with *ex vivo* experiments using a laboratory model of pediatric CPB, as well as with *in vivo* studies during congenital heart operations.

**Results:** Our laboratory studies have shown that the vast majority (~99%) of air emboli within the venous line are eliminated by the oxygenator and the arterial filter. Of the microemboli detected in the post-filter arterial line, a similar majority (~99%) are smaller than 40 microns. Microemboli transmission across the CPB circuit was increased with higher flow rates, lower temperatures, pulsatile flow, and vacuum-assisted drainage. Our preliminary clinical studies have incorporated the emboli detector into the CPB circuit at the venous line and the post-filter arterial line. We found that the numbers of microemboli detected in the arterial line represented a small fraction (10-20%) of that detected in the venous line, suggesting that most of emboli entering the circuit were cleared by the circuit components. Of the microemboli detected in the arterial line, the majority (~95%) were smaller than 40 microns. We also found a temporal pattern of emboli detection in the circuit, with the greatest numbers associated with the initiation of bypass and with the deairing maneuvers associated with the removal of the aortic cross clamp.

**Conclusions:** Thousands of microemboli smaller than 40 microns may be transmitted to pediatric patients during congenital heart surgery. Most of these microemboli are below the detection threshold of standard transcranial Doppler ultrasound. Although the clinical significance of microemboli remains unknown, increased awareness of this phenomenon may lead to improved practices to minimize microembolization, with potential improvement in neurologic outcomes.
The Challenge of Congenital Valve Disease

Giovanni Battista Luciani, MD, University of Verona, Verona, Italy.

Congenital valve disease (CVD) represents the most common group of inborn cardiac defects in nature. Epidemiology is unique, as they typically occur in a young, often growing, and socially active patient population. As a consequence, history of multiple prior procedures (surgical, transcatheter) and expectation of future ones is the rule. Clinically, CVD presents in isolated form or in the context of more complex malformations: associated pathology, be it congenital or acquired is highly prevalent. In addition, critical onset (endocarditis, dissection) is not uncommon. Given the expectation of long-term survival and satisfactory quality of life (education, employment, exercise, pregnancy, socialization) typical of a young patient population, surgical management of CVD is highly challenging. Reparative approaches, which represent by far the most suitable strategy to CVD, have since evolved into more reproducible techniques, yet freedom from repeat intervention late after surgery remains an issue. Traditional replacement devices (biological, mechanical), on the contrary, offer a second best option with dependable functional behavior. However, quality of life is limited by prosthetic valve-related morbidity.

Experimental and clinical research in the last decade has brought about trans-catheter valve therapies, which have become a less invasive management alternative for native and post-operative semilunar (pulmonary, aortic) valve disease in select patients. Investigation in the field of trans-catheter atrio-ventricular valve repair and replacement is also growing rapidly and clinical applications are foreseeable in the future. In complex clinical settings, such as the ones often encountered in CVD, combination of off-pump surgical and transcatheter percutaneous approaches may result in hybrid therapeutic solutions.

Progress in the field of biomaterial research, to identify more biocompatible devices, and application of mathematical (finite element model analysis) and bioengineering (computational fluid dynamics) methodologies to the patho-physics and management of valve lesions have also been instrumental in facing the formidable challenge posed by CVD to scientists and clinicians.
Systematic Engineering of an Expandable Polymeric Heart Valve for Neonates with Congenital RVOT Defects

Ulrich Steinseifer, PhD¹; Ute Urban, Dipl.-Ing.¹; Ingo Nadzeyka, Dipl.-Ing., Nicole Kiesendahl, PhD¹; Yara Safi¹, MS; Georg Lutter, MD² and Thomas Schmitz-Rode, MD¹

¹ Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany
² Dept. of Cardiovascular Surgery, Christian-Albrechts-University of Kiel, School of Medicine, Germany

Purpose:
Congenital heart defects affect approximately 0.5% of all neonates. In about one fifth of these cases a surgical reconstruction of the right ventricular outflow tract RVOT becomes necessary. The most common therapy is the surgical revision with a heart valve prosthesis. However, this requires the exposure, cardioplegic arrest and cardiopulmonary bypass of the heart, and bears the risk of injuries, which is additionally increased by potential intergrowths at repeated interventions. In cases of a moderate stenosis of the RVOT and an insufficiency as the major indication for the correction, the interventional application of a heart valve prosthesis might be feasible. Initial clinical results with bovine jugular valves placed in a balloon-expandable stent showed promising results. However, the major limitations of that valve assembly were the size of the delivery sheath required (18F), rendering the application in smaller children very difficult. In this study we present the systematic engineering of a polymeric, expandable cardiac valve PECAV with optimal flow performance, biocompatibility and durability. Moreover, it allows the manufacturing and crimping to smaller sizes in order to fit in smaller delivery sheets.

Methods:
The PECAV comprises an expandable Nitinol stent and three flexible leaflets made from Polyurethane. Major engineering challenges are the optimization of the stent and leaflet design with regard to the applied loads, a durable connection of the polymer to the Nitinol stent, the manufacturing of the leaflets and the safe and effective anchoring of the prosthesis in the intended position. The stent and leaflet designs were based on the anatomic design of natural heart valves. Their structures were optimized by numerical simulation of the crimping process and the leaflet kinematics. Various technologies were evaluated and optimized for manufacturing the leaflets and a sealing against paravalvular leakage, including dip coating and polymer spraying. The safe and effective anchoring was simulated in virtual fitting studies based on MRI and CT images and validated in anatomical studies using porcine and ovine hearts.

Results:
An optimum stent design was developed that allows crimping to a diameter of less than 4 mm within acceptable stress tolerances. It consists of 2 rings that are connected via several cross beams. The polymeric leaflets are attached to the upper ring via a proprietary silica coating of the Nitinol surfaces and an additional adhesion promoter. Several anchoring methods were investigated and evaluated for the pulmonary and aortic position and may be used for the interventional application of the valve. Lab prototypes of the valve were manufactured and initially tested in vitro.

Conclusions:
The systematic engineering of a flexible polymer valve makes the interventional application of a heart valve in neonates with RVOT defects more feasible, and thus opens new options for paediatric therapies.
The Launch and Plans for the NHLBI PumpKIN Contract Program

Timothy Baldwin, Ph.D.*, Jonathan Kaltman, M.D.†, Gail Pearson, M.D., Sc.D.†, Victoria Pemberton, RNC, M.S., CCRC†, Karen Ulisney, M.S.N, CCNP*
*Advanced Technologies and Surgery Branch, †Heart Development and Structural Diseases Branch, Division of Cardiovascular Diseases, National Heart, Lung, and Blood Institute, Bethesda, MD, USA

Program Origin:
In 2004, NHLBI launched the Pediatric Circulatory Support Program to fund the development of five devices specifically to provide circulatory support for children with heart failure who are less than 25 kg. The 5-year program was successful in meeting its objectives, paving the way for the next phase of rigorous pre-clinical testing and analysis, manufacturing development, and clinical trial planning and implementation. To this end, NHLBI issued a Request for Proposals (RFP) on October, 2008 for the Pumps for Kids, Infants, and Neonates (PumpKIN) program. The purpose of this program is to help make the most promising devices available to meet the clinical needs of the youngest heart failure patients.

Award Process:
NHLBI received a robust response to the PumpKIN RFP in February, 2009. The initial peer and secondary reviews of the proposals were held in April and May, 2009, respectively. NHLBI negotiated with institutions that submitted proposals determined to be in the competitive range based on the results of the reviews. Four contracts totaling $23.6M were awarded effective January 15, 2010 to the institutions listed in Table 1.

Program Content and Plans:
The devices in the PumpKIN program include: a magnetically-levitated, mixed-flow VAD for children up to 15 kg (PediaFlow); a hydrodynamically-levitated, axial-flow VAD for children up to 25 kg (Infant Jarvik 2000); a compact ECMO system composed of a magnetically-levitated pediatric ventricular assist system and oxygenator made of standard microporous hollow fiber membranes (PediPL); and a compact ECMO system that uses a heparin-based engineered surface coating for the device’s hollow fiber membrane (pCAS). Both ECMO systems have modular components that can be changed out multiple times in order to provide longer patient support.

The contractors are each working toward the goals of submitting pre-IDE requests to the FDA, submitting an HUD designation request within one year, submitting an IDE application within 30 months, and obtaining IDE approval by the end of three years.

The NHLBI will be issuing an RFP in 2010 for the PumpKIN Data and Clinical Coordinating Center (DCCC). The DCCC will work with the contractors to design the appropriate clinical trials, oversee related clinical issues, and run the clinical trials once the IDEs are approved. The current plans calls for the PumpKIN clinical trials to begin in January, 2013 and be completed within three years.

Table 1. NHLBI PumpKIN Contractors

<table>
<thead>
<tr>
<th>Contractor Institution</th>
<th>Principal Investigator</th>
<th>Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Pittsburgh</td>
<td>Harvey Borovetz, Ph.D.</td>
<td>PediaFlow™ Pediatric VAD</td>
</tr>
<tr>
<td>University of Maryland, Baltimore</td>
<td>Bartley Griffith, M.D.</td>
<td>Pedi PumpLung (PediPL)</td>
</tr>
<tr>
<td>Jarvik Heart, Inc.</td>
<td>Robert Jarvik, M.D.</td>
<td>Infant Size Jarvik 2000 Heart</td>
</tr>
<tr>
<td>Enson, Inc.</td>
<td>Mark Gartner, Ph.D., MBA</td>
<td>Pediatric Cardiopulmonary Assist System (pCAS)</td>
</tr>
</tbody>
</table>
Inflammatory and Hemostatic Response to Cardiopulmonary Bypass in Pediatric Population: Feasibility of Seriological Testing of Multiple Biomarkers

Mehmet Ağirbaşli, MD*, My-Le Nguyen, MD, Khin Win, MD, Allen R. Kunselman, MA, J. Brian Clark, MD, John L. Myers, MD, Akif Ündar, PhD
Marmara University, Department of Cardiology, Istanbul, Turkey; Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, & Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA

**Purpose:** Cardiopulmonary bypass (CPB) causes alterations in the levels of biomarkers related to inflammation, tissue damage, and other tissue pathologies. Perioperative myocardial and cerebral damages are the major determinants of postoperative morbidity and mortality. Early and accurate evaluation of inflammation and tissue damage would therefore be clinically useful. Multi-Analyte Profiling (MAP) technology platform (Rules Based Medicine, Austin, TX) allowed us to analyze 90 different biomarkers using only 100 μl of plasma to detect any changes in the levels of 90 biomarkers at 5 different time points. Our objective is to assess the suitability of using MAP in pediatric cardiac surgery as a potential surrogate marker of clinical outcome.

**Methods:**
The pilot protocol included 10 patients with similar Jenkins risks stratifications who underwent non-pulsatile CPB. The patients’ ages ranged from 3 month to 4 years. Plasma samples were collected at five different time points:
1. before mid-line incision,
2. on CPB for three to five minutes,
3. at the end of CPB
4. 1 hour (h) after CPB
5. 24 h after CPB

We detected changes in the levels of 90 biomarkers. The average values and standard deviations of each biomarker at each time point were then compared to each other and to the base-line (sample 1) to identify any change as a result of CPB procedure. Biomarkers were grouped and scores were defined based on the number of fold increase or decrease in the level compared to baseline. Linear mixed effects models were fit to compare all pairwise sample times within each protein. P-values were adjusted to control for the false discovery rate using the method of Benjamini and Hochberg. All hypotheses tests were two-sided and all analyses were performed using version 9.1 of the SAS System for Windows (SAS Institute Inc., Cary, NC). The study was approved by the Institutional Review Board.

**Results:**
Striking increases were noted in the early markers of necrosis (myeloperoxidase, pregnancy associated plasma protein (PAPP-A), and heart-type fatty acid-binding protein (FABP)) as early as 3-5 minutes after CPB. Myeloperoxidase and PAPP-A increased 18 and 49 fold after the onset of CPB respectively (p<0.001). FABP increased 25,193, 151 and 4 fold at time points 2,3,4 and 5 respectively (p<0.001). Other markers of myocardial necrosis (creatine kinase (CK) MB, myoglobin) increased later in the course (2,16,25,7 fold for CK-MB, 4,21,16,1 fold for myoglobin at time points 2,3,4,5 respectively p<0.001 (Figure 1). Moderate but steady rises were noted among markers of inflammation,
hemostasis and plaque stability (i.e. matrix metalloprotease 9, CD40L, plasminogen activator inhibitor 1). By 24 hours, levels of early necrosis markers normalized, yet striking increases in the levels of inflammatory markers (C-reactive protein (CRP), interleukin 6 (IL 6) were noted. IL 6 increased 45 fold 1 h post CPB (p<0.001), CRP increased 161 fold 24 h post CPB (P<161). Figure 1 demonstrates the top 7 biomarkers with most significant increase after CPB. Time dependent increases were noted in the serial assessment of insulin, CD40 L, IL 10, MMP 9, growth hormone, calcitonin and ferritin levels.

Discussion

MAP is a feasible method to assess necrosis, inflammation and hemostasis after pediatric CPB. The most sensitive marker for necrosis appears to be time dependent. PAPP-A rose immediately on CPB, whereas increase in FABP was noted after CPB. Markers of inflammation (IL 6, CRP) and hemostasis (PAI-1, WF) rose later in the course. Similarly, IL 6 surge was 1 h after CPB, followed by CRP surge at 24 h. Therefore, following a panel rather than a single marker may elucidate the complex metabolic profile after CPB. Our findings may also help us to understand temporal course of potential complications after CPB in the pediatric population.

Figure 1. The top 7 biomarkers with most significant increase after CPB. Y axis indicates the number of fold increase compared to baseline.

Conclusions:
1. MAP is a feasible method to monitor patients after CPB in pediatric population.
2. The best marker for myocardial necrosis appears to be a time dependent phenomenon.
3. PAPP-A and myeloperoxidase are early markers of necrosis that can potentially direct clinician during CPB, whereas FABP may prove to be more useful after CPB.
4. Moderate but steady rises were noted among markers of hemostasis and plaque stability.
5. Future studies are needed to compare biomarker panel at pulsatile vs. non-pulsatile CPB and to determine the relationship between the panel and clinical outcomes.
6. Necrosis and inflammatory risk scores may be derived from the panel to predict complications.
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

**Mechanical Support and Medical Therapy Reverse Heart Failure in Infants and Children**

Hannah Zimmerman, MD, Diane Covington, RN, Richard G Smith, MSEE, and Jack G. Copeland, MD

**University of Arizona Department of Surgery, Section of Cardiothoracic Surgery**

**Purpose:**
Most infants and children implanted with ventricular assist devices go on to cardiac transplantation. Recovery of dilated dysfunctional hearts with ventricular assist device decompression and maximal medical therapy has been possible in some adults, and may be more feasible in infants and children.

**Methods:**
We conducted a Human Subjects approved retrospective chart review of pediatric patients that had a mechanical assist device placed at our institution. We used pulsatile and continuous flow ventricular assist devices and total artificial heart (TAH). Candidates for heart recovery were treated with maximum medical therapy for congestive heart failure and short term dobutamine prior to weaning off device support.

**Table 1. Outcomes by Age**

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Recovery</th>
<th>Transplant</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>(No. of patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 2 (13)</td>
<td>6</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>2 to 6 (5)</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7 to 16 (10)</td>
<td>0</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total (28)</strong></td>
<td><strong>10</strong></td>
<td><strong>10</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>

**Competing Outcomes Analysis**

<table>
<thead>
<tr>
<th>X axis – days on device</th>
<th>Y axis – No. patients</th>
</tr>
</thead>
</table>

**Results:** Since 1997, 28 patients, infants and children, ages 1 month to 16 years, were implanted for durations of 3-107 days (mean 27). Eighteen received LVADs (Left Ventricular Assist Devices), 7 BiVADs (Biventricular Assist Devices), and 3 TAHs (Total Artificial Hearts). Device related mortality was 7/28 (25%), leaving 21/28 (75%) surviving to transplantation or weaning from device support and 20/28 (71%) discharged from hospital and currently surviving for 2 months to 9 years. Ten of eleven transplant recipients (90%) have survived 2 to 9 years. All 10 recovered hearts are alive and well for 2 months to 5 years. Eight of 12 (67%) LVAD patients with dilated hearts recovered.

**Conclusions:** Infants and children who have failed inotropic therapy may be treated with an LVAD and medical therapy for congestive heart failure anticipating native heart recovery. A variety of devices have tried. All small LVADs yielded comparable results. Larger and older children may have also a good of recovery, but experience with them is too small except to note that they do well with larger devices and transplantation.


Extracorporeal Membrane Oxygenation in Infants After Stage One Palliation: the Impact of Shunt Type and ECMO Indication on Mid-term Survival

Mark A Scheurer MD,1,3, Joshua W Salvin MD,1,3, Peter C Laussen MBBS1,3, Elizabeth Sherwin MD,1,3, Francis Fynn-Thompson MD,2,4, Sitaram Emani MD,2,4, Ravi T Thiagarajan MBBS1,3

The Departments of Cardiology1 and Cardiac Surgery2, Children’s Hospital Boston; and the Departments of Pediatrics3 and Surgery4, Harvard Medical School, Boston MA

Purpose:
The use of extracorporeal membrane oxygenation (ECMO) after stage one palliation (S1P) has been reported in small case series. The impact of ECMO utilization after S1P on longitudinal survival has not been described.

Methods:
All infants at our institution who underwent S1P from January 2000 through June 2009 were included for analysis and followed until death, loss to follow-up or September 1, 2009.

Results:
Of the 333 infants undergoing S1P, 219 received a modified Blalock-Taussig shunt (BTS), while 114 underwent a right ventricle to pulmonary artery conduit (RV-PA). Thirty-eight of those with a BTS (17.4%) underwent 41 total runs of ECMO, compared to 17 patients (14.9%) undergoing 18 runs in the RV-PA group (p=0.57). Of those patients undergoing ECMO in the BTS group, 64.9% were initiated during CPR (ECPR) while 50% of runs in the RV-PA group were ECPR (p=0.29). A low cardiac output state (LCOS) was the principal indication for ECMO support in 56.8% of cases in the BTS group, compared to 72.2% in the RV-PA group (p=0.38). Of all patients supported with ECMO for LCOS (n=34), hospital survival was 32.4% versus 61.9% for those supported for hypoxemia (n=21) (p=0.03). Survival after S1P for those undergoing ECMO was 32.9% at 3 years, versus 79.4% for all others (log-rank p<0.001). Only LCOS as a primary indication for ECMO was found to be an independent risk factor for death through the typical period of Fontan completion [HR 2.5 (1.2 – 5.4)], when controlled for shunt type and the use of ECMO as ECPR.

Conclusions:
Infants after S1P who require ECMO for LCOS are at high risk for death through the typical period of staged palliation. In a center with an experienced ECMO program, neither shunt type, nor the use of ECPR independently impact longitudinal survival in those undergoing ECMO after S1P.
Improved Cerebral Oxygen Saturation and Blood Flow Pulsatility with Pulsatile Perfusion during Pediatric Cardiopulmonary Bypass

Xiaowei W. Su, BS, Yulong Guan, MD, Mollie Barnes, CNIM, J. Brian Clark, MD, John L. Myers, MD, Akif Ündar, PhD
Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Purpose:
Few studies exist comparing pulsatile and non-pulsatile perfusion with regards to neuro-protection and current brain monitoring techniques during pediatric cardiopulmonary bypass (CPB) procedures. The present study utilized near infrared spectroscopy (NIRS) to measure regional cerebral oxygen saturation ($rSO_2$) and transcranial Doppler ultrasound (TCD) to measure cerebrovascular pulsatility index (PI) in patients randomized to pulsatile or non-pulsatile perfusion in order to evaluate the merits of the respective perfusion modes.

Methods:
The INVOS 5100B pediatric NIRS monitor and Pioneer TC8080 TCD monitor were employed. Statistical analysis inclusion criteria were: 1) Age 10 days – 5 years, 2) Weight 2.5-16.5 kg, 3) Patients must receive crossclamp (XC), 4) Complete NIRS & TCD data at either 40 or 60 min after XC; yielding 67 patients in the pulsatile group and 33 patients in the nonpulsatile group.

NIRS, TCD and MAP were recorded at baseline, on bypass prior to XC, and 5, 20, 40, and 60 min after XC. Statistical analysis was performed using StatView 5 (SAS).

Results:
There were no significant differences in patient characteristics (age, weight, gender) or intraoperative characteristics (Jenkins risk category, total CPB time, XC time, nadir temperature) between groups. At all time points measured the decrease in $rSO_2$ from baseline was lower in the pulsatile vs. non-pulsatile group, with a statistically significant difference at the longest time point. At all time points measured the decrease in PI from baseline was lower in the pulsatile vs. non-pulsatile group, with significant differences at 5, 20 & 40 min after XC. At all time points measured the decrease in MAP from baseline was lower in the pulsatile vs. non-pulsatile group, however results were not statistically significant. Relevant data reflecting these results are presented in Table 1.

Conclusions:
Results in this pilot study suggest improvements in $rSO_2$, PI & MAP when pulsatile perfusion is used. This may provide improved cerebral and other vital organ perfusion. We believe this may be a factor in improving neurologic and post-operative outcomes.

### Table 1. Intra- and Postoperative Physiologic Data

<table>
<thead>
<tr>
<th>Time</th>
<th>Pulsatile</th>
<th>Non-Pulsatile</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>66.6 ± 2.2</td>
<td>69.4 ± 1.8</td>
<td>0.391</td>
</tr>
<tr>
<td>Before XC</td>
<td>-3.8 ± 3.2</td>
<td>-7.7 ± 3.5</td>
<td>0.453</td>
</tr>
<tr>
<td>5 min after XC</td>
<td>-9.9 ± 3.0</td>
<td>-14.2 ± 2.7</td>
<td>0.383</td>
</tr>
<tr>
<td>20 min after XC</td>
<td>-2.9 ± 3.6</td>
<td>-11.7 ± 2.6</td>
<td>0.111</td>
</tr>
<tr>
<td>40 min after XC</td>
<td>-4.8 ± 3.7</td>
<td>-14.5 ± 3.1</td>
<td>0.094</td>
</tr>
<tr>
<td>60 min after XC</td>
<td>-6.2 ± 4.3</td>
<td>-19.7 ± 3.2</td>
<td>0.041</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Pulsatile</th>
<th>Non-Pulsatile</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>60.9 ± 1.9</td>
<td>64.2 ± 2.2</td>
<td>0.286</td>
</tr>
<tr>
<td>Before XC</td>
<td>-24.2 ± 3.9</td>
<td>-31.1 ± 5.0</td>
<td>0.292</td>
</tr>
<tr>
<td>5 min after XC</td>
<td>-36.8 ± 3.0</td>
<td>-37.3 ± 3.7</td>
<td>0.922</td>
</tr>
<tr>
<td>20 min after XC</td>
<td>-31.3 ± 3.1</td>
<td>-34.9 ± 3.0</td>
<td>0.450</td>
</tr>
<tr>
<td>40 min after XC</td>
<td>-25.9 ± 3.2</td>
<td>-31.7 ± 3.3</td>
<td>0.265</td>
</tr>
<tr>
<td>60 min after XC</td>
<td>-22.6 ± 3.8</td>
<td>-30.1 ± 4.2</td>
<td>0.231</td>
</tr>
</tbody>
</table>
Impact of oxygen delivery rich perfusion on regional brain perfusion during pediatric cardiopulmonary perfusion

Hideshi Itoh, CCP, Sadahiko Arai, MD, Shinya Ugaki, MD, Ko Yoshizumi, MD, Shingo Kasahara, MD, Shunji Sano, MD
Department of Cardiovascular Surgery, Okayama University Hospital, Okayama, Japan.

Purpose: To provide both adequate systemic oxygen delivery (DO\textsubscript{2}) and oxygen demand (VO\textsubscript{2}) is a valuable purpose of cardiopulmonary bypass. Mixed venous oxygen saturation (SvO\textsubscript{2}) is a good marker of an adequate balance between DO\textsubscript{2} and VO\textsubscript{2}. Our purpose is to investigate the effect of DO\textsubscript{2} rich perfusion (monitored by SvO\textsubscript{2}) on regional oxygen saturation (rSO\textsubscript{2}) that reflects brain protection during cardiopulmonary bypass. We measured rSO\textsubscript{2} using near-infrared spectroscopy (NIRS).

Methods: We studied 60 pediatric cardiopulmonary perfusion cases since September 2008 to December 2009. We divided into two groups: high SvO\textsubscript{2} (group H (n=30); SvO\textsubscript{2}>80 %) and low management (group L (n=30); 70% < SvO\textsubscript{2}< 80%). We measured in-line SvO\textsubscript{2} by Terumo CDI-500. Early transfusion, high flow and high FiO\textsubscript{2} management established DO\textsubscript{2} rich perfusion. Backgrounds of patients of both groups are similar as shown in Table 1. We compared lowest hemoglobin concentration, maximum cardiopulmonary perfusion flow, lowest rSO\textsubscript{2} (by NIRS; INVOS 5100), lowest lactate, lowest base excess, urine output, fluids balance, amount of blood transfusion, and phenylephrine hydrochloride dose during pediatric cardiopulmonary perfusion. We used non-parametric Mann-Whitney U test for statistical analysis. Statistical significance was accepted at \( p < 0.05 \).

Results: There are significantly differences in lowest hemoglobin and rSO\textsubscript{2} as shown in Table 2. The lowest hemoglobin and rSO\textsubscript{2} in Group H is higher than Group L.

Conclusions: These results suggest that oxygen delivery rich perfusion to maintain SvO\textsubscript{2} over 80% improved regional brain perfusion and may improve brain protection in pediatric cardiopulmonary perfusion.

