CONFERENCE PROCEEDINGS

Volume 9, May 2013

The Proceedings of the Ninth International Conference on

Pediatric Mechanical Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion

Akif Ündar, PhD, Editor

May 8-11, 2013, Hershey, PA, USA

The Ninth International Conference Is Dedicated In Honor Of John A. Waldhausen, MD, For His Life-Long Contributions As The Founding Chair Of The Department Of Surgery At Penn State Hershey And As A Pioneering Surgeon And Educator Of The Development Of Pediatric Cardiac Surgery In The United States.

PENNSTATE HERSHEY Children's Hospital

PENNSTATE HERSHEY Pediatric Cardiovascular Research Center

Conference Founder & President

Akif Ündar, PhD

Honorary Co-Chairs

Aydin Aytaç, MD, Turkey
William S. Pierce, MD, USA
William Williams, MD, Canada

Keynote Lecturers

Shunji Sano, MD, PhD, Japan
Jeffrey Towbin, MD, USA

International & Local Members, Moderators & Wet Lab Instructors

Mehmet Aĝirbaşli, MD, Turkey
Atif Akcevin, MD, Turkey
Tijen Alkan-Bozkaya, MD, Turkey
Erle H. Austin, III, MD, USA
Larry Baer, CCP, USA
Paula Baldridge, MSN, MHA, RN, USA
Emre Belli, MD, France
Roosevelt Bryant, MD, USA
Gary D. Ceneviva, MD, USA
J. Brian Clark, MD, USA
Thomas K. Chin, MD, USA
Jaesoon Choi, PhD, Korea
Hannah Copeland, MD, USA
Jack G. Copeland, MD, USA
Stephen E. Cyran, MD, USA
Megan Del Corral, USA
Yves Durandy, MD, France
Mohammed-Adel Elgamal, MD, Egypt
Christoph Fusch, MD, PhD, FRCPC, Canada
Roberta L. Hales, MHA, RRT-NPS, RN, USA
Allen R. Kunselman, MA, USA
Giovanni Battista Luciani, MD, Italy
Steven E. Lucking, MD, USA
Thomas Markmann, MBA, Germany
David Morales, MD, USA
John L. Myers, MD, USA
Vinay M. Nadkarni, MD, USA
David Palanzo, CCP, USA
Kerem Pekkan, PhD, Turkey
William S. Pierce, MD, USA
Chitra Ravishankar, MD, USA
Tami Rosenthal, BS, CCP, MBA, USA
Shunji Sano, MD, PhD, Japan
Neal J. Thomas, MD, USA
Jeffrey Towbin, MD, USA
Theodor Tirilomis, MD, PhD, Germany
Riza Türköz, MD, Turkey
Akif Ündar, PhD
Shigang Wang, MD, USA
Bonnie Weaver, RN, MSN, CCRN, CCNS, USA
Ronald P. Wilson, VMD, USA
Sung Yang, PhD, Korea
Jeffrey D. Zahn, PhD, USA

Conference Coordinator

Heather Stokes

Welcome to the Ninth Annual Event

Akif Ündar, PhD

Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA

On behalf of the organizing committee, we are pleased to welcome you to **the 9th International Conference on Pediatric Mechanical Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion** at the HERSHEY LODGE, Hershey, PA, USA, May 8-11, 2013. The main purpose of the proposed meeting is to bring together internationally known clinicians, bioengineers, basic scientists, and industry participants involved in research on pediatric mechanical cardiac support systems and pediatric cardiopulmonary bypass procedures (1). The primary focus will be to describe explicitly the problems with current pediatric mechanical circulatory support systems, methods, techniques during acute and chronic support and suggest solutions with novel approaches. During the past nine years, we have not changed our main focus, but we have added more hands-on wet-labs and simulations with the newest devices and techniques to give the highest possible educational opportunities to the diverse participants (2-5).

Learning Objectives of the 9th annual event are 1) Evaluate the impact of unique features and outcomes for pediatric ventricular assist device (VAD) support, 2) Compare the benefits and risks of current and new extracorporeal life support systems (ECLS) and cardiopulmonary bypass (CPB) equipment and techniques, 3) Determine how and where to implement cutting edge bioengineering approaches in their practice of pediatric cardiovascular medicine, and 4) Critique new and current devices including pediatric heart pumps, oxygenators, etc., and the areas where additional physician training may be required for successful implementation.

The Ninth International Conference Is Dedicated In Honor Of John A. Waldhausen, MD, Professor Emeritus, For His Life-Long Contributions As The Founding Chair Of The Department Of Surgery At Penn State Hershey And As A Pioneering Surgeon And Educator Of The Development Of Pediatric Cardiac Surgery In The United States. Therefore, the ninth annual event will start with a special lecture about the remembrance of John A. Waldhausen, Founding Chair of the Department of Surgery at the Penn State Hershey College of Medicine by Professor of Emeritus William S. Pierce, MD and John L. Myers, MD, from Penn State Hershey College of Medicine. The opening of the event will continue with Keynote lectures by two distinguished international scholars. The first Keynote lecture is titled "Pediatric Heart Failure Etiologies And The Outcomes Of Children With Mechanical Circulatory Support" by Jeffrey Towbin, MD, Executive Co-Director, The Heart Institute, Professor and Chief, Pediatric Cardiology Kindervelt-Samuel Kaplan Chair in Cardiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio and the Second Keynote lecture is titled "Stem Cell Therapy In Children With HLHS" by Shunji Sano, MD, PhD, Professor and Chairman Department of Cardiovascular Surgery, Okayama University School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama City, Japan.

There will be two Plenary Sessions in the afternoon of the first day. While the first plenary session will cover the Pediatric MCS: 2013 update including several devices and outcomes for pediatric patients, the second plenary session's

focus will be neuromonitoring and neuroprotection during CPB by several invited lecturers.

Second day of the event will start with the third plenary session on ECLS systems: 2013 Update followed by a Mini-symposium on Nursing Perspectives of ECLS. Ten regular slide presenters (all selected from submitted abstracts) will cover the latest research results of the pediatric MCS, ECLS and CPB procedures. Six Wet-labs and Simulations sessions (3 hour block) will be performed and all participants will be exposed to the latest devices in the field. Following this special session, a Wine and Cheese Reception will be held at The Hershey Story that is a new museum at the sweetest place on earth. "The Hershey Story is an uplifting celebration of the great American dream. Each of the five permanent, engaging, interactive exhibits tells you a pivotal part of Milton Hershey's amazing rags to riches journey. Discover the town through immersive exhibits and engaging interactives, as well as a digital state-of-the art model of the community. See how this community became the cornerstone of one man's legacy through interactive touch-screens and mini-theaters. At the Hershey story, as expected, we will attend the Chocolate Lab. It explores the unique qualities of chocolate through playful, hands-on experiences and interactive demonstrations. Guaranteed to bring out the kid in you, the Chocolate Lab offers participatory classes such as tempering, molding, dipping and even making chocolate from scratch." Guests should be prepared for more surprises such as live music from our invited lecturers and participants on the second night. All guests will be transported to and from The Hershey Story by Hershey Trolley Works. Each trolley ride will also provide a 30 minute tour of a historic journey through the town built on chocolate.

The last day of the event will start with the plenary session on pediatric perfusion followed by a mini-symposium on bioengineering approaches in pediatric cardiovascular medicine. The conference will end with two sessions on regular slide presentations selected from abstracts.

New Penn State Hershey Children's Hospital Tours

This 263,000 square feet of space has five dedicated pediatric operating rooms, a cardiac catheterization lab, two procedure rooms and a pediatric radiology space. A 12 bed state-of-the-art pediatric intensive care unit and a 6 bed Pediatric Cardiac Care unit.

Other amenities designed to encourage healing and to let kids be kids, even while at the hospital, include a performing arts area, a meditation space, interactive play areas, a learning wall and healing gardens, including a "green" roof on the third floor. The building incorporates natural light in most spaces and architectural details and finishes that evoke the natural world, such as the "waterfall" window on the east end of the building, and large wall images of plant and animal life that adorn many public areas. A safety store and a family resource center provide all parents in the community with the tools and information they need to help keep kids safe and healthy. Join us for a tour of this fabulous hospital at the pre-conference on Wednesday, May 8, 2013 or Saturday at the last day of the event, May 11, 2013.

PICU Tours

These sessions will be held in the PICU at The Penn State Hershey Children's Hospital and lead by PICU 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 75 minutes duration, and space is restricted to 25 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.

Conference Awards

This event will continue to recognize young investigators' original research; therefore special

awards will be given to young investigators based on their full manuscript. All details regarding awards can be accessed via conference web site. http://pennstatehershey.org/web/pedscpb/home

Artificial Organs

If an abstract is accepted either for oral or poster presentation, then the presenters are required to submit original manuscripts to the Artificial Organs prior to the conference. All original manuscript will be peer-reviewed. The January 2014 issue of the Artificial Organs is dedicated to our conference manuscripts (all peer-reviewed), in addition to the April 2013 issue for accepted abstracts. Special thanks to Angela T. Hadsell, Executive Editor, and Paul Malchesky, D. Eng, Editor-in-Chief, for making this issue possible and for their continued support year after year. To date, over 400 manuscripts, including original articles, editorials, special reports, and case reports have been peer-reviewed and published. These publications have become the largest resource for investigators in their research projects related to pediatric CPB and MCS.

To date, over 2,055 investigators from 33 countries have participated in the last eight events. All of the past eight conference proceedings, 400 publications, young investigator awardees, and all conference related details including conference, hotel and exhibitor registrations can be also found on the conference web site.

Financial support

We thank the Penn State Hershey Pediatric Cardiovascular Research Center, the Penn State Hershey Children's Hospital, and the International Society for Pediatric Mechanical Cardiopulmonary Support for providing financial support to this event year after year. In addition, we received confirmations or funds from the following companies (as of April 1, 2013):

- MEDOS MEDIZINTECHNIK AG (Germany);
- TERUMO CARDIOVASCULAR SYSTEMS (USA);
- COVIDIEN (USA);
- MAQUET MEDICAL SYSTEMS (USA);
- SYNCARDIA SYSTEMS, INC. (USA); and
- WILEY-BLACKWELL (USA).

Our Motto

As we have written several times before, 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."

Acknowledgments:

I would like to thank Bonnie Weaver, MSN, RN for leading the Pre-Conference events including the new Children's Hospital and PICU tours. Wet-lab co-chairs, Tami Rosenthal, BS, CCP, MBA, and David Palanzo, CCP have also spent a significant amount of time selecting the new pediatric devices and organizing the hands-on experience. Special thanks go to Heather Stokes and Dr. Shigang Wang for the coordination and support of this event. We also appreciate Ann Hagan's invaluable help for organizing CME from the Department of Continuing Medical Education of the Children's Hospital of Philadelphia. As always, I also have "unconditional support and love" from my family, my wife, Pinar and children, Damla and Akifcan during the past nine years. My family and I consider this event our third child while the **International Society for Pediatric Mechanical Cardiopulmonary Support** is our fourth child. Parts of this Welcome Letter were extracted from Dr. Ündar's earlier publication (6).

References:

1. Ündar A, Wang S, Krawiec C. Impact of a unique international conference on pediatric mechanical circulatory support and pediatric cardiopulmonary perfusion research [Invited editorial]. Artificial Organs 2012; Nov;36(11): 943-50.
2. Ündar A, Akçevin A, Alkan-Bozkaya T, et al.. Outcomes of the eighth international conference on pediatric mechanical circulatory support systems and pediatric cardiopulmonary perfusion [Guest Editorial]. Artificial Organs 2013; 37 (1) 1-9.
3. Ündar A, Ravishankar C, Gaynor JW, Baer LD, Clark JB, Wernowsky G, Myers JL. Outcomes of the seventh international conference on pediatric mechanical circulatory support systems and pediatric cardiopulmonary perfusion and second annual meeting of the international society for pediatric mechanical cardiopulmonary support. Artif Organs 2011 Nov;35(11):975-82.
4. Ündar A. Outcomes of the sixth international conference on pediatric mechanical circulatory support systems and pediatric cardiopulmonary perfusion and first annual meeting of the international society for pediatric mechanical cardiopulmonary support. Artificial Organs 2010; 34(11): 865–868.
5. Ündar A. Outcomes of the fifth international conference on pediatric mechanical circulatory support systems and pediatric cardiopulmonary perfusion. Artificial Organs 2009; 33:879-882.
6. Ündar A. Welcome to the 9th international conference on pediatric mechanical circulatory support systems & pediatric cardiopulmonary perfusion. Artif Organs 2013;27(4):354-6.

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Selected Posters from Penn State Hershey Pediatric Cardiovascular Research Center

Scientific Program

Wednesday, May 8, 2013 - Pre-Conference Program

ECLS Workshop, Hospital Tours and ICU Rounds

2:00 – 5:00pm Registration

9:00am – 5:00pm Pediatric ECLS Workshop:

Hands-On Experience With The Newest Pediatric ECLS Systems (Pediatric Cardiovascular Research Center)

Instructors: Larry Baer, CCP, David Palanzo, CCP, Bonnie Weaver, RN, MSN, CCRN, CCNS, Shigang Wang, MD, Akif Ündar, PhD

9:00am – 12:00pm Group #1: 15 participants (PRE-REGISTRATION is required)

1:00 – 4:00pm Group #2: 15 participants (PRE-REGISTRATION is required)

Parallel Session I New Penn State Hershey Children's Hospital Tours

Instructors: Bonnie Weaver, RN, MS, CCRN, CCNS, Gary D. Ceneviva, MD, J. Brian Clark, MD, Neal J. Thomas, MD, Steven E. Lucking, MD, and John L. Myers, MD

These sessions will provide a guided tour of the new, Children's Hospital. This facility is new to our campus as of 2013. (PRE-REGISTRATION is required)

This 263,000 square feet of space has five dedicated pediatric operating rooms, a cardiac catheterization lab, two procedure rooms and a pediatric radiology space. A 12 bed state-of-the-art pediatric intensive care unit and a 6 bed Pediatric Cardiac Care unit.

Other amenities designed to encourage healing and to let kids be kids, even while at the hospital, include a performing arts area, a meditation space, interactive play areas, a learning wall and healing gardens, including a "green" roof on the third floor. The building incorporates natural light in most spaces and architectural details and finishes that evoke the natural world, such as the "waterfall" window on the east end of the building, and large wall images of plant and animal life that adorn many public areas. A safety store and a family resource center provide all parents in the community with the tools and information they need to help keep kids safe and healthy. Join us for a tour of this fabulous hospital.

10:00am – 12:00pm	**Group #1: 25 participants (PRE-REGISTRATION is required)**
1:00 – 3:00pm	**Group #2: 25 participants (PRE-REGISTRATION is required)**
3:00 – 5:00pm	**Group #3: 25 participants (PRE-REGISTRATION is required)**
Parallel Session II	**Cardiac ICU and PICU Tours:**
	Instructors: Gary D. Ceneviva, MD, Thomas K. Chin, MD, J. Brian Clark, MD, Stephen Cyran, MD, Linda Pauliks, MD, Neal J. Thomas, MD, Steven E. Lucking, MD, John L. Myers, MD
	These sessions will be held in the PICU at The Penn State Hershey Children's Hospital 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 75 minutes duration, and space is restricted to 25 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.
10:00am – 12:00pm	**Group #1: 25 participants (PRE-REGISTRATION is required)**
1:00 – 3:00pm	**Group #2: 25 participants (PRE-REGISTRATION is required)**
3:00 – 5:00pm	**Group #3: 25 participants (PRE-REGISTRATION is required)**

Thursday, May 9, 2013 – Scientific Program

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

8:00 – 8:15am **WELCOME**
Akif Ündar, PhD, Penn State Hershey Children's Hospital & Penn State Hershey College of Medicine, Hershey, PA, USA

8:15 – 9:00 am **Remembrance Of John A. Waldhausen, MD**
William S. Pierce, MD and John L. Myers, MD, Hershey, PA, USA

9:00 – 10:00 am **KEYNOTE LECTURE #1**

IL1. **Pediatric Heart Failure Etiologies And The Outcomes Of Children With Mechanical Circulatory Support**
Jeffrey Towbin, MD, Executive Co-Director, The Heart Institute, Professor and Chief, Pediatric Cardiology Kindervelt-Samuel Kaplan Chair in Cardiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

10:00 – 11:00 am **Coffee Break/Exhibits/Posters/Wet-Labs**

11:00 – Noon **KEYNOTE LECTURE #2**

IL2. **Stem Cell Therapy In Children With HLHS**
Shunji Sano, MD, PhD, Professor and Chairman Department of Cardiovascular Surgery, Okayama University School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama City, Japan

Presentation of Young Investigators' Awards

Noon – 13:00 pm **LUNCH**

1:00 – 3:00pm **PLENARY SESSION #1: Pediatric MCS: 2013 Update**

Moderators: Shunji Sano, MD, PhD, Okayama, Japan; William S. Pierce, MD, Hershey, PA, USA; Jeffrey Towbin, MD, Cincinnati, Ohio, USA

IL3. **The Berlin Heart Experience Across North America**
Roosevelt Bryant, MD, Cincinnati, Ohio, USA

IL4. **VAD Support As A Bridge To Recovery In Pediatric Cardiac Patients**
Hannah Copeland, MD, Loma Linda, CA, USA

IL5. **TAH As Bridge To Transplantation In Pediatric Patients**
Jack Copeland, MD, San Diego, CA, USA

IL6. **Animal Model For Pediatric MCS Research**
Ronald P. Wilson, VMD, Hershey, PA, USA

IL7. **VAD Coordinator's Impact On Successful Outcomes**
Megan Del Corral, RN, Cincinnati, Ohio, USA

IL8. **Novel therapy options for neonatal and pediatric Extracorporeal Life Support using the ROTASSIST 2.8**
Thomas Markmann, MBA, Germany

Discussion

3:00 – 3:45pm **Coffee Break/Exhibits/Posters/Wet-Labs**

3:45 – 5:45pm **PLENARY SESSION #2: Neuromonitoring / Neuroprotection During CPB**
Moderators: Erle H. Austin, III, MD Louisville, KY, USA; J. Brian Clark, MD, Hershey, PA, USA; Giovanni Battista Luciani, MD, Verona, Italy

IL9. **Neuromonitoring During Pediatric CPB**
Erle H. Austin, III, MD Louisville, KY, USA

IL10. **Biomarkers For Neurologic Injury During Pediatric CPB Procedures**
Mehmet Agirbasli, MD, Istanbul, Turkey

IL11. **Neurological Outcomes After Normothermic CPB**
Emre Belli, MD, Paris, France

IL12. **Cerebral Protection In Congenital Heart Surgery**
Giovanni Battista Luciani, MD, Verona, Italy

IL13. **Brain Protection In Pediatric Aortic Arch Repair: Deep Hypothermic Circulatory Arrest, Selective Cerebral Perfusion Or Combined Technique**
Riza Türköz, MD, Istanbul, Turkey

IL13a **Impact of cerebral embolization during pediatric cardiac surgery on neurocognitive outcomes at intermediate follow-up**
J. Brian Clark, MD, Hershey, PA, USA

IL14. **Collaborating with a Statistician to Enhance Pediatric Cardiovascular Research**
Allen R. Kunselman, MA, Hershey, PA, USA

Discussion

Friday, May 10, 2013

7:00 – 8:00 am — **Breakfast / Conference registration**

8:00 – 10:00am — **PLENARY SESSION #3: ECLS systems: 2013 Update**

Moderators: Emre Belli, MD, Paris, France; Chitra Ravishankar, MD, Philadelphia, PA, USA

IL15. Cardiac Neonatal ECLS At CHOP
Chitra Ravishankar, MD, Philadelphia, PA, USA

IL16. Development Of Microfluidic Oxygenators As Lung Assisting Devices For Term And Preterm Newborn Infants
Christoph Fusch, MD, PhD, FRCPC, Hamilton, Ontario Canada

IL17. Epidemiology and Outcomes of Pediatric CPR & E-CPR
Vinay M. Nadkarni, MD, Philadelphia, PA, USA

IL18. Pulsatile ECLS Systems
Akif Ündar, PhD, Hershey, PA, USA

IL19. Adjunct therapies for pediatric Acute Lung Injury
Neal Thomas, MD, MPH, Hershey, PA, USA

10:00 – 10:45am — **Coffee Break/Exhibits/Posters/Wet-Labs**

10:45 – Noon — **MINI-SYMPOSIUM #1: PEDIATRIC EXTRACORPOREAL LIFE SUPPORT: NURSING PERSPECTIVE (20 min each)**

Moderators: Paula Baldridge, MSN, MHA, RN and Bonnie Weaver, RN, MSN, CCRN, CCNS

IL20. Expanded Resources Through Utilization Of A Primary Care Giver Extracorporeal Membrane Oxygenation Model
Paula Baldridge MSN, MHA, RN, Ann Arbor, MI, USA

IL21. Pediatric ECMO simulation training pioneered at CHOP
Roberta L. Hales MHA, RRT-NPS, RN, Philadelphia, PA, USA

IL22. Pediatric ECLS @ The Penn State Children's Hospital: 2013 Update
Bonnie Weaver, RN, MS, CCRN, CCNS, Hershey, PA, USA

Discussion (15 min)

Noon – 1:00 pm — **LUNCH**

1:00 – 3:00pm — **Regular Slide Presentations #1:**

Moderators: Hannah Copeland, MD, San Diego, CA, USA; Jaesoon Choi, PhD, Seoul, Korea; Mohammed-Adel Elgamal, MD, Egypt

(9 min. Presentation and 3 min. Discussion)

S1 Extracorporeal life support following cardiac surgery in children: outcomes in a single institution
Takashi Sasaki, Toshihide Asou, Yuko Takeda, Yasuko Onakatomi, Yokohama, JAPAN

S2 Initial Experiences with Medos Deltastream DP3 Pediatric Extracorporeal Life Support System
Sertac Haydin, Ersin Erek, Halime Ozkan, Ismihan Selen Onan, Perihan Yivli, Mehmet Yeniterzi, Ihsan Bakir, Istanbul, Turkey

S3 Impact of Pulsatile Flow on Hemodynamic Energy in a Medos Deltastream DP3 Pediatric Extracorporeal Life Support System
Conrad Krawiec, MD, Shigang Wang, MD, Allen R. Kunselman, MD, and Akif Ündar, PhD, Hershey, PA, USA

S4 NeonatOx II – 12 Hour Pumpless Extracorporeal Lung Support on Premature Lambs
Jutta Arens; Mark Schoberer; Aileen Erben; Thorsten Orlikowsky; Daan Ophelders; Reint K. Jellema; Boris W. Kramer; Jan L. Bruse; Petra De Brouwer; Thomas Schmitz-Rode; Ulrich Steinseifer, Aachen, Germany

S5 Novel Inflow Cannula for Mechanical Circulatory Support in Patients with Total Caval Pulmonary Connection
Michael F Swartz PhD, Doran Mix BS Christopher Cistrone BS, Andrew Hagar BS, Alexander Kotelsky BS, Ron Angona CCP, Karl Schwarz MD, George M. Alfieris MD, Rochester, NY, USA

S6 Incidence and Outcome of Pediatric Patients with Intracranial Hemorrhage while supported on Ventricular Assist Devices
Robert A. Niebler MD, Sean Lew MD, Steven D Zangwill MD, Ronald K Woods MD, Michael E Mitchell MD, James S Tweddell MD, and Nancy S Ghanayem MD, Milwaukee, WI USA

S7 Five-year Experience with Mini-Volume Priming in Infants ≤5 kg: Safety of Significantly Less Transfusion Volume
Hyoung Woo Chang, MD, Jinhae Nam, MD, Jae-Hee Cho, Woo Sung Jang, MD, Kwangho Choi, MD, Jeong-Ryul Lee, MD, PhD, Yong-Jin Kim, MD, PhD, Woong-Han Kim, MD, PhD, Seoul, Republic of Korea

S8 The Influence of Lower Body Circulatory Arrest on the Acute Kidney Injury after Surgery for Congenital Heart Disease in Neonate
Ko Yoshizumi, MD, Shingo Kasahara, MD, Atsushi Tateishi, MD, Takuya Kawabata, MD, Yosuke Kuroko, MD, Sadahiko Arai, MD Shunji Sano, MD, Okayama, Japan

S9 **Is There a Difference between Pulsatile and Nonpulsatile Perfusion Mode According to the Regional Brain Perfusion via Using NIRS in Patients Which Underwent to Pediatric Cardiac Surgery with CPB?**
Alkan-Bozkaya T., Karacı AR., Sasmazel A., Ersoy C., Türkoğlu H., Akçevin A., Karaaslan P., Gökay Vural B.,Ündar A., Istanbul, TURKEY

S10 **Cardiac Surgery in Neonates with Body Weight Less Than 2500 Gram**
Jeng-Wei Chen,MD; Shu-Chien Huang, MD; Yih-Sharng Chen, MD; Chung-I Chang, MD; Ing-Sh Chiu, MD, Nai-Kuan Chou, MD, Taipei, Taiwan

3:00 – 3:45pm **Coffee Break/Exhibits/Posters/Wet-Labs**

3:30 – 6:30 pm **WET-LABS & SIMULATIONS**

Moderators: ***Tami Rosenthal BS, CCP, MBA, Philadelphia, PA, USA, David Palanzo, CCP, Hershey, PA, USA, Shigang Wang, MD, Hersheym PA, USA***

6 WET-LABS (30 min each)

6:30pm **SOCIAL PROGRAM**

Guests will be transported to and from The Hershey Story by Hershey Trolley Works. Each trolley ride will provide a 30 minute tour of a historic journey through the town built on chocolate!

7:00 – 9:30pm **Wine & Cheese Reception at The Hershey Story**

A place devoted to Hershey – the man, the company, and the town! During the reception, guests can be fascinated, inspired and filled with wonder as they explore the Museum Experience. The Hershey Story is an uplifting celebration of the great American dream. Each of the five permanent, engaging, interactive exhibits tells you a pivotal part of Milton Hershey's amazing rags to riches journey. Discover the town through immersive exhibits and engaging interactives, as well as a digital state-of-the art model of the community. See how this community became the cornerstone of one man's legacy through interactive touch-screens and mini-theaters.

Chocolate Lab

Explores the unique qualities of chocolate through playful, hands-on experiences and interactive demonstrations. Guaranteed to bring out the kid in you, the Chocolate Lab offers participatory classes such as tempering, molding, dipping and even making chocolate from scratch.

The Special music this evening is brought to us by Heidi Watts, Vocalist, Tim Vallati, Guitarist, and Professor Emre Belli on the Saxophone.

Heidi Watts began singing as soon as she could talk. She enjoys singing in her church choir and with the newly formed Penn State Hershey Hospital Choir which is made up of physicians, nurses, and staff. In 2007 she won the Elizabethtown Fair's singing idol competition. Heidi performed at our 2010 Conference in Boston, MA, USA.

Tim Vallati is owner/instructor of Vallati Guitar. He has over 35 years of experience as a professional musician and more than 20 years as a private guitar instructor. Tim has played lead guitar in many local bands, and currently collaborates with several artists and groups comprised of top-notch musicians. While Tim is trained in a wide range of musical genres, like Soul, Jazz, Country, Folk and Bluegrass music. He has particular skill and interest in Rock, Blues, and Contemporary music. "Tim believes that sharing his love of music with the next generation of artists is a gift"

Professor Emre Belli provided us all with wonderful background music as we set sail on the Bosphorus last year while in Istanbul, Turkey.

We look forward to an evening of wonderful music.