Table 1. Backgrounds of patients

<table>
<thead>
<tr>
<th></th>
<th>Age (months)</th>
<th>Body Weight (Kg)</th>
<th>Heights (cm)</th>
<th>Body Surface Areas (m\textsuperscript{2})</th>
<th>CPB time (min)</th>
<th>Cross Clamp Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group H</td>
<td>19.7 ± 8.8</td>
<td>7.6 ± 7.1</td>
<td>72.1 ± 12.3</td>
<td>0.38 ± 0.01</td>
<td>99 ± 41</td>
<td>62 ± 33</td>
</tr>
<tr>
<td>Group L</td>
<td>14.5 ± 23.1</td>
<td>7.7 ± 4.1</td>
<td>72.4 ± 7.8</td>
<td>0.38 ± 0.01</td>
<td>111 ± 60</td>
<td>72 ± 38</td>
</tr>
<tr>
<td>P value</td>
<td>0.65</td>
<td>0.26</td>
<td>0.52</td>
<td>0.65</td>
<td>0.7</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Table 2. Results

<table>
<thead>
<tr>
<th></th>
<th>Lowest Hgb (g/dL)</th>
<th>Lowest Ht (%)</th>
<th>Max. Perfusion Flow (mL/kg)</th>
<th>Lowest rSO\textsubscript{2}</th>
<th>Lowest Base Excess</th>
<th>Urine Output</th>
<th>Fluid Balance</th>
<th>Amount of blood transfusion</th>
<th>Phenylephrine hydrochloride dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group H</td>
<td>9.2 ± 2.8</td>
<td>28.7 ± 5.1</td>
<td>168.6 ± 29.6</td>
<td>57.2 ± 10.8</td>
<td>2.03 ± 1.38</td>
<td>142 ± 153</td>
<td>44.8 ± 155</td>
<td>118 ± 126</td>
<td>2.27 ± 3.18</td>
</tr>
<tr>
<td>Group L</td>
<td>8.1 ± 2.7</td>
<td>25.4 ± 4.9</td>
<td>157.8 ± 19.0</td>
<td>50.2 ± 7.9</td>
<td>1.78 ± 0.68</td>
<td>209 ± 211</td>
<td>72.6 ± 247</td>
<td>125 ± 149</td>
<td>1.79 ± 2.05</td>
</tr>
<tr>
<td>P value</td>
<td>0.027</td>
<td>0.128</td>
<td>0.007</td>
<td>0.86</td>
<td>0.47</td>
<td>0.19</td>
<td>0.08</td>
<td>0.75</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Hgb: Hemoglobin concentration, Ht: Hematocrit
Purpose:
Cardiopulmonary bypass (CPB) is known to initiate a Systemic Inflammatory Response (SIR) which can result in a variety of post operative complications which may continue long after the discontinuation of CPB. The damaging effects of CPB procedure are more severe in infants and neonates, who are more susceptible to inflammatory responses due to their high metabolism rate and immature organs. Even though postoperative morbidity and mortality after CPB have been declining, they are still significant. The goal of this study is to develop a real-time microfiltration microdevice to continuously separate blood proteins and components of the blood involved in inflammatory responses, such as complements and cytokines from whole blood during CPB procedures. This will enable researchers to track the development of and better understand the inflammation process in order to better control and prevent these systemic responses. Additionally, integration of the proposed microfiltration device with a continuous microimmunoassay would create an integrated microanalysis system for point-of-care diagnostics, reducing analysis times, costs and volume of blood samples required for the assays.

Methods:
The microfiltration system consists of a two compartment mass exchanger with two sets of polydimethylsiloxane (PDMS) microchannels separated by a porous polycarbonate membrane. Whole blood flows on one side of the membrane (reservoir channel) and plasma filtrate flows through the membrane to the other channel (filtrate channel). Large particles in the blood, such as blood cells and platelets cannot enter the filtrate channel due to the small pore size diameter of the membrane (200 nm). Figure 1 (Right) shows a schematic of the device which was designed with 32 parallel channels in each compartment to maximize the transport area to allow a high enough filtrate flowrate so that ~50-100µl of fluid can be collected at the filtrate outlet within a reasonable period of time while maintaining high recovery. The performance of the microfiltration device was evaluated using heparinized human blood within an in-vitro model normothermic CPB circulation loop. The normothermic CPB circulation loop was primed with 500 ml freshly drawn heparinized human blood, hemodiluted to 27.5% Hct in lactated Ringers solution and circulated at a rate of 500 ml min⁻¹ at an arterial circuit pressure of 100 mmHg. A small portion of the blood was redirected from the arterial port of the membrane oxygenator through the reservoir channels at a flow rate of ~80 µl min⁻¹, driven by the pressure generated within the CPB circuit. Discrete samples were collected every 20 minutes from the microfiltration device channels (Reservoir and Filtrate) and directly from the CPB membrane oxygenator arterial port (Blood Sample). The samples were then analyzed for cytokines TNFα, IL-1β, IL-6, and IL-8 concentrations using immunofluorocytometry.

Results:
The results shows the cytokine concentrations in the reservoir and filtrate samples were comparable to those from direct blood draws, indicating very high recovery of the microdevice. Additionally the cytokine concentration increased significantly compared to baseline values over the circulation time for all cytokines analyzed (Fig.1 Left). The high protein recovery, absence of hemolysis and low level of biofouling on the membrane surface were all indications of effective and reliable device performance for future clinical applications.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

PENN STATE HERSHEY PEDIATRIC CARDIOVASCULAR RESEARCH CENTER: 2010 UPDATE

Akit Ündar, PhD, Linda Pauliks, MD, J. Brian Clark, MD, Jeffrey Zahn, PhD, Allen R. Kunselman, MA, Feng Qiu, MD, Qi Sun, MD, PhD, Kerem Pekkan, PhD, Elizabeth Carney, DVM, Timothy K Cooper DVM, Neal Thomas, MD, MSc, Dennis Chang, MD, Willard Freeman, PhD, Kent Vrana, PhD, Aly El-Banayosy, MD, Serdar H. Ural, MD, Ronald Wilson, VMD, MS, Sung Yang, PhD, Sarah Sturgis, MSN, Jennifer Stokes, RN, Jessica Beiler, MPH, Heidi Watts, RN, Amyee Monagle, RN, Julie Vallati, RN, Larry D. Baer, CCP, David Palanzo, CCP, Robert Wise, CCP, Karl Woitas, CCP, Robert McCoach, CCP, Stephen E. Cyran, MD, Vernon M. Chinchilli, PhD, Deborah Reed-Thurston, MD, Nikkole Haines, BS, Ashley Rogerson, BS, Bonnie L. Weaver, RN, MSN, CCRN, Mollie Barnes, CNIM, Lawrence Sasso, BS, Kiana Aran, BS, Xiaowei Su, BS, Jonathan Talor, BSE, Mehmet Uluer, MS, Sophia Peng, BS, Chiajung Karen Lu, MS, Tijen Alkan-Bozkaya, MD, Atif Akçevin, MD, Mehmet Agirbasli, MD, Kyung Sun, MD, PhD, MBA, Shigang Wang, MD, Yulong Guan, MD, Cun Long, MD, John L. Myers, MD

Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, Public Health Sciences, Pharmacology, Comparative Medicine, Obstetrics & Gynecology, and Anesthesiology, Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA.

Background:
Over the past 6 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 and mechanical circulatory support. The Penn State Hershey Pediatric Cardiovascular Research Center has been established with the collaboration of teams from multiple academic departments and representing multiple disciplines. This center combines basic science, engineering, and clinical applications under the unified mission of pediatric cardiovascular research. Scientists and clinicians in the center represent the departments of Pediatrics, Surgery, Bioengineering, Anesthesiology, Comparative Medicine, Public Health Sciences, Pharmacology, Obstetrics & Gynecology, and Nursing Education & Professional Development.

Objective:
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 reducing the associated morbidities of cerebral, myocardial, pulmonary, and renal injury.

Our long term aspirations are to: 1) establish The Penn State Hershey Pediatric Cardiovascular Research Center as a leading center for further development of novel treatments and cutting edge devices for cardiovascular health in pediatric populations, both at the Penn State Hershey Children's Hospital and at other pediatric heart centers around the world; 2) educate more bioengineers, medical students, residents, post-doctoral fellows and junior faculty members in pediatric cardiovascular research; and 3) ensure that our international conference continues to be the leading conference for defining the problems of current mechanical circulatory support systems in pediatric patients and suggesting appropriate solutions for these pediatric cardiac patients.

Current Projects
Impact of Pulsatile CPB on Vital Organ Recovery (Clinical/Basic Science/Engineering)

Neonatal Extracorporeal Life Support Systems with Pulsatile and Non-Pulsatile
Sixth International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

**flow: Research and Education at Penn State Hershey Children’s Hospital (Clinical/Engineering)**

Comparison of retrograde flow between three centrifugal blood pumps in a pediatric ECLS model (Clinical/Engineering)

Comparison of perfusion quality in hollow-fiber membrane oxygenators for neonatal extracorporeal life support (Clinical/Engineering)

Microemboli Detection and Classification by Innovative Ultrasound Technology During Cardiopulmonary Bypass Procedures (Clinical/Engineering)

Application of real time intra operative neurologic monitoring on management of pediatric cardiopulmonary bypass (Clinical)

Microfluidic Dialysis Platforms for Monitoring Cardiopulmonary Bypass Systemic Inflammation (Engineering/Basic Science)

Noninvasive Cardiac Imaging (Clinical)

Ecuador Mission Program (Clinical)

**Air Handling Capabilities of Blood Cardioplegia Systems (Clinical/Engineering)**

Discovery Proteomics During Pediatric Cardiac Surgery (Clinical/Basic Science)

Microdevices for Measuring CPB Systemic Inflammation (Engineering/Basic Science)

Sixth International Conference on Pediatric Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion (Clinical/Basic Science/Engineering)

Medos Pulsatile DP3 Device for ECLS (Engineering)

Animal models will be developed for testing the new devices (Basic Science/Engineering)

**Summary**

The Penn State Hershey College of Medicine, Department of Pediatrics contributed over $600,000 in funds to support the creation of the new pediatric cardiac research center. Many research components in the center (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 heart pumps and oxygenators for future clinical studies in pediatric patients in the United States and around the globe.

Within the past 6 years, our pediatric cardiac research group has generated over 122 articles, over 160 national and international presentations and invited lectures, as well as over $7.7 million in grants. Additionally, we have trained dozens of medical students, post-doctoral fellows, and undergraduate and graduate biomedical engineering students.

With the creation of the Penn State Hershey Pediatric Cardiovascular Research Center, we strive to become one of the leading centers 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 our conference (The International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion - http://www.hmc.psu.edu/childrens/pedscp/) in order to provide a scientific venue for the pioneering research being performed in pediatric mechanical circulatory support and cardiopulmonary perfusion.
Purpose:
Hematocrit (Hct) level is one of the critical information for accessing patient’s condition during transfusion procedure in intensive care units or during cardiopulmonary bypass (CPB) procedures. A microfluidic based hemocytometer for continuous measurement of Hct is proposed in this study. The performance of the proposed µ-hemocytometer is characterized under various Hct levels as well as electrode configurations including width, gap between electrodes.

Methods:
The whole blood sample was freshly harvested from a healthy donor and collected into a 3.0ml vacutainer (B&D) containing EDTA as anticoagulants. In order to simulate various Hct conditions, the blood sample was centrifuged at 3000 rpm for 20 min and 6 sets of blood samples were prepared from 0% (pure plasma) to 50% Hct. Figure 1 shows a fabricated microfluidic-based sensor and schematics of experimental setup. Electric field forms between electrodes, and is disturbed by a number of RBCs placed between electrodes. The electrical sensing module of sensor is composed of a series of low pass filter, high pass filter and differential amplifier to reduce noise signals. The output signal was acquired by using a conventional A/D board. All experiments were conducted at a flow rate of 0.2ml/hr, and a modulation frequency of 100 kHz with 1 V_{pp}.

Results:
As shown in figure 2, the conductivity (signal output) decreased with increasing Hct levels since a current could not penetrate through RBCs membrane at low frequency of 100 kHz. The Type 1 sensor is similar with the Type 3 in performance due to the large surface area of the electrodes. A sensor with the smaller spacing between electrodes has the larger signal output.

Conclusions:
A µ-hemocytometer for the measurement of Hct level has been proposed and successfully demonstrated under the various Hct levels. It was also possible to improve the sensitivity of the dynamic range by controlling the electrode configurations.

Acknowledgement:
This research was partially funded by grants from the MEST (WCU Program, No. R31-2008-000-10026-0), the MCT (07SeaHeroB01-03), and the Institute of Medical System Engineering (iMSE, GIST), Republic of Korea.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion
PH-stat versus alpha-stat perfusion strategy during antegrade cerebral perfusion

Stanford University

Purpose:
The superiority of the pH-stat to the alpha-stat acid-base strategy during antegrade cerebral perfusion (ACP) as a neuroprotective method is still controversial.

Methods:
Twelve neonatal piglets (3.6 ± 0.2 kg) were randomized to pH-stat (n = 6; group P) or alpha-stat (n = 6; group A) management. Cardiopulmonary bypass was started with the initial flow rate of 200 ml/kg/min. After cooling to 18°C, the flow was decreased to 100 ml/kg/min (half flow; HF) for 15 minutes and ACP was conducted with a flow rate of 40 ml/kg/min for 45 minutes. Cerebral blood flow (CBF) was measured using fluorescent microspheres at HF and ACP. Cerebral oxygen extraction (CEO2) and lactate values were monitored. Cranial oxygen saturation (rSO2) was continuously recorded with near-infrared spectroscopy.

Results:
Cooling time was 27±9.4 (P) and 35.5±7.2 (A) minutes (p= 0.11). There was no difference in CBF and CEO2 between the groups (CBF (HF): 31.3±7.1 and 27.2±24.6 ml/100g/min, p= 0.71, CBF (ACP): 33.3±18.1 and 24.6±10.7 ml/100g/min, p= 0.33, CEO2 (HF): 9.5±4.2 and 11.2±3.9 %, p= 0.51, CEO2 (ACP): 17.3±11.4 and 18±7.3 %, p= 0.91). However, lactate was greater in group A at HF (3.7±0.7 and 2.8±0.7 mmol/l, p= 0.03) and ACP (4.1±0.6 and 2.8±0.6 mmol/l, p= 0.003). The rSO2 was significantly lower in group A at HF (80.7±5.2 and 90.9±5.4 %, p= 0.001), and trended lower at ACP (72.8±6.5 and 87.5±13.2 %, p= 0.056).

Conclusions:
In both groups, CBF and CEO2 were similar at each bypass condition. However, the difference of rSO2 between the groups implied better perfusion of peripheral brain tissue in group P and lactate values corroborate the finding.
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Perioperative Monitoring of Thromboelastograph on Blood Protection and Recovery for Severe Cyanotic Infants Undergoing Complex Cardiac Surgery

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(¹Department of Cardiopulmonary Bypass, ²Department of Anesthesiology, Cardiovascular Institute and Fuwai Hospital, CAMS and PUMS, Beijing, 100037, China)

Purpose:
The complex cardiac operations for severe cyanotic infants are often associated with coagulation disturbances and bleeding complications. They usually consume more blood products and need longer operative recovery period than others. We assessed a new transfusion therapy guided by thromboelastograph (TEG) on blood protection and clinical effect.

Methods:
This study included 31 severe cyanotic infants with HCT higher than 54%, who were diagnosed as transposition of the great arteries (TGA) and underwent arterial switch operation (ASO) or double roots transplantation (DRT). We divided them into two groups: In group F (n=17), the transfusion therapy after CPB was performed with fibrinogen administration combined with traditional transfusion, guided by TEG; in group C (n=14), was traditional transfusion only. We recorded some parameters from the beginning of operation to the 24-hours after surgery, including: sternal closure time, fresh frozen plasma (FFP) and platelet (PLT) amount used in closure time(closure FFP, closure PLT), FFP amount used in ICU(ICU FFP), total FFP, platelet and red blood cells amount used in operation and ICU(total FFP, total PLT, total RBC). Chest drainage at 1h, 6h, 24h, and the mechanical ventilator time, ICU stay, hospitalization time were also collected.

Results:
There were no differences between the baselines of these patients, such as age, body weight, pre-operative HCT, CPB time, aortic-clamping time, FFP and RBC amount for priming (p>0.05, respectively). In surgery, the closure time, closure FFP and closure PLT had no significant reduction in group F (p>0.05), and there were also similar in chest drainage at very time points between two groups (p>0.05). The total platelet and total RBC usage were same too (p>0.05). But the ICU FFP and total FFP had significantly dropped in group F (p<0.05), the mechanical ventilator time, ICU stay, hospitalization time in group F were much shorter than them in group C (p<0.05).

Conclusions:
TEG was effective in blood protection. The new transfusion therapy could reduce the use of allogeneic blood products, and shorten the operative recovery period. It might be better for those server cyanotic infants underwent complex cardiac surgery.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

A Dynamic Study on The Hemolytic Effect of Negative Pressure on Blood

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Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany
‡ Both Authors contributed equally to this manuscript

Purpose:
It is often regarded as common knowledge that negative pressure applied on circulating blood causes hemolysis, e.g. during ECMO or cardiac surgery. But in literature there are only few studies with different outcomes and most studies were performed only with static test settings. Therefore, we designed a dynamic test set up to study the effect of negative pressure on hemolysis during a 6 hour test period.

Methods:
The general test set up was according to ISO 7199, comparing four identical circuits with hydrostatically adjusted pressures of 0 mmHg, -40 mmHg, -80 mmHg, -120 mmHg. The tests were performed with fresh heparinized porcine blood. Test duration was 6 hours with a flow rate of 2.4 l/min. Each circuit consisted of a venous hardshell reservoir (Medos), an oxygenator (Medos Hilite® 7000), a Maquet RPM 20-230 roller pump H20, and Raumedics PVC tubing in identical lengths. All roller pumps had similar rotation speed of 105 rpm ± 3. The combination of pumps, oxygenators, and reservoirs was changed randomly after each test. The adjustment of blood parameters (pO₂, pCO₂, glucose, base excess, and temperature) followed the ISO 7199 protocols. Samples were taken from each circuit at 0, 10, 30, 90, 180, 270, 360 min. Plasma free hemoglobin was measured photometrically.

Results:
Different hemolysis rates occurred in the four parallel measured circuits, but after 6 tests no correlation between hemolysis and the height of negative pressure could be found. Also there was no correlation between hemolysis and neither the different pumps, oxygenators nor reservoirs.

Conclusions:
As we could find no correlation between hemolysis and the negative pressure, we hypothesize that a negative pressure up to -120 mmHg in dynamic systems, such as ECMO devices or heart lung machines, does not cause increased hemolysis rates. Though, further tests should be performed to reach higher level of statistic evidence.
Differential Immune Activation During Simulated Cardiopulmonary Bypass Procedure Using Freshly Drawn and Week Old Blood - A Pilot Study

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Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
A simulated cardiopulmonary bypass (CPB) procedure is commonly used to evaluate pressure-flow relationships along the circuit, emboli production, circuit components (e.g., pumps, oxygenators, cannulae, length and diameter of the tubing etc.). In particular, simulated circuits allow the study of the response of blood and immune activation to perfusion through the circuit in the absence of other major factors such as surgical trauma or cardiotomy suction. Additionally simulated circuits allow data to be collected with relative ease compared to the use of animal models or drawing blood from patients undergoing CPB procedure for analysis. The goal of this study is to assess whether the use of different aged blood, used during the simulated Penn State Hershey Pediatric CPB model affects immune activation.

Methods:
In order to study and compare the cytokine release involved in the humeral immune response during simulated CPB, both freshly drawn whole blood used less than 1 hour after donation and reconstituted whole blood (1 week old) were circulated in a simulated CPB circuit. In each experiment the normothermic CPB circulation loop was primed with 500 ml of either heparinized freshly drawn human blood (n=2) or a reconstituted whole blood sample drawn 1 week prior (n=3). Each sample was hemodiluted (Hct 27-30) in lactated Ringers solution and circulated at a rate of 500 ml min⁻¹ at an arterial circuit pressure of 100 mmHg. Over the course of each experiment, discrete samples were collected every 20 minutes for fresh blood and every 15 minutes for reconstituted blood directly from the CPB membrane oxygenator arterial port. The blood samples were then centrifuged, the plasma removed and flash frozen at -80°C and analyzed for the cytokines TNFα, IL-6, and IL-8 concentrations using immunofluorocytometry.

Results:
The results shown in figure 1 indicate that the cytokine concentrations of freshly drawn blood increased significantly compared to the reconstituted blood over the CPB circulation time. The fresh blood activation was 2 to 3 orders of magnitude larger than the week old blood for all cytokines analyzed. These results indicate that the use of fresh blood during simulated CPB increases the production of inflammatory mediators and should be used in studies of immune activation during CPB. However, these results cannot be used to predict the actual intensity of the inflammatory response during surgery. Further research is needed to clarify the effects of blood storage on immune activation in both simulated and surgical CPB circuits.

Figure 1: Comparison of outlet cytokine (TNFα, IL-8 and IL-6) concentrations from 5 different experiments using freshly drawn blood (n=2) and reconstituted week old blood (n=3).
A New, Innovative Model of Chronic Ischemic Cardiomyopathy Induced by Multiple, Coronary Ligations in Sheep

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²Department of Anesthesiology, Emergency and Intensive Care Medicine, University of Goettingen, Germany
³Department of Cardiac Imaging, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

Background - Heart failure is one of the fastest growing worldwide epidemics in healthcare today. Although a wide variety of animal models exist to create chronic heart failure, there are few truly successful, reproducible models with ischemic dilation and mitral regurgitation.

Methods and Results – Six healthy sheep (36 ± 5 kg) underwent multiple, strategic coronary artery ligations on the left ventricle (LV). Six to eight ligations were performed transmurally on 3 of 4 segments of the LV: anterior, lateral and posterior. Side branches of the left anterior descending and circumference arteries were ligated to create multiple, patchy areas of myocardial infarction. Cardiac function was evaluated using echocardiography and MRI. The overall mortality rate was 16.7% (1/6 animals). The average ejection fraction of the remaining animals had significantly decreased from 60 ± 5 % to 28 ± 7%; additionally, two of the remaining 5 (40%) animals developed mild to moderate mitral regurgitation on cardiac MRI. Furthermore, each animal displayed clinically significant evidence of heart failure (tachycardia, dyspnea and tachypnea) with global, dilated cardiomyopathy on MRI.

Conclusions – Creating and reproducing a model of global, ischemic cardiomyopathy with mitral regurgitation is an arduous task. We have developed a promising model of ischemic heart failure using multiple ligations, which mimics the sequelae of human cardiomyopathy. Besides being highly effective, our proposed model is also reproducible and may be used for experimental research on heart failure (cardiac assist devices, heart transplant).
Myocardial Contractility and Relaxation after Deep Hypothermic Circulatory Arrest in Neonatal Piglets

Theodor Tirilomis, Aron-Frederik Popov, Oliver J. Liakopoulos, Marc Bensch, Jan D. Schmitto, Katja Steinke, K. Oguz Coskun, Friedrich A. Schoendube
Department for Thoracic, Cardiac, and Vascular Surgery, University of Goettingen, Goettingen, Germany

Purpose:
Deep hypothermia may influence outcome of cardiac surgery due to alterations on myocardial performance of left ventricle. The aim of the present study was the analysis of myocardial contractility and relaxation after deep hypothermic circulatory arrest (DHCA).

Methods:
Newborn piglets (younger than 7 days of age) were operated on deep hypothermic circulatory arrest (18°C; DHCA group; n=8) and then the data were compared with the data of neonatal piglets after mild hypothermic cardiopulmonary bypass (32°C; MH-CBP group; n=10). Total CPB time was for both groups 180 minutes; perfusion data are shown on Table 1. Left ventricular (LV) pressures were measured through a transapical Millar catheter and dP/dt\textsubscript{max} and -dP/dt\textsubscript{max} calculated. The regional myocardial contractility was determined as sonomicrometric measured myocardial wall thickening (WT).

Results:
The LV systolic pressures remained one hour after separation from CPB in all animals stable. Changes in dP/dt\textsubscript{max}, -dP/dt\textsubscript{max}, and WT are presented in Table 2. The differences between the two groups were not statistically significant.

Table 1: Time intervals during DHCA / MH-CPB.

<table>
<thead>
<tr>
<th>group</th>
<th>perfusion /cooling</th>
<th>circulatory arrest</th>
<th>cardiac arrest</th>
<th>rewarming/reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHCA</td>
<td>30 min</td>
<td>90 min</td>
<td>-</td>
<td>60 min</td>
</tr>
<tr>
<td>MH-CBP</td>
<td>30 min</td>
<td></td>
<td>90 min</td>
<td>60 min</td>
</tr>
</tbody>
</table>

Table 2: LV contractility and relaxation data after DHCA / MH-CPB.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>CPD end</th>
<th>1 hour after CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>dP/dt\textsubscript{max} [mmHg/s]</td>
<td>1720 ± 131</td>
<td>1771 ± 131</td>
<td>1875 ± 131</td>
</tr>
<tr>
<td>-dP/dt\textsubscript{max} [mmHg/s]</td>
<td>-1242 ± 120</td>
<td>-1173 ± 120</td>
<td>-1146 ± 120</td>
</tr>
<tr>
<td>WT [mm]</td>
<td>1,37 ± 0,06</td>
<td>1,17 ± 0,06</td>
<td>1,19 ± 0,06</td>
</tr>
</tbody>
</table>

Conclusions:
Left ventricular dP/dt\textsubscript{max} increased after DHCA and after mild hypothermic CPB while -dP/dt\textsubscript{max} decreased after DHCA and increased after mild hypothermic CPB. Nevertheless, the differences between the two groups did not reach statistical significance.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Air Handling Capabilities of Blood Cardioplegia Systems in a Simulated Pediatric Model

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Purpose:
Blood cardioplegia systems are employed in most pediatric open heart cases to arrest the heart and keep it preserved during aortic crossclamping. They are also used as part of the modified ultrafiltration (MUF) system at the end of cardiopulmonary bypass (CPB). We evaluated and compared the air handling capabilities of different types of blood cardioplegia devices.

Methods:
A simple circuit incorporating a cardiotomy reservoir, a roller pump, a cardioplegia test system and two emboli detection and classification (EDAC) sensors was used to investigate the air handling capabilities of the following cardioplegia systems: GISH BIOMEDICAL Vision, MAQUET Plegiox, Medtronic Trillium™ MYOtherm™ XP, Sorin Group BCD Vanguard™, Sorin Group CSC14 and Terumo Conducer. The ¼” circuit was primed with 400 ml of Lactated Ringer’s. Outdated packed red blood cells were added to obtain a hematocrit of 24-28%. System pressure was maintained at 50 mmHg. Air (0.1, 0.3, 0.5 ml) was rapidly injected into the circuit just after the pump head. Gross microemboli (GME) were measured prior to the cardioplegia system and after the device to evaluate the air handling characteristics. The tests were run at 100 and 200 ml/minute blood flow for both 4°C and 37°C.