Poster Presentations:

(8 am, Thursday, May 9, 2013 – 5 pm, Saturday, May 11, 2013 – All posters will be displayed throughout the conference)

P1 Handling Ability of Gaseous Microemboli of Two Pediatric Arterial Filters in a Simulated CPB Model
Ashton Strother, Shigang Wang, MD, Allen R. Kunselman, MA, Akif Ündar, PhD, Hershey, PA, USA

P2 Is NIRS (Near infrared spectroscopy) Monitoring Important during Pediatric Aortic Coarctation and/or Arch Repair?
Alkan-Bozkaya T., Akçevin A., Ersoy C., Türkoğlu H., Karaaslan P., Gökay Vural B., Ündar A, Istanbul, TURKEY

P3 In Vitro Comparison of the Delivery of Gaseous Microemboli and Hemodynamic Energy for a Rotary and Roller Pump
Ranjodh Dhami, BS, Shigang Wang, MD, Akif Ündar, PhD, Hershey, PA, USA

P4 Impacts of Pulsatile Settings on Hemodynamic Energy Output of a Diagonal Pump in a Simulated ECLS System
Shigang Wang, MD, Allen R. Kunselman, MD, Akif Ündar, PhD, Hershey, PA, USA

P5 Hemodynamic Energy Change Depends on Position of Patients during Extracorporeal Circulation
Chi Bum Ahn, PhD, Kuk Hui Son, MD, Sung Ho Lee, MD, Ho Sung Son, MD, Jae Seung Jung, MD, Kyung Sun, MD, Seoul, Korea

P6 In Vitro Performance Analysis of Novel Pulsatile Diagonal Pump in Simulated Pediatric Mechanical Circulatory Support System
Shigang Wang, MD and Akif Ündar, PhD, Hershey, PA, USA

P7 Impact of Pulsatile Flow Settings on Hemodynamic Energy Levels Using the Novel Diagonal Medos DP3 Pump in a Simulated Pediatric ECLS System
Pelumi Adedayo, MS, Shigang Wang, MD and Akif Ündar, PhD, Hershey, PA, USA

P8 A Rare Reason of Right Ventricular Failure: The Decortication Requiring because of Constructive Pleuritis at Redo Case who had Tetralogy of Fallot
Turkoglu H., Sarıtas T., Alkan-Bozkaya T., Gunluoglu MZ., Oktem S., Ersoy C., Karaaslan P., Gökay Vural B., Akcevin A., Istanbul, TURKEY

P9 **In Vitro Evaluation of Medos Deltastream DP3 Pulsatile ECLS System**
Shigang Wang, MD, Allen R. Kunselman, MD, and Akif Ündar, PhD, Hershey, PA, USA

P10 **Evaluation of Capiox and Quadrox-i Hollow Fiber Membrane Oxygenator in a Simulated CPB Circuit for Adolescents**
Shigang Wang, MD, Allen R. Kunselman, MD, and Akif Ündar, PhD, Hershey, PA, USA

P11 **MIFS (Minimal Incision Full Sternotomy) in Pediatric Cardiac Surgery Indications, Technique and Results**
Ersoy C., Alkan-Bozkaya T., Akcevin A., Türkoğlu H., Istanbul, TURKIYE

P12 **Postoperative Cerebral Perfusion Monitoring with NIRS in Pediatric Patients Undergoing Cardiac Surgery**
Alkan-Bozkaya T., Karaaslan P., Gökay Vural B., Türkoğlu H., Akçevin A., Ersoy C., Ündar A, Istanbul, TURKEY

P13 **Using a Secondary Reservoir for Pump Suckers to Avoid the Generation of Foam during CPB Procedures in Pediatric Patients**
Akif Ündar, PhD, David Palanzo, CCP, Robert Wise, CCP, Larry Baer, CCP and Shigang Wang, MD, Hershey, PA, USA

P14 **Monitoring Biomarkers after Pediatric Heart Surgery: A New Paradigm on the Horizon**
Mehmet Aĝirbaşli, MD, Istanbul, TURKEY and Akif Ündar, PhD, Hershey, PA, USA

Selected Posters from Penn State Hershey Pediatric Research Center

P15 **Approaches Toward Continuous Monitoring of Pediatric Cardiopulmonary Bypass Procedures Using Cytometric Bead Processing within a Microfluidic Device.**
Yang S, PhD, Ündar A, PhD, Zahn JD, PhD, Hershey, PA, USA

P16 **A Two Compartment Microdialysis Microdevice for Continuous Protein Extraction from Whole Blood.**
Aran K, PhD, Fox A, PhD, Zahn J, PhD, Ündar A, PhD, Hershey, PA, USA

P17 **Neonatal Extracorporeal Life Support: Will the Newest Technology Reduce Morbidity?**

Reed-Thurston D, Shenberger J, Qiu F, MD, Ündar A, PhD, Hershey, PA, USA

P18 **Extracorporeal Life Support Systems: Alternate vs. Conventional Circuits**

Sameer Khan, BS, Rahul Vasavada, MS, Feng Qiu, MD, Allen Kunselman, MA, Akif Ündar, PhD, Hershey, PA, USA

P19 Hemodynamic Evaluation of Arterial and Venous Cannulae Performance in a Simulated Neonatal Extracorporeal Life Support Circuit

Feng Qiu, MD, Joseph B. Clark, MD,†, Allen R. Kunselman, MA, Akif Ündar, PhD, John L. Myers, MD, Hershey, PA, USA

P20 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 Ündar, PhD, Hershey, PA, USA

Saturday, May 11, 2013

7:00 – 8:00 am **Breakfast**

8:00 – 10:00am **PLENARY SESSION #4: Pediatric Perfusion: 2013 update**

Moderators: Larry Baer, CCP, Hershey, PA, USA & Tami Rosenthal BS, CCP, MBA, Philadelphia, PA, USA,

IL23. Neonatal & Pediatric CPB Techniques At CHOP
Tami Rosenthal BS, CCP, MBA, Philadelphia, PA, USA

IL24. Applications for Perfusion Simulation
Debra Zarro, Terumo Cardiovascular Systems, Ann Arbor, MI, USA

IL25. Choosing a Pump for Extracorporeal Life Support
David Palanzo, CCP, Hershey, PA, USA

IL26. Minimizing Systemic Inflammation During CPB In Pediatric Population
Yves Durandy, MD, Paris, France

IL27. Microemboli Detection And Capturing During CPB
Shigang Wang, MD, Hershey, PA, USA

10:00 – 10:45am **Coffee Break/Exhibits/Posters/Wet-Labs**

10:45 – Noon **MINI-SYMPOSIUM #2: Bioengineering Approaches in Pediatric Cardiovascular Medicine (25 min each)**

Moderators: Kerem Pekkan, PhD, Istanbul, Turkey; Jeffrey D. Zahn, PhD, Piscataway, NJ, USA

IL28. Impact Of Computational Fluid Dynamics On Pediatric CPB Procedures
Kerem Pekkan, PhD, Istanbul, Turkey

IL29. A Hand-Held Microhemocytometer: Prototype And More
Sung Yang, PhD, Korea & USA

IL30. Real-Time Monitoring Of Systemic Inflammation During CPB & ECLS
Jeffrey D. Zahn, PhD, Piscataway, NJ, USA

Noon – 1:00 pm **LUNCH**

1:00 – 3:00pm **Regular Slide Presentations #2:**

Moderators: Tijen Alkan-Bozkaya, MD, Istanbul, Turkey; Yves Durandy, MD, Paris, France; Theodor Tirilomis, MD, Germany
(9 min. Presentation and 3 min. Discussion)

S11 **An Implementation of Computer Graphic Simulator Framework for the Training of Congenital Heart Disease Surgery with Interactive Virtual Vessel Re-configuration**
Duck Hee Lee, MS, Song E Choi, BA, Seoung Joon Song, PhD, Song Cheol Kim, MD, PhD, Jaesoon Choi, PhD, Seoul, Republic of Korea

S12 **Valsartan Improves Myocardial Cardioplegic Protection and Oxidative Stress Tollerance during Ischemia/ Reperfusion In Isolated Neonatal Rat Heart.**
Gianluca Lucchese, MD, PhD, Giulia Elisa Cambi, ScD, Rocco Tabbi, CP, Stiljan Hoxha, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Pietro Amedeo Modesti, MD, PhD, Giovanni Battista Luciani, MD, Verona, Italy

S13 **Carotid artery Doppler flow pattern after deep hypothermic circulatory arrest in neonatal piglets**
Theodor Tirilomis, MD, PhD, Stella Malliarou, MD, K. Oguz Coskun, MD, Friedrich A. Schoendube, MD, PhD, Göttingen, Germany

S14 **Near Infrared Spectroscopy Monitoring in the Pediatric Cardiac Catheterization Laboratory**
Ibrahim Cansaran Tanidir, Erkut Ozturk, Isa Ozyilmaz, Murat Saygi, Neslihan Kiplapinar, Sertac Haydin, Alper Guzeltas, Ender Odemis, Istanbul, Turkey

S15 **A Computerized Mock Circulatory Loop System Using Servo Control Flow Regulator for Time-varying Hemodynamic Characteristics Simulation**
Youngjin Moon, PhD, Jaesoon Choi, PhD, Seoul, Korea

S16 **Quantitation of Fetal Heart Function with Tissue Doppler Velocity Imaging – Reference Values for Color Doppler Velocities and Comparison with Pulsed Wave Doppler Imaging**
Ashish P. Saini, MD, Serdar Ural, MD, Linda B. Pauliks, MD, MPH, Hershey, PA

S17 **Could ECMO Be Weaned Off for a Child with Acute Fulminant Myocarditis under the Status of Low Left Ventricular Ejection Fraction?**
Shye-Jao Wu, MD, Taipei, TAIWAN

S18 **The Dynamic Observation of Plasma Concentration of Antimicrobial Agents during Balanced Ultrafiltration in Vitro**
Yulong Guan, MD, Zhida Fu, MD, Ju Zhao, MD, Peng Sun, MD, Cun Long, MD, Beijing, P. R. China

	S19	**Universal Method for Object Detection and Tracking in Robot-assisted Laparoscopic Surgery Images** *Jiwon Ryu, Jaesoon Choi, PhD, Hee Chan Kim, PhD, Seoul, Korea*
	S20	**Aortic Outflow Cannula Tip Design and Orientation Impacts Cerebral Perfusion in Pediatric Cardiopulmonary Bypass** *Prahlad G Menon, MS, Akif Ündar, PhD, Kerem Pekkan, PhD, Pittsburgh, PA, USA*
3:45 pm– 4:55pm		**MINI-SYMPOSIUM #3: Penn State Hershey Pediatric Cardiovascular Research Center – International Collaborations: 2013 Update** **Moderator: Akif Ündar, PhD, Hershey, PA, USA** **Panel Discussion: Mehmet Agirbasli, MD, Istanbul, Turkey; Yves Durandy, MD, Paris, France; Kerem Pekkan, PhD, Istanbul, Turkey; Akif Ündar, PhD, Hershey, PA, USA**
	I.	**2013 International Collaborations: An overview** *Akif Ündar, PhD, Hershey, PA, USA*
	II.	**High throughput technologies and overwhelming amount of biomarkers of clinical value. Where are we heading?** *Mehmet Agirbasli, MD, Istanbul, Turkey*
	III.	**Novel Neonatal Cannula Design** *Kerem Pekkan, PhD, Istanbul, Turkey*
	IV.	**A Nonocclusive Pediatric Pulsatile Roller Pump** *Yves Durandy, MD, Paris, France*
Parallel Session I		**New Penn State Hershey Children's Hospital Tours** ***Instructors: Bonnie Weaver, RN, MS, CCRN, CCNS, Gary D. Ceneviva, MD, J. Brian Clark, MD, Neal J. Thomas, MD, Steven E. Lucking, MD, and John L. Myers, MD***
Parallel Session II		**Cardiac ICU and PICU Tours:** **Instructors: Gary D. Ceneviva, MD, Thomas K. Chin, MD, J. Brian Clark, MD, Stephen Cyran, MD, Linda Pauliks, MD, Neal J. Thomas, MD, Steven E. Lucking, MD, John L. Myers, MD**
1:00 – 3:00pm		**Group #1: 25 participants (PRE-REGISTRATION is required)**
3:00 – 5:00pm		**Group #2: 25 participants (PRE-REGISTRATION is required)**
5:00pm		**CLOSING REMARKS**

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- **Nurses:** **24.6 Category 1 CEU's**

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MAQUET MEDICAL SYSTEMS (USA)

SYNCARDIA SYSTEMS, INC. (USA)

WILEY-BLACKWELL (USA)

IL1. Pediatric Heart Failure Etiologies and the Outcomes of Children with Mechanical Circulatory Support

Jeffrey A. Towbin, MD
The Heart Institute, Cincinnati Children's Hospital Medical, Cincinnati, Ohio, USA

Like adult forms of cardiomyopathy, children also are affected by 5 potential types of disease. These classified forms of cardiomyopathy include 1) dilated cardiomyopathy (DCM), 2) hypertrophic cardiomyopathy (HCM), 3) restrictive cardiomyopathy (RCM), 4) left ventricular cardiomyopathy (LVNC), and 5) arrhythmogenic right ventricular cardiomyopathy (ARVC). In all forms, heart failure (HF) is a potential clinical outcome, as is sudden cardiac death (SCD). However, the clinical features of these heart muscle diseases may differ in children compared to adults and the percentage and types of genetic and acquired etiologies may also be different in children.

The mechanisms of cardiomyopathy and HF in children rely on disturbance of "final common pathways" of disease and may differ between forms and even within disease forms. For instance, HCM appears to be due to disturbed sarcomere function which may occur due to mutations in sarcomere-encoding genes or inborn errors of metabolism, resulting in abnormal development or utilization of energy needed by the sarcomere. RCM appears to also result from these disturbances. DCM can occur by disruption of the sarcomere and/or cytoskeleton/sarcolemma and again mutations in genes that encode these proteins or in errors of metabolism can cause these features. In addition to genetic causes, acquired disease, especially viral myocarditis is responsible for DCM and heart failure. ARVC appears to be result from disturbed desmosome function while LVNC appears to result from overlap of these disturbances.

The annual incidence of DCM in children <18 years is 0.57 cases per 100,000/year overall, higher in boys than girls, in blacks than whites, and in infants (<1 year) vs. children. The 1- and 5-year rates of death or transplantation are 31% and 46%, respectively. Independent risk factors at DCM diagnosis for t death or transplantation included older age, HF, lower LV fractional shortening Z score, and etiology. Utilization of MCS in myocarditis in children has been shown to lead to >75% survival, either with normalization or successful transplantation. For HCM, the annual incidence of pure HCM is 4.7/1 million children with a higher incidence in boys than girls and in children diagnosed at <1 year of age vs. older. HCM due to inborn errors of metabolism and malformation syndromes had significantly worse survival than the other groups. Patients with idiopathic HCM diagnosed before 1 year of age had worse survival from the time of diagnosis than those diagnosed later, with HF being common in this group. MCS in this group leads to improved survival. For RCM, an incidence of 0.03 to 0.045 cases/100 000 children is notable, accounting for 4-5% of pediatric cardiomyopathy cases. Freedom from death is 82%, 80%, and 68% at 1-, 2-, and 5-years after diagnosis but transplant-free survival is 48%, 34%, and 22%. Overall, RCM outcomes are worse than for all other cardiomyopathies. MCS may improve outcome as a bridge to transplant.

References:

1. Maron BJ, Towbin JA, Thiene G, et al. Contemporary Definitions and Classifications of the Cardiomyopathies: An American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. Circulation 113:1807-1816, 2006.
2. Towbin JA, Lowe AM, Colan SD, et al. Incidence, causes and outcomes of dilated cardiomyopathy in children. JAMA. 2006 Oct 18;296(15):1867-76.
3. Wilmot I, Morales DL, Price JF, Rossano JW, Kim JJ, Decker JA, McGarry MC, Denfield SW, Dreyer WJ, Towbin JA, Jefferies JL. Effectiveness of mechanical circulatory support in children with acute fulminant and persistent myocarditis. J Card Fail. 2011 Jun;17(6):487-494.

IL4. Mechanical Support and Medical Therapy Reverse Heart Failure in Infants and Children

Hannah Copeland (Zimmerman), MD, Diane Covington, RN, Richard Smith, MSEE, Jack Copeland, MD

Loma Linda University, Loma Linda, CA 92354, United States

Objective:

Most infants and children implanted with ventricular assist devices go on to cardiac transplantation. Recovery of dilated cardiomyopathies with the combination left ventricular decompression with a ventricular assist device and treatment with maximal medical therapy has been possible in some adults, and may be more feasible in infants and children.

Methods:

We used pulsatile and continuous flow ventricular assist devices and the total artificial heart (TAH) as bridges to transplantation or to recovery. Candidates for native heart recovery were treated with maximal medical therapy for congestive heart failure and short term dobutamine prior to weaning off device support.

Results:

Since 1997, 28 infants and children, ages 1 month to 16 years, were implanted for durations of 3-107 days (mean 27). Eighteen received LVADs (left ventricular support 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 the hospital and currently surviving for 2 months to 9 years. Ten of eleven transplant recipients (90%) have survived 2 to 9 years. All 10 with recovered hearts are alive and well for 2 months to 5 years. Eight of 12 (67%) LVAD patients with dilated hearts recovered. None of the recovery patients were over 6 years old.

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 been tried. All small LVADs yielded comparable results. Larger and older children also have a chance of recovery, but our experience with them is too small except to note that they do well with larger devices and transplantation.

IL5. SynCardia TAH Experience in Patients Under 22 Years of Age

Jack Copeland, MD
Division of Cardiothoracic Surgery, University of California San Diego, La Jolla, CA

Over 1100 Syncardia TAHs have been implanted since 1992. Of these, only 51 have been in patients under age 22 years. The usage pattern may well change when 50ml ventricles become available this year. A 28% size reduction is anticipated to allow TAH implantation in patients with a BSA of 1.2 m^2 or weight of around 40 kg. We have reviewed preliminary data on the first 51 "pediatric" patients implanted with 70 ml ventricles for any survival differences that might exist in comparison to the adult population.[1,2]

A retrospective review included all patients under the age of 21 from July 1986 through November 2012. This is an international experience that comes from the SynCardia Systems Inc database. There were 51 patients, 20 % females. Nineteen were in the 19 to 21 year group. The overall mean age was 17.8 years (range 13 to 21). Duration of implantation ranged from 1 day to 318 days. Of the 31 supported for ≤ 30days 61%, survived, of 7 supported for >30 and ≤ 60 days, 70% survived, and for 15 supported for > 60 days 87% survived. Overall survival was 69%. Pre-implant diagnosis, number of patients, and deaths on device are listed in the table.

Pre-implant diagnosis	Number of patients	Death on Device Support
Acute rejection	2	1
Cardiomyopathy	20	3
Congenital heart disease	6	0
Giant cell myocarditis	1	0
Hypertrophic	6	3
Ischemic	1	1
Malignant arrhythmias	1	0
Myocarditis	1	1
Not listed	4	1
Peri-partum	2	2
Restrictive	1	0
Scleroderma	1	1
Valvular	2	2
Viral	3	1

11/16 (69%) deaths were in the first 2 post-implant weeks suggesting a very sick population. Data on adverse events are currently not available.

This experience in young patients is very similar to previously published experiences with older groups where survival to transplantation has been 70-80% and most mortality has been in the first few days to weeks after implantation. If the early deaths are related to poor pre-implant patient condition, selecting better candidates is likely to improve early post-implantation survival.

References:

1. Copeland J, Copeland H, Gustafson M, Mineburg N, Covignton D, Smith R, Friedman M. Experience with Over 100 Total Artificial Heart Implants. J Thorac Cardiovasc Surg. 2012 Mar; 143(3): 727-34. Epub 2012 Jan 14. PMID 22245242
2. Copeland JG, Smith RG, Arabia FA, Nolan PE, Sethi GK, Tsau PH, McClellan D, Slepian MJ. Cardiac replacement with a total artificial heart as a bridge to transplantation. N Engl J Med 351(9):859-67, 2004.

IL6. Development of Animal Models for Pediatric Mechanical Circulatory Support Research and Training

Ronald P. Wilson, V.M.D., M.S., DACLAM, William J. Weiss, Ph.D., Akif Ündar, Ph.D.

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

Design, development and refinement of cardiac assist devices ranging from total artificial hearts pediatric ventricular assist devices has been a major focus of research at the Penn State Hershey College of Medicine and M. S. Hershey Medical Center for four decades. Animal models have included calves, sheep and goats, each species presenting unique features and challenges. Since 2004 a multidisciplinary team of surgeons, bioengineers, scientists and veterinarians have designed, developed and tested implantable cardiac assist devices and extracorporeal life support systems (ECLS) specifically for the neonate and pediatric patient. Selection of appropriate animal models for testing of and training on various devices for mechanical circulatory support in the pediatric patient is challenging. Many factors must be considered in model selection; from the objective of the study to consideration of the anatomy, hemodynamics, and size and growth rate of the species selected (1).

The Penn State Hershey Center for Pediatric Cardiovasular Research utilizes a swine model for experimental investigations of and training on pediatric ECLS. Current research focuses on comparison of continuous versus pulsatile flow systems and contribution of the circuit elements contributing to gaseous microemboli and inflammation during cardiopulmonary bypass (2). Neonatal patients are modeled by piglets (5 – 7 days of age; 3 – 5 kg body weight), while juvenile pigs (3 – 4 weeks of age; 20 – 25 kg body weight) are used to model pediatric patients. For research investigations, animals are supported by ECLS for variable time intervals up to 24 hours. Pigs are maintained under ECLS support up to 6 hours for training laboratories (3). Anesthesia for the procedures is induced by ketamine-midazolam and maintained with isoflurane initially delivered by mechanical ventilation and subsequently through the bypass circuit supplemented with constant-rate infusion (CRI) of fentanyl citrate. Animals are typically maintained normothermic but some experimental paradigms require hypothermic cardiopulmonary bypass (28°C). All studies to date have been non-survival but future survival studies are planned.

In 2004, the research team at Penn State College of Medicine was one of 5 awardees of contracts from the National Heart, Lung and Blood Institute to develop devices for circulatory support in infants and children. A pneumatically actuated infant ventricular assist device (VAD) with a dynamic stroke volume of 12 – 14 ml was developed based on the design of the Pierce-Donachy (Thoratec) adult VAD. Wanting to conduct *in vivo* testing of the device in an animal model that approximated the size and hemodynamics of the human infant/child patient, juvenile goats, lambs and adult goats (Pygmy breed) were used in initial experiments (1). Although several goats had been used in early design studies, both juvenile and adult goats used initially for the current series of experiments experienced numerous intra- and post-operative complications and did not easily acclimate to the restraint and handling required for a chronically instrumented animal. Furthermore, the contractor had limited experience with data derived from this species. For these reasons a juvenile Dorset-cross sheep model (Fig. 1) was selected but challenges, especially respiratory compromise during surgery and the immediate post-operative period were experienced (4). Modifications to the anesthetic regimen and airway management during and after surgery were critical to overcoming the respiratory complications. In addition, aggressive post-operative pain management utilizing a multi-modal analgesia approach combining systemic opioids and NSAIDS with local anesthesia has been key to the animals' rapid recovery and return to normal food and water intake which is critical to the health of the juvenile ruminant. Details of the anesthesia, airway and pain management of the lambs is provided in the reference by Carney, et al (5).

Fig. 1. Male Dorset-Finn lamb (16 kg) implanted with 12 ml pediatric VAD.

Selection of the appropriate animal model for testing of circulatory support devices intended for pediatric patients must take into consideration species-related and study related factors. Although size of the animal and its rate of growth may be the primary factor, species differences in anatomy, thrombogenicity, hemodynamics and tissue response, as well as study duration and adaptability of the animal (1). Involvement of a multidisciplinary team with each member contributing their expertise to the project is essential to a successful outcome.

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IL9. Neuromonitoring during Pediatric CPB

Erle H Austin III, MD, Christopher E Mascio MD, Harvey L Edmonds Jr, PhD*

*Division of Cardiothoracic Surgery, Department Surgery and Department of Anesthesiology**
University of Louisville, Louisville, Kentucky, USA

The significant improvement in pediatric cardiac surgery over the past three decades has changed the focus of outcome assessment from survival to quality of life. Neurologic outcome has therefore become an area of increasing scrutiny. Although in many cases neurologic dysfunction noted in infants after surgery for congenital heart disease can be attributed to factors other than the operation or its management, the surgeon must always remember that the operation places the child's brain and spinal cord in jeopardy and during that time the brain is the surgeon's responsibility. A simple lapse in the course of an operation can result in a devastating neurologic insult. If such a lapse is recognized at its onset, the surgeon can immediately rectify the problem and minimize or avoid the neurologic injury. This is the concept behind intraoperative neuromonitoring during pediatric cardiopulmonary bypass.

We began multimodality intraoperative neuromonitoring at our center in 1994 and have continued to apply it routinely. We analyzed our early experience and noted an initial reduction of neurologic complications from 26 to 10%.[1] As we continue to apply it, we still encounter unanticipated threats related to cannula position, gaseous embolism, suboptimal cooling and rewarming, seizure activity, and other less expected events. With this early recognition we have been able to correct the problem before a serious injury might occur.

In our opinion more than one neuromonitoring modality is required for this approach to be effective. We utilize 1) four-channel EEG, 2) transcranial Doppler, 3) near-infrared spectroscopy (NIRS), and 4) somatosensory-evoked potentials. Having more than one modality improves the sensitivity and specificity of a single modality and permits the development of algorithms for intervention.

The use of intraoperative neuromonitoring in pediatric heart surgery has spread to many other centers in the last decade. Unfortunately most of those centers have elected to limit their technique to a single modality: NIRS. This is understandable because NIRS alone is less expensive, easy to apply, and can be monitored by the anesthesiologist alone. Unfortunately, it has led to a controversy related to the value of neuromonitoring in general. Recent reviews have questioned the strength of published evidence related to this question.[2] In fact, the most recent review[3], using classes of benefit and levels of evidence, stated: "There is insufficient evidence of an association with improved neurological outcomes to recommend the use of any *single* modality as a neuromonitoring strategy during CPB." (Italics – mine). That review did note that ".one retrospective observational study of *multimodality* neuromonitoring demonstrated an improvement in clinical outcome." (Italics – mine). At present, the only study that has demonstrated improved outcomes with intraoperative neuromonitoring was done with the multimodality approach. That study is our study!!

Thus we continue to recommend intraoperative neuromonitoring, as we feel it has significantly reduced adverse neurologic outcomes in our patients, but that reduction has been achieved with a multimodality approach, not NIRS alone.

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IL10. Biomarkers of Neurological Injury during Pediatric CPB Procedures

Mehmet A. Ağirbaşli, MD[1], Jianxun Song, MD[2], Fengyang Lei, MD[2], Shigang Wang, MD[3], Allen R. Kunselman, MA[4], Joseph B. Clark, MD[3], John L. Myers, MD[3], Akif Ündar, PhD[3,*]

[1]Marmara University College of Medicine, Department of Cardiology, Istanbul, Turkey; [2]Department of Microbiology and Immunology; [3]Pediatric Cardiac Research Laboratories, Departments of Pediatrics, Surgery, and Bioengineering; [4]Department of Public Health Sciences, Penn State Milton S. Hershey Medical Center, Penn State Hershey College Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Cardiopulmonary bypass (CPB) procedure cause disturbance in the levels of biomarkers related to inflammation, tissue damage, and other tissue pathologies (1, 2). Central nervous system (CNS) injury is the most dreadful complication of CPB as it associates with significant morbidity after pediatric cardiac surgery (3, 4). Nearly 50 % of the children experience impaired neurological outcomes after complex heart surgery (5, 6). Several modalities attempt to identify and protect children from CNS injury during CPB (i.e. EEG, sensory- or motor-evoked potential, transcranial Doppler, near-infrared spectroscopy, imaging methods). Novel neuroprotective strategies such as pulsatile flow and/or improved bubble detection can provide CNS protection and improve the outcome. However, current standards of care and expectations of the patients and families warrant further research on continuous and precise monitoring of CNS injury after CPB. Studying biomarkers that can promptly identify patients with CNS injury is therefore critical in children with congenital heart disease. Traditional biomarkers of neurological injury include creatine kinase brain band (CK-BB), neuron specific enolase (NSE), and S100β protein (7-12). The major limitations of the conventional biomarkers are related to poor specificity for brain tissue and delayed peak after CNS injury. Therefore, the search for novel and ideal biomarkers is moving target in clinical studies. For instance ubiquitin C-terminal hydrolase 1 (UHCL1) and phosphorylated axonal neurofilament heavy chain (pNF-H) have potential for more specificity for the brain (13) and show promise for better specificity in brain injury, especially in neonates after HIE from birth asphyxia. Other potential biomarkers for CNS injury include plasma TNFα, IL-1β, IL-6, high-mobility group box-1, IL-6 and IL-1β mRNA (7-12). Glial fibrillary acidic protein (GFAP) is a biomarker with previous studies linking to intracerebral hemorrhage (ICH) in patients with symptoms of acute stroke (14). Pediatric patients with brain ischemia or cerebral infarct display GFAP elevations above the 95th percentile of healthy controls (15).