Results:
There were no significant differences among the groups when comparing pre-cardioplegia system GME thus demonstrating that all devices received the same amount of injected air. When comparing the groups for post-cardioplegia system GME, significant differences were noted. For the trials performed at 37°C and 4°C, the devices ranked differently in regards to the ones that handled the air the best compared to those who handled it the worst. (See Table 1).

Table 1. Air Handling Capabilities of the Blood Cardioplegia Systems

<table>
<thead>
<tr>
<th>Blood Cardioplegia System</th>
<th>4°C</th>
<th>37°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAQUET Plegiox</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medtronic Trillium™ MYOtherm™ XP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sorin Group BCD Vanguard™</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sorin Group CSC14</td>
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<tr>
<td>Terumo Conductor</td>
<td></td>
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<tr>
<td>GISH BIOMEDICAL Vision</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAQUET Plegiox</td>
<td>Sorin Group BCD Vanguard™</td>
</tr>
</tbody>
</table>

Conclusions:
These results suggest that for the devices compared in this study, the MAQUET Plegiox and the Medtronic Trillium™ MYOtherm™ XP eliminated GME the best.
Surgical Correction with Single Approach to the Combination of Aorticopulmonary Window and Interrupted Aortic Arch in Neonatal Period

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Purpose:
Aorticopulmonary window (APW), a congenital abnormality, is a rarely seen case and its accompaniment with Interrupted Aortic Arch (IAA) is even more rarely encountered. Early diagnosis and surgical intervention is life-saving in such cases. The objective of this study was to discuss our results and management methods of this rare pathology complex.

Methods:
Between 2002 to 2008, 6 patients which had APW and IAA pathologies with the signs of cardiac failure mainly were operated in our clinic. All of them were low birth weight (under 1500 grams) and mean weight was 1.2 kg. They were taken to the surgery emergently by echocardiographic diagnosis. In all of the six cases, complete correction was successfully achieved in a single session via median sternotomy and with cardiopulmonary bypass (CPB) and total circulatory arrest (TCA,18oC). Pulsatile perfusion mode was used in all cases during CPB.

According to our clinical experience, early surgical intervention to aortic arch obstructions and accompanied intracardiac pathologies in a single session by median sternotomy can be performed with an acceptable risk potential. Only one patient was died at early postoperative period because of pulmonary hypertensive crises.

Results:
Early and late postoperative periods of our 5 cases in the 4-16 monthly follow-up have no problem. Because of these rare cases, we think that surgical correction in a single session can be possible and safely applied in neonatal period in such combined arch pathologies. We thought that especially pulsatile perfusion mode is more suitable choice in this high risk group pathologies (according to improved patient outcome in maintaining better cardiac, renal and pulmonic function) in the early postoperative period. Short intubation period (12±10.08 hours) and short ICU (2.21±1.23 days) and hospital stay (7.4±2.08 days) were observed in all five patients.
Cardiac Surgery of Prematures and Low Birth Weight Newborns: Is It Possible to Change of Fate?

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Purpose:
Low-birth weight (LBW) continues to be a high risk factor in surgery for congenital heart disease. This risk is particularly very high in LBW infants under 1500 grams and extremely LBW (ELBW) infants under 1000 grams.

Methods:
From January 2005 to December 2008, 43 consecutive LBW neonates underwent cardiac surgery in our clinic. Their weight range were between 800 gram to 1,900 gram. Nine of them were under 1000 grams. Cardiopulmonary bypass (CPB) was used in 17 patients (%39.54) and pulsatile perfusion mode was applied to all of CPB group. Selective cerebral perfusion technique was used in complex arch pathologies. Median gestational age was 36 weeks with 11 (40.7%) premature babies (≤ 37 weeks). Multivariate analysis by logistic regression was used to identify survival predictors. Pathologies were: single ventricle (n= 3), pulmonary atresia-ventricular septal defect (n= 3), aortic coarctation (n= 10), aortcopulmonary window and interrupted aortic arch combination (n= 6), patent arterial duct (n= 11), critical aortic stenosis (n=8), tetralogy of Fallot with pulmonary atresia (n= 2).

Results:
Median follow-up was 18 months. There were two early postoperative deaths. None of the cases showed a need for early reoperation. ELBW found to be that had a significant negative influence on survival.

Conclusions:
The acceptable early and mid-term mortality rates in this group suggest that these operations could be successfully performed. We thought that the use of pulsatile flow could be an important factor in improved patient outcome. There is a need for further and multicentered studies to evaluate of these high risk groups.
Effects of Pulsatile and Nonpulsatile Perfusion on Cerebral Oxygen Saturation And Endothelin-1 in Tetralogy Of Fallot Infants Undergoing Correcting Heart Surgery

Ju Zhao MD#, Jiuguang Yang MD#, Jinping Liu MD#, Shoujun Li MD&, Jun Yan MD&, Ying Meng MD*, Xu Wang MD*, Cun Long MD#

# Department of Cardiopulmonary Bypass; & Surgery department of Pediatric Heart Center, * ICU of pediatric heart center, Fuwai Cardiovascular Hospital Peking Union Medical College & Chinese Association of Medical Science, Beijing, 100037, P.R. China

**Purpose:**

Benefits of pulsatile flow during cardiopulmonary bypass (CPB) in pediatric heart surgery is still controversial and nonpulsatile CPB is still wildly used in clinical cardiac surgery, however, pulsatile CPB must be reconsidered because of its physiologic feature.

Objectives: To evaluate the effects of pulsatile perfusion (PP) and nonpulsatile perfusion (NP) on cerebral oxygen saturation (ScO2) and endothelin-1 (ET-1) in pediatric Tetralogy of Fallot (TOF) patients undergoing open heart surgery with CPB.

**Methods:**

40 pediatric patients was randomly divided into pulsatile group (PP, n=20) and nonpulsatile group (NP, n=20). Pulsatile patients used modified roller pump pulsatile perfusion during cross-clamping period in CPB, although NP patients used roller pump continuous flow perfusion. ScO2 of every patient was monitored from the operation beginning until 6hrs after patients back to ICU. We also monitored hemodynamic status and ET-1 concentration and plasma free hemoglobin (PFH) in blood samples over time in all patients.

**Results:**

Effective PP can be monitored in PP patients and pulse pressure (delta P) was significantly higher in PP group than NP group (p<0.01). ScO2 of PP group was higher than that of NP group (p<0.01) during cross-clamping period and this advantage of PP patients would be maintained until 2hrs after patients back to ICU (p<0.05). ET-1 level in blood was lower when CPB weaned off in PP group than NP group (p<0.01), but there was no different after patients were transferred to ICU between two groups. PFH concentration in PP group at preclamp off and CPB weaned of were higher than that of NP group (p<0.05) in these cyanotic patients.

**Conclusions:**

ScO2 can sensitively indicate the variety of patients cerebral oxygenation during operation. Pulsatile perfusion can increase ScO2 and improve microcirculation during cross-clamping period in TOF pediatric patients, but PP would cause severe hemolysis in these cyanotic patients than NP.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Therapeutic Value of Somatotropin in Treatment of Postoperative Recurrent Serous / Chylous Drainage in Patients with Fontan Circulation.

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Purpose:
Chylothorax is a very rare complication in patients who have undergone cardiac surgery for complex congenital heart disease. Systemic venous hypertension (>17-20 mmHg) causes increased capillary permeability, leading to interstitial oedema, pleural and pericardial effusions, and ascites. This condition is also reflected onto ductus thoracicus, causing multiple lymphatic drainage sites, resulting in chylothorax.

Methods:
In our study, somatotropin (3 mcgr/kg/h for 5 days) was used for treatment of seven patients who underwent Fontan modifications for complex pathologies with functional single ventricles (three with postoperative chylothorax, and two with recurrent serous drainage resistant to conventional medical therapy).

Results:
All five patients were completely cured. One case had late (postoperative third month) pericardial effusion underwent surgical drainage. Following table summarizes our results. The functional capacities of all the patients are in NYHA class I-II. Mean follow-up period is: 6 ± 18 months.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Operative procedure</th>
<th>Chilous*/serous** drainage (ml/day)</th>
<th>Initiation day of STH</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>BY</td>
<td>6</td>
<td>M</td>
<td>VSD-PFO-PS</td>
<td>LT-BDG</td>
<td>550*</td>
<td>POD5</td>
<td>Cured</td>
</tr>
<tr>
<td>MO</td>
<td>3</td>
<td>M</td>
<td>TA-PS-ASD-VSD-LBTS BDG</td>
<td>TCPC (f)</td>
<td>400*</td>
<td>POD7</td>
<td>Cured</td>
</tr>
<tr>
<td>AS</td>
<td>4</td>
<td>F</td>
<td>TA-PS-ASD-VSD-BDG</td>
<td>TCPC</td>
<td>580**</td>
<td>POD7</td>
<td>Cured</td>
</tr>
<tr>
<td>EG</td>
<td>2</td>
<td>F</td>
<td>TA-VSD (r)-ASD-BDG</td>
<td>TCPC (f)</td>
<td>500*</td>
<td>POD8</td>
<td>Cured</td>
</tr>
<tr>
<td>AG</td>
<td>3</td>
<td>M</td>
<td>TA-PS-BDG</td>
<td>TCPC (f)</td>
<td>600**</td>
<td>POD7</td>
<td>Cured</td>
</tr>
<tr>
<td>FT</td>
<td>4</td>
<td>F</td>
<td>TA-PS-BDG</td>
<td>TCPC (f)</td>
<td>450**</td>
<td>POD6</td>
<td>Cured</td>
</tr>
<tr>
<td>EE</td>
<td>4</td>
<td>F</td>
<td>TA-VSD (r)-ASD-BDG</td>
<td>TCPC (f)</td>
<td>400**</td>
<td>POD7</td>
<td>Cured</td>
</tr>
</tbody>
</table>


STH: Somatotropin, POD: Postoperative day

Conclusions:
We think that somatotropin is a good therapeutic modality for treatment of postoperative recurrent serous / chylous drainage in Fontan patients resistant to conventional medical treatment.
Innovative Safety Valve for Prevention of Total Massive Air Embolism

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Ashwini Co-op. Hospital & Research Centre, Maharashtra, India

**Purpose:**
The clinical occurrence of Massive Air Embolism is life threatening event. A number of cases of Massive Air Entry in Cardio Pulmonary Bypass (CPB) circuit have been documented. The reported incidental rate is 1:1000 cases. (CPB Principles and Management; KENNITH M TAYLOR). Incidence of venous Reservoir emptying due to inadequate venous return remains a life threatening problem during CPB because of Massive air embolism. Neurological complications from air embolism are documented by (STONEY.et al). Therefore the need for an Effective Device to Protect the patient from Massive air embolism is needed. We have designed a Safety Valve which prevents the massive air from entering the Aortic line and protects the patient from Massive Air Embolism.

**Methods:**
The safety valve is placed in the Cordiotomy reservoir on the reservoirs outlet opening. It consists of a cylindrical tube attached to the outlet orifice with two holes at the bottom for blood to flow out. Inside the cylindrical tube there is a piston with a air tight float at the top and a rubber stopper at the bottom. This piston moves up and down freely inside the cylindrical tube according to fluid level of the reservoir. As the fluid level reaches the minimum level the piston moves down and the rubber stopper blocks the inside outlet opening of the reservoir due to suction pressure of arterial pump. A minimum level of fluid is thus always ensured in the Cordiotomy Reservoir.

**Results:**
We have tested the valve at various pump flows on experimental basis. The maximum flow achieved was 7.5 liters/mint and the minimum flow was 0.5 liters/mint. It was also tested for various temperatures from 42°C to 18°C and various type of fluid viscosities like Ringer lactate, Coloid Soln, and Blood. No incidence of Massive Air Entry was recorded.

**Conclusions:**
The Safety Valve never allow any massive air to enter the Arterial line from the Cordiotomy Reservoir at any conditions. Also it is very easy to re-establish CPB immediately after getting sufficient return volume in the Reservoir. There was no need to remove air from the Oxygenators and arterial tubing. It requires no special training to operate this new device.
Relation between Renal Dysfunction Requiring Renal Replacement Therapy and Promoter Polymorphism of the Erythropoietin Gene in Cardiac Surgery

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Purpose:
Some genetic polymorphism has been identified as factor in the occurrence and progression of renal dysfunction after cardiac surgery with cardiopulmonary bypass (CPB). Recently, it was demonstrated that the T allele of SNP rs1617640 in the promoter of the EPO gene is significantly associated with proliferative diabetic retinopathy (PDR) and end stage renal disease (ESRD). This disease risk-associated gene and his potential pathway mediating severe microvascular complications in T-allele carriers could play also a role on renal dysfunction in patients who underwent cardiac surgery with CPB.

Methods:
We conducted a prospective single centre study between April 2006 and May 2007. In 481 adult patients who underwent cardiac surgery with CPB we prospectively examined the SNP rs1617640 in the promoter of the EPO gene by DNA-sequencing. The patients were grouped according to their genotype (GG, GT, and TT).

Results:
Genotype distribution of SNP rs1617640 in the promoter of the EPO gene was 36% (TT), 49 % (TG), and 15% (GG). The groups did not differ in age, body-mass-index, gender, CPB time, length of stay in intensive care unit, and hospital stay were unaffected by genotypes. No difference was shown in Euroscore, SAPS II, APACHE II, ARF Score, and RIFLE Score. The mortality was quite uniform across the genotypes. However, an association between TT genotype and acute renal replacement therapy (p=0.03) and IABP usage (p=0.02) were observed after cardiac.

Conclusions:
The analysis suggests that the risk allele (T) of rs1617640 show a significant role in the development of renal dysfunction after cardiac surgery with CPB. Patients with the TT risk allele required more frequent acute renal replacement therapy. Since our result is close to the border of significance, this question should be clarified in larger, prospective studies with long term follow up in the future, if this polymorphism could serve as a risk factor.
The prototype of Polish extracorporeal pulsatile pediatric heart assist device – POLVAD-PED

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(1)Foundation for Cardiac Surgery Development, Artificial Heart Laboratory, Zabrze, Poland; (2)Foundation for Cardiac Surgery Development, Biocybernetics Laborator

Purpose:
The construction of the Polish pediatric extracorporeal ventricular assist device POLVAD-PED (Fig. 1) has been developed and wide range of numerical and physical analyses have been performed.

Methods:
The pump development consisted of the following phases:

1. Computer modeling CAD and CFD: The numerical CAD model design has been supported with computer fluid dynamics (CFD) simulations. The steady-state analyses (ANSYS CFX) for pump’s maximal filling position and maximal ejecting position have been performed; the assumptions of SST turbulence model and Newtonian fluid (constant density $\rho =1060$ kg/m$^3$, dynamic viscosity $\nu =3.4$ mPa·s) have been set.

2. Physical model: The first physical model has been produced in rapid 3D prototyping technology with the performance accuracy of 0.01 mm. The second physical model has been made of biocompatible polyurethane equipped with single disc heart valves Medtronic Hall™.

Hydrodynamic evaluation: The hydrodynamic examination consisted of two phases focused on: general hydrodynamic properties and local fluid dynamics. General hydrodynamic properties evaluation has been performed on physical Windkessel’s model of vascular system. The input pump’s load was a column of water (equivalent pressure $= 15$ mmHg) and adjustable resistance, the output load consisted of resistance and 80 cm$^3$ compliance, fluid temperature has been stabilized at the level of 37°C. The flow (with non-invasive ultrasonic flowmeter) and pressure were measured. Local fluid dynamics evaluation has been done with the usage of pulsed ultrasound Doppler velocimetry (UDV) and laser flow visualization (LFV) techniques. Steady (flow rate: 2.7 L/min) and pulsatile flow examinations (pump frequency 30 beat/min and mean flow 1.7 L/min) have been performed. The following features by UDV have been analyzed: velocity profiles with standard deviation, the level of maximal shear stress values (NSS) and Reynolds Stress values (RNS) at all measuring points. LFV examination: water (viscosity 1.0 cP, density 1.0 g/cm$^3$) used as a working fluid with particles 0.4 ÷ 0.6 µm in diameter and 0.5% concentration.

In-vitro blood testing: For in-vitro examinations the adopted thrombogenesis procedure developed by Schima H. has been used. Heparinized blood circulated in a mock circulatory system with ACT decreasing from level of 4 times to 1.5 times of physiological value - then the test was finished and the pump was inspected regarding thrombus identification. Porcine blood circulated in the system on conditions: pressure 90 mmHg, flow 4.1 L/min and temperature 37°C.

Results:
The safe pump work on blood has been confirmed – the few areas of fluid stagnation were recognized (mainly in the inlet connector area; CFD flow velocity $<0.01$ m/s), dp/dt values in all measuring points are below 3500.0 mmHg, driving pressure influence on pump stroke volume changes has been presented (Fig. 2). Maximal NSS values at all measuring lines do not exceed 0.27 Pa. In the in-vitro thrombogenicity test after 4h of blood circulation the pump was free of massive thrombus. The thin white thrombus localized on the valve and thin red thrombus inside pump were observed.

Conclusions:
The prototype of pediatric pump has been developed with the preservation of an unique asymmetrical geometry and technological assumptions used in adult pump. Hydrodynamic evaluation revealed the correct pump properties, whereas observed flow stagnation regions in the inlet area will be minimized with further detailed device geometry improvement. The pump interior has a low thrombogenicity potential. Mechanical valves utilized in the prototype generate thrombi, which correspond to those observed in vivo in adult pump.
ECMO for Pediatric Cardiac Failure

Robert H Bartlett, MD
Professor of Surgery, Emeritus, University of Michigan Medical School

Extracorporeal life support (ECLS or ECMO) is the use of mechanical devices to replace heart and lung function for cardiopulmonary failure in intensive care. ECMO was first used successfully to treat ARDS in an adult in 1971, cardiac failure in a child in 1972, and respiratory failure in a newborn infant in 1975. ECMO was used primarily in newborn respiratory failure from 1980 to 1990. Success with neonates led to wider application to respiratory failure in children and adults, and to treatment of cardiac failure as a bridge to recovery, VAD support, or transplantation. The extracorporeal life-support organization (ELSO) was established in 1989 to share experience, education, and to maintain a registry of cases. They are now more than 40,000 patients in the registry including over 9000 pediatric cardiac failure cases.

The applications of ECMO in pediatric cardiac failure are postoperative, post-cardiopulmonary bypass cardiogenic shock, myocarditis, myocardiopathy, septic shock, and as an adjunct to cardiopulmonary resuscitation (ECPR). The mode of access is always veno-arterial with major vascular access gained via the jugular and carotid in small children, or using the cardiac cannulas placed for a patient who cannot be weaned from bypass in the operating room. The extracorporeal circuit used today is quite different than the complex circuit used in the past. The current circuit uses a low resistance membrane lung, a safe centrifugal pump, and a small heat exchanger. With the newer devices the management of ECMO is much simpler, safer, and automatic than in the past.

The indication for ECMO is cardiogenic shock unresponsive to optimal treatment, preferably before cardiac arrest occurs. Unresponsiveness is defined as poor perfusion, metabolic acidosis, and oliguria, for an hour or more despite optimal pharmacologic management. The only contraindication is a condition incompatible with normal life after recovery from the (severe brain injury). However the results are best when ECMO is instituted early in severe cardiogenic shock. Profound acidosis and anuria for more than six hours are considered too late, therefore a contraindication in many centers. The indication for ECPR is ongoing resuscitation with chest compressions or direct cardiac massage, but there must be good evidence of adequate perfusion to justify adding extracorporeal support.

ECMO is considered a bridge to decision, recovery, possibly to VAD, possibly to transplant. ECMO is not treatment but a merely life support to allow time for evaluation, diagnosis, and management. When ECMO is used for cardiac support it is important to determine whether the patient is a VAD and transplant candidate on the first day of ECMO. If the answer is yes the patient should be listed for transplant and appropriate steps instituted. If not a timetable for futility should be defined, typically seven to 10 days beyond which cardiac recovery is unlikely.

The outcome of ECMO for cardiac failure in children is 30% survival for ECPR to 80% survival in experienced centers.
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ECMO Research in the Current Regulatory Environment

P. Pearl O’Rourke, MD, Partners HealthCare, Boston, MA

Four separate factors merit consideration: What is ECMO research? Who does ECMO research? What is the broad clinical research environment? What are the relevant regulations?

What is ECMO Research?
ECMO research in 2010 is research on an invasive, device-dependent, costly procedure that is standard, accepted care for some seriously ill patient populations. These descriptors of ECMO, alone and in combination, define the scope of research, for example:
- Invasive and device-dependent: research may focus on new pumps, oxygenators, tubing, new methods of vascular access, anticoagulation, workforce issues re: bedside oversight.
- Costly: research may focus on ways to decrease ECMO costs. Research may also address cost-effectiveness.
- Seriously-ill patient populations: research should focus on identifying appropriate inclusion and exclusion criteria for groups of patients as well as individual patients; comparative effectiveness, outcomes.

Who does ECMO research?
There is no single ECMO-researcher type – but a large category of ECMO researchers that merits specific consideration is that of ECMO clinicians. These are people who are strong advocates for ECMO and who are intimately involved in not only ECMO, but non-ECMO care of patients. In addition, many are involved in various aspects of device development.

What is the broader clinical research environment?
Specific elements to high-light include: Decreased research funds – not only for specific protocols, but also for research infrastructure; the 80-hour resident work-week that limits residents’ ability to participate in clinical research; increased scrutiny on research versus clinical billing; focus on privacy and security; focus on comparative effectiveness and potentially cost effectiveness. AND, HANDLING OF CONFLICTS OF INTEREST.

What are the relevant regulations that must be considered?
Virtually all of them! IRB regulations (Common Rule and FDA regulations) to cover human subjects research. FDA regulations as they pertain to device development. HIPAA and the HiTech Act, as well as numerous new state laws as they relate to privacy, confidentiality and security. Finally there are CMS billing requirements. And, conflicts of interest requirements permeate regulations as well as conditions of funding agencies.

The take home message:
ECMO research has always faced numerous challenges. In 2010 some of these old challenges may be more daunting. For example:
- Reliance on registry databases: the ELSO Registry is invaluable. There is interest in increased scrutiny re: the oversight of any database of patient information. HIPAA in concert with the HiTech Act place some new requirements on the sharing of identifiable data.
- Conflict of interest issues: Most ECMO researchers will now face increased requirements for financial disclosure as well as more intense review of potential COI in any research activity.
- Comparative effectiveness – and possibly cost effectiveness research: While there is increased demand for this area of research – ECMO has always suffered from the lack of accurate real-time control groups. This will require some additional attention.
Extracorporeal Membrane Oxygenation for Cardiopulmonary Resuscitation

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Despite advances in the knowledge, recognition, education, and standardization of the conduct of cardiopulmonary resuscitation survival to hospital discharge for children and adults who suffer an in-hospital cardiac arrest remain poor. Extracorporeal membrane Oxygenation has been shown to be useful in aiding cardiopulmonary resuscitation during cardiac arrest in children and adults who suffer an in-hospital cardiac arrest [1, 2]. ECMO used for this indication i.e. support of cardiopulmonary resuscitation also called ECPR has been shown to promote survival compared to use of standard resuscitation techniques. Furthermore many survivors following ECPR have been shown to have good neurological outcomes [3]. The American Heart Association guideline for the conduct of CPR in children and adults published in 2005 recommends consideration of ECPR in institutions that have ECPR services for patients with easily reversible causes for cardiac arrest and in patients considered to be candidates for cardiac transplantation.

The use of ECMO to support CPR is growing, and accounts for 10% of approximately 1,200 ECMO uses reported to the Extracorporeal Life Support Registry (ELSO) a central data registry that collects information on ECMO uses and outcomes from approximately 116 member centers [2]. Despite increasing use patient selection for ECPR, conduct of ECPR including team logistics, patient management during ECPR, and adjunct therapies used during ECPR such as therapeutic hypothermia remain controversial and widely variable. Furthermore, long-term functional neurological outcomes following ECPR are not available to help patient selection or conduct of ECPR. Current research indicates that early recognition and good cardiopulmonary resuscitation are essential to survival and good neurological outcomes following ECPR.

This talk will explore survival outcomes and predictors of survival and good neurological outcomes for ECPR users. In doing so we will try to define a patient population best suited for ECPR. In addition we will also explore an ideal ECPR program using the experience from Children’s Hospital Boston as an example.

References:

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Inter-Hospital Transport of Children Supported with Extra-Corporeal Membrane Oxygenation

Katherine Clement, MD, Richard Fiser, MD, William Fiser, MD, Carl Chipman, CRNFA, Bonnie Taylor, MD, Mark Heulitt, MD, Michele Moss, MD, James Fasules, MD, Sherry Faulkner, CCP, Michiaki Imamura, MD PhD, Eudic Fontenot, MD, Robert Jaquiss, MD
ECMO Program, Departments of Pediatrics and Surgery, University of Arkansas for Medical Sciences College of Medicine, Arkansas Children’s Hospital, Little Rock, Arkansas, USA

Purpose:
Patients with refractory cardiopulmonary failure may benefit from extracorporeal membrane oxygenation (ECMO), but ECMO is not available in all medical centers. We report our institution’s 20-year experience with inter-hospital ECMO transport.

Methods:
Data (age, weight, diagnosis, ECMO course, hospital course, mode of transport, and outcome) were obtained and compared to the most recent Extracorporeal Life Support Organization (ELSO) registry report.

Results:
Inter-hospital ECMO transport was provided to 112 patients from 1990-2008. Eight were transferred between outside facilities (TAXI group); 104 were transported to our hospital (RETURN group). Transport was by helicopter (75%), ground (12.5%), and fixed wing (12.5%). No patient died during transport. Indications for ECMO in RETURN patients were cardiac failure in 46% (48/104), neonatal respiratory failure in 34% (35/104), and other respiratory failure in 20% (21/104). Overall survival from ECMO for the RETURN group was 71% (74/104); overall survival to discharge was 58% (61/104).

Patients with cardiac failure had a 46% (22/48) survival to discharge. Neonates with respiratory failure had an 80% (28/35) survival to discharge. Other patients with respiratory failure had a 62% (13/21) survival to discharge. None of these survival rates were statistically different from survival rates for in-house ECMO patients or for survival rates reported in the international ELSO Registry ($p > 0.1$ for all comparisons).