Our recent work indicated that fibrinolytic system components can offer clinical use after pediatric heart surgery. In addition to their role in vascular disease, the components of the fibrinolytic system, tissue plasminogen activator (tPA) and its endogenous inhibitor plasminogen activator inhibitor-1 (PAI-1) regulate various neurophysiological and pathological responses in brain (16). Fibrinolytic balance depends on PAI-1 and tPA concentrations (16). Endothelial cells are the major source of t-PA release. Elevated t-PA and decreased PAI-1 levels associate with white matter brain lesions in adult patients with ischemic stroke (17). Studies indicate evidence for the endothelial activation in small vessel brain injury, associated with low levels of PAI-1. In a small pilot study, we in fact observed that PAI-1 levels drop significantly minutes after cardiopulmonary bypass in pediatric population (1). In a different study, we measured plasma PAI-1 antigen and tPA antigen in children who underwent CPB. We observed persistently elevated t-PA /PAI-1 ratio at the end of 24 hours after CPB which might be a potential novel biomarker for CNS injury. Further studies are needed to define the clinical significance of fibrinolytic balance as a biomarker of CNS injury.

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IL12. Cerebral Protection in Congenital Heart Surgery

Giovanni Battista Luciani, MD

Division of Cardiac Surgery, University of Verona, Verona, Italy

Neurologic injury, be it reversible or permanent, remains the major source of early and late morbidity and loss of active life years after repair of congenital heart disease (CHD) in children and adults. Whereas neuro-monitoring and neuro-protective strategies have dramatically evolved during the past decade, a variety of other patient and treatment-related variables have also concomitantly changed. These circumstances have practically resulted in the impossibility to compare current with historic neuro-protective approaches. In addition, the heterogeneity inherent with complex or recurrent CHD, particularly those involving aortic arch repairs, has represented an obstacle to the set up of randomized controlled trials. All this notwithstanding, methods entailing regional cerebral perfusion (RCP) have gained increasing favor in surgery for CHD. Technical aspects and clinical outcome of RCP in children and adults will be discussed, along with experimental animal and computational models.

IL13. Brain Protection in Pediatric Aortic Arch Repair: Deep Hypothermic Circulatory Arrest, Selective Cerebral Perfusion or Combined Technique

Rıza Türköz, MD

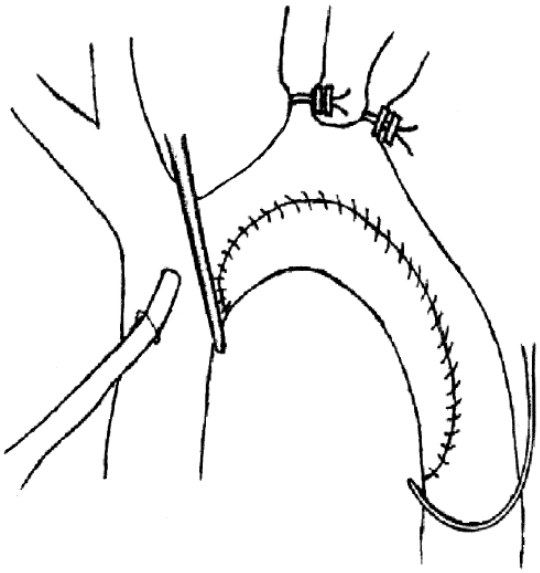
Departments of Cardiovascular Surgery, Baskent University, Istanbul Teaching and Medical Research Center, Istanbul, Turkey

Traditionally deep hypothermic circulatory arrest (DHCA) has been used for more than four decades as the standard intraoperative technique to perform whole aortic arch reconstruction in neonatal and infants. DHCA creates a bloodless operative field without clamps or cannula. On the other end, DHCA has been associated with early and late neurodevelopmental morbidities (1). Another disadvantage of DHCA is the prolongation of myocardial ischemia. Selective cerebral perfusion (SCP), after first used in 1996 as an alternative to DHCA, has recently started to be used as a perfusion method that could prevent the negative effects of DHCA in neonatal and infant arch reconstruction (2).

By using the selective cerebral and myocardial perfusion (SCMP) technique, coarctation with aortic arch hypoplasia (CoAAH) with concomitant cardiac defects can be repaired without the long duration of DHCA. A variety of cannulae positions can be used to achieve antegrade cerebral perfusion to the brain while performing aortic arch reconstruction. Usually, The cannulation of the the innominate artery have been used in SCMP either through a PTFE graft or by a direct cannulation. Another technique of cannulation of the the innominate artery is advancing the aortic cannula into the innominate artery (3).

The cannulation of the the innominate artery either through a PTFE graft or by a direct cannulation adds an additional procedural time, increases the required effort and/or is technically challenging in small innominate artery. The other technique for arch reconstruction is combination with SCMP and short term total circulatory arrest (TCA) (5-10 min) through ascending aortic cannulation.

In our clinical practice, with this technique, 40-50 ml/kg/min flow for SCMP and less than 10 min TCA at 24-26ºC has been used in CoAAH patients (Figure 1). 37 cases with aortic arch and isthmus hypoplasia accompanying cardiac defects were operated with SCMP and short TSA between January 2007 and September 2012. All VSD-CoAAH patients without complex cardiac anomalies were extubated with SCMP and short TSA on the day of surgery or on the first morning following surgery. Most of the neonatal and infants requiring aortic arch reconstruction have simple or complex intracardiac defects. Simple, safe, fast and effective arterial cannulation is especially advantageous in the arch reconstruction accompanied with complex intracardiac repair. SCMP and short term TCA (less than 10 min) through ascending aortic cannulation is a simple and safe technique.



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IL13a. The Impact of Cerebral Embolization during Pediatric Cardiac Surgery on Neurocognitive Outcomes at Intermediate Follow-up

Clark JB[1,2], Naik RJ[1], Wagner JB[1], Barnes ML, Wagner DS[3], Burson KC, Eslinger PJ[1,3]

Departments of Pediatrics[1], Surgery[2], and Neurology[3], Penn State College of Medicine, Hershey, PA

Objective: Pediatric cardiac surgery is associated with neurologic morbidity including decreased performance on late neurodevelopmental tests. Brain monitoring during pediatric cardiac surgery has been shown to reduce acute neurologic events. Transcranial Doppler ultrasound is a neuromonitoring tool that detects embolic signals within the cerebral vasculature. Cerebral embolization during cardiac surgery is a known risk factor for stroke in adults, but has not been shown to be associated with adverse neurologic events in children. We hypothesized that increased cerebral embolic signals during infant cardiac surgery would be associated with worse neurodevelopmental outcomes at intermediate follow-up.

Methods: Internal Review Board Approval was obtained. Inclusion criteria included cardiac surgery at age less than 1 year, absence of genetic syndromes or preoperative neurologic abnormalities, and age 3-6 years at follow-up. At surgery, a transcranial Doppler ultrasound probe was positioned over the middle cerebral artery and provided quantification of embolic signals. At follow-up, child participants were evaluated using two standardized neurocognitive tests, and parents completed two standardized questionnaires to assess observed developmental behaviors. Statistical analysis was performed to evaluate the relationship between embolic signal counts and testing and questionnaire scores.

Results: The study group consisted of 24 children (14 males) who had infant cardiac surgery. The median age and weight at surgery were 113 days (range 3-361) and 4.9 kg (range 2.0-11.2). The case mix was heterogeneous, with the most common operations including repair of Tetralogy of Fallot (4), repair of ventricular septal defect (3), and hemi-Fontan cavopulmonary connection (3). The median number of intraoperatively detected cerebral embolic signals was 17 (range 0-55). No acute adverse neurologic events were appreciated in the postoperative period. The median hospital stay was 6 days (range 2-33). The mean age at neurocognitive testing was 3.8 years (range 3.1-4.9). A total of 30 separate parameters from the 2 parental questionnaires were analyzed for association with the number of cerebral embolic signals, and no significant associations were found. A total of 37 separate parameters were analyzed from the 2 child neurodevelopmental assessments, and 5 parameters showed significant association ($p<0.05$) with the number of embolic signals: imitating hand positions, non-dominant hand positions, omissions, and hit reaction time standard error and variability. However, these 5 parameters all correlated in the opposite direction of the intuitive clinical hypothesis, suggesting that increased cerebral embolic signals were associated with improved neurocognitive performance.

Conclusions: The number of cerebral embolic signals detected during infant cardiac surgery was not shown to be associated with worse neurodevelopmental outcomes at intermediate follow-up in this small cohort of children. A larger study is likely necessary to ascertain the potential influence of cerebral embolic signals on eventual neurologic outcomes in children. The clinical relevance of cerebral embolic signals during pediatric cardiac surgery remains undetermined and deserves further investigation.

IL14. Collaborating with a Statistician to Enhance Pediatric Cardiovascular Research

Allen Kunselman, MA

Division of Biostatistics and Bioinformatics, Department of Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania, USA

Pediatric cardiovascular research and medical research in general is becoming increasingly more collaborative in nature as experts from a variety of disciplines are needed to address novel scientific investigations. For example, in the evaluation of a pediatric simulated cardiopulmonary bypass model a research team may consist of pediatric clinicians and biomechanical engineers. Another key member of many research teams should be a statistician. However, clinical investigators are often apprehensive to involve a statistician. Reasons for reluctance to involve a statistician may include: unfamiliarity of the benefits of having a statistician as a collaborator, belief that their training qualifies them to analyze their own data regardless of the complexity of the study, ease of using statistical software (often incorrectly), fear that the statistician will conclude the study design or analysis is flawed, fear that the statistician will prevent them from publishing their data, and inability to justify funds for a statistician. These reasons are unfounded. There should be a symbiotic relationship between the statistician and other investigators of the research team, and communication is a key component. Clinical investigators and engineers provide scientific knowledge of the disease, outcomes being studied, device being used, etc. and the statistician provides the technical skills to incorporate the investigator's scientific knowledge into an appropriate study design and statistical analysis.

The statistician's role in the research process should start during the planning phase of the study whether it is a clinical trial, laboratory experiment, or simulation study (1). The statistician can determine the most efficient design and appropriate sample size for a trial that will ensure a strong prospect of detecting effects of clinical or scientific interest. The more complex the study design (e.g., crossover trial) or analysis (e.g., analysis of repeated measurements or addressing missing data) for a pediatric cardiovascular research project, the greater the need to collaborate with a statistician. To make valid inferences from the observed data, the use of advanced statistical methodology is often required but should only be applied with a clear understanding of why the methodology is being used, what the limitations or assumptions of the methodology are, and how to properly interpret the data using the methodology.

Statisticians are not the enemy! Statisticians contribute and support investigator research in order to obtain valid results. Statistical support can make your grant proposal, research study, or manuscript stronger as they are less likely to have statistical or scientific flaws and may be more cost effective (2). Some suggestions are made as to how to foster that collaboration.

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IL15. Cardiac Neonatal ECLS/ECMO

Chitra Ravishankar, MD, Associate Professor of Pediatrics

Division of Cardiology, The Children's Hospital of Philadelphia

While conventional therapy with inotropic support and afterload reduction remains the mainstay of treatment for the failing heart, the role of mechanical circulatory support is well established in the pediatric population. The majority of the pediatric experience consists of the use of Extracorporeal Membrane Oxygenation (ECMO). ECMO which is the use of mechanical devices to replace heart and lung function for cardiopulmonary failure was first used successfully for cardiac failure in a child in 1972, and respiratory failure in a neonate in 1975 (1). The success of ECMO in neonates with respiratory failure led to wider application to treatment of cardiac failure as a bridge to recovery or transplantation, and as a bridge to a long-term ventricular assist device (VAD) in the current era. The Extracorporeal Life Support Organization (ELSO) was established in 1989 to share experience, education, and to maintain a registry of cases. There are now more than 40,000 patents in the registry including over 9000 pediatric cardiac cases.

As the familiarity and experience with ECMO has grown, new indications have emerged including emergent resuscitation (2, 3).

Indications for ECMO are as follows:

Cardiac Surgery

- Pre-operative stabilization
- Failure to wean from cardiopulmonary bypass (CPB)
- Post-operative low cardiac output syndrome (LCOS)
- Cardiopulmonary arrest or E-CPR

Non-Cardiac Surgery

- Myocarditis and cardiomyopathy
- Intractable arrhythmias
- Respiratory indications

Post-cardiotomy cardiopulmonary failure is the most common indication for ECMO in children with congenital heart defects as a bridge to recovery or transplantation. ECMO may be required in the postoperative period either due to the inability to separate from CPB, progressive LCOS, or cardiac arrest caused by a number of factors such as ventricular dysfunction, pulmonary hypertension, progressive hypoxemia or intractable arrhythmias.

Complications of ECMO include bleeding, neurologic events, circuit related complications, sepsis and multi-organ failure. The incidence of complications increases with time, thus limiting the use of ECMO for long-term support. ELSO reports survival to discharge of 39% after neonatal cardiac ECMO. Risk factors for poor outcome include the presence of significant acidosis prior to initiation of ECMO, prolonged CPB time, and renal dysfunction. Use of ECMO has increased in neonates with single ventricle heart disease, however survival has not improved.

Cardiac ECMO can be effective for several indications and can salvage over a third of infants. Long-term follow-up that includes assessment of neurodevelopmental outcome and quality of life is important in this high-risk patient population.

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IL16. Development of Microfluidic Oxygenators as Lung Assisting Devices for Term and Preterm Newborn Infants

Christoph Fusch, MD, PhD, FRCPC

Div. of Neonatology, McMaster Children's Hospital, University, Hamilton, Ontario Canada

Respiratory insufficiency is a major cause of neonatal mortality and long-term morbidity, especially in preterm infants. Mechanical ventilation is an accepted treatment to provide respiratory support to newborns with respiratory insufficiency. However, in infants with severe respiratory insufficiency mechanical ventilation reach the limit of efficacy.
An alternative approach is to provide extra-pulmonary gas exchange through the use of extracorporeal membrane oxygenation (ECMO). Current ECMO systems are invasive, requiring vascular cut down, full body anticoagulation, and cardiovascular assistance with pumps which limits the application to the preterm infant population.

To overcome these restrictions a lung assist device is needed, which could substitute lung gas exchange of newborn preterm and term infants by mimicking functions of the natural placenta (Fig. 1). Such a device would be pumpless only driven the infant heart and characterized by a low priming volume, low resistance, achieve sufficient vascular access via umbilical vessels, high gas exchange, and hemocompatibility.

We have developed a low volume lung assist device (LAD) composed of a stack of microfluidic single oxygenator units (SOU) made of polydimethyl-siloxane (Fig. 2). The vascular network of SOUs is designed to maximize the surface to volume ratio of blood for higher gas exchange. The LAD takes oxygen-deficient and carbon dioxide rich blood from the umbilical artery and returns oxygen-saturated and carbon dioxide depleted blood to the umbilical vein. The LAD works under ambient air, no additional oxygen is needed.

Figure 1: Approach of lung assist device

The feasibility of our LAD was first tested in invitro using various membranes types to enhance gas-exchange. Second, the prototype has been tested in a hypoxic piglet model (FiO2: 0.12, PIP: 6 mbar, PEEP: 0 mbar, Freq.: 35/min). Extracorporeal blood flow rates only driven by the piglet heart were achieved by up to 20 mL/kg/min. Peripheral O2 saturation (SaO2) increased from 60% to 100% when LAD was applied indicating effective gas exchange in the LAD and showed the feasibility of the LAD. In conclusion, the development of such a low volume, biocompatible LAD with effective gas exchange has the potential to become a rescue treatment for newborn infants with end-stage lung failure. Hemocompatibility and improvement of the vascular access are further developments.

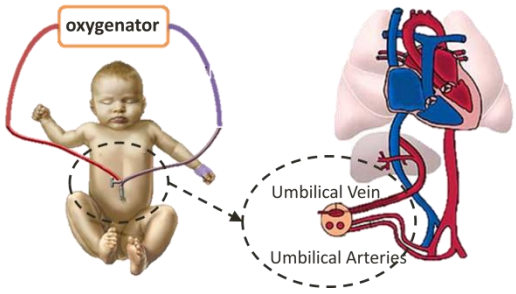

Figure 2: Lung assist device composed of 7 back-to-back units (14 microfluidic oxygenators); left: schematic of the stacking oxygenators; middle: blood perfused device; right: single oxygenator unit.

IL18. Pulsatile Extracorporeal Life Support Systems for Neonatal and Pediatric Patients

Akif Ündar, PhD, Shigang Wang, MD, Allen R. Kunselman, MA, and Conrad Krawiec, MD, and Yves Durandy, MD*

Pediatric Cardiovascular Research Center, Departments of Surgery, Pediatrics, Bioengineering, and Penn State Hershey Pediatric Critical Care Unit, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA
** Intensive Care and Perfusion, CCML – Le Plessis Robinson France*

Introduction: Extracorporeal Life Support (ECLS) Technology is and will continue to advance. Each improvement made to the circuit must be scrutinized and perfected, preferably prior to clinical use. Pulsatile flow has been expecting to be used in ECLS system because it could preserve microcirculation, reduce the inflammatory response, and improve patient outcomes.

Two circuits have been evaluated in our research center: **1). Non-Occlusive Pulsatile Pump:** A simple, inexpensive pediatric pulsatile roller blood pump has been utilized for routine CPB, ECLS, and MCS for decades in France (1,2). This particular non-occlusive pulsatile system has many advantages including several safety features for patients as well as an extremely lower cost. This particular pump can only generate pulsatile mode of perfusion. **2). New generation Diagonal Pulsatile Pump:** The Medos Deltastream DP3 system uses a novel diagonal pump to provide non-pulsatile and pulsatile flows for pediatric and adult ECLS. This system is small, compact, and user-friendly. It has been approved for extended clinical ECLS use in children and adults in Europe (3,4).

Objective and methods: The objective of this study is to evaluate the two particular systems for ECLS in pulsatile mode in a simulated ECLS model. The experimental ECLS circuits consisted of the two pumps, Medos Hilite 2400 LT hollow-fiber oxygenator, arterial and venous cannula, primed with human blood (HCT 35%). All trials were conducted at different flow rates and pulsatile flow setting.

Results: Our results showed that the two ECLS systems can generate physiological quality of flow and pressure waveforms (Figure 1,2). 1). The non-occlusive roller pump automatically created pulsatile flow at certain frequencies depending on flow rates. Higher flow rates generated higher hemodynamic energy output. 2). The new-generation diagonal DP3 pump was easily switched between nonpulsatile and pulsatile mode, generated effective pulsatile flow without backflow, and create surplus hemodynamic energy (SHE) and more total hemodynamic energy (THE) than non-pulsatile flow at all pump flow rates.

Conclusions: 1). The non-occlusive pulsatile roller pump performed well during all of the experimental conditions and generates adequate quality of pulsatile pressure-flow waveforms using ECLS circuitry. Although this novel concept was first introduced in 1990 (1, 2), we believe that there is still need for this technology because of significant advantages including safety, no back flow, higher hemodynamic energy, and significantly reduced cost (5). **2).**The new-generation Medos Deltastream DP3 ECLS system can provide adequate quality of pulsatility without backflow, and generate more hemodynamic energy under pulsatile mode in our simulated pediatric ECLS system (6).

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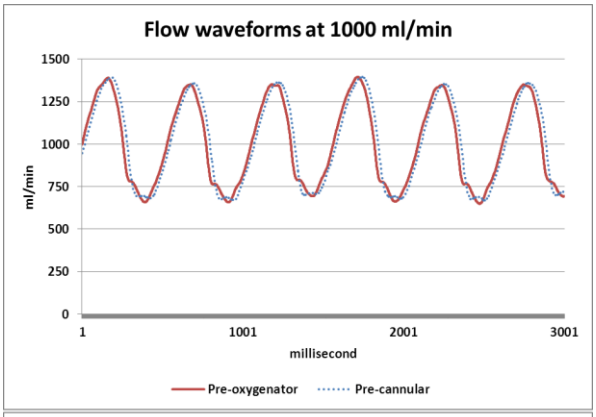
Figure 1. Flow/pressure waveforms in non-occlusive roller pump ECLS system.



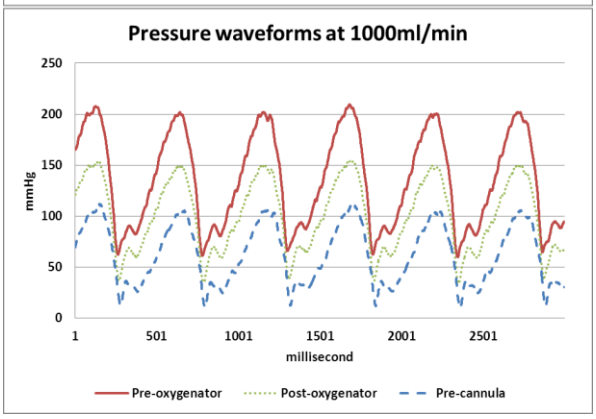
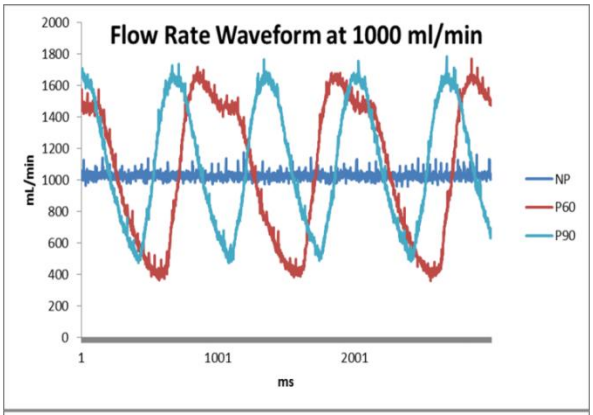
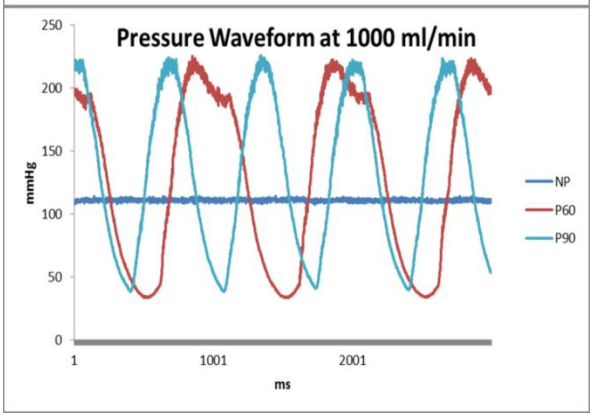
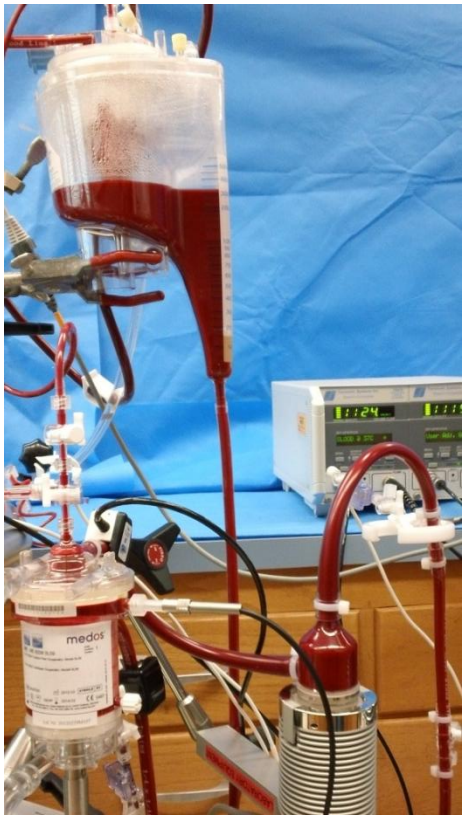


Figure 2. Flow/pressure waveforms in Medos DP3 ECLS system.







IL19. Adjunct Therapies for Pediatric Acute Lung Injury

Neal J. Thomas, MD, MSc

Pediatric Critical Care Medicine, Departments of Pediatrics and Public Health Sciences, Penn State University College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Since the advent of the treatment of pediatric patients with acute lung injury (ALI), practitioners have been faced with multiple dilemmas related to their care. ALI in children appeared to be more similar to the "acute respiratory distress syndrome" (ARDS) described by Ashbaugh and Petty (1) than the "respiratory distress syndrome" seen in neonates, yet significant and important differences existed. Children have considerable variability in the predisposing conditions and etiology; their response to therapy is different and often better; and preexisting conditions and underlying etiology appear to influence outcome to a greater extent than the severity of the lung injury itself (e.g., ALI due to respiratory syncytial virus in a previously healthy child vs. ALI due to respiratory syncytial virus in a children who has undergone repair of hypoplastic left heart syndrome). A number of important questions still persist in 2013: Is "ALI" in children a specific entity? How best can we treat this heterogeneous population and does one approach fit all? Can we advance the care of these children if we apply a uniform approach to what appears to be a multifaceted disease process?

One of the main issues related to the study of therapies for pediatric ALI is the definitions. In 1994, and again in 2011, consensus conferences attempted to define this spectrum of adult patients. (2,3). Both of these conferences resulted in working definitions of ALI and ARDS, but also had significant shortcomings. The definitions are focused on ADULT acute lung injury and ignore differences in risk factors, etiologies, and pathophysiology in children. Moreover, the criteria still require arterial blood gas sampling, overlooking the use of non-invasive measures of hypoxemia now more commonly used. Therefore, a group of experts was recently assembled to form the Pediatric Acute Lung Injury Consensus Conference (PALICC). This group will meet three times over 18 months, with the goal of develop a better taxonomy to define pediatric ALI, specifically predisposing factors, etiology, and pathophysiology. In addition, this group will attempt to outline optimal treatment of pediatric ALI (4). The 9 topics that PALICC will cover are listed in Table 1.

Table 1: Topics of PALICC
(1) Definition, incidence, and epidemiology
(2) Co-morbidities and severity
(3) Ventilatory support
(4) Pulmonary specific ancillary treatment
(5) Non-pulmonary treatment
(6) Monitoring
(7) Non-invasive support and ventilation
(8) Extracorporeal support
(9) Morbidity and long-term outcomes

Therapies for pediatric ALI based on high-quality research specifically in children are extremely limited. Therefore, much of the treatment that is offered in children is based on adult studies, or small pediatric studies. There are many therapies utilized in adult patients which may or may not be applicable to children. The adjunct therapies that require further study and discussion include: low tidal volume ventilation, corticosteroids, fluid management, exogenous surfactant, non-conventional ventilation, prone positioning, nitric oxide, and extracorporeal support.

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IL20. Expanded Resources through Utilization of a Primary Care Giver Extracorporeal Membrane Oxygenation (ECMO) Model

Regi Freeman, MSN, RN, CNS, Chrissy Nault, BSN, RN, CCRN, Jole' Mowry, MS, RN, Paula Baldridge, MSN, MHA, RN.

University of Michigan, Ann Arbor, MI, USA

The University of Michigan ECMO program was established in 1980 by Dr. Robert H. Bartlett and currently accommodates approximately 75 to 90 Extracorporeal Life Support (ECLS) patients per year. The ECMO specialist staff is comprised of critical care nurses and respiratory therapists. The ECMO specialist remains at the bedside 24 hours per day to ensure that the circuit is safely managed in accordance with physician directives.

During a period of time between 2006 and 2009, the ECMO Program, encumbered by a small core of highly specialized personnel, struggled to meet increasing, unpredictable, demand for ECLS services. Selective recruitment, cumbersome training processes, expanding geographic locale, and staff attrition all played a role in limiting the human resources needed for a rapidly changing ECMO landscape. Human resource was clearly identified as the limiting factor when ECMO demand outstripped ECMO supply.

To accomplish such an undertaking required careful planning of a large scale educational offering, coordinated by members of the ECMO Program and ICU nursing staffs, with cooperation of the ICU medical staff. Educational content was developed to meet the role description of the ECMO specialists, bedside RNs, nurse practitioners, and physicians. At all levels, documentation of attendance and competency were recorded.