Table 1. Comparison of Return Group to ELSO Registry Control Group

<table>
<thead>
<tr>
<th></th>
<th>Weaned from ECMO*</th>
<th>Survived to Discharge*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RETURN Group</td>
<td>ELSO</td>
</tr>
<tr>
<td>Cardiac</td>
<td>60% (29/48)</td>
<td>59%</td>
</tr>
<tr>
<td>Neonatal</td>
<td>91% (32/35)</td>
<td>85%</td>
</tr>
<tr>
<td>Other Respiratory Failure</td>
<td>71% (15/21)</td>
<td>64%</td>
</tr>
<tr>
<td>Overall</td>
<td>71% (74/104)</td>
<td>75%</td>
</tr>
</tbody>
</table>

*p>0.1 for all RETURN vs. ELSO comparisons
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**Conclusions:**
Outcomes of patients transported by an experienced ECMO team to a busy ECMO center are very equivalent to outcomes of non-transported ECMO patients as reported in the ELSO registry. As has been previously reported, inter-hospital ECMO transport is feasible and can be accomplished safely. Other experienced ECMO centers may wish to consider developing inter-hospital ECMO transport capabilities to better serve patients in different geographic regions.
Anticoagulation in ECMO: Time for Proper Evaluation

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Introduction:
Moderate duration extracorporeal life support (ECLS), extracorporeal membranous oxygenation (ECMO) is currently reserved for management of severe respiratory and/or cardiac failure as a bridge to recovery or transplant. The use of various types of oxygenators, pumps and artificial circuits as well as the patient's underlying illness, in some cases eg sepsis, activates hemostasis and results in thrombin generation and the balance of hemostasis becomes shifting toward the development of thrombosis. In an attempt to bring hemostatic balance back to normal and prevent thrombosis of ECMO components as well as the patient, anticoagulation is used. Unfractionated heparin (UFH) currently the agent of choice has a number of challenges associated with its management, including hemostatic differences in children vs adults influencing UFH effect, poor bioavailability of UFH resulting in the need for constant monitoring, a number of imperfect laboratory monitoring techniques (PTT, heparin levels, ACT, TEG and others) and development of antibodies resulting in catastrophic thrombosis (heparin induced thrombocytopenia). The safety and efficacy of UFH in ECMO has not been established through properly designed studies.

Purpose:
To report on inadequacies of current anticoagulation dosing and monitoring as published in the medical literature. To propose a multi centre study using one agreed upon anticoagulation protocol (including monitoring) from which safety and efficacy can be determined.

Methods:
Literature review up to present and evaluation of ELSO data base reports, if appropriate, on UFH use in ECMO.

Results:
The reported current inadequacies of UFH dosing and monitoring will hopefully result in facilitating the establishment of an expert group prepared to design a multicentre study with a common anticoagulation protocol following input and agreement from participating centres and ELSO.

Conclusions:
Current anticoagulation protocols for ECMO vary between centres thus determination of safety and efficacy is challenging. Completion of a properly designed study using an agreed upon anticoagulation protocol with defined outcome measures will provide evidence based guidelines for ECMO which are currently lacking.
Purpose:
Patients suffering from cardiogenic shock refractory to conventional medical treatment experience high morbidity and mortality. The CentriMag pump is a new generation magnetically levitated centrifugal pump. We hypothesized that utilization of the CentriMag pump as a percutaneous ECMO might improve outcomes in this patient population.

Methods:
Between June 2008 and September 2009 twenty-three patients between the ages of 14 and 79 years, 15 male and 8 female, were treated with the CentriMag-ECMO in our institution. Refractory CS etiology comprised: inability to wean from cardiopulmonary bypass following cardiac surgery (n=6), post-partum myocarditis (n=1), primary graft failure following cardiac transplantation (n=1), acute rejection (n=1), cardiac arrest (n=3), cardiopulmonary failure (n=7), and acute myocardial infarction (n=3). All patients were in CS despite inotropic drugs. Pre-implant mean serum lactate was 6.5 m mol/l. ECMO was initiated at the bedside or in the OR in postcardiotomy cases. All patients were monitored in the ICU with routine critical care. Anticoagulation was maintained with Heparin drip to achieve an aPTT level between 50-60 seconds.

Results:
The CentriMag-ECMO functioned appropriately in all patients. Average maximum pump speed was 3,500-4,500 rpm with an average maximum flow rate of 3.5 to 5 L/min. Average support duration was 5.2 days (range 1-14 days) and overall survival to discharge was 57% (13 patients). Five patients received long term LVAD (4 survivors), 8 patients fulfilled our weaning criteria and were successfully weaned and discharged. Five patients achieved sufficient organ recovery to support weaning from ventilator. Nine patients did not survive with causes of death comprising: multi-system organ failure (n=8) and severe neurological disorder (n=2). Other major complications comprised: compromised cannula insertion site (n=18), bacteremia (n=3), hemolysis (n=1), and TE (n=1).

Conclusions:
CentriMag-ECMO represents a novel technology with the potential to reduce morbidity and mortality in select patients suffering from persistent cardiogenic shock. Further clinical investigation is required to determine the magnitude and mechanism of this benefit.
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Constructing the Ideal ECMO Circuit: Analysis of Each Component Using In Vitro and In Vivo Testing

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Purpose:
To construct an ideal ECMO circuit in terms of hemodynamics, each component of the circuit should be evaluated. In previous studies conducted in our laboratory the hemodynamics of the oxygenator have been compared. In this study, we evaluated different sizes of cannulae in a simulated neonatal extracorporeal life support (ECLS) circuit.

Methods:
The neonatal ECLS circuit used included a Capiox Baby RX05 oxygenator, a Rotaflow centrifugal pump and a heat & cooler unit. Seven combinations of arterial and venous cannulae were tested (8F-10F, 8F-12F, 10F-10F, 10F-12F, 10F-14F, 12F-12F, 12F-14F). Both the arterial tubing (1/4 inch) and the venous tubing (3/8inch) length was 2 feet. A Hoffman clamp was located upstream the pseudopatient to maintain a constant patient pressure of 40, 60 and 80 mmHg. Three pressure transducers were placed at post-oxygenator, pre-arterial cannula and post-arterial cannula sites. In each circuit, we measured the pressure drops of arterial cannula, as well as the flow rates at different RPMs (2500 to 4000, 500 intervals). The system was primed with Lactate Ringer's solution, human blood was added to maintain the hematocrit at 40%. The priming volume of the circuit including all of the components was 115ml. The volume the of pseudo patient was 500ml. For each setup, six trials were conducted at 37°C.

Results:
Flow rates increased linearly with increasing size of both venous and arterial cannulae at the same pump RPMs. The increase in flow rate was greater when changing the arterial cannulae (next size larger) compared to changing the venous cannulae (next size larger) by a factor of four. Figure 1 summarizes the results at a constant pseudo patient pressure of 60 mmHg.

Conclusions:
These results suggest that the size of the arterial cannulae has the largest impact on flow rates.
The essential components of an ECMO system have not significantly changed but advances in design and function continue to evolve. Improvements to ECMO platforms that incorporate all components have occurred as systems used for cardiopulmonary bypass continue to be adapted for long-term ECMO applications. While roller pumps have been reliable, centrifugal pumps with pump heads designed for longer duration and minimal adverse effects on red blood cells have gained considerable prominence. The availability of polymethylpentene-coated diffusion membranes has been a welcomed addition, with purported benefits of low resistance, integral heat-exchangers, and ease of priming and de-airing greatly improving and simplifying the ECMO circuit. Future technical developments will be aimed at coupling the pump head with the membrane in an effort to simplify and shorten the ECMO circuit, and in conjunction with smaller controls and platforms, enhance portability and improve deployment in emergency situations.
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How to Build and Train an ECMO Team

Catherine Allan, MD, Boston, MA, USA.

Studies of non-medical high risk enterprises (aviation, nuclear power industry) have shown that human factors, including sub-optimal teamwork, contribute substantially to accidents or catastrophic failures. Likewise, multiple studies across high acuity medical specialties have demonstrated that human factors contribute to substantially to adverse events. In the field of pediatric cardiac surgery, de Leval and colleagues have demonstrated through direct observation of congenital cardiac operations that minor compensated or uncompensated errors, including errors of teamwork and communication, are additive and contribute substantially to the risk death or serious adverse events. In the aviation industry, teamwork and communication skills are taught through a simulation-based program called Crew Resource Management. The principles of Crew Resource Management have been widely adopted in high acuity medical fields, first by David Gaba in anesthesia, under the moniker "Crisis Resource Management" (CRM) Training. CRM Training teaches 5 essential components of team function, including role clarity, communication, personnel support, resource utilization, and global assessment.

Similar to the pediatric cardiac surgery clinical microsystem, a system for providing ECPR is highly complex and susceptible to human error. Contributing factors include 1) high technical complexity, 2) need for high level of cognitive performance, 3) presence of a large, complex multidisciplinary team, and 4) dependence on sophisticated organization structure. In the clinical microsystem of the pediatric cardiac intensive care unit, CRM courses have been used to train teams in effective teamwork and communication utilizing highly discipline-specific scenarios in an effort to overcome these factors. In this session we will review how a traditional CRM course taught in a pediatric cardiac intensive care unit can be adapted to meet the unique needs for teamwork training around ECPR and ECMO emergencies, incorporating key safety protocols organizational structural requirements.
Noninvasive Assessment of Cardiac Function on Mechanical Circulatory Support

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Purpose: Outside of the operating room, mechanical circulatory support is used as bridge to recovery, bridge to transplant and potentially as destination therapy even for pediatric patients. In this situation, the Pediatric Cardiologist may be called upon to assess cardiac recovery. However, conventional echocardiographic markers of cardiac function fail in this situation. Commonly used ejection phase markers like ejection fraction or fractional shortening, myocardial thickening and even dp/dt are somewhat load-dependent. This limits their utility in the unloaded ventricle and even during weaning attempts. This presentation will define the challenge and present alternative function markers including tissue Doppler imaging (TDI) myocardial velocities, isovolumic contraction acceleration (IVA) and strain rate imaging (SR). The relative merits and limitations of these techniques will be illustrated with examples.

Methods: Literature review and case presentations of experimental and clinical data.

Conclusions: Pediatric echocardiographers increasingly face the challenge to assess myocardial function in patients on mechanical circulatory support under non-physiological ventricular loading conditions and/or during weaning attempts. A good understanding of the strength and limitations of the various function markers is essential. While not routinely used in daily practice yet, strain rate imaging and other advanced markers of myocardial deformation are now widely available on standard echocardiographic machines. They may fill an important gap in the diagnostic tool box of the Pediatric Cardiology consultant.
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Pneumatic Pulsatile Ventricular Assist Device as a Bridge to Heart Transplantation in Pediatric Patients

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Purpose:
Despite the remarkable advances with the use of ventricular assist devices (VAD) in adults, pneumatic pulsatile support in children is still limited. We report on our experience in pediatric population.

Methods:
Retrospective review of 17 consecutive children offered mechanical support with Berlin Heart as a bridge to heart transplant from 02/02 to 02/10.

Results:
The median patient age was 4.2 years (75 days to 13.7 years). The median patient weight was 15.8 Kg (4 to 52 Kg). Prior to VAD implantation, all children were managed by multiple intravenous inotropes and mechanical ventilation (14) or ECMO (3). Nine patients required biventricular mechanical support (BVAD), but in all other cases a single left ventricular assist device (LVAD) proved sufficient (47%). The median duration of VAD support was 45 days (2 to 151 days). Nine patients were successfully bridged to heart transplantation after a median duration of mechanical support of 46 days (5 to 131 days), meanwhile two patients are waiting heart transplantation. Six deaths occurred (35%). Since 2007, the survival rate of our patients has increased from 40% to 75%.

In 2 patients with Rpi> 6 WU/m² unresponsive to medical therapy, Rpi dropped to 2.2 and 2 WU/m², after 40 and 23 days of BVAD support, respectively. Seven patients (41%) required at least one pump change. Of 9 patients undergoing heart transplant, 3 developed an extremely elevated (>60%) panel reactive antibody. All 3 experienced at least one acute episode of rejection in the first month after heart transplant. The survival rate after heart transplantation was 100% with a median follow-up of 30.2 months (8 to 7.5 yrs).

Conclusions:
Mechanical support in children with end-stage heart failure is an effective strategy as a bridge to heart transplantation with a reasonable morbidity and mortality. BVAD support may reverse extremely elevated pulmonary vascular resistance.
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Extracorporeal Membrane Oxygenation Following Norwood Stage 1 Procedures

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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 Jan 1998 to Dec 2009 retrospectively.

Results:
Of the 91 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 28±30 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 hypoxemia 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.
Extracorporeal Membrane Oxygenation for Pediatric Cardiopulmonary Resuscitation

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Purpose:
To describe the 10 years experience of extracorporeal cardiopulmonary resuscitation (ECPR) for in-hospital pediatric cardiac arrest in a university affiliated tertiary care hospital.

Methods:
The pediatric patients who received extracorporeal membrane oxygenation (ECMO) during active cardiopulmonary resuscitation from 1999 to 2009 were included in the retrospective study. The venous-arterial (V-A) ECMO were applied in all patients. The primary outcome was survival to hospital discharge. The secondary outcome was neurological status after ECPR at hospital discharge and late follow-up. Good neurological outcome was defined as Pediatric Cerebral Performance Categories (PCPC) 1, 2, and 3.

Results:
We identified 54 ECPR events. The survival rate to hospital discharge was 46% (25/54). The duration of ECMO support was 131+/-84 hours in the survivors and 245+/- 380 hours in the non survivors. The duration of cardiopulmonary resuscitation (CPR) was 39+/-17 minutes in the survivors and 52+/- 45 minutes in the non-survivors (p=N.S). The non-survivors had higher serum lactate level (13.4+/-6.4 vs 8.8+/-5.1 mmol/L, p < 0.01) more renal failure after ECPR (66% [19/29] vs 20% [5/25], p < 0.01). The survival rate of the first three years was 0% and improved to 55% in the recent 7 years. Among the 25 survivors, 21(84%) of them had good neurological outcomes.

Conclusions: ECPR successfully rescued some pediatric patients who failed rescue with conventional in-hospital CPR. Good neurological outcomes were achieved in the majority of the survivors. Higher pre-ECPR lactate level and post-ECPR renal failure were associated with mortality.
Comparison of Perfusion Quality in Hollow-Fiber Membrane Oxygenators for Neonatal Extracorporeal Life Support

Purpose:
Perfusion quality is an important issue in extra-corporeal life support (ECLS); without adequate perfusion of the brain and other vital organs, multi-organ dysfunction and other deficits can result. The authors tested three different pediatric oxygenators (Medos Hilite 800 LT, Medtronic Minimax Plus, and Capiox Baby RX) to determine which gives the highest quality of perfusion at flow rates of 400, 600, and 800 mL/min using human blood (36°C, 40% hematocrit) under both non-pulsatile and pulsatile flow conditions.

Materials and Methods:
Clinically identical equipment and a pseudo-patient were used to mimic operating conditions during neonatal ECLS. Traditionally, the post-oxygenator surplus hemodynamic energy value (SHE\textsubscript{post}, extra energy obtained through pulsatile flow) is the one relied upon to give a qualitative determination of the amount of perfusion in the patient; the authors also examined SHE retention through the membrane, as well as the contribution of SHE\textsubscript{post} to the post-oxygenator total hemodynamic energy (THE\textsubscript{post}):

\[
\frac{SHE\textsubscript{post}}{THE\textsubscript{post}} = 1 - \frac{MP\textsubscript{post}}{EEP\textsubscript{post}},
\]

where MP is the mean arterial circuit pressure and EEP is the energy equivalent pressure. In this way, one can calculate the contribution of SHE to THE using solely the pressures measured independent of the oxygenator and can be used to determine which how much of the initial energy applied to the blood will end up improving perfusion quality.

Results:
At each experimental condition, pulsatile flow outperformed non-pulsatile flow for all factors contributing to perfusion quality. For both pulsatile and non-pulsatile flow, the Capiox Baby RX oxygenator was found to deliver the highest quality of perfusion, while the Minimax Plus oxygenator delivered the least perfusion.

Table 1: Pulsatile vs. Non-Pulsatile Flow

<table>
<thead>
<tr>
<th>Flow (mL/min)</th>
<th>ΔP</th>
<th>SHE\textsubscript{pre} (ergs/cm\textsuperscript{3})</th>
<th>SHE\textsubscript{post} (ergs/cm\textsuperscript{3})</th>
<th>THE\textsubscript{post} (ergs/cm\textsuperscript{3})</th>
<th>SHE:THE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 LT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600 P</td>
<td>44.8</td>
<td>46555±890</td>
<td>29488±632</td>
<td>233091±1564</td>
<td>12.65%</td>
</tr>
<tr>
<td>600 NP</td>
<td>44.0</td>
<td>7176±21</td>
<td>4341±18</td>
<td>199150±349</td>
<td>2.18%</td>
</tr>
</tbody>
</table>

Conclusion:
It is the authors’ recommendation that the Baby RX oxygenator running under pulsatile flow conditions be used for pediatric ECLS, but further studies need to be done in order to establish its effectiveness beyond the FDA approved time span.
Comparison of Retrograde Flow between Three Centrifugal Blood Pumps in a Pediatric ECLS Model

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Purpose:
During extracorporeal life support (ECLS), retrograde flow may occur once the pump
revolutions decrease below a critical value determined by the patient’s blood pressure and
circuit resistance. It is crucial to select proper blood pump to avoid this adverse event. In this
special ECLS model, retrograde flow of centrifugal blood pump was evaluated.

Methods:
The experimental circuit included a centrifugal blood pump head (RotaFlow, CentriMag or Bio-
Medicus® BP-50), Capiox® Baby RX05 oxygenator (Terumo Corporation, Tokyo, Japan) and Sorin pediatric tubing package (Sorin S.p.A., Milano, Italy). HL-20 heart-lung machine (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) was utilized to mimic the native heart with pulsatile perfusion. The circuit was primed with heparinized human packed red blood cells and Lactated Ringer’s solution (total volume 480 ml, corrected Hematocrit 40%). Trials were conducted at normothermia (36°C). Under isoresistance conditions, performance including circuit pressure and flow rate was measured for every setting analyzed.

Results:
The zero pump flow rates of CentriMag pump were highest whereas those of Bio-Medicus® pump were lowest at same test conditions (p < 0.001). At same rotation speed, RotaFlow pump has significant higher pump flow rate than CentriMag pump (82–272ml/min at 60mmHg, 32–172ml/min at 80mmHg and 31–132ml/min at 100mmHg) and less retrograde flow (p < 0.001).

Table 1. Pump flow rate of ECLS with three different pump head at different circuit pressure

<table>
<thead>
<tr>
<th>Circuit Pressure (mmHg)</th>
<th>Pump head</th>
<th>Pump Rotation speed (rpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1000</td>
<td>1100</td>
</tr>
<tr>
<td>60 Bio-Medicus</td>
<td>-14.83</td>
<td>22.86</td>
</tr>
<tr>
<td>RotaFlow</td>
<td>-96.30</td>
<td>-57.97</td>
</tr>
<tr>
<td>80 Bio-Medicus</td>
<td>-98.08</td>
<td>-63.02</td>
</tr>
<tr>
<td>RotaFlow</td>
<td>-189.64</td>
<td>-159.18</td>
</tr>
<tr>
<td>CentriMag</td>
<td>-222.11</td>
<td>-197.22</td>
</tr>
<tr>
<td>100 Bio-Medicus</td>
<td>-159.94</td>
<td>-127.99</td>
</tr>
<tr>
<td>RotaFlow</td>
<td>-239.85</td>
<td>-211.27</td>
</tr>
<tr>
<td>CentriMag</td>
<td>-271.11</td>
<td>-250.36</td>
</tr>
</tbody>
</table>

At each rpm, statistically significant differences (p < 0.0001) were observed among three centrifugal pumps (Biomedicus vs. Rotaflow vs CentriMag).

Conclusions:
The results obtained in this experiment demonstrate retrograde flow may occur in all of the three centrifugal pumps with low rotation speed. At same rotation speed, RotaFlow pump has significant higher pump flow rate than CentriMag Pump and less retrograde flow.
Advantages of Pulsatile Perfusion Mode on Vital Organ Recovery in Pediatric Patients

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Purpose:
This study was undertaken to evaluate the effects of cardiopulmonary bypass (CPB) on vital organ recovery and thyroid function in pediatric patients undergoing open heart surgery under pulsatile or nonpulsatile perfusion modes.

Methods:
289 consecutive pediatric patients undergoing open heart surgery for repair of congenital heart disease were prospectively entered into the study and randomly assigned to either the pulsatile (Group P, n = 208) or nonpulsatile perfusion group (Group NP, n = 81). 148 of the patients were in the neonatal and infantile age group (neonatal Group P, n = 112 and neonatal Group NP, n = 36). All patients received identical surgical, intra-perfusion, and postoperative care. Study parameters included intubation time, duration of ICU and hospital stay, requirements for inotropic support, pre- and postoperative enzymes (ALT, AST), CRP, lactate, albumin, blood count (leukocytes, hematocrit, platelets), thyroid hormones (TSH, FT3, FT4), creatinine levels , mean urine output (ml/day) and total drainage (ml). Major complications and clinical outcomes were documented.

Results:
There were no statistically significant differences in preoperative or operative parameters between the two groups (age, BSA, weight, X-Clamp and CPB time, base flow, flow rates and hemofiltration). All age groups (neonatal and older than neonatal) were evaluated according to the same age category in the study.

Group P had significantly less inotropic support compared to Group NP (number of agents 1.6±0.08 vs 2±0.12, p = 0.0015; dopamine 6.21±0.58 vs 9.02±0.46 μg/kg/min, p = 0.00024; dobutamine 4.32±0.5 vs 5.4±0.6 μg/kg/min, p = 0.038, adrenalin 0.018±0.004 vs 0.046±0.004 μg/kg/min, p = 0.021), less intubation time (8.14±2.04 vs 14.26±1.99 hours, p = 0.018), as well as shorter duration of ICU (1.35±0.07 vs 2.54±1.19 days, p = 0.015) and hospital stays (5.78±1.18 vs 10.06±1.58 days, p = 0.0024).

Although there were no significant differences in either creatinine, enzyme levels and drainage amounts between two groups, lower lactate levels (12.32±2.02 vs 19.67±2.05 mg/dL, p = 0.00034), higher albumin levels (3.21±0.03 vs 2.95±0.06 μg/kg/min, p = 0.046) and higher urine output (624.52 ± 21.5 vs 512.55 ± 24.2 ml/day, p = 0.018) during ICU period was observed in Group P.

Mean preoperative thyroid hormone levels were similar between groups. TSH, Total T3-T4 and FT3-FT4 levels were markedly reduced versus their preoperative values in both groups. There were significantly lower decreases in FT3 and FT4 levels in the pulsatile group during CPB and at postoperative 72 hours. Thyroid hormones changes after CPB were as follows in the pulsatile (Group P) and nonpulsatile groups (Group NP), respectively: FT3, during CPB 2.18 ± 0.4 pg/mL vs 1.33 ± 0.2 pg/mL (p<0.00018), postoperative 72 h 2.41 ± 1.21 pg/mL vs 1.98 ± 1.34 pg/mL (p<0.0041), FT4, during CPB 1.58 ± 0.16 ng/dL vs 0.64 ± 0.14 ng/dL (p<0.0025), postoperative 72 h 1.91 ± 0.8 ng/dL vs 1.71 ± 0.6 ng/dL (p<0.0038).

There were no significant differences in other hormones levels between 2 groups in the early postoperative period.
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Conclusions:
Statistically significant differences in outcomes were observed when comparing pulsatile to nonpulsatile perfusion systems (shorter ICU and hospital stay durations). We postulate that the use of pulsatile flow results in enhanced preservation of cardiac function and better maintenance of renal and pulmonary function in the early post-bypass period, possibly contributing to improved patient outcomes. Results also indicate enhanced preservation of thyroid hormone homeostasis with pulsatile perfusion, which may improve patient outcomes. Further research is required to elucidate the exact mechanisms responsible effects on thyroid homeostasis.
Pulsatile Flow Improves Cerebral Blood Flow in Pediatric Cardiac Surgery

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Purpose:
The objection of this study is to evaluate the effect of pulsatile flow on cerebral blood flow in infants undergoing cardiac surgery with mild hypothermic Cardiopulmonary bypass (CPB).

Methods:
Thirty infants scheduled for open-heart surgery were randomized to pulsatile group (Group P, n = 15) and non-pulsatile group (Group NP, n = 15). In Group P, pulsatile perfusion was applied during aortic cross-clamping period, whereas non-pulsatile perfusion was used in Group NP. Systolic blood velocity (Vs), diastolic blood velocity (Vd), mean blood velocity (Vm) as well as pulsatile index (PI) and resistant index (RI) were measured by Transcranial Doppler (TCD) during anesthesia (T1), at the beginning of CPB (T2), 10 minutes after aortic cross-clamping (T3), 3 minutes after declamping (T4), the cessation of CPB (T5), and the end of the operation (T6). Clinical parameters and arterial blood gas were also recorded.