Review of the Primary Care ECMO patient data base (n=12) 1 year after its inception revealed even distribution of mode of support between veno-arterial (6) and veno-venous (6) ECMO. No sentinel or adverse events occurred over this period of time. Survival rates at the University of Michigan

We conclude that in a setting that provides for immediate response to bedside ECMO emergencies by qualified personnel, training the bedside RN to monitor the ECMO circuit is a safe and effective practice. The PCG ECMO model provides a safe, flexible, and fiscally responsible staffing model for variable ECMO activity.

IL22. Pediatric ECLS at the Penn State Hershey Children's Hospital: A Look at the Program as of 2013

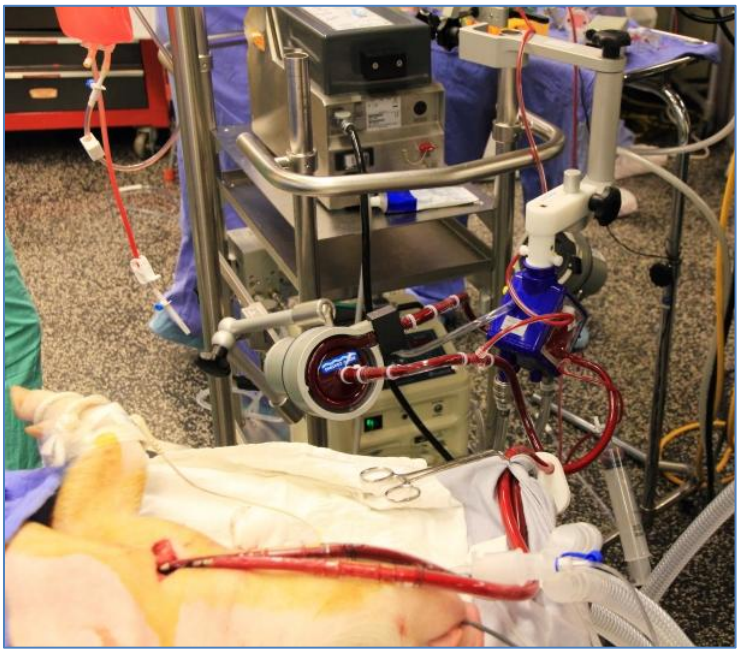
Bonnie Weaver, RN, MSN, CCRN, CCNS

Nursing Education & Professional Development, Penn State Children's Hospital, Hershey, Pennsylvania, USA

As of January of 2009, the Pediatric ECLS program at the Penn State Hershey Children's Hospital was completely redesigned (Figure 1). This change was in response to improvements with devices and protocols which have emerged during the past half century. In addition to these changes, the staffing model utilized to deliver care to these patients was also re-designed.

The approach utilized to make decisions related to both equipment & personnel changes from ECLS programs have been based on the following aspect: scientific data, translational research all through the lens of clinical experiences of over thirty years of an ECLS program designed to care for patients from birth to adulthood requiring Extracorporeal Life support.

The rapid development of Pediatric ECLS technology will continue. With the goal in mind to minimize mortality and morbidity of ECLS support, we must continue to modify components of the circuitry as well as techniques and methods used in daily basis. Therefore, the evidence based research is a must not an option for better outcomes.



The following is a report of the current status of the Pediatric Program at the Penn State Hershey Children's Hospital. Various aspect of the current program will be described. In addition challenges which lie ahead for all of us invested in caring for our youngest patient's requiring Extracorporeal Life Support.

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IL23. Optimizing Strategies for Pediatric Cardiopulmonary Bypass

Tami Rosenthal CCP, MBA, FPP

Chief Perfusionist, Children's Hospital of Philadelphia

Techniques in pediatric perfusion continue to evolve and improve through research and experience. Over the last ten years at CHOP the perfusion team has incorporated many new devices and techniques to improve care for pediatric patients.

A number of new oxygenators have become available with smaller prime volumes and in some cases integrated arterial line filtration which has made a dramatic difference in circuit size. Smaller tubing sizes and the use of vacuum assisted venous drainage has brought the CPB circuit closer to the surgical field and helped to reduce blood usage.

Trends in temperature management have evolved over time and have effected flow requirements. Adaptive blood gas management strategies and neurologic monitoring are changing the management of pediatric patients on CPB. Evolving ideas about optimal cardioplegia solutions and delivery modes are common. This discussion will provide a brief overview of current methods and techniques at CHOP and in use throughout pediatric centers.

IL24. Applications for Perfusion Simulation

Deb Zarro, Senior Clinical Specialist
Terumo Cardiovascular Systems, Ann Arbor, MI, USA

Perfusion education has traditionally relied on training with real patients in actual clinical settings. Hands-on and experiential learning are indispensable with mistakes being an expected and inevitable part of the learning process; however, mistakes are a real risk to patient safety. Simulation learning provides an opportunity for clinicians to develop and/or refine their skills without putting patients at risk. The skills required for perfusionists include multi-tasking and reacting to events compared to those of an airline pilot; but the airline industry provides intensive remedial training and the opportunity for assessing those skills in a real-time simulated environment.

Perfusion simulation advances medical learning, instills confidence, and allows for repetitive practice while preparing students for clinical activity. It elevates the standard level of clinical competence for practicing perfusionists leading to improved patient safety. A simulation environment allows students and clinicians to perform critical but low occurrence events while experiencing real-time clinical conditions. Perfusion simulation is also used to develop and/or improve protocols for emergency procedures and device failures. Cardiac surgeon resident training programs in perfusion simulation provides residents an opportunity to learn and understand the tasks and responsibilities of perfusionists as well as hands-on experience with cardiopulmonary bypass circuits and equipment.

Simulation is used in industry to train engineers and manufacturing associates to enhance their knowledge of clinical applications of hardware and disposable devices, for product design and development requirements, for product enhancement projects, to investigate product complaints and/or failures, to test and validate new/enhanced products, and understand why devices need to meet specific requirements for clinical application. Simulation operating rooms at manufacturing facilities provide an opportunity for clinicians to trial new techniques, devices and paradigms in a safe environment. These simulated operating rooms also offer clinicians the ability to explore failure modes and mitigations of any product in a safe environment and develop strategies and/or protocols.

Although serious accidents during cardiopulmonary bypass are infrequent, potential adverse events from both disposables and hardware do still occur and require immediate and well-coordinated responses. Due to the reliability of the products manufactured today the failure rate of devices is very low; therefore clinicians rarely experience or may never experience a device failure during bypass. The integration of simulation into clinical practice provides clinicians the opportunity to practice a myriad of crisis management drills and appropriate remedies in real-time. Regular crisis management competency training is an important element in optimizing patient safety.

The benefits of perfusion simulation are multifactorial and its applications are numerous. It provides trainees unlimited opportunities to practice emergency situations without the pressure and risk involved in a real-life procedures, it's an effective learning tool, and it's an extremely valuable asset for manufacturers of perfusion devices.

IL25. Choosing a Pump for Extracorporeal Life Support

David A. Palanzo[1], Larry D. Baer[1], Aly El-Banayosy[1], Shigang Wang[2], Akif Ündar[2] and Walter E. Pae[1]

[1]Heart and Vascular Institute, Penn State Milton S. Hershey Medical Center, [2]Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery and Bioengineering; Penn State Hershey
College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Background:
When choosing a pump for extracorporeal life support (ECLS), there are many factors to consider. One needs to carefully analyze the performance of the pump especially in regard to the creation of hemolysis, but there are other areas to evaluate such as ease of set-up, pump safety, ease of use and cost.

Methods:
One hundred and sixty pediatric and adult patients placed on ECLS at the Penn State Milton S. Hershey Medical Center with a simplified, streamlined circuit containing a Bioline-coated Quadrox-D membrane oxygenator (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) and a centrifugal pump (CentriMag®, Levitronix LLC, Waltham, MA, USA or Rotaflow, MAQUET Cardiopulmonary AG) were reviewed. Comparisons were made in all areas of pump evaluation.

Results:
Many of the factors compared including creation of hemolysis, ease of set-up and ease of use showed no differences among the pumps. Differences were noted in the safety and cost of the different pumps.

Who sits?	CentriMag®	ROTAFLOW	ROTAFLOW (ICU Package)	CardioHelp
Perfusionist	✓	✓	✓	✓
ECMO Specialist	✓		✓	✓
Bedside Nurse	✓			✓
Cost per circuit	$14,000	$2,447	$2,447	$13,781

Conclusions:
The final choice on what pump to use was a result of who would be sitting at the bedside with the ECLS circuit.

IL26. Minimizing Systemic Inflammation during CPB in Pediatric Population

Yves Durandy M.D.

Intensive Care and Perfusion, CCML – Le Plessis Robinson France

Inflammation is a physiologic protective response involving immune and coagulation cascades. During cardiopulmonary bypass systemic inflammation is triggered by blood contact to foreign surfaces. The intensity of systemic inflammation response depends on modifiable factors such as polymers of the bypass circuit components, air-blood contact, blood transfusion, endotoxins, ischemia-reperfusion injury and hemolysis, but also on non-modifiable genetic factors. When over expressed systemic inflammation, via vasoactive proteins and pro-coagulant factors, alters systemic vascular resistance and vascular permeability and may induce reversible or irreversible end-organ dysfunction or damage. Therefore, minimizing systemic inflammation is expected to improve patient outcome. Extensive works were done to measure inflammation biomarkers, to limit inflammatory response and to assess attempts to antagonize drawbacks of inflammation. Therapeutic strategies are mainly directed to prevention and to treatment of inflammation, the two strategies being often associated.

Prevention of inflammation:

Inflammation begins with activation of factor XII (a factor of the coagulation cascade) and of C3 (a factor of the complement cascade) followed by activation of endothelial cells, monocytes, macrophages, leukocytes and platelets. The optimal prevention would be a total blockage of F XII and C3 activation but that is currently not feasible. However, polymers coating is likely to decrease this initial activation. Others strategies include mainly:

- Miniaturization of the bypass circuit, decreasing blood contact to foreign surfaces

- Use of closed bypass circuits reducing air-blood contact

- Pre-bypass patient treatment with steroid or antifibrinolytic products that decrease cellular activation and production of damaging compounds.

Treatment of inflammation:

Once inflammation is present, the main strategy is to eliminate deleterious humoral factors through hemofiltration techniques.

In the recent past, refinements in cardiopulmonary bypass have probably decrease systemic inflammation response, contributing to the well-acknowledged improvement in initial outcome. However, recent meta-analysis on attempts to minimize inflammation failed to demonstrate improvement in end-organ injury. It is easy to decrease plasma concentration of inflammatory mediators by ultrafiltration, but results are often short-term for cell activation is still on going. Nevertheless, a reasonable hope is that the use of several beneficial though non-significant therapies in a single patient may result in a significant clinical improvement.

Future research will be directed at finding new refinements in cardiopulmonary bypass protocols (like full-flow pulsatile warm perfusion trying to improve end-organ perfusion and to limit ischemia-reperfusion injury) and biologic agents that may effectively minimize inflammation without increasing infectious risk (inflammation being the first protective step of immune response against sepsis).

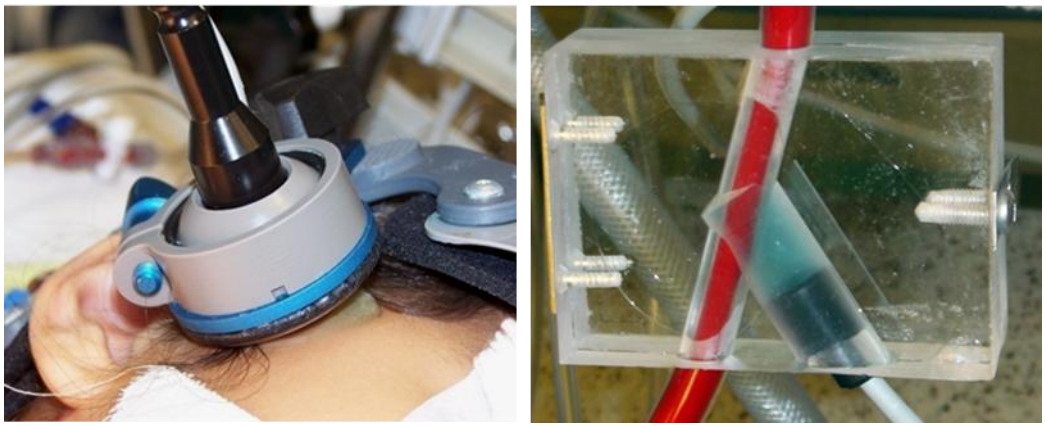
IL27. Microemboli Detection and Capturing During CPB

Shigang Wang, MD, Yulong Guan, MD, Feng Qiu, MD, Ryan K. Mathis, BS, Natalie M. Dogal, BS, Judith Lin, BS, Ashton Strother, Allen R. Kunselman, MS, J. Brian Clark, MD, John L. Myers, MD, Akif Ündar, PhD

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

Gaseous microemboli formed in the closed circuit during CPB may cause postoperative brain injury and complications through blood vessel occlusion and neurological damage (1). To monitor the amount of microemboli generated during CPB, transcranial Doppler (**TCD**) ultrasound is used to detect microemboli larger than 40μm in the middle cerebral artery of the patient (**Figure 1**) (2), and Emboli Detection and Classification (**EDAC**) is used to detect microemboli larger than 10μm and classify them by size in the circuit (**Figure 2**) (2-4). Oxygenators, cardiotomy reservoirs and arterial filters in the circuit are designed with membrane filters to trap microemboli by size in order to reduce the amount of microemboli reaching the patient.

Figure 1. Transcranial Doppler (TCD).



In order to reduce the priming volume and eliminate a separate arterial filter in the circuit, manufacturers recently developed new hollow-fiber membrane oxygenators with integrated arterial filters. We have evaluated the Quadrox-i neonatal/pediatric oxygenators (Maquet, Herrlingen, Germany) and Capiox Baby FX05 (Terumo Corporation, Tokyo, Japan) in terms of hemodynamic energy levels(5-8), but we are also interested in comparing the effectiveness of these neonatal/pediatric oxygenators in the flow range of neonatal patients in terms of reducing microemboli load delivered to the patient. In this lecture, we would like to compare the performance of circuit components (oxygenators with and without IAF, arterial filters, venous and cardiotomy) in terms of microemboli delivery to the neonatal/pediatric patient.