Results:
There were no significant differences in clinical parameters and arterial blood gas in both groups. During the aortic cross-clamping period, the blood flow showed an apparent pulsatile characteristic in group P. However, the flow was flat in Group NP. (Figure) At T3 and T4, Vs in Group P was significantly higher than that in Group NP, while Vd and Vm did not show any differences. PI and RI in Group P were also higher than those in Group NP (both p < 0.05), and closer to the baseline level. At T5, Vd and Vm were significantly higher in Group P (p < 0.05), whereas Vs didn’t show significant difference between two groups. Additionally, PI and RI in Group P were significantly lower than in Group NP (p < 0.05). However, at T6, none of cerebral blood velocity, PI and RI were different in Group P and Group NP. (Table)

<table>
<thead>
<tr>
<th></th>
<th>Vs (cm/s)</th>
<th>Vd (cm/s)</th>
<th>Vm (cm/s)</th>
<th>PI</th>
<th>RI</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>100.3 ± 19.0</td>
<td>35.1 ± 11.8</td>
<td>56.8 ± 13.4</td>
<td>1.186 ± 0.257</td>
<td>0.655 ± 0.0814</td>
</tr>
<tr>
<td>Group P</td>
<td>99.4 ± 18.1</td>
<td>40.8 ± 15.8</td>
<td>60.3 ± 15.6</td>
<td>1.042 ± 0.392</td>
<td>0.590 ± 0.119</td>
</tr>
<tr>
<td>T2</td>
<td>59.9 ± 11.3</td>
<td>27.1 ± 9.4</td>
<td>38.0 ± 7.2</td>
<td>0.895 ± 0.421</td>
<td>0.530 ± 0.189</td>
</tr>
<tr>
<td>Group P</td>
<td>61.5 ± 11.0</td>
<td>28.7 ± 7.9</td>
<td>39.7 ± 7.6</td>
<td>0.853 ± 0.306</td>
<td>0.529 ± 0.121</td>
</tr>
<tr>
<td>T3</td>
<td>61.1 ± 13.6</td>
<td>28.1 ± 7.5</td>
<td>39.1 ± 7.5</td>
<td>0.857 ± 0.349</td>
<td>0.527 ± 0.136</td>
</tr>
<tr>
<td>Group P</td>
<td>42.0 ± 10.6*</td>
<td>33.9 ± 9.7</td>
<td>36.8 ± 9.9</td>
<td>0.233 ± 0.116*</td>
<td>0.197 ± 0.083*</td>
</tr>
<tr>
<td>T4</td>
<td>56.3 ± 12.2</td>
<td>28.7 ± 8.9</td>
<td>37.9 ± 8.1</td>
<td>0.752 ± 0.361</td>
<td>0.478 ± 0.155</td>
</tr>
<tr>
<td>Group P</td>
<td>46.1 ± 13.7*</td>
<td>33.2 ± 10.4</td>
<td>37.5 ± 11.0</td>
<td>0.346 ± 0.179*</td>
<td>0.271 ± 0.112*</td>
</tr>
<tr>
<td>T5</td>
<td>88.8 ± 21.2</td>
<td>32.1 ± 10.0</td>
<td>51.0 ± 11.2</td>
<td>1.119 ± 0.367</td>
<td>0.622 ± 0.146</td>
</tr>
<tr>
<td>Group P</td>
<td>80.0 ± 18.1</td>
<td>21.3 ± 7.8*</td>
<td>41.9 ± 9.6*</td>
<td>1.451 ± 0.360*</td>
<td>0.726 ± 0.100*</td>
</tr>
<tr>
<td>T6</td>
<td>93.9 ± 19.0</td>
<td>29.2 ± 8.4</td>
<td>50.8 ± 10.3</td>
<td>1.299 ± 0.285</td>
<td>0.686 ± 0.0830</td>
</tr>
<tr>
<td>Group P</td>
<td>90.9 ± 18.0</td>
<td>32.8 ± 12.9</td>
<td>52.2 ± 13.0</td>
<td>1.162 ± 0.399</td>
<td>0.638 ± 0.119</td>
</tr>
</tbody>
</table>

No: * p < 0.05 (Group P vs Group NP)  # p < 0.001 (Group P vs Group NP)

Conclusions:
Pulsatile perfusion may increase cerebral blood flow and decrease cerebral vascular resistance in early period after mild hypothermic CPB.
Blood Transfusion in Pediatric Surgery

Y. Durandy, MD, France.

Purpose:
To quantify the volume of blood needed for pediatric cardiac surgery.

Methods:
Inclusion criteria: Patients operated-on with a blood prime, from September 2009 to January 2010. Miniaturized bypass circuit and microplegia were always used. Prime volume was 100 ml for patients up to 3.5 Kg, 125 ml for 3.6 Kg to 7.5 Kg patients and 160 ml for 7.6 to 15 Kg patients. Prime was composed of reconstituted blood. After weaning from bypass, the circuit blood was collected with remaining blood bank products. This blood was used for post-bypass transfusion. After the last transfusion, the remaining blood volume was measured and the total amount of blood transfused was calculated from the difference between the blood volume of packed red cells and fresh frozen plasma units and the remaining blood volume.

Results:
45 patients were operated with a mean weight of 5 kg (1.9 to 8.6). No platelets infusion were needed during the hospital stay. If we assume a patient blood volume of 80 ml/kg the mean blood transfused during the hospital stay was equivalent to 68 % of the total blood mass.

<table>
<thead>
<tr>
<th>Volume transfused mL</th>
<th>Hb before surgery g/dL</th>
<th>Hb during surgery g/dL</th>
<th>Hb after surgery g/dL</th>
<th>Time to extubation hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± S.E. 271 ± 112 Median 248</td>
<td>Mean ± S.E. 10.3 ± 1.7 Median 9.7</td>
<td>Mean ± S.E. 11.0 ± 1.5 Median 10.8</td>
<td>Mean ± S.E. 12.3 ± 2.4 Median 12.1</td>
<td>Mean ± S.E. 12± 33 hours Median 5.5 hours</td>
</tr>
</tbody>
</table>

Conclusions:
There is no dramatic increase in blood requirement in the post-antifibrinolytic therapy era. Blood free surgery remains a difficult challenge in small infants but a more restrictive transfusion decision with a trigger for blood transfusion mainly based on clinical tolerance rather than on hemoglobin level may decrease blood transfusion and thus, complication related with blood bank use.
Cerebral Oxygen Metabolism During Total Body Flow and Antegrade Cerebral Perfusion at Deep and Moderate Hypothermia

Stanford University

Purpose:
Objectives: To evaluate the effect of temperature on cerebral oxygen metabolism at total body flow bypass and antegrade cerebral perfusion (ACP).

Methods:
Neonatal piglets were put on cardiopulmonary bypass with the initial flow rate of 200 ml/kg/min. After cooling to 18°C (n= 6) or 25°C (n= 7), flow was reduced to 100 ml/kg/min (half-flow; HF) for 15 minutes, ACP was initiated at 40 ml/kg/min for 45 minutes. Following re-warming, animals were weaned from bypass and survived for four hours. At baseline, HF, ACP, and 4-hours post bypass (post 4h), cerebral oxygen extraction (CEO2) and lactate values were monitored. Regional cranial oxygen saturation (rSO2) was continuously recorded through the procedure using near-infrared spectroscopy.

Results:
At 18°C, CEO2 trended lower at HF and ACP (p= 0.114, 0.656), and higher at post 4h (p= 0.31) compared with baseline. Cranial rSO2 was significantly higher at HF and ACP (p<0.001, <0.001) and equal at post 4h (p= 0.88). Lactate trended higher at all time points (p= 0.59, 0.51, 0.11) compared with baseline but there was no significant difference. At 25°C, CEO2 was equal at HF and ACP (p= 0.80, 0.99) and trended higher at post 4h (p= 0.45) compared with baseline. Cranial rSO2 was significantly higher at HF (p= 0.01), equal at ACP (p= 0.60), and lower at post 4h (p= 0.030). Lactate was significantly higher at all time points (p= 0.036, <0.001, <0.001).

Conclusions:
At 18°C, each bypass condition provided more than enough oxygen to the brain and post-bypass cranial rSO2 was maintained in the pre-bypass range. At 25°C, ACP provided minimum oxygen to the brain and post-bypass cranial rSO2 was lower than baseline. At 25°C, since brain oxygen demand is not so reduced as at 18°C, a higher ACP flow might be needed to supply more than enough oxygen to the brain.
A Newly Developed Miniaturized Heart Lung Machine – Expression of Systemic Inflammation in a Small Animal Model

Heike Schnoering, MD¹‡, Jutta Arens, Dipl.-Ing.²‡, Estela Terrada, PhD¹ Joerg S. Sachweh, MD¹, Maximilian W. Runge¹, Thomas Schmitz-Rode, MD², Ulrich Steinseifer, Dr. Ing.² and Jaime F. Vazquez-Jimenez, MD¹

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² Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany
‡ Both Authors contributed equally to this manuscript

Purpose:
Cardiopulmonary bypass may cause severe inflammatory reactions and multi organ failure, especially in low weight newborns and premature in part due to the large extrinsic surface contact area and the essential addition of foreign blood. Thus, we developed a new miniaturized heart lung machine (MiniHLM) for neonates with a total static priming volume of 102 ml (including arterial/venous line) and tested it in a small animal model.

Methods:
Seven Chinchilla Bastard rabbits were perfused with the MiniHLM (dynamic priming volume 120 ml). Seven animals were perfused with Dideco Kids® and Stöckert roller pump (modified dynamic priming volume 175 ml) served as control. The rabbits were anesthetized and sternotomized, followed by cannulation of the aorta and the right atrium. The Aorta was clamped for one hour. Blood for examination of inflammation (TNFα, IL8, IL 6, IL10 und IL1β) and blood gas analysis was taken before skin incision, 5 min before opening aorta, 15 min after opening aorta and 4 hours after the beginning of cardiopulmonary bypass. The parameters of inflammation were expressed by the comparative C_T method (ΔΔC_T method). After gradually reducing HLM, the heart was decannulated and the sternum was closed.

Results:
All rabbits were successfully weaned from the cardiopulmonary bypass. Blood gas analysis was unremarkable in all cases. Foreign blood was not administered in all cases. There was a tendency for lower inflammatory expression in the MiniHLM, though statistically not significant.

Conclusions:
The newly developed MiniHLM prototype was tested successfully in a small animal model in terms of technical function and expression of inflammation. Upcoming tests with the industrially manufactured MiniHLM may uncover the advantages of the MiniHLM in comparison to the conventional HLM.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Evaluation of Neonatal Membrane Oxygenators with respect to Gaseous Microemboli Capture and Transmembrane Pressure Gradients

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Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, and Bioengineering, Penn State College of Medicine, Penn State Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
A series of studies performed in our center demonstrate gaseous microemboli (GME) remain a challenge in cardiac surgical procedures. Evaluation of novel oxygenators must address hemodynamic parameters and microemboli capture capability. The objective of this study is to compare two neonatal membrane oxygenators, Quadrox-i and Capiox RX05, with respect to gaseous microemboli capture and transmembrane pressure drops.

Methods:
The experimental circuit included a Maquet HL-20 heart-lung machine, a Heater-Cooler Unit HCU 30 (MAQUET Cardiopulmonary AG, Hirrlingen, Germany), membrane oxygenator (Quadrox-i Neonatal or Capiox RX05) and a Capiox® cardiotomy reservoir CX*CR10NX (Terumo Corporation, Tokyo, Japan). The circuit was primed with Lactated Ringer’s solution and de-aired according to clinical priming procedures then human packed red blood cells were added into the circuit to maintain hematocrit at 30% in both groups. The total volume of the system was 400ml. Heparin (5000IU) was added into the circuit. Pump flow rate was set at 500ml/min or 1000ml/min with 100mmHg of circuit pressure at normothermia (35°C). Bolus air (0.5ml) was injected into the circuit at pre-pump site over 5 seconds. Gaseous microemboli elimination as well as relevant hemodynamic parameters were compared between respective oxygenators.

Results:
Total emboli counts and total emboli volume was significantly reduced by Quadrox-i neonatal membrane oxygenator compared to Capiox® RX05 membrane oxygenator. Classification and quantification of gaseous microemboli detected at post-oxygenator site at two different flow rates indicated Quadrox-i Neonatal captures the majority of microemboli larger than 40 microns in diameter. The Quadrox-i neonatal membrane oxygenator had a higher trans-membrane pressure drop at 500ml/min whereas it had a lower pressure drop at 1000ml/min compared to Capiox Baby RX05 oxygenator.

Table 1. The count and volume of GME and membrane pressure drop of the two tested oxygenators

<table>
<thead>
<tr>
<th>Flow rate (ml/min)</th>
<th>Count</th>
<th>Post-oxy</th>
<th>Volume (ml)</th>
<th>Pressure drop (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-oxy</td>
<td>&lt; 40µm</td>
<td>&gt; 40µm</td>
<td>Pre-oxy</td>
</tr>
<tr>
<td>Qua-i 500</td>
<td>554±43</td>
<td>19±2</td>
<td>1±1</td>
<td>9.7E-02±1.5E-02</td>
</tr>
<tr>
<td>1000</td>
<td>582±781</td>
<td>1051±201</td>
<td>26±14</td>
<td>6.3E-02±1.9E-02</td>
</tr>
<tr>
<td>RX05 500</td>
<td>560±133</td>
<td>126±23</td>
<td>4±5</td>
<td>1.6E-02±9E-03</td>
</tr>
<tr>
<td>1000</td>
<td>554±461</td>
<td>3015±265</td>
<td>150±58</td>
<td>3.9E-02±1.4E-02</td>
</tr>
</tbody>
</table>

Conclusions:
Compared to Capiox® RX05 membrane oxygenator, Quadrox-i Neonatal membrane oxygenator has significantly improved microemboli handling capacity. In terms of pressure drop, Quadrox-i Neonatal is higher than that of Capiox RX05 at 500ml/min, but is lower at 1000ml/min.
Comparison of a Miniature Centrifugal Rotary Pump (TinyPump) and Roller Pump in Neonatal Piglets

Purpose:
A seal-less, ultraminiature rotary centrifugal blood pump (TinyPump) with a priming volume of 5 ml was developed. The purpose of this study was the evaluation and comparison of the effects of the miniature centrifugal rotary pump (TinyPump) and a roller pump on the coagulation system, inflammatory response and cardiac function in a neonatal piglet model.

Methods:
Twelve neonatal piglets (body weight 3.8 ± 0.3kg) were divided into two groups based on the driving pump system; Group R (roller pump) and Group T (TinyPump). The CPB system consisted of the membrane oxygenator (Capiox Baby RX, Terumo Corp., Tokyo, Japan) with its corresponding hard-shell venous reservoir connected to coated biocompatible 3/16 internal diameter arterial and venous polyvinyl chloride tubing lines, which measured a total of 90 cm in length. These were connected to a driving unit (TOWNOK compo, Tonokura Medical, Inc., Tokyo, Japan) with a remote roller pump head or TinyPump. The total priming volume was 170 ml and in both groups. CPB was established by cannulation of the aorta and the right atrium. These animals were placed on the mild hypothermic CPB (30-32 ℃) at 120ml/kg/min for 2 hours. No cardiac arrest or blood transfusion was performed. Inotropic and vasoactive drugs were not used in this study.

Results:
These factors showed significant differences after CPB:

<table>
<thead>
<tr>
<th></th>
<th>Pre-CPB</th>
<th>Post-CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group R</td>
<td>Group T</td>
</tr>
<tr>
<td>PAP (mmHg)</td>
<td>20±4</td>
<td>20±7</td>
</tr>
<tr>
<td>RVCI (l/min/kg)</td>
<td>0.29±0.09</td>
<td>0.26±0.04</td>
</tr>
<tr>
<td>PVRI (dynes/cm(^5)/kg)</td>
<td>3104±1202</td>
<td>3039±1799</td>
</tr>
<tr>
<td>SVRI (dynes/cm(^5)/kg)</td>
<td>11690±3053</td>
<td>11512±3063</td>
</tr>
<tr>
<td>Lung water content (%)</td>
<td>88.9±1.1</td>
<td>86.9±0.7†</td>
</tr>
<tr>
<td>Thrombin-antithrombin complex (ng/ml)</td>
<td>2.4±1.1</td>
<td>2.3±0.8</td>
</tr>
<tr>
<td>Platelet counts (x10(^4) μl)</td>
<td>29±10</td>
<td>31±8</td>
</tr>
</tbody>
</table>

* P < 0.05, Group R vs. Group T; † P < 0.01, Group R vs. Group T; ‡ P < 0.001, Group R vs. Group T. RVCI, right ventricular cardiac index; PVRI, pulmonary vascular resistance index; SVRI, systemic vascular resistance index.

Conclusions:
This study demonstrated that this newly developed TinyPump particularly reduced the activation of the coagulation system to a greater extent than the roller pump. Furthermore, the TinyPump showed an excellent hemodynamic performance with less lung edema and pulmonary vascular resistance in comparison to the roller pump in neonatal piglets.
The Role of Phospho-AMPK and VEGF in a Model of Chronic Heart Failure

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The first two authors contributed equally the same to this study

Objective:
We established a stable and reproducible animal model of chronic-heart-failure (CHF) in sheep to investigate biomolecular changes. AMP-activated-protein-kinase (AMPK) plays an important role in cellular energy homeostasis and its increase is associated with myocardial ischemia. Vascular-endothelial-growth-factor-A (VEGF-A) acts as an important signalling-protein for neoangiogenesis.

Methods:
We examined 15 juvenile sheep (mean-weight 32±4kg, control n=3, ShamOP n=2, coronary microembolization (CME) n=10). CHF was induced under fluoroscopic-guidance by multiple sequential microembolization through bolus-injection of polyester-microspheres (90µm, n=25,000) into the left main coronary artery (Fig. 1). CME was repeated up to three times in two to three week intervals until animals started to develop stable signs of CHF. All animals were followed for 3 months. Phosphorylation of AMPK, marking the activated protein form, was detected by Western-blotting, VEGF-A and VEGF-receptor2 (VEGF-R2)-mRNA were detected by real-time-PCR. Glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) was used as housekeeping-gene.

Results:
All 10 CHF-animals developed clinical signs of CHF. Western-bLOTS showed a significant phosphorylation of AMPK in CME-animals compared to control-group (Phospho-AMPKα/GAPDH control: 0.0, CME left ventricle (LV): 0.39 ± 0.20, CME right ventricle (RV): 0.53 ± 0.30; p<0.05). VEGF-A and VEGF-R2-expression in CME-animals myocardium was located in the range of control-group but this data could not reach statistical significance caused by to the small size of each group. While microinjection was performed into the left main coronary artery, phosphorylation of AMPK and expression of VEGF-A und VEGF-R2 were higher in the right than left ventricle.

Conclusions:
Multiple sequential intracoronary microembolization can effectively induce myocardial dysfunction with clinical and biomolecular signs of chronic ischemic cardiomyopathy. Quantitative analysis of biomolecular markers showed significant higher phosphorylation of AMPK in chronic heart failure animals compared to control myocardium.

Figure 1: Multiple infarcted areals in myocardium after autopsy (see arrows)
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Pediatric Extracorporeal Life Support (ECLS) Systems: Education and Training at Penn State Hershey Children’s Hospital

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Penn State Hershey Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, Comparative Medicine and Perfusion Services, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose: We share our experience in transitioning from our old Extracorporeal Life Support (ECLS) system to our current system. This was not an evolutionary change but a revolution in support since ECLS has advanced in simplicity and reliability, using a long-term hollow fiber oxygenator and centrifugal pump. Whereas the operation of the circuit was previously in the hands of perfusionists, the aim of the current project was to familiarize all clinicians (physicians, fellows, residents, practitioners, nurse educators, perfusionists, and ICU nurses) with our new simplified circuit. This aim was met by involving the pediatric cardiovascular research center and animal research facility in the training program.

Methods: Our new ECLS circuit used a Quadrox-D hollow-fiber membrane oxygenator and Rotaflow centrifugal pump (Maquet Inc., Bridgewater NJ, USA). This circuit had already been tested in vitro in our research laboratory. During the didactic part of the course, the circuit was demonstrated as a wet lab. The final part of the course was a voluntary visit to the animal research facility. The main objective of this training was to provide an opportunity for all of our clinicians to have “hands on” experience with the next generation oxygenators and blood pumps. Both normal operation and emergency procedures were reviewed. The session concluded with clinical case scenarios to reinforce the education and training.

Animal Labs: The entire staff was provided 2-hour sessions, focused on setup, priming and normal operation of the ECLS system. Clinical situations requiring intervention were viewed. The session included the participants demonstrating and verbalizing normal parameters and appropriate interventions in the event of an emergency. A handout with documentation of the session, clinical scenarios and evaluation was provided.

ECLS Model in piglets: Domestic swine (n = 5), ranging in size from 17.3 – 20.9 kg were anesthetized with Ketamine (20 mg/kg) and Acepromazine (1 mg/kg), given intramuscularly. Following intubation, mechanical ventilation was initiated using 1.5 % Isoflurane in 100% oxygen. Peripheral venous access was established using auricular veins for fluid and Fentanyl continuous rate infusions (CRI). Following a 50 mcg IV Fentanyl bolus, a Fentanyl CRI (6-8 mcg/kg/hr) was maintained for the duration of the procedure. Heparin (2000 units IV) was administered prior to cannulae placement in the right carotid artery and right internal jugular vein. Activated clotting time was measured every 45-60 minutes, with a target range of 200-250 seconds; additional doses of heparin were administered as needed. Arterial blood pressure and blood gasses were measured via a right femoral artery catheter. Other physiologic parameters measured included heart rate, ECG, oxygen saturation, respiratory rate, end tidal CO₂, tidal volume, and body temperature. Total time on circuit ranged from 5-6 hours; pigs were euthanized with a commercial euthanasia solution (Euthasol®) at the conclusion of the training laboratory.
We used intra-operative echocardiography for this study. Echocardiographic monitoring was provided as guidance for the instrumentation of the animal. This involved transthoracic and epicardial imaging as appropriate. A GE Vivid I system was used (GE Healthcare, Milwaukee, WI) with 3.5 MHz or 5 MHz transducers as needed. The position of the cannulae was ascertained with 2D echocardiography. Cardiac function was assessed using conventional parameters such as fractional shortening and ejection fraction and color tissue Doppler imaging. The animal was monitored for complications such as pericardial effusion, thrombus or valvular insufficiency.

**Protocol for Training Sessions:** The sessions were designed in 2 hour increments. The initial content provided a demonstration of the normal operating procedures of the Rotaflow console and drive unit, oxygenator and input to the entire ECLS circuit. An “ECLS patient” and circuit were reviewed for both normal and abnormal clinical presentations during support.

Participants were required to identify derangements of “normal” ECLS operation (without the participants awareness that the circuit had been changed) and demonstrate corrective interventions and reassessment.

**Results:** In the fall of 2009, the entire pediatric ECLS team had an opportunity to train in the animal laboratory. These training sessions were also available to clinicians in the adult and neonatal units that offer ECLS. A total of 54 participants were trained in 5 days of training. The PICU at the Penn State Children’s hospital has a total of 29 ECLS trained nurses or 93% of the total PICU nursing staff.

The participants valued the following aspects of the experience:

1. The scenarios encouraged critical thinking in order to arrive at the best intervention given the patient’s condition.
2. The animal laboratory setting provided a “safe” environment to learn more about normal and abnormal equipment function.
3. Corrective interventions and reassessment of potential emergency situations were offered in a guided, constructive approach.

**Conclusions:** With the revolutionary change in ECLS, we took an entirely new view of support from the ground up. Most of the changes had little or nothing in common with our old ECLS system: personnel, training and management of support. Involving the pediatric research and animal research facility proved to be invaluable in the education and training of the ECLS team. We strongly feel that education and training for all clinicians involved in ECLS support is a key to safe support. The effort throughout this process was to build a competent ECLS team that could deal with any clinical situation that may arise. We feel the patient requiring support has a new level of safety both in equipment and staff training. With the less offensive nature of the new ECLS system, the patient has a greater chance for a full recovery.

**Acknowledgment:** This research was supported by the Children’s Miracle Network Funds.
Purpose: Efficacy of desensitization therapy, in pediatric patients, with VAD support as a bridge to heart transplantation.

Background: the effect of ventricle assist device (VAD) in pediatric patients on the development of anti-human leukocyte (HLA) antigen antibodies and their impact on orthotopic heart transplantation (OHT) outcome have not been extensively evaluated.

Methods: a retrospective review of all patients undergoing VAD implant at our Institution between 2007 and 2009 was performed. Serial panel reactive antibody (PRA) was obtained prior to VAD implant, during VAD support and after OHT. The donor specific antibodies(DSA) were detected after OHT. Patients who became sensitized (PRA >10%) underwent desensitization therapy consisting in plasmapheresis associated to a low dose of IgG infusion. The second step consisted in repeated immunoabsorption procedures associated to rituximab infusion.

Conclusions: VAD therapy was associated with the development of anti HLA sensitization in 60% of recipients. We believe that the long time of VAD support, the transfusions and the immaturity of the immunological system in the very young children can predicted sensitization. There were no differences in overall survival or outcomes after OHT.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Mechanically Assisted Total Cavopulmonary Connection with a New Axial Flow Pump

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Background: Up to 40% of patients with total cavopulmonary connection (TCPC) experience late failure with systemic venous hypertension and liver dysfunction. A prototype of mechanically assisted TCPC using a new “child version” of the Jarvik axial flow pump, capable of flow rates between 1-3 L/min in a range of 5,000-9,000 rpm, was tested in a sheep model.

Methods: Six sheep (42-45 Kg) underwent extracardiac TCPC, classic in 2 and “assisted” in 4. In the latter model, a 16 mm reinforced Gore-tex tube was interposed between the two cavae and T-connected to the pulmonary artery via a composite graft including, in sequence, another 16 mm reinforced Gore-tex tube, the Jarvik axial pump (positioned as distal as possible) and a short-segment 12 mm regular Gore-tex tube. Both groups were weaned off cardiopulmonary bypass. In the assisted group, the axial pump was titrated to maintain the baseline cardiac output. Pressures, cardiac output, systemic and pulmonary vascular resistance, lactate levels and blood gasses were recorded for three hours.

Results: In the unsupported group, a gradual circulatory deterioration, with increasing lactate levels, occurred after one hour. In the assisted group there were stable cardiac index of 2.85 ± 0.60 l/min/m², systemic venous pressures of 10 ± 1 mmHg and a mean pulmonary artery pressure of 12 ± 1 mmHg with a 2 mmHg trans-device pressure step-up at a cardiac output of 2.2 l/min. Systemic and pulmonary vascular resistance, blood gasses and arterial lactate levels remained stable to baseline. There was no caval collapse even with pump rates over 10,000 rpm.

Conclusion: A new child axial flow pump in a T-shaped composite Gore-tex graft provides normal cardiac output and physiologic stability in a sheep model of TCPC. This experimental arrangement will serve to further evaluate the potential for mechanical support in patients with Fontan failure.
The Changes of Inflammatory Cytokines in the Support of Extracorporeal Membrane Oxygenation (ECMO)

Feilong Hei, MD, Hong Sun, MD, Shuyi Lu, MD, Kun Yu, MD, Liang Sun, 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:
In order to know the changes of the inflammatory cytokines of these patients and to provide the evidence for the prevention and treatment of the inflammatory complications, we observe the changes of the inflammatory cytokines during the ECMO support in this study.

Methods:
Eleven post-cardiac surgery patients who had cardiogenic shock and undergone ECMO support were observed. Four milliliters of blood was drawn from the radial artery at 30 min (T1), 12 h (T2), 24 h (T3), 48 h (T4), 72 h (T5) after ECMO started. The INF-α, IL-1β, IL-4, IL-6, IL-8 and IL-10 were analyzed using the radioimmunoassay.

Results:
The concentration of INF-α, IL-1β, IL-4, IL-6, IL-8 and IL-10 was significantly higher than the normal value at all time point during the ECMO support. The concentration of INF-α, IL-1β, IL-6 and IL-8 got to its peak value at 12 hours (T2) of the ECMO support and decreased gradually at 24 hours (T3) of the ECMO support. At the 72 hours (T5) of the ECMO support the concentration was significantly reduced compared to that of the 30 min (T1). The concentration of IL-4 and IL-10 arrived at its peak value at the 24 hour (T3) of the ECMO support and the 72 hours (T5) was still significantly higher than that of 30 min (T1) (P<0.05).

Conclusions:
(1) In the early stage of ECMO support, the secretion of the inflammatory cytokines increased. When the internal environment became stable, the secretion of cytokines decreased. (2) The peak secretion of the anti-inflammatory cytokines was late than that of the inflammatory cytokines. But the duration of its peak secretion is longer. (3) We should take the anti-inflammatory measures on the first day of ECMO support to alleviate the morbidity of severe inflammatory reaction.
Extra Corporeal Circulation in Pediatric Accidental Hypothermie

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Purpose:
In the pediatric population, deep accidental hypothermia with drowning or near-drowning is still an emergency with a very poor prognosis requiring rapid active core re warming. This study reviews retrospectively our surgical experience with extracorporeal re warming in patients with deep hypothermia and cardiopulmonary arrest.

Methods:
We reviewed thirteen patients being re warmed in our clinic between 1987 and 2007 because of accidental deep hypothermia. The average age of the patients was 3.2 years; four were female and nine were male. All patients were intubated and ventilated. Resuscitation was immediately started and continuously performed during the transport until initiation of Cardiopulmonary bypass (CPB). Rectal temperature at admission ranged from 20ºC to 29ºC (mean 25.3ºC).

Results:
All of the patients were re warmed and restoration of spontaneous circulation was achieved in 11 patients (84.6%) with CPB, in 2 (15.4%) patients treatment was ended in the operating room who could not be weaned from CPB despite adequate re warming due to severe cardiopulmonary insufficiency. In 2 patients Extra Corporeal Membrane Oxygenation was used to treat oxygenation due to severe pulmonary oedema. Six of the 11 successfully weaned patients (54.5%) could finally be discharged home, but except one completely recovered patient all suffered a severe neurological deficit. Mortality and morbidity is influenced by pulmonary, and transient neurological complications. Modes of re warming, age, sex, rectal temperature, serum electrolytes did not influence mortality.

Conclusions:
Severe accidental hypothermia remains a challenging emergency. Extracorporeal circulation is the treatment of choice, providing efficient re warming and circulatory support. Therefore maximal efforts at resuscitation should be made until normotherma is achieved while pediatric patients can survive accidental deep hypothermia even after prolonged circulatory arrest.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

The Choice of ECMO and VAD in Children

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Purpose:
Objective: The objective of this study is to summarize the case supported with ventricular assist device (VAD) and extracorporeal membrane oxygenation (ECMO) in Shanghai Children’s Medical Center.

Methods:
From March, 2004 to April, 2009, 16 cases were supported with mechanical circulatory devices after open-heart surgery in Shanghai Children’s Medical Center. Nine of them were support with the VAD and 7 with ECMO. ECMO and VAD were set up routinely. During the support, the flow rates were maintained between 80-120ml/kg.min in both groups. ACT was kept between 150-180s with the continuous infusion of heparin.

Results:
Nine children were supported with VAD for 3-111 hours, 5 (56%) of them were weaned and 3 (33%) were discharged. And 7 were supported with ECMO for 65-498 hours, 4 (58%) were weaned and 3 (42%) were discharged. The duration for support was longer in ECMO group (P=0.04), and there was no significant difference between two groups in wean ratio and discharged ratio.

The coagulation system complications, including bleeding and embolism, were the most frequent complication. The most frequent cause of death is bleeding too (4 cases). In addition, other 4 cases died from neurological event, mechanical failure, hepatic failure and right ventricular failure respectively. After being weaned, 2 cases passed away because of cardiac failure and severe mal-nutrition condition. The costs of VAD (USD 5,000-22,000) were lower than (P=0.01) those of ECMO (USD 11,000-45,000).

Conclusions:
Both VAD and ECMO can support the cardiac function post-operatively. VAD results in less complication and lower costs. ECMO is preferred to the patients with worse respiratory function, severe right heart failure, and young infants. VAD has its advantages to vent left heart completely, accelerate recovery and spend less.
Mechanical Performance Comparison between two Centrifugal Blood Pumps in an Adolescent-Adult ECLS Model

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Purpose:
Centrifugal blood pumps have been widely adopted in conventional adult cardiopulmonary bypass and circulatory assist procedures. Different brands of centrifugal blood pumps incorporate distinct designs which affect pump performance. In this adult extracorporeal life support (ECLS) model, the performance of two brands of centrifugal blood pump (RotaFlow blood pump and CentriMag blood pump) was compared.

Methods:
The simulated adult ECLS circuit used in this study incorporated a centrifugal blood pump, Quadrox D membrane oxygenator and Sorin adult ECLS tubing package. A Sorin Cardiovascular® VVR® 4000i venous reservoir (Sorin S.p.A., Milano, Italy) with a Hoffman clamp served as pseudo-patient. The circuit was primed with 900ml heparinized human packed red blood cells and 300ml Lactated Ringer’s solution (total volume 1200 ml, corrected Hematocrit 40%). Trials were conducted at normothermia (36 °C). Performance including circuit pressure and flow rate was measured for every setting analyzed.

Results:
The shut-off pressure of RotaFlow was higher than CentriMag for all points measured at the same rotation speed (p < 0.0001). The shut-off pressure differential between the two centrifugal blood pumps was significant and increased given higher rotation speeds (p < 0.0001) (Figure 1). RotaFlow blood pump has higher maximal flow rate (9.08 ± 0.01L/min) compared with CentriMag blood pump (8.37 ± 0.02L/min) (p < 0.0001). The blood flow rate differential between the two pumps when measured at the same RPM ranged from 1.64L/min to 1.73L/min.

Conclusions:
Findings support the conclusion that RotaFlow has better mechanical performance than CentriMag. The benefits of RotaFlow versus CentriMag are currently being evaluated in clinical studies.
Implantable Cardioverter Defibrillator in Familial Friedrichs Ataxia

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Purpose:
Friedrichs ataxie (FRA) is an autosomal recessive disease of the central nervous system which is associated with familial cardiomyopathy. Cardiac involvement is seen in more than 90% of the patients and is the most common cause of death in these patients.

Methods:
This review discusses retrospectively the indication of implantable cardioverter defibrillators (ICD) in five pediatric patients (4 female and 1 male, mean age 17.4 years) who underwent ICD implantation between 2007 and 2008 in the University Hospital of Goettingen. The diagnosis of FRA was established by standard clinical criteria and proven in each case by genotyping at the frataxin locus.

Results:
The mean duration of illness in all pediatric patients was 10.4 years from apparent onset to time of ICD implantation. All patients received transvenous lead systems. There was no intraoperative and postoperative complications.
At the follow up, the neuromuscular symptoms had no further progressed, and quality of life improved. In electrocardiogram were minor repolarisation changes. All patients had normal echocardiograms and no angina has been reported. Coronary angiographies were normal.

Conclusions:
Increasing evidence indicates that many of these patients develop ventricular dysfunction. In the absence of definitive surgical cure an ICD is generally indicated in the young with hemodynamically significant sustained ventricular tachyarrhythmia’s. The use of ICD in children with FRA is safe.
Subpectoral generator implant is preferable. Only with a multidisciplinary approach to overall management survival can be improved.
Biocompatibility Evaluation of the TinyPump™ for Pediatric Left Ventricular Assist Device Application

Background:
Pediatric patients with end-stage heart failure require mechanical circulatory support as adult patients. However, there are very few ideal circulatory support devices for small patients, and pumps for adult patients have been used widely in neonates and infants, resulting in poor outcomes. In order to meet the requirements for neonates and infants, pediatric circulatory support devices must be compact with low priming volume, easily controllable with low flow, less traumatic to blood cells and tissues, and bio-compatible with minimum anti-coagulation.

Purpose:
We have designed and developed an ultra-miniature rotary centrifugal blood pump, TinyPump™ with a priming volume of 5 ml, which has already demonstrated the controllable performance for low flow and durability in vitro. To evaluate feasibility of TinyPump™ for left ventricular assist device (LVAD) application in neonates and infants, we have evaluated the biocompatibility and hemodynamic performance of the TinyPump™ in pediatric animal model using Shiba-goats. In vivo, the TinyPump™ was implanted in Shiba-goats as LVAD, and the biocompatibility was evaluated to improve the pump design as reflected in the outcome for the future long term use.

Materials and Methods:
TinyPump™ is a disposable, centrifugal pump developed at Tokyo Medical and Dental University since 2004. The devise weighing 150 g comprises of a disposable pump head with a 30mm diameter impeller having six straight vanes, and a reusable motor driver. TinyPump™ implantations were performed in twenty one (17 female and 4 male) 1 year-old Shiba-goats, with body weight ranging from 8.4 to 17.5 kg. Under gas anesthesia, through left lateral thoracotomy, 22 Fr inflow cannula was inserted through left ventricular apex, while 6mm outflow graft was anastomosed to descending aorta, followed with connection to TinyPump™ mounted back of the animal. Postoperatively, hemodynamic monitoring included heart rate, arterial and central venous pressure, pump flow and rotation speed. Target flow in all animals was maintained at 0.9±0.1 L/min which is approximately half of the native PA flow measured in control animals. Blood samples were collected to evaluate peripheral organ functions, hemolysis and thrombosis.

Results:
Goats were divided into three groups, acute phase (6hours; n=4), sub-chronic phase (6hours-2POD; n=11), and chronic phase (3POD- 21POD; n=6) based on the survival duration. In the early experiments, hemolysis and thrombus generated at the bearing of the impeller resulted in termination of the study. The modification in bearing design, pump housing and magnetic coupling helped minimize the hemolysis and thrombosis related complications, resulting in longer survival of animals.

Conclusions: Our experience to date has shown that the TinyPump™ can maintain the hemodynamics with minimum adverse effects to the blood components and organ functions in Shiba-goats for the duration of two weeks. With further improvement in pump durability and hemocompatibility, the TinyPump™ can be a suitable circulatory support device for neonates.
Evaluation of Capiox FX05 Oxygenator with an integrated arterial filter on trapping gaseous micro-emboli and pressure drop with open and closed purge line

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Purpose:
The gaseous micro-emboli (GME) during cardiopulmonary bypass is still a problem because there is a positive correlation between micro-emboli exposure during CPB and post-operative neurological injury. It is important to minimize the number of GME delivered to the patients undergoing cardiopulmonary bypass procedure. In this study, we evaluated the capturing of GME as well as membrane pressure drop of a new membrane oxygenator Capiox BabyFX05 which has an integrated arterial filter with open and closed purge line in a simulated CPB model.

Methods:
We used all the components in this study identical to our clinical CPB circuit. Three Emboli Detection and Classification (EDAC) quantifier transducers were placed at pre-pump, pre-oxygenator and post-oxygenator site in the circuit. Two flow probes as well as three pressure transducers were placed at both upstream and downstream the oxygenator. The system was primed with Lactate Ringers solution and added human blood to maintain the hematocrit at 30%. 1ml of air was injected in pre-pump site under nonpulsatile perfusion modes at three flow rates (500, 750 and 1000ml/min) at 35°C with changing the purge line open and closed. As a total of 36 trials, n = 6 were done for each unique set-up. Circuit pressure was kept constant at 100mmHg. Both of the size and quantity of micro-emboli at post-oxygenator site were recorded for 5 mins after each injection.

Results:
Total counts of GME were significantly reduced with the purge line open when compared to keeping the purge line closed. At all flow rates, most GME were under the size of 20micron. In terms of micro emboli greater than 40micron, the counts were significantly higher without the purge line compared to keep the purge line open at the flow rates of 750 and 1000 ml/min. There is a tiny difference less than 1 mmHg in membrane pressure drop between the open and close of the purge line under all flow rates due to the small A-V shunt.

Table 1. Microemboli count, classification and membrane pressure drop under different flow rates (Mean±SD)

<table>
<thead>
<tr>
<th>Flow rate (ml/min)</th>
<th>Purge line</th>
<th>Total count</th>
<th>0 - 20 µm</th>
<th>20 - 40 µm</th>
<th>&gt;40µm</th>
<th>Pressure drop (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
<td>open</td>
<td>69±17</td>
<td>59±14</td>
<td>9.8±3.7</td>
<td>0.33±0.52</td>
<td>36.3±0.08</td>
</tr>
<tr>
<td></td>
<td>close</td>
<td>143±21</td>
<td>102±12</td>
<td>40±9</td>
<td>2.2±0.75</td>
<td>35.6±0.01</td>
</tr>
<tr>
<td>750</td>
<td>open</td>
<td>2139±264</td>
<td>1757±228</td>
<td>364±42</td>
<td>17±8</td>
<td>50.3±0.18</td>
</tr>
<tr>
<td></td>
<td>close</td>
<td>2550±306</td>
<td>2118±246</td>
<td>407±58</td>
<td>25±5</td>
<td>49.7±0.22</td>
</tr>
<tr>
<td>1000</td>
<td>open</td>
<td>5719±646*</td>
<td>4688±499*</td>
<td>960±133*</td>
<td>50±12*</td>
<td>63.5±0.03</td>
</tr>
<tr>
<td></td>
<td>close</td>
<td>7830±1448</td>
<td>6383±1168</td>
<td>1360±266</td>
<td>87±20</td>
<td>62.6±0.10</td>
</tr>
</tbody>
</table>

*p<0.0001, purge line open vs. close.

Conclusions:
These results suggest that the integrated arterial filter of Capiox FX05 oxygenator significantly improve the capturing of GME with little impact on membrane pressure drop.
Rare Cardiac Pathology:
Unilateral Absence of Pulmonary Artery with Tetralogy of Fallot

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Purpose:
Patients with unilateral absence of pulmonary artery and tetralogy of Fallot (TOF) are a high-risk group for whom there is no consensus on the correct approach to surgical management. The aim of this report is to review our clinical experience in the treatment of those patients.

Methods:
Between July 1995 and May 2008, 432 patients underwent correction of TOF in our clinic, 5 of those patients with unilateral absence of pulmonary artery (2 had absence of right pulmonary artery, 3 had absence of left pulmonary artery).
Right ventricular patches were used in all patients and transannular patch with a monocusp that was made of patient’s autolog pericardium was used in last 2 patients.

Results:
Five patients with absence unilateral pulmonary artery (2 right and 3 left) with TOF underwent successful surgical correction. Pulsatile perfusion mode was used in last 3 cases. Prophylactic peritoneal dialysis was used in all patients at early postoperative (24-48 hrs) period for negative fluid balance and protection to mediators. Median follow-up from date of first operation was 4 years. There was no operative and early postoperative deaths. All of the patients had good early and late clinical outcome (according to echocardiographic findings and exercise tests).

Conclusions:
Unilateral absent pulmonary artery with TOF is a very rare congenital cardiac anomaly. The major important factor is the size of pulmonary artery to decision for total correction of those patients. However right ventricular outflow transannular patch with a monocusp (pericardial or goretex membrane) should be used for infundibular stenosis. Our opinion that early intervention, pulsatile perfusion mode and prophylactic peritoneal dialysis may be useful to the early postoperative management in these complex cardiac pathologies.
Surgical Approach to “Swiss cheese” VSDs

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Purpose:
The main handicap of surgical approach to “Swiss Cheese” VSDs is residual VSDs or formation of septal dysfunction. In our series of 6 cases, we repaired the multiple VSDs by using a “single patch” on the right aspect of septum by right atrial approach and double patch on two of the cases. In this paper, we would like to discuss our surgical approach and present our results.

Methods:
Eight consecutive patients (5 male, 3 female) with diagnosis of VSD were operated in our clinic between January 2000-March 2006. Patients were between 2 months – 2 years old (mean age 7.6 +/- 6.2 months) VSD was accompanied by ASD and pulmonary hypertension (subsystemic in 6 cases) in all cases. Also, coarctation of aorta in 2 cases, tricuspid insufficiency in 2 cases, Ipsuc in 2 cases and in one case Holt-Oram syndrome were present. In 6 of the cases VSDs were repaired with a single dacron patch. In the remaining two cases muscular VSD was repaired with a single patch, perimembranous VSD was repaired with a second patch.

Conclusions:
In neonatals and infants surgical intervention of “Swiss Cheese” VSDs are complicated and present high post-operative morbidity and mortality rates. In the early and late post-operative period follow-up of septal wall motion by echocardiography is crucial. New modes of therapy such as hybrid approaches with preoperative catheter application or intraoperative closure techniques with “devices” may assist accompanying pathologies and lower risk rates in this complex and risky patient group.
Ventricular Assist Device Implantation With A Prior Mechanical/Prosthetic Valve: A Retrospective Review Of A Single-Center Experience

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Division of Cardiac Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

Purpose:
The presence of a mechanical or bioprosthetic valve had previously been considered a relative contraindication for ventricular assist device (VAD) implantation. The purpose of this study was to review our experience of patients with a prior mechanical or prosthetic valve undergoing VAD placement.

Methods:
From 2002 to 2009, 133 patients underwent VAD implantation at the Brigham and Women’s Hospital. There were 7 patients with a mechanical or prosthetic valve who required VAD support. Patient demographics and operative characteristics were assessed with primary endpoints including post-operative complications and mortality.

Results:
Among the 7 patients, there were 5 males (71.4%) with a mean age of 58 years. Preoperative patient characteristics included: diabetes mellitus (3/7, 42.9%), hypertension (3/7, 42.9%), chronic lung disease (6/7, 85.7%), NYHA Class IV (4/7, 57.1%) and cardiogenic shock (2/7, 28.6%). At the time of VAD implantation, 3 patients had a bioprosthetic aortic valve, 1-mechanical mitral valve, 2-mechanical aortic valve, 1-combination mechanical aortic/mitral valve. The indications for VAD included: bridge to transplantation (2/7, 28.6%), bridge to recovery (1/7, 14.3%) and postcardiotomy ventricular failure (4/7, 57.1%). One patient with a mechanical mitral/aortic valve developed a thromboembolic event (stroke) after VAD implantation. The long-term mortality was 4/7 (57.1%), 3/7 patients died in the immediate postoperative period from multisystem organ failure. Four patients survived the immediate postoperative period: 3 underwent transplantation (1/3 died from right heart failure) and 1 patient underwent successful VAD explantation.

Conclusions:
Although a mechanical or bioprosthetic valve is not an absolute contraindication for VAD placement, the presence of such devices appears to confer increased morbidity and mortality.
Surgical Approach to Aortic Coarctation in the Neonatal-Infant group

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Purpose:
The timing for surgical intervention on the aorta coarctation (AoCoA) in the neonatal and infant group shows difference from center to center because of the fact that this group bears a high risk. We aim to present the pre and postoperative monitoring and results of AoCoA cases in the neonatal and infant group whom we operated in a single center with a surgical approach.

Methods:
During the period of January 2000-May 2006, 32 aorta coarctation cases of neonatal (n = 14) and infant age (n = 18) groups were taken to operation and resection and end-to-end anastomosis was applied on them. The mean age of the Neonatal group was: 12±10.4 days and their mean weight was: 2.8±1.2 kg while the mean age for the infant group was: 5.2±2.8 months and their mean weight was: 6.1±2.1. In 5 cases AoCoA was concomitant with VSD. For these cases both AoCoA and VSD repair was applied through the median sternotomy approach. A wide anastomosis was applied on 11 cases with aortic arch hypoplasia to also make arch reconstruction possible. Medical records, catheter and ecocardiographic findings of all cases as well as their postoperative clinical monitoring were evaluated during our retrospective data analysis. Mean X-clamp time was: 35±5 minute.

Results:
Mean follow-up period was 56 ± 12 months, the recoarctation was 2/14 (% 14.3) in the neonatal group, and 1/18 (%5.5) in the infant group. (p=0.19) Balloon angioplasty was applied and recoarctation developed in 3 cases. 2 of these cases were re-operated. Another 2 cases showed trivial degrees of gradient (20 mmHg) (in the 4th and 6th postoperative months) and closely monitored.

Conclusions:
In our series the results of surgical approach to the aortic coarctation in the neonatal and infant group was showed that low morbidity and mortality. Recoarctation frequency was low. Another important advantage is the possibility to treat the hypoplastic aortic arch in the one stage. Close postoperative ecocardiographic monitoring of the cases should be done. Any value over 20 mmHg should be considered as risky. Balloon angioplasty is a treatment option to be preferred for the recoarctation developed after the operation.
Pattern Width Variation by Printer Control Parameters in a Hydrogel-based Bioprinting System

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Purpose:
Bioprinting techniques have been an interest for constructing tissue or artificial organ in complex 3D structure because of its repeatability and high precision in printing resolution at macro- and micro-scales. To implement minimal pattern width in a hydrogel-based bioprinting system, a study on the printing characteristics has been performed by varying printer control parameters.

Methods:
The bioprinting system consists of three axis of x-y-z motion control stage and one axis of nozzle control. We prepared line pattern design in an image format from which CAD/CAM data were constructed for input to the system. The system control software was developed in Labview™ (National Instruments Co. U.S.A.). Combinations of linear printing speed [1.67, 3.33, 6.67 mm/sec], injection needle inner diameter [0.26, 0.11 μm], injection nozzle head linear speed [4.17, 5.21, 8.33, 13.89, 41.67 μm/sec] as available in the used bioprinting system structure were used for the variation of the pattern width. The biomaterial we use for the printing was a hyaluronic acid (HA) based hydrogel. HA is one of the extra-cellular matrix proteins. Acrylated HA is crosslinked with PEG. Cell or other biochemical components were not contained in the hydrogel.

Results:
The experiments showed that pattern width could have wide variation largely depending on the printing speed parameters. The minimal pattern width was 141.38 μm. (The maximal from current combinations was 603.218 μm.)

Table 1. Comparison printing pattern width with various printing parameters.

<table>
<thead>
<tr>
<th>Needle Inner Diameter [μm]</th>
<th>Linear Printing Speed [mm/sec]</th>
<th>Nozzle Head Speed [μm/sec]</th>
<th>Pattern Width (Average) [μm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.26</td>
<td>1.67</td>
<td>8.33</td>
<td>382.068</td>
</tr>
<tr>
<td>0.26</td>
<td>3.33</td>
<td>8.33</td>
<td>301.378</td>
</tr>
<tr>
<td>0.26</td>
<td>6.67</td>
<td>8.33</td>
<td>266.430</td>
</tr>
<tr>
<td>0.26</td>
<td>6.67</td>
<td>41.67</td>
<td>603.218</td>
</tr>
<tr>
<td>0.26</td>
<td>6.67</td>
<td>13.89</td>
<td>445.058</td>
</tr>
<tr>
<td>0.26</td>
<td>6.67</td>
<td>5.21</td>
<td>244.596</td>
</tr>
<tr>
<td>0.26</td>
<td>3.33</td>
<td>4.17</td>
<td>193.102</td>
</tr>
<tr>
<td>0.11</td>
<td>3.33</td>
<td>4.17</td>
<td>141.38</td>
</tr>
</tbody>
</table>

(a) Result of 1), (b) Result of 2) and (c) Result of 3) in Table 1

Conclusions:
In the used system, conventional micro injection syringe instead of custom fabricated nozzle is used and the study showed that wide variations in the pattern width can be implemented by controlling printing system parameters, which could be applied into various tissue structure printing.
Evaluation of HL-20 Roller Pump and Rotaflow Centrifugal Pump on Perfusion Quality and Gaseous Microemboli Handling

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*Pediatric Cardiovascular Research Center, Department of Pediatrics, †Department of Surgery, ‡Department of Bioengineering, §Department of Public Health Sciences, Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children’s Hospital, Hershey, Pennsylvania, USA

Purpose:
The objective of this study was to evaluate the effects of two types of blood pump (HL-20 roller pump and Rotaflow centrifugal pump) on hemodynamic energy production as well as gaseous microemboli (GME) handling capacity.

Methods:
This study employed a simulated pediatric cardiopulmonary bypass (CPB) model which included a Jostra HL-20 heart-lung machine or Rotaflow centrifugal pump, respectively; a Capiox BabyRX05 oxygenator; Capiox pediatric arterial filter; and ¼ inch tubing. Total experimental system volume was 700ml (500ml for the circuit and 200ml for the pseudo-neonatal patient). Hematocrit was maintained at 30% using human blood. At the beginning of each experiment a 5ml bolus of air was injected into the venous line and both GME data as well as pressure values were recorded at post-pump, post-oxygenator and post-arterial filter sites. All experiments were conducted under non-pulsatile perfusion at three flow rates (500, 750 and 1000ml/min) and three blood temperatures (35°C, 30°C and 25°C). With n=6 for each setup a total of 108 trials were conducted.

Results:
Total numbers of gaseous microemboli increased as temperature decreased from 35°C to 25°C in trials using the HL-20 roller pump while the opposite effect occurred when using the Rotaflow centrifugal pump. At a given temperature total GME counts increased with increasing flow rates for both pumps. Total microemboli counts were significantly less using Rotaflow compared to HL-20 roller pump especially under high flow rates. Less than 10% of total microemboli were larger than 40µm in diameter with the majority of GME presenting in the 0-20 µm class in all trials. Post-pump total hemodynamic energy (THE) increased with increasing flow rates and decreasing temperatures in both circuits using the respective pumps. HL-20 roller pump delivered more THE than Rotaflow centrifugal pump at all measured flow rates and temperatures.

Table1. GME delivery and THE production at post-pump site at 30°C (Mean ± SD)

<table>
<thead>
<tr>
<th>Flow rate (ml/min)</th>
<th>Total count</th>
<th>Total Volume (ml)</th>
<th>THE (erg/cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HL-20</td>
<td>Rotaflow</td>
<td>HL-20</td>
</tr>
<tr>
<td>500</td>
<td>1.2±2.0</td>
<td>1.3±2.4</td>
<td>4.0E-09±6.6E-09</td>
</tr>
<tr>
<td>750</td>
<td>37±18</td>
<td>3.2±2.4</td>
<td>5.3E-08±3.5E-08</td>
</tr>
<tr>
<td>1000</td>
<td>972±177</td>
<td>251±77</td>
<td>2.1E-06±5.9E-07</td>
</tr>
</tbody>
</table>

Conclusions:
Results suggest HL-20 roller pump has diminished gaseous microemboli handling capacity compared to Rotaflow centrifugal pump while generating greater hemodynamic energy.
Objective: CircuLite has developed a miniature pump intended for partial support in adult patients. Due to its small size, the Synergy device could be used to provide support to children with congenital heart defects and acquired heart failure. Through modifying the inlet geometry of the pump, 5 designs were conceptualized. The feasibility of using the Synergy device in children was assessed by completing computational, in vitro, and in vivo studies.

Methods: Through fit studies inporcine animal models and child hearts from a heart museum, 3 design concepts were selected to be pursued further. Computational fluid dynamic (CFD) was used to further screen these designs. In vitro hemolysis and hydrodynamic performance studies were conducted to confirm performance and biocompatibility. These studies lead to five two-week animal experiments that were performed in juvenile ovine animals using the final 2 design concepts.

Results: Both concepts demonstrated adequate support and hemodynamic performance in clinically acceptable ranges. The surgical procedure to implant proved to be easy and was accomplished in approximately 1 hour. The in-vivo results confirmed that the Child System provides adequate LV unloading, normal end-organ function and no device malfunctions during the evaluations.

Conclusions: These results demonstrate that the CircuLite Synergy System has the potential to provide circulatory support in children. One concept has been selected for further evaluation to refine the design and prove its long term performance.
The DELTASTREAM blood pumps belong to a special type of rotary blood pumps, so called diagonal flow pumps. Diagonal flow pumps represent a mixture of axial and radial pumps. End of the nineties the development of the DELTASTREAM blood pumps was initiated at the Helmholtz institute Aachen. The intention was to design a pump of small size, which is however able to generate a high flow and a high pressure to fulfill the requirements of a wide range of applications within the clinical field. From simplified bypass systems for routine applications to ECLS and short term ventricular assist applications in pediatrics and adults. Besides that the pump system should be able to perform continuous as well as pulsatile flow.

During development different impeller designs were tested to improve and optimize the hydraulic as well as hematologic characteristics. A shrouded design of the impeller with washout holes was the result to meet these multiple requirements.

In 2001 the DP1 was introduced to the market. With its integrated motor and the approval for 24 hours of use the DP1 engaged a unique position at that time. To strengthen the position of the DELTASTREAM concept for routine applications (minimized bypass systems, beating heart support), the DP2 was developed. A new external motor drives the impeller by means of a magnetic coupling.

The DP3 represents the main part in the next generation of DELTASTREAM blood pump technology. Especially by using a new bearing concept the performance for longer pump runs was optimized radically. In a first step the DP3 is actually approved and CE-marked for 7 days of use. Combined with the option to run the pump in continuous as well as pulsatile mode, the DELTASTREAM system meets the requirements on new perfusion concepts nowadays. Besides excellent hydraulic capabilities, the first clinical results showed low thrombogenity and also a very low hemolysis.

Especially the small design and resulting low priming of the new pump qualifies the DP3 for neonatal and pediatric applications. Besides that the pump can be adjusted exactly at very low flows. Additional safety and control functions of the console lead to an outstanding position of the new DELTASTREAM perfusion system.
Pediatric Berlin Heart

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Purpose:
The pediatric Berlin Heart system, which is based on the fundamental work of the group of Prof. Bücherl in the late 60’s and early 70’s, has been commonly used in clinical practice for pediatric support in Europe since 1994 and is in clinical study in the US. Over the years a pump family in a size range from 10 to 80 ml was created with optimized technical parameters and production methods. A scientific overview of the EXCOR system will touch on the history and technical details.

Methods:
From the beginning up to now only 3 different hemocompatible blood contact materials were used: Polyurethane, silicon and titanium alloy Ti6Al4V. The methods used for blood flow investigation changed over the years from simple flow visualization to high end PIV analysis. For polyurethane and silicone processing, production methods also changed over years from deep drawing to injection molding. Today titanium polishing is under investigation with the aim to make the change from simple manual polishing to laser polishing.

Results:
As previously mentioned over the period of ongoing product and production development there have been significant improvements in a variety of areas. One of the latest results has been improvements in the field of titanium component polishing. The process parameters for laser polishing have been successfully transferred from flat samples to the three-dimensional geometries of all components. In comparison to manual polishing techniques the results of the functional checks show that the laser polishing of Ti6Al4V components leads to similar functional surfaces in terms of damage and activation levels of the pumped blood.

Conclusions:
Ongoing research into improved manufacturing processes with continuously evolving technical equipment has resulted in a system, originally designed for adults about 30 years ago, that has now developed into an improved device which is successfully used in a variety of applications including pediatric.
Pulsatile Blood Flow in the Microcirculation

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**Purpose:**
The efficacy of pulsatile flow in circulatory support has long been a subject of interest. Numerous studies have delineated the relations between flow and pressure gradient in elastic tubes with the aim of describing the physics of flow comparable in size to vessels of the macro- and micro-circulations. Although the impedance to flow in elastic vessels and the effects of pulsatility on shear stresses for a Newtonian fluid is well understood, much remains to be revealed about cell-cell interactions between blood cells, and between blood cells and the endothelium. To shed light on a possible role of molecular processes that may be affected by pulsatile flow, observations were made by direct intravital microscopy of the mesenteric microcirculation in a low flow state induced by occlusion of microvessels with a blunted probe. This derangement in flow was selected because of similarities to transient events of flow stoppage normally present in all tissues that arise from stochastic blood cell interactions and transient mechanical forces.

**Methods:**
The intestinal mesentery of either anesthetized rats or cats was exteriorized through a midline abdominal incision, draped over a clear support and superfused with warmed Ringer’s solution. The tissue was observed by intravital microscopy using either brightfield trans- or epi-fluorescence illumination. Intravascular pressures and pressure drops (ΔP) were measured using the dual servo-null technique with micropipettes held in a micromanipulator. Red cell velocities (V_{RBC}) were measured using the two-slit photometric method. To examine details of pulse components of pressures and flow, the signals were averaged in synchrony with the r-r interval of the cardiac cycle obtained from EKG measurements.

**Results:**
As typified in the above figure for flow in a 35 µm diameter arteriole, at all levels of the microcirculation (arterioles, capillaries and venules) a significant pulsatile component of upstream to downstream pressure drop (ΔP) and red cell velocity (V_{RBC}) is present during normal flow. Examination of the phasic relationships between pressure gradient and flow in single unbranched microvessels reveals differences attributable to variations in microvessel elasticity (compliance) and the topographical pattern of arterioles, capillaries and venules. Upon cessation of the steady component of flow, as induced by obstruction of the distal portion of a capillary, oscillations in red cell position along the capillary length arise due to elastic distension of capillaries with the pressure pulse. These oscillations reflect shear stresses that appear to affect red cell aggregation. Oscillatory movements of rouleaux appear to decrease the amount of red cell aggregation during net zero shear. Oscillatory shear stresses acting on the endothelium can be observed to distort the molecular layer of polysaccharides (glycocalyx) on the surface of the endothelium. This can be seen by observing the oscillatory movement of 100 nm beads coated with lectins that cause them to bind to the surface of the endothelium. During a pure oscillatory flow, a 180 nm amplitude shear displacement of the glycocalyx can be visualized by tracking movement of the beads.
Conclusions:
These results suggest that oscillatory shear stresses acting on the surfaces of the endothelium and aggregates of red cells in the low flow state may have a significant effect on the molecular dynamics of cell adhesion. Pulsations of flow proximal to transient obstructions in capillaries arise due to radial distension of the capillary lumen. Concomitant fluid movements create oscillatory shear stresses that act to disrupt red cell aggregates and distort the endothelial glycocalyx.
(Supported by NIH R01 HL-39286)
Autonomous Continuous Flow Microimmunofluorocytometry Assay for Real Time Tracking of Biomarkers during CPB

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Purpose: Cardiopulmonary bypass (CPB) is known to initiate a systemic inflammatory response syndrome which is one of the major factors for mortality and morbidity in high risk pediatric populations. Considerable evidence suggests that systemic inflammation causes many post-CPB complications, including vital organ dysfunction that can lead to multi-organ failure and even death. The intensity of the inflammatory response appears to be directly correlated with the severity of CPB-related morbidity. The objective of this research is to develop and test a microdiagnostic system for online monitoring of inflammatory biomarkers during the CPB procedure.

Methods: This microanalytical system is designed to continuously measure inflammation biomarkers in a continuous, fashion based upon a sandwich immunofluorocytometry assay using a magnetically controlled incubation process with antibody conjugated paramagnetic beads allowing serial processing steps of the beads to be performed autonomously: from antibody-antigen binding in the antigen stream, bead washing, fluorescently tagged secondary antibody labeling and finally optical detection in a detection area. Since the beads are continuously infused and mixed with analyte solution in a well controlled incubation process, as analyte concentration changes, the corresponding bead fluorescence also changes allowing continuous tracking of fluctuating biomarker concentrations.

The device has been validated against an ELISA standard for detecting C3a within a blood plasma sample. Freshly drawn human blood (500 ml) was circulated in a normothermic circulation loop, hemodiluted to 27.5% Hct and perfused at a rate of 500 ml/min at an arterial circuit pressure of 100 mmHg. Throughout the circulation time, blood samples were collected every 20 minutes from the arterial port of the membrane oxygenator. The plasma was then analyzed by both C3a ELISA plate or using the whole concentrated sample perfused through the device.

This device was also used to directly measure C3a concentrations using filtered plasma directly sampled from a circulation loop. The outlet of the microdevice containing incubated beads in wash solution was collected in 1.5 ml Eppendorf tubes for 20 minute intervals. Following bead collection, the beads were labeled with a fluorescent secondary antibody and analyzed via flow cytometry.

Results: For device validation, a pairwise scatterplot was constructed with the standard ELISA concentration on the x-axis and the novel measurement on the y-axis (Figure 1 left). A linear fit of the correlation line shows a slope of 1.02 and a correlation coefficient between the two measurement methods of r=0.98. A plot tracking temporal C3a concentration changes during blood circulation is shown in Figure 1 right demonstrating the device’s ability to track time varying antigen concentrations.

Figure 1: (Left) Pairwise scatterplot comparing C3a measurements by the device with those made using ELISA. (Right) Temporal tracking of C3a concentration using the device.
Microfluidic Devices for A Fully Integrated Blood Test System

Yang Jun Kang, MS, Jae Seong Park, BS, Sang Young Lee, BS, Min Su Son, BS, Jong Chan Choi, BS, Sun Young Oh, BS, Donghee Lee, MS, Myoung Gon Kim, MS, Sang Youl Yoon, PhD, Seon Hwa Lee, BS, Ji A Choi, BS, Sung Yang, PhD

Purpose:
Most biomedical sample analyses require either chemical or mechanical methods for precise analyses of a sample depending on its purpose. Especially, blood test requires various methodologies to investigate clinically relevant information. Recently, a microfluidic system for the applications of blood tests has been highlighted and extensively studied in many research groups because of its numerous advantages over conventional methods including small sample consumption and fast analysis time. In this presentation, a few of microfluidic devices, which might be applicable to clinical blood tests, are introduced as individual components for the development of a fully integrated blood test system.

Methods:
All microfluidic devices were prepared by a standard PDMS replica molding techniques (Duffy et al. 1998; Xia et al. 1998). In designing stage of the microfluidic devices, a series of analytical and numerical (CFD-ACE+, ESI Group, France) studies were extensively conducted to ensure each device’s function. In experimental stage, a freshly harvested donor blood or a laboratory cultured cell lines were used in entire experiments.

Results:
The presentation is composed of two parts. First part is microfluidic devices for sample preparation. Second part is microfluidic devices for sample analysis. In each part, both mechanical and chemical methods for the sample preparations and analyses are introduced.

Sample Preparations
The microfluidic devices for the sample preparation include a blood separation (plasma, WBCs, RBCs) using hydrodynamics, a cell positioning for cellomics study, a cell lysis using for DNA or protein extraction.

Sample Analyses
The microfluidic devices for the sample analysis include a micro viscometer, a micro aggregation index measurement system, and a micro immunoassay platform.

Both sample preparations and analyses devices utilize mechanical, chemical or electrical method to prepare or analyze samples. In this presentation, the detailed working principles and their quantitative performance are extensively discussed and compared with conventional methods.

Conclusions:
Microfluidic technologies provide numerous advantages over conventional laboratory technologies. In addition, by integrating all these microfluidic components, it is believed that a true meaning of a micro total blood test system (μTBTS) could be realized.

Acknowledgements:
This research was partially supported by grants from the MEST (WCU Program, No. R31-2008-000-10026-0, KOSEF, No.2009-0076858), and the Institute of Medical System Engineering (iMSE, GIST), Republic of Korea.
Purpose: Multifactorial causes contribute to the adverse effects of cardiopulmonary bypass (CPB) procedures and mechanical circulatory support (MCS) systems in pediatric and adult patients. One of the primary causes of adverse effects is poor CPB or ECLS circuit component selection. Independent circuit component evaluation is rarely performed. A majority of centers select circuit components without adequate scientific justification. The objective of this presentation is to detail methods used to select and justify different components (all FDA approved) for acute and chronic use at the Penn State Hershey Children’s Hospital.

Methods: As a standard protocol we evaluate each new CPB or ECLS component in the laboratory prior to use in the operating room. The experimental circuits employed during evaluations are identical to those used in clinical practice. A custom-made data acquisition system which utilizes LabView software is used to measure pressure and flow; hemodynamic energy parameters; energy loss in roller or centrifugal pumps with pulsatile and non-pulsatile perfusion; membrane oxygenator pressure drops; and relative merits of arterial cannulae as well as tubing lengths in real-time. We use Emboli Detection and Classification System (EDAC) to evaluate microemboli handling in oxygenators, pump heads, and cardioplegia systems in our simulated pediatric design.

The results of following projects will be presented in this lecture:

- Mechanical Performance Comparison between two Centrifugal Blood Pumps in an Adolescent-Adult ECLS Model (Engineering/Clinical)
- Comparison of Eight Different Pediatric 10 FR Aortic Cannulae During Pulsatile vs. Non-Pulsatile Perfusion in a Simulated Neonatal Model of CPB (Engineering/Clinical)
- Comparison of perfusion quality in hollow-fiber membrane oxygenators for neonatal/pediatric CPB and ECLS (Engineering/Clinical)
- Air Handling Capabilities of Blood Cardioplegia Systems (Engineering/Clinical)

Results: All of the components of CPB and ECLS systems were selected based on scientific data which generated by a multi-disciplinary team at the Penn State Hershey Pediatric Cardiovascular Research Center.

Conclusions: Translational research supported by clinicians, engineers, and scientists is necessity for optimal component selection in CPB and ECLS systems.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

Continuum of Cardiac Support Ranging From Neonates to Teenagers

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Abiomed Inc., USA

Purpose:
Intracorporeal cardiac support based on catheter based rotary blood pump technology can be developed to support the left or right heart without the need for externalizing blood flow. The intravascular device with its displacement volume of app. 2cc complies with the need of reducing the prime volume in volume critical patients. The Impella platform of rotary axial catheter based pumps comprises the world’s smallest commercially available device. It, however, remains to be too large for patients with a BSA < 1m². As such modified or further miniaturized pumps are needed.

Methods:
The commercially available adult version of the 12F Impella 2.5 blood pump for temporary left heart support has recently been successfully applied in pediatric patients with an age ranging from 6 – 16 years. Patients, so far, have been treated for cardiomyopathy, myocarditis and donor organ rejection post transplantation with an overall survival of 80%. For smaller patients, however, the usage is limited due to the length and design of the inflow cannula, which is adapted to optimally fit the adult left ventricular cavity and outflow geometries. Smaller patients require a modified inflow cannula as previously discussed and for neonates a reduction in rigid length of the device and a further miniaturization down to 9F is indicated.

Results:
Modifications of the commercially available adult version of the 12F Impella 2.5 have been conducted leading to a short inflow cannula. The portion, which extends across the native aortic valve, is only 9F and increases in diameter to 12F at the pump. Alongside with a modest hydraulic downsizing the pump can provide 1.6l/min support at physiologic pressures. Small target flows of only 0.5l/min can be achieved by device pulsation. Cadaver fit studies have helped to define the patient range by weight ranging from 5kg to app. 25kg. For patients < 5kg a shorter and smaller device is necessary in order to avoid any flow obstruction within the aortic root. Therefore a 9F downsized version is being developed and hydraulic tests of the impeller are presently being assessed.

Conclusions:
A continuum of care of pediatric patients from 2kg to 70kg appears to be feasible with a family of Impella catheter based pumps. Specific modifications of the Impella 2.5 are deemed necessary for patients smaller 25kg. Patients smaller 5kg will furthermore require a size reduction from 12F down to 9F for the pumphead and cannula.
Development of an Ultra-Durable Heparin-Free ECMO System and Its Clinical Application to Pediatric and Adult Patients in Japan

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Background:
ECMO is used for treating the patients with life threatening severe respiratory and/or circulatory failure. This modality is extremely important especially in pediatric cases. The current system, however, has two major limiting barriers to its extensive use: 1) poor durability due to plasma leak in long-term use, and 2) poor antithrombo-genicity necessitating systemic heparinization. At the National Cardiovascular Center of Japan, an ultra-durable heparin-free ECMO system has been developed. This system has been already used in clinical settings in Japan in pediatric and adult patients, and demonstrating very good outcomes.

ECMO System:
Our ECMO system consists of a compact leakless oxygenator (BioCube-NCVC series), and a sealless durable centrifugal pump (RotaFlow). The oxygenator is made of PMP membrane (Dainippon Ink & Chemicals) in which micropores are blind-ended at the blood contacting surface to prevent plasma leak. There are three different sizes of oxygenators. Membrane area and priming volume of S-size (infant size), M-size (child size) and L-size (adult size) are 0.4, 0.8 and 1.2 m², and 45, 95 and 130 ml, respectively. Total priming volume of the S-size ECMO circuit is only 147 ml. The entire blood-contacting surface is coated with a novel heparin-bonding material (T-NCVC coating) to impart extremely potent antithrombogenicity for long-term use.

In vivo Evaluation:
In order to clarify durability and thrombo-resistant property of the system, heparin-free veno-arterial bypass ECMO was carried out in chronic animal experiments using 22 goats weighing 19–64 kg. Systemic anticoagulation was not conducted at all, except for one-shot heparin injection at cannulation. As a result, over one month (34-92 days) heparin-free ECMO could run in 20 out of 22 animals until elective termination. Bypass flow was maintained between 1.4-3.3 L/min according to the oxygenator size. In these animals gas-exchange function was kept stable at sufficient level for provided blood flow in each size oxygenator. Plasma leak was not observed in any case. Platelet count, ACT, APTT, and fibrinogen levels were within normal limits, and the blood heparin concentration was always less than detectable level. In postmortem observation, a small amount of clot formation was found at the inlet and outlet of oxygenator where the blood tended relatively stagnant, but the fiber bundle was always surprisingly clean against prolonged heparin-free perfusion. The other parts of the circuit were also free of thrombus formation.

Clinical Application:
Clinical application of this ECMO system was carried out in sixteen adult patients with active bleeding complication (Age: 18 to 82 years, completely heparin-free) and five pediatric postcardiotomy patients (Age: 18 days to 2 months, BW: 2.5-4.5 kg, low dose heparin administration with ACT control at 150-200 sec). The longest ECMO duration in adult patients was 9 days, and that in pediatric patients was 41 days. As a result, ten out of sixteen adults patients and two out of five pediatric patients were successfully salvaged.

Conclusions:
The newly developed ECMO system for pediatric and adult patients showed excellent durability and thrombo-resistant property in both in vivo testing and clinical cases. We conclude that this system can be used for prolonged cardiopulmonary support with minimum or without systemic heparinization.
Abstract:
Neonatal and pediatric heart surgery, CPB and ECLS are highly demanding – for perfusionists, surgeons, anesthesiologists and nurses as well as for the devices and equipment used. Both the literature and our interviews with perfusion and surgical teams confirm that minimal hemodilution and blood trauma are crucial factors that contribute to effective, safe and stable extracorporeal circulation.

The characteristic QUADROX-i design from MAQUET Cardiovascular guarantees high gas transfer rates and heat exchange performance at an unrivalled low pressure drop and a low priming volume. With the new QUADROX-i Neonatal & Pediatric oxygenators, MAQUET is confirming its commitment to the smallest and most challenging patients, and completes the QUADROX-i family. These new Quadrox-i oxygenators have a maximum blood flow rating of 1.5 and 2.8 l/min respectively. Both oxygenators are available with BIOLINE COATING.

The unique rectangular design of all QUADROX oxygenators, with its 90 degree crosswise orientated fibers combines highly efficient gas transfer with a low pressure drop. QUADROX-i Neonatal & Pediatric are designed and available with and without an integrated arterial filter. The filter adds only 2 ml or 18 ml respectively to the static priming volume. Its separate pre- and post- filter de-airing mechanism makes the priming process quick, effective and safe.

During ECLS applications babies and children benefit from the low priming volume, smooth blood handling and wide flow range that the QUADROX-i Pediatric oxygenator can offer. This oxygenator connectors in order to optimize hemodynamics during long-term use.

The integration of a TPU hollow fiber heat exchanger reduces priming volume by approx. 50% compared to a design concept with a separate oxygenator and heat exchanger.

With its unique Volume Efficiency Index of 35.57\(^1\) it is ideal for ECLS in newborns, infants and children.

With the QUADROX-iD Pediatric, MAQUET Cardiovascular provides the first and only plasma tight oxygenator for neonatal and pediatric extracorporeal life support which is approved for long-term use for up to 30 days.

\(^1\) Maximum blood flow divided by static priming volume
Capiox FX: A New Generation of Pediatric Oxygenators with Fully Integrated Arterial Filter

Andreas Becker, PhD
Terumo Europe, Leuven, Belgium

The reduction of priming volume is a constant goal in the development of products for extracorporeal perfusion. Especially in neonates and infants, the priming volume of the perfusion circuit causes significant hemodilution resulting in greater need for blood transfusion. Both hemodilution and blood transfusion induce inflammatory response and increase the risk of myocardial and pulmonary dysfunction.

To further reduce these adverse effects of extracorporeal perfusion, Terumo has developed a new generation of oxygenators, the Capiox FX series. FX oxygenators feature an integrated 32µ arterial filter and offer significantly reduced priming volume and foreign surface area compared to a circuit with oxygenator and a separate arterial filter.

The filter membrane is located inside the oxygenator housing surrounding the hollow fiber bundle. This design requires minimal priming volume (0-9 ml depending on oxygenator size), does not significantly increase the pressure drop and has no negative effect on the gas and heat exchange performance of the oxygenator. Although the active surface area of the integrated filter is similar to stand-alone arterial filters, the foreign surface area of the entire perfusion circuit is significantly reduced as no separate filter housing is required and the connectors and tubing of the filter bypass line within the arterial side of the circuit are not necessary.

Unlike conventional arterial filters, FX oxygenators eliminate air via the inner lumen of the hollow fibers and through the gas outlet of the oxygenator. This patented self-venting technology allows easier priming and de-airing, while particulate and gaseous emboli are trapped or removed as effectively as with a separate arterial filter.

Pediatric Capiox FX oxygenators come in two different sizes. The FX05 oxygenator for neonates and infants with 0.5 m² fiber surface area and a priming volume of 43 mL and the FX15 oxygenator, a mid-size oxygenator with 1.5 m² surface area and 144 ml priming volume for pediatric patients. Clinical studies have demonstrated that both oxygenators are easy to set up and prime, offer the additional safety of an integrated arterial filter and the same performance as Terumo’s established Capiox RX oxygenators (1,2). Capiox FX oxygenators thus represent a useful tool to reduce priming volume, hemodilution and inflammatory response in pediatric perfusion.

Table 1. Specifications of Pediatric Capiox FX Oxygenators with Integrated Arterial Filter

<table>
<thead>
<tr>
<th></th>
<th>Capiox FX05</th>
<th>Capiox FX15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hollow Fiber Surface Area (m²)</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Priming Volume (ml)</td>
<td>43</td>
<td>144</td>
</tr>
<tr>
<td>Maximum Blood Flow (l/min)</td>
<td>1.5</td>
<td>5</td>
</tr>
<tr>
<td>Arterial Filter Surface Area (cm²) / Filter Pore Size (µm)</td>
<td>130 / 32</td>
<td>360 / 32</td>
</tr>
<tr>
<td>Oxygen Transfer Capacity at Maximum Blood Flow (ml/min)</td>
<td>100</td>
<td>330</td>
</tr>
<tr>
<td>Air Elimination (%)</td>
<td>94±4 (1)</td>
<td>93±5 (2)</td>
</tr>
</tbody>
</table>

Purpose:
Mortality rate in Neonatal patients is still reported as the highest in Cardiac Surgery practice. Dynamic Priming Volume of blood oxygenators and CPB systems in general is the major contributor in hemodilution and in the addition of banked blood and blood products. Stimulated by the medical community, Sorin Group is probing the ground for CPB System substantial Priming Volume reduction, in the attempt of further reducing CPB impact for the neonatal patients.

Methods:
Priming Volume calculation of different size arterial and venous lines has been accomplished. Priming Volume of low prime Kids D100 neonatal oxygenator and Kids D130 arterial filter were measured. Kids D100 Venous Reservoir dynamic hold-up volume and minimum operating level were also measured. Several CPB system architectures have been simulated and partly tested by using S5 pump console with mast mount system. Priming Volume of simulated combinations of 1/4” – 3/16” – 1/8” I.D. of Arterial, Venous and Suction line size tubing have been charted. Flow related pressure drop values post-main pump, and of all downstream individual parts of the CPB system (arterial filter, tubing set and arterial cannulae) have been measured for the simulated CPB system architectures. Test conditions were: bovine blood Hb 12±1 g/dl, blood flow 100 to 500 ml/min, blood temperature 37°C and 25°C. The graphs including systemic blood flow, CPB system architecture, arterial line pressure drop values and system cumulative dynamic priming volume have been built.

Results:
Kids D100 oxygenator high connectability allows to decrease priming volume by reducing A/V and suction lines length and size. Venous line may be considerably shortened by simulating S5 console mast mount set-up type architecture, and made smaller in size in case VAVD technique is used. Arterial line size and length may be lowered considerably to reach a very small priming volume especially when mast mount set-up configuration is put in place. A further contribution in arterial line priming volume reduction is coming from VAVD technique allowing shorter and smaller lumen size. 1/8” ID arterial line seems to be a feasible option. CPB system architecture is directly linked to the ability of handling flow especially on the arterial side while generating a safe post-main pump pressure. Arterial cannulae size is heavily influencing arterial line pressure. Suction lines can be brought down to 1/8” ID when setting-up a dedicated mast mounted CPB system.

Conclusions:
Preliminary evaluation shows that it is possible to think of industrially available CPB systems allowing dynamic priming volume close to 120 ml for the smallest neonatal patients. Arterial line size and mainly arterial cannulae size are directly influencing maximum perfusion flow that may be in the region of 300-400 ml/min.
A Microfluidic Device For Continuous WBC Separation And Lysis From Whole Blood

Seung Mo Jung, MS, Myoung Gon Kim, MS, Donghee Lee, MS, Jong Chan Choi, BS, Sung Youl Yoon, PhD, Sung Yang, PhD

Purpose:
DNA in human white blood cells (WBCs) has critical information about specific diseases, such as Hepatitis B virus (HBV) and human immunodeficiency virus (HIV). The WBC separation and WBC lysis are essential steps for the diagnosis. This study aims to develop a microfluidic device for continuous WBCs separation and lysis to isolate DNA from whole blood without any additional steps.

Methods:
Figure 1 shows the operation principle and schematics of the proposed device. In the CCO (Cell Cross Over) region, relatively large WBCs pass through the bifurcation channels, and cross over into the lysis solution continuously, while RBCs, platelets, and blood plasma run into the bifurcation channels. The whole blood sample was freshly harvested from a healthy donor and collected into a 3.0ml vacutainer (B&D) containing EDTA as anticoagulant. The WBCs lysis solution mixed with RNase and Proteinase K (Q-Lysis) was prepared.

Results:
The superimposed images in time during the separation and lysis are represented in figure 2. The WBCs successfully are separated from the whole blood and crossed over into the lysis solution. The WBCs was completely lysed within 500 ms. The recovery rate of WBCs was measured as 97.2%. The DNA concentration and the purity of the lysed DNA samples were compared with the ones obtained from a commercial lysis kit (Gentaur). The ratio of absorbance at 260/280 nm was measured as 1.82±0.11 by a UV-Vis spectrometer. The DNA concentration of 28.80±11.18 μg/ml is in agreement with the one from the commercial WBCs lysis kit.

Conclusions: This study has successfully demonstrated continuous WBCs separation and lysis with high efficiency in the developed microfluidic device. The proposed microfluidic device and method could be applicable in clinical fields for diagnosis of diseases.

Acknowledgement:
This research was partially funded by grants from the MEST (WCU Program, No. R31-2008-000-10026-0), the KOSEF (No. 2009-0076858), and the Institute of Medical System Engineering (iMSE, GIST), Republic of Korea.
Highly Accurate and Consistent Microfluidic Viscometer for Continuous Viscosity Measurement

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Purpose:
It is well known that high blood viscosity is strongly correlated with cardiovascular diseases such as atherosclerosis, stroke, myocardial infarction, etc. For this reason, blood viscosity measurement is of importance, and necessary step for patient’s monitoring. In this study, a microfluidic viscometer, which provides a continuous measurement of blood viscosity, is proposed.

Methods:
Figure 1 represents the proposed microfluidic viscometer for blood viscosity measurement. This device is designed with two inlets for a blood sample and a PBS sample, and a microfluidic channel array (MCA) which consists of a diverging channel (DC) and counting channels (CCs) of the same size and shape. The relative viscosity ($\mu_r = \mu_{\text{Blood}}/\mu_{\text{PBS}}$) is expressed as $\mu_r = (N_{\text{Blood}}/N_{\text{PBS}})(Q_{\text{PBS}}/Q_{\text{Blood}})$. Therefore, a relative viscosity of blood sample could be calculated by counting the number of the counting channels filled with each sample. For the verification of the microfluidic viscometer, the blood viscosities measured by the proposed viscometer are compared with those measured by conventional HAAKE MARS viscometer.

Results:
As shown in Figure 2, the blood viscosity values measured by the proposed viscometer are in good agreement with those measured by the conventional viscometer. In addition, the proposed viscometer could provide more consistent viscosity value, especially at low shear rates. Furthermore, the required measurement time for each shear rate was less than 1 min, and total volume consumption was less than 0.1 ml.

Conclusions:
The proposed microfluidic viscometer could measure the viscosity of blood sample with high accuracy and convenience in measurement by simply counting the number of channels filled with each sample without calibration or correction. Furthermore, it could have the ability to measure the viscosity in short time with extremely small blood sample consumption.

Figure 1. A schematic drawing of the proposed microfluidic viscometer for blood viscosity measurement.

Figure 2. Comparison of the relative viscosity measured by the proposed microfluidic viscometer and HAAKE MARS viscometer.

Acknowledgement:
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A Microdevice for Immunological Synapse Formation of T Cells Utilizing Protein Patterning on the PDMS Structure by Hydrophilic Surface Treatment

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Purpose:
T cells play an integral role in the immunity system as an activator in immune system by secreting interleukin and as phagocyte when it detects antigen representing cell. The interface between an antigen-presenting cell and T cell is called an immunological synapse (IS). T cells could be influenced in severely different environment such as CPB surgery (Cardiopulmonary bypass) by inflammatory response with foreign materials, unusual fluidic condition, and low temperature comparing to normal state. In here, a microdevice, which might be applied in evaluation of immunological function of T cell, is proposed.

Methods:
The three dimensional circular post structure made of PDMS (Poly Dimethyl Siloxane) with 2μm in diameter, 2.5μm in height was fabricated applying PDMS replica molding. Fig.1 (a) shows the fabricated PDMS microdevice on the slide glass. TS2/4 protein to derive the formation of T cell’s IS was adsorbed physically onto the side and bottom parts of PDMS structure utilizing autonomous capillary flow by hydrophilic surface treatment on PDMS microdevice. The open channel between PDMS and slide glass was selectively filled by capillary-driven flow. After incubating overnight, TS2/4 could be immobilized at the engraved part of PDMS microdevice. After protein patterning, T cell was loaded on the PDMS microdevice and the formation of immunological synapse was investigated based on morphology of T cell.

Results:
Fig. 1 (b) shows the fluorescence image of PDMS microdevice on which Cy3 (Orange color) labeled TS2/4 protein was patterned. The orange color region by Cy3 coincided with engraved part of PDMS microdevice. Fig. 2 shows confocal microscope image of FITC (green color) labeled T cell on PDMS microdevice patterned with TS2/4 protein. The pseudopidia-like morphology of T cell was found at the interface between T cell and TS2/4 protein patterned PDMS microdevice.

Conclusions:
We suggest that the microdevice to investigate immunological function of T cell with respect to formation of immunological synapse utilizing PDMS microdevice fabricated by replica molding and TS2/4 protein patterning with hydrophilic surface treatment.

Acknowledgement
This research was partially funded by grants from the MEST (WCU Program, No. R31-2008-000-10026-0), the KOSEF (No. 2009-0083811), and the Institute of Medical System Engineering (iMSE, GIST), Republic of Korea.
In Vitro Flow Dynamics of Pediatric Right Ventricular Outflow Tract Reconstruction with Bicuspid Valved PTFE Conduit

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Purpose:
Conduits that are used in right ventricular outflow tract (RVOT) reconstruction, effect valve function, can become stenotic and/or insufficient due to calcification. In order to reduce the incidence of reoperations and improved function we have developed and used a bicuspid valved polytetrafluoroethylene (PTFE) conduit for the RVOT reconstruction. The purpose of this study is to investigate the hemodynamic performance of the new design using a pediatric in vitro right heart mock loop and computational fluid dynamics.

Methods:
PTFE conduit has been used for the complete biventricular repair of 20 patients (age: 1.7±6) with cyanotic congenital defects. To account for the large variability of conduit sizes, 14mm and 22 mm conduit sizes were evaluated using in vitro flow loop comprised of a pulsatile pump (CO: 2-5 LPM), bicuspid valved RVOT conduit, pulmonary artery and venous compartments, and the flow visualization setup. We recorded the diastolic valve leakage, pre- and post-conduit pressures and flow in static and pulsatile settings. In vitro valve function and overall hemodynamic performance was evaluated using high speed cameras and ultrasonic flow probes. Three-dimensional flow fields for different in vivo conduit curvatures and inflow regimes were calculated by computational fluid dynamics (CFD) analysis to further aid the conduit design process and determine optimal valve location, leaflet number.

Results:
The static pressure drop over the valved conduit was calculated to be 3±5 mmHg depending on the CO. High speed videos captured the diastolic valve closure and asymmetrical valve opening which indicated unbalanced opening forces on leaflets during the systole. CFD simulations demonstrated the flow skewness towards the major curvature of the conduit based on the in vivo conduit shape. Right ventricle model demonstrated its utility by generating physiological flow and pressure waveforms.

Conclusions:
Preliminary in vitro data with the bicuspid valved PTFE conduit coincides well with the excellent early clinical performance (no insufficiency), with relatively low pressure drop, reduced flow leakage and intact valve motion. These findings may indicate the prognosis such as no conduit stenosis and may be used to quantify the long-term viability of the conduit.
Development of a Force-reflecting Robotic Platform for Cardiac Catheter Navigation

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Purpose:
Cardiac catheterization is one of minimally invasive intervention procedures mostly used in cardiac ablation and stent implantation. To facilitate more accurate and precise catheter navigation, systems for robotic cardiac catheter navigation have been developed and commercialized. The authors have been developing a novel force-reflecting robotic catheter navigation system. The paper documents and discusses the initial in vitro performance test results.

Methods:
The system is a network-based master-slave configuration 3-DOF (Degree-Of-Freedom) robotic manipulator for operation with conventional cardiac ablation catheter installed. The master manipulator implements force feedback using force/torque signal either measured by the sensor (forward/backward motion) or estimated from the motor status (roll motion) in the slave manipulator. The slave manipulator implements a robotic catheter control platform in which conventional cardiac catheter is installed and the motions - forward/backward, roll, catheter tip articulation – are controlled. The system runs on a realtime OS based system software that implements master-slave motion synchronization control of the robot system.

Results:
The master-slave motion synchronization performance tested with step, sinusoidal, arbitrarily varying motion commands showed satisfactory results with insignificant level of steady state motion error.

Conclusions:
The current system successfully implemented the motion control function and will undergo safety and performance evaluation in animal experiment. Further study on the force feedback control algorithm and active motion catheter with embedded actuation mechanism are underway.
Filament Support Spindle for an Intravascular Cavopulmonary Assist Device

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Purpose:
We are developing an intravascular, axial flow, blood pump to support adolescent and adult Fontan patients. To protect the blood vessel, this pump has an outer cage with radially arranged filaments and a newly designed spindle at the pump outlet. The spindle is included for two reasons: 1) to physically limit the axial movement of the rotor, and 2) to house bearings which support the rotor. This study evaluates the impact of the new spindle on pump performance.

Methods:
Figure 1 illustrates the protective cage with filaments and a spindle. The prototype for the protective cage was constructed from 5 stainless steel 1/16" diameter rods and 2 stainless steel 1/2" diameter bars. We used a CNC lathe to machine the spindle shape. We then drilled five holes through the bar for insertion of the filaments. To create the individual filaments, we cut the rods to length and bent them to the desired shape. We machined an acrylic housing to support the cage. The inner diameter of the housing was 18 mm with the cage filaments in full extension. The drive-shaft extended through the spindle into the cage. We mounted the impeller inside of the cage on the distal end of the drive-shaft. We placed this prototype into our hydraulic test loop and measured the pressure-flow performance using a blood analog fluid.

Results:
The pump with the cage filaments and spindle generated 2 to 15 mmHg of pressure rise for flow rates of 0.5 to 4 L/min over rotational speeds of 4000 to 7000 RPM (Figure 2). This range is suitable to support a failing Fontan physiology.

Conclusions:
These results support the continued development of this cavopulmonary assist device with a spindle at the pump outlet. The next step is to incorporate biocompatible and flexible materials into the cage design.
Description of a Flow Optimized Oxygenator with Integrated Pulsatile Pump

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**Purpose:**
Current oxygenators cause several adverse reactions due to their large extrinsic surface contact area and the high filling volumes. By means of an optimized flow pattern inside the hollow fiber bundle the efficiency of an oxygenator can be increased. With additional integration of a pulsatile pump the extracorporeal priming volume can be reduced.

**Methods:**
Various ideas are combined in the ExMeTrA oxygenator. A hexagonal fiber bundle avoids shunt flows and a defined flow pattern within the oxygenator is possible due to the integration of flow distribution plates. Silicone tubes embedded into the fiber bundle generate a pulsatile flow through the oxygenator. Therefore, the use of an additional pump is unnecessary to operate this gas exchanger. Hence, the additional volume of a pump can be saved. Moreover, the distribution of blood inside the fiber bundle is improved by adequate positioning of these pumping tubes. Investigations show that pulsating tubes generate microcurrents between surrounding fibers. These currents seem to increase the gas exchange. Automatic and individual positioning of fibers in a predefined configuration allows to generate a uniform flow around those fibers. These methods improve the flow pattern within the oxygenator. Hence, an increase of efficiency is expected.

**Results:**
Experiments show the practicability of pulsatile pumping silicone tubes as well as the potential to distribute the flow by using distribution plates. Numerical simulations show that different flow patterns can be generated by changing the arrangement of the silicone tubes or by modifying the geometry of the distribution plates. Automatic positioning of single fibers in a predefined configuration was also investigated successfully.

**Conclusions:**
The positive achievements of the different ideas referring to the flow pattern within an oxygenator have been demonstrated. Particularly the embedded pulsating silicone tubes are promising to increase the efficiency of gas exchange inside an oxygenator. This may reduce the extrinsic surface contact area and the filling volume and expand the range of applications for oxygenators significantly.
Improving Oxygenator Performance Using Computational Simulation and Flow Field Based Parameters

Roland Graefe, Dipl.-Ing.; Ralf Borchardt, Dipl.-Ing.; Peter Schlanstein, Dipl.-Ing.; Jutta Arens, Dipl.-Ing.; Johannes Dieter, Dipl.-Ing.; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD
Department of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

Purpose:
Current goals in the development of oxygenators are to reduce extrinsic surface contact area, thrombus formation, hemolysis and priming volume. The ExMeTrA oxygenator is a highly integrated device currently under development. In order to minimize priming volume, remove stagnation areas and provide a favorably concentration gradient for the gas-exchange throughout the fiber bundle, the flow has to be guided by an optimized geometry.

Methods:
This study focuses on the design of the in- and outlet to the fiber bundle. For a given fiber arrangement, the inlet and the outlet geometry determine the flow field in the bundle. This investigation was based on computational fluid dynamics (CFD) and its experimental validation. Parameters derived from the simulation results lead to an automated quantitative evaluation of geometry changes and a practical assessment of the quality of the flow. The experimental flow visualization setup used ink and a camera. The CFD results were generated assuming non-Newtonian fluid properties and laminar flow at a steady-state.

Results:
The experimental and numerical results agreed well. Geometry variations concerned the in- and outlet tubes, the introduction of different distribution plates and the casing geometry at the in- and outflow. Two parameters were invented, one based on the velocity distribution and the second calculated from the residence time of massless particles representing erythrocytes. Significant improvements between optimized and initiate configurations were found. Depending on the parameter, differences of up to 74% could be achieved. Therefore, using an optimized geometry, less stagnation areas, a more uniform velocity distribution and saturation level can be expected. This may lead to a reduction of thrombus formation, hemolysis, inflammation response, and improved oxygenation allowing for a decrease in membrane area and priming volume.

Conclusions:
There is a big potential improving the flow field within oxygenators. CFD proofed to be a powerful tool to quickly improve designs of oxygenators whereas experiments are tedious, yield less detailed and comprehensive results and are more costly.
Purpose:
This study examined the interactive fluid dynamics between a cavopulmonary assist device and the univentricular Fontan circulation. We conducted 2-D particle image velocimetry (PIV) measurements on an idealized total cavopulmonary connection (TCPC) with an axial pump prototype in the inferior vena cava (IVC).

Methods:
The experiment was performed on an idealized TCPC constructed of glass. The model consisted of rigid vessels having diameters of 14 mm and a 1-mm diameter vessel offset at the TCPC junction. We compensated for distortion generated by the curvature of the model by immersing it in fluid of matching refractive index. Fluid velocity profiles were examined under several conditions: SVC/IVC pressure differentials of 30/70%, 40/60%, and 50/50%; cardiac outputs of 3, 5, and 7 L/min; and pump rotational speeds from 3000 to 9000 RPM. A blood analog mixture of water-glycerin was employed and seeded with buoyant silver-coated 8-10 micron diameter particles. A 2-D plane along the mid-span of the TCPC was illuminated, and 300 sequential vector snapshots were taken and averaged.

Results:
The velocity profiles for all cases demonstrated the expected shunting of flow from the IVC toward the right pulmonary artery. Figure 1 shows the velocity profiles along the midspan plane for two pump rotational speeds. Few flow vortices were captured in the image plane downstream of the pump in the TCPC junction. A rotational component in the pump outflow was observed forcing flow to the periphery as compared to the flow profile without a pump present in the IVC. The inclusion of the pump provides a pressure rise of 3 to 9 mmHg.

Conclusions:
These results indicate a rotational component of the flow leaving the pump and support the continued development of the intravascular axial flow pump for Fontan patients. The next step involves stereo 3-D PIV measurements with a patient-specific geometry.
Sixth International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

ECMO Support for Pediatric Patients with Acute Fulminant Myocarditis

Shye-Jao Wu, MD, Chun-Chi Peng, MD, Ming-Ren Chen, MD
Departments of Surgery, Pediatrics, MacKay Memorial Hospital, Taipei, Taiwan

Purpose:
Myocarditis is usually a self-limited disease entity, but acute fulminant myocarditis with circulatory collapse is associated with significant morbidity and mortality in children. We reported our preliminary experience of ECMO support for the pediatric patients with acute fulminant myocarditis.

Methods:
From July 2000 through June 2008, 9 consecutive pediatric patients, 4 boys and 5 girls, with acute fulminant myocarditis were treated with ECMO support with centrifugal pump and hollow fiber membrane oxygenator due to failure of traditionally conservative treatments. The patient’s median age was 8 months old (range: 11 days old to 14.6 years old). The median body weight of the patients was 8.4kg (range: 3.0-52.5kg). Presenting symptoms included fever in 5, herpangina in 1, myoclonic jerk in 3, and shortness of breath in all the patients. Inotropic support included dopamine and dobutamine of 20µg/kg/min for all the patients, epinephrine of 2µg/kg/min for 3 patients, and norepinephrine of 1µg/kg/min for 1 patient. Pre-ECMO cardiopulmonary resuscitation (CPR) was performed for 3 patients. VA-mode ECMO was set up through exploration of right carotid artery and right internal jugular vein. The initial ECMO blood flow ranged from 80ml/min/kg to 150ml/min/kg due to wide range of body weight.

Results:
The ECMO supporting time ranged from 7 to 159 hours. The ECMO weaning rate was 67%(6/9), the percentage of discharge from hospital was 56%, and the long-term survival rate was 44%. For the 6 patients without pre-ECMO CPR, the ECMO weaning rate was 83%(5/6), the percentage of discharge from hospital was 83%, and the long-term survival rate was 67%. For the 3 patients with pre-ECMO CPR, one survived the ECMO support.

Conclusions:
ECMO may provide a chance to support the critically ill patients with acute fulminant myocarditis with circulatory collapse. The survival benefit that ECMO offers might be slashed if pre-ECMO CPR occurs.
Short-term Circulatory Support – Preclinical Animal Testing of the Medos® Deltastream DP3 Diagonal Flow Pump

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Pediatric Cardiac Surgery, Pathology, Laboratory Animal Science and Applied Medical Engineering, RWTH Aachen University, Aachen, Germany

Purpose:
The Medos® (Stolberg, Germany) DP3 diagonal flow pump was designed to provide a cost-effective means of mechanical circulatory support up to 7 days duration combined with low priming volume (<30 ml), a wide range of flow rates (0–8 l/min), and low morbidity. The results of preclinical animal testing are presented.

Methods:
For device testing 12 sheep (body weight 70 – 80 kg) were selected. The pumps were used as right-heart bypass aiming at permanent flow rates >3 l/min. Small outflow cannulae facilitated high line pressures (>200 mmHg) mimicking systemic flow conditions. Using the lung as end-organ detection of peripheral thromboembolism was eased. Immediately after implantation the sheep were extubated and were allowed to move in a cage. Activated clotting time (ACT) aimed at 180-200s. Clinical data, pump parameters, and laboratory data were obtained regularly. After 7 days of testing pump hardware, heart and lungs were subjected to autopsy.

Results:
The testing was done in two series. In the initial series 3 of 6 pumps failed 0.5–15 hours after implantation because of thrombosis of the flushing canals of the rotor. After technical modifications including the flushing canals the second series of testing was done. Five of six animals had an uneventful clinical course over 7 days. Laboratory data did not suggest relevant or progressive hemolysis. In one animal a fabrication defect (askew bearing pin) of these prototypes caused pump failure after 6 days. Anticoagulation was mostly inadequate with low ACTs. Very tiny thrombus formation on the rotor or the bearing pin was found in all survivors not altering function. One animal revealed a minimal (2mm) pulmonary thrombus.

Conclusions:
Prototype animal testing of the Medos® Deltastream® DP3 revealed reliable function and low morbidity over 7 days of implantation. Industrial fabrication is planned.
Impact of tubing length on hemodynamics in a simulated neonatal ECLS circuit

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Purpose:
In extracorporeal circulation, a large portion of the hemodynamic energy is lost to various components of the circuit. Minimization of this loss in the circuit leads to better vital organ perfusion and decrease the risk of systemic inflammation. In this study, we evaluated the hemodynamic properties of a simulated neonatal extracorporeal life support (ECLS) circuit with differing lengths of tubing.

Methods:
The neonatal ECLS circuit used in this study included a Capiox Baby RX05 oxygenator, a Rotaflow centrifugal pump and a heater & cooler unit. An 8Fr Biomedicus arterial and a 10Fr Biomedicus venous cannula were connected to the pseudopatient. 1/4inch tubing was used for both the arterial and the venous line. A Hoffman clamp was located upstream from the pseudopatient to maintain a certain patient pressure. Three pressure transducers were placed at different sites: post-oxygenator, pre-arterial Cannula and post-arterial cannula. The system was primed with Lactate Ringer’s solution, human blood was then added to maintain a hematocrit of 40%. The volume of the pseudopatient was 500ml. We hemodynamically evaluated three circuits with different lengths of tubing (6, 4 and 2 feet for both arterial and venous lines), the priming volumes including all of the components of the circuits were 195ml, 155ml and 115ml respectively. In each circuit, we measured the pressure drops of the arterial tubing and the arterial cannula, as well as the flow rates at different RPMs (1750 to 3000, 250 interval) under three patient pressures (40, 60 and 80 mmHg). All the experiments were conducted at 37°C.

Results:
The pressure drop across the arterial cannula is much larger than that of arterial tubing in all set-ups, especially under high flow rates. Upon cutting the tubing from 6 feet to 2 feet, the pressure drop of the arterial tubing decreased by half, while the pressure drop of arterial cannula increased due to the slightly higher flow rates.

![Fig1. Pressure drop of Arterial tubing and arterial cannula at 60mmHg](image)

Conclusions:
These results suggest that the arterial cannula has the largest impact on the hemodynamics of the circuit.
Utilization of Discovery Proteomics to Identify Plasma Biomarkers in Pediatric Patients Undergoing Cardiopulmonary Bypass

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Penn State Center for Host defense, Inflammation, and Lung Disease (CHILD) Research1 and Penn State Hershey Pediatric Cardiovascular Research Center2 and the Department of Pediatrics1, 2, and the Departments of Pharmacology3, Surgery4, Public Health Sciences3 and Bioengineering6, Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA

Purpose:
Despite major advances in cardiopulmonary bypass (CPB) technology and procedures, systemic inflammatory response syndrome (SIRS) remains a major problem in pediatric patients undergoing CPB. Complications such as multiple end organ dysfunction, neurodevelopmental abnormalities, and even death are potential long-term outcomes in the pediatric population. Studies designed to identify plasma biomarkers related to systemic inflammation associated with CPB could prove useful in predicting, monitoring, and preventing adverse outcomes. Our study utilized a dual-platform proteomics approach of two-dimensional difference gel electrophoresis (2D-DIGE) and a multi-analyte profile (MAP) immunoassay to identify and quantify more than 100 potential biomarkers related to tissue damage, inflammation, and other pathologies from the plasma of pediatric CPB patients. A thorough understanding of the plasma biomarkers and the changes they undergo during CPB may aid in future treatments and improve patient outcome.

Methods:
Blood samples from 10 patients were collected 30 minutes before CPB and 24 hours after weaning from CPB. Plasma was isolated and one aliquot was used for MAP immunoassays. A second aliquot 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% using 2D-DIGE. A total of 150 microliters of plasma was used to compete both assays.

Results:
A total of 556 protein spots were visualized in gels from all samples by 2D-DIGE. Protein identification was obtained for 269 of the 566 spots, which constituted 44 distinct proteins and accounted for 88% of the total expressed protein resolved by the gel system. MAP analysis detected an additional 90 proteins. Of the total 129 proteins identified by both methods, 71 underwent significant changes in expression after CPB (p<0.05 after Bonferroni correction for multiple comparisons), with 34 increases and 37 decreases. The PANTHER gene ontology database was used to help categorize and determine the molecular functions and biological processes involving the proteins with significant changes. 4 groups that included the greatest number of proteins with significant changes were: immunity and defense, protein metabolism and modification, signal transduction, and transport. Additional analysis using the Ingenuity Pathways Analysis software demonstrated that numerous proteins with significant increases 24 hours after CPB, including C-reactive protein, ferritin, interleukin (IL)-6, lipopolysaccharide binding protein (LBP), serum amyloid P component, and von Willebrand factor (vWF), were involved in the “acute phase response signaling” pathway.

Conclusions:
This study utilized a novel approach combining two proteomics techniques to identity and quantify potential plasma biomarkers in children undergoing CPB. The results demonstrated significant changes in many proteins involved in the acute phase response pathway and systemic inflammation.
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