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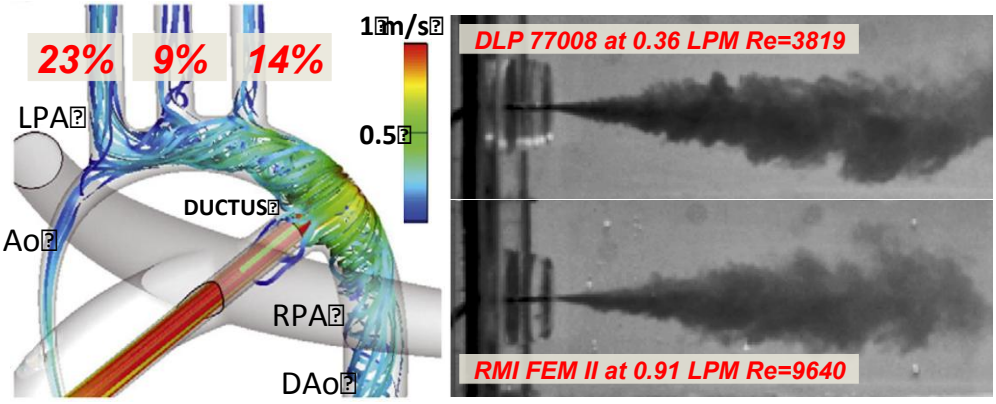
IL28. Impact of Integrated Computational Fluid Dynamics and Lumped Parameter Modeling on Neonatal CPB and Congenital Heart Surgery

Kerem Pekkan, PhD[1,3], Berk Yigit[1], Prahlad Menon[3], Senol Piskin[1], William Kowalski[3], Ahmet Sasmazel, MD[2]

[1]Pediatric Cardiovascular Fluid Mechanics Laboratory, Departments of Mechanical and Biomedical Engineering, Koc University, [2]Siyami Ersek Cardiothoracic Research Hospital, Istanbul, Turkiye and [3]Carnegie Mellon University, Pittsburgh, USA

Poor cerebral perfusion through the congenital neonatal aortic arch and immature Circle of Willis is a suspected cause for peri- and post-operative neurological complications associated with cardiopulmonary bypass (CPB). Likewise local high-speed jets from 8-10Fr neonatal cannulae delivering high blood can result sub-lethal hemolytic and endothelial damage (1). Using flow visualization techniques jet-wake flow structures of commercially available cannulae are qualitatively compared (Figure). We emphasize the importance of cannulation strategy and engineering better CPB perfusion through a redesigned aortic cannula tip and orientation (2). Altering the cannula tip to include a diffuser cone angle ensured a net positive outflow at the brachicephalic artery. Integrated multi-scale computational models of complex congenital heart circulation and three-dimensional hemodynamics have been applied to various clinical problems with advanced distal boundary condition treatment (3). We applied this methodology to pre-surgical neonatal CPB evaluation, where the *entire* hypoplastic left ventricle circuit is modeled (Figure). This approach also allowed us to evaluate a number of recent clinical applications including hemodynamic comparison of fetal to post-natal circulation transition of major congenital heart disease templates, detailed cerebral perfusion predictions through inclusion of cerebral arterial circulation of various cardiopulmonary by-pass scenarios and comparison of pulmonary perfusion of alternative Glenn stage circuits.



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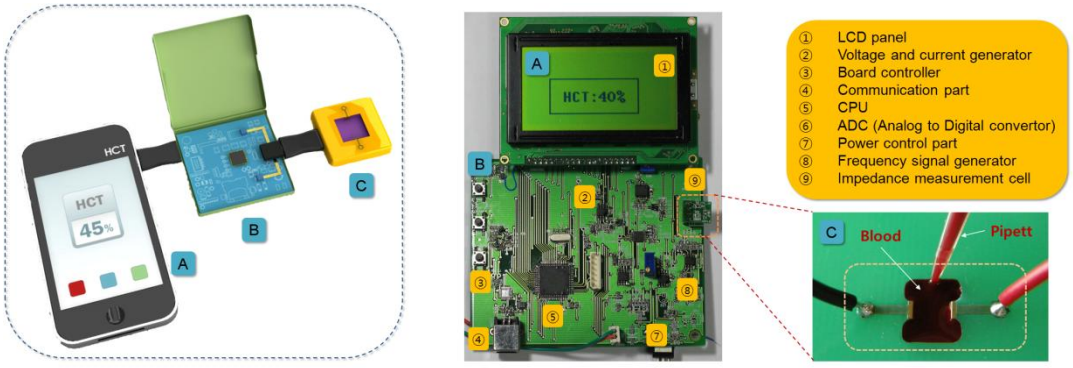
IL29. A Hand-held Microhemocytometer: Protoype and More

[1]Myounggon Kim, MS, [3]Taekeon Jung, BS, [*1,2,3]Sung Yang, PhD
*[1]School of Mechatronics, [2]Department of Medical System Engineering, and [3]Department of Nanobio Materials and Electronics, Gwangju Institute of Science and Technology, Gwangju, Republic of Korea, *Email: syang@gist.ac.kr*

Background:
Rapid and reliable blood hematocrit (HCT) measurement is critical procedure in the medical process. Electrical HCT measurement method using a novel HCT estimation parameter was developed in the previous study. Particularly, this method gives an accurate HCT measurement result regardless of change in plasma's electrical conditions and an end-user easily handles the system owing to simple blood dropping procedure using a pipette. A development of the prototype of the hand-held microhemocytometer is presented in this study.

Methods:
The prototype is mainly composed of three parts; blood impedance measurement cell, circuit board for measurement of blood impedance, and LCD panel for display of the measured HCT level. The measurement cell is constituted two plane-parallel gold electrodes mounted on each of its side walls and it is fabricated by using a commercial printed circuit board (PCB) manufacturing process. The main role of the circuit board is generation of the frequency signal from a battery power, production a constant ac current signal, and signal processing of the measured the impedance for calculation of the HCT level. The last one is LCD panel for showing a measured HCT ($HCT_{meas.}$) level. The measurement cell is disposable device and all parts have a USB port to connect with other parts.

Results:
Figure 1 shows (a) a schematic drawing of the final goal of the prototype, (b) a photograph of the prototype (LCD panel and circuit board), and (c) a measurement cell. The prototype is currently being optimized and compared with a gold standard method. We are expecting that the current prototype will be coupled with a conventional cellular phone such as Android or iPhone for providing convenient measurement of HCT as well as manipulation of data acquired.



(a) (b) (c)

Conclusions:
This study has attempted to develop a smartphone based hand-held HCT measurement. We believe that our study is first step towards the creation of new hand-held system for blood total analysis.

Acknowledgement:
This work was partially funded by grants from the Ministry of Education, Science and Technology (MEST, KRF-20110028861), World Class University Program (R31-2008-000-10026-0) and the institute of Medical System Engineering (iMSE), GIST, Republic of Korea.

IL30. A Continuous Biomarker Monitor for Tracking Systemic Responses during Pediatric Circulatory Support

Jeffrey D. Zahn, PhD

BioMEMS Laboratory, Department of Biomedical Engineering, Rutgers University, Piscataway, New Jersey, USA

Background:

For the past several years we have been developing a microdiagnostic platform to allow biomarker monitoring during pediatric circulatory support. These are based on microfluidic platforms that can perform sample blood preparation and/or plasma protein analysis.

Our microdevices have been used to continuously isolate plasma via a cross-flow microfiltration device (1) and more recently to fractionate non-homogeneous cell suspensions, especially blood using a multicompartmental filtration approach (2). Once the sample preparation has occurred, protein biomarkers can be quantified via a designed immunoassay which automates the serial incubation steps required using magnetic microbead immunofluorocytometric assays.The device uses a magnetic actuation scheme to transfer microbeads into a blood sample and subsequent reagents required for the assay (3). Finally, this system was used to sample blood from an extracorporeal circulatory loop through a sampling manifold connected to the arterial port of the membrane oxygenator and measure C3a concentrations within the device (4).

Conclusions:

The long term goal will be to use this diagnostic device as a clinical monitor during surgery. At present, clinicians can only react to physiological changes (e.g., Mean Arterial Pressure (MAP), Heart Rate (HR) and blood oxygenation) that occur, and many times these changes are a late finding in a patient's response to CPB and surgery. Having the ability to follow biomarkers real-time and continuously, and make clinical changes based on these biomarkers, would rapidly alter the way pediatric cardiac surgery and critical care is practiced.

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S1. Extracorporeal Life Support Following Cardiac Surgery in Children: Outcomes in a Single Institution

Takashi Sasaki, Toshihide Asou, Yuko Takeda, Yasuko Onakatomi

Department of Cardiovascular Surgery, Kanagawa Children's Medical Center, Yokohama, JAPAN

Background:
Extracorporeal life support (ECLS) is used in congenital heart surgery for several indications including failure to separate from cardiopulmonary bypass, postoperative low cardiac output syndrome, and pulmonary hypertension. We assessed the results of postcardiotomy ECLS in our institute.

Methods:
Medical records of all children who required postoperative ECLS at our institute were reviewed.

Results:
Between 2003 and 2011, 36 (1.4%) among 2,541 cardiac surgical cases required postoperative ECLS. Median age was 64.5 days (range: 0 day- 4.1 years). Extracorporeal membrane oxygenation (ECMO; n= 23) and ventricular assist system (VAS; n= 13) were used. Mean duration of ECLS was 4.9±4.2 days. Overall 25 patients (69%) were successfully weaned off ECLS and 17 patients (47%) were discharged alive. Nineteen patients underwent biventricular repair and 17 patients underwent single ventricular repair (palliation, BCPS, TCPC, DKS, etc.) Compared to single ventricle (SV) patients, biventricular patients had higher rate of survival to ECLS discontinuation and at hospital discharge (p= 0.04, p= 0.007). Regarding ECLS type, VAS showed higher rate of survival to ECLS discontinuation in SV patients (p= 0.02) compared to ECMO, but survival rate at hospital discharge was not different. Surgical interventions such as banding of BT shunt to reduce pulmonary blood flow or placing BCPS to reduce volume overload were effective for weaning from ECLS in SV patients.

Conclusions:
The rate of survival to ECLS discontinuation and at hospital discharge was almost same as the ECLS registry report from Extracorporeal Life Support Organization. Biventricular patients were likely weaned off ECLS and survival rate to hospital discharge was better than SV patients. VAS was a better option for SV patients because of higher weaning rate, although survival rate at hospital discharge was not different from ECMO. Additional intervention to reduce ventricular volume load might be needed to discontinue ECLS in SV patients. (300words)

S2. Initial Experiences with Medos Deltastream DP3 Pediatric Extracorporeal Life Support System

Sertac Haydin[1], Ersin Erek[1], Halime Ozkan[2], Ismihan Selen Onan[1], Perihan Yivli[2], Mehmet Yeniterzi[1], Ihsan Bakir[1]

[1] Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Education and Research Hospital, Dept. of Cardiovascular Surgery, Istanbul, Turkey

[2] 1Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Education and Research Hospital, Dept. of Cardiovascular Perfusion, Istanbul, Turkey

Objective:

The new Medos Deltastream DP3 system includes a novel diagonal pump and a micro porous hollow fiber membrane oxygenator (Plasma tight, RHEOPARIN® coated) that provides pediatric extracorporeal life support (ECLS). Our ECLS system has been switched from Medos Deltastream DP2 to DP3 since last November. The aim of this study is to investigate the efficiency of this new system.

Methods:

Between March 2011 and February 2013, the Medos Deltastream ECLS system was used in 33 patients. The system was DP2 in 25 patients before November 2012 and DP3 in 8 patients since then. The mean age was 24 months and mean ECLS duration was 2.8 days in the last 8 patients. All applications were performed following open heart surgery. Non-pulsatile flow was used in all patients.

Results:

Hemodynamic stability was established as soon as starting of ECLS. Lactate levels were decreased to 50% after 8th hour of treatment and remained less than 3.5 mg/dl during the support. Urine output was more than 2mg/kg/hr. There was not microscopic or macroscopic hematuria. 7 of 8 patients (87.5%) were successfully weaned from ECLS and 3 of 7 patients (43%) survived. In DP2 system, these numbers were 36% (9/25) and 55% (5/9), respectively. There was not any mechanical problem during system run.

Conclusions:

Weaning success from ECLS is higher in DP3 than in DP2. DP3 can provide better hemodynamic stability during ECLS support.

S3. Impact of Pulsatile Flow on Hemodynamic Energy in a Medos Deltastream DP3 Pediatric Extracorporeal Life Support System

Conrad Krawiec, MD[1,4], Shigang Wang, MD[1], Allen R. Kunselman, MD[2], and Akif Ündar, PhD[1,3]

Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics[1], Health Evaluation Sciences (ARK)[2], Surgery and Bioengineering[3], Penn State Hershey Pediatric Critical Care Unit[4], Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Background: The Medos Deltastream DP3 system is made up of a novel diagonal pump and hollow-membrane oxygenator that provides non-pulsatile and pulsatile flows for extracorporeal life support (ECLS). The objectives of this study are to 1) evaluate the efficacy of the hemodynamic energy provided by Medos Deltastream DP3 system in non-pulsatile and pulsatile mode and 2) to evaluate the pulsatile mode under different frequencies.

Methods: The experimental ECLS circuit was used in this study, primed with Ringer's Lactate and packed red blood cells (HCT 35%). All trials were conducted at flow rates of 500, 1000, 1500, and 2000 ml/min with modified pulsatile frequencies of 60, 70, 80, and 90 bpm at 36ºC. Simultaneous blood flow and pressures at the pre/post oxygenator and pre/post cannula sites were recorded for quantification of the pulsatile perfusion-generated energy-equivalent pressure (EEP), surplus hemodynamic energy (SHE), and total hemodynamic energy (THE).

Results:

The experiments showed that under pulsatile flow conditions, at all flow rates and frequencies, 1) the EEP, SHE, and THE were significantly higher when compared to the non-pulsatile group and 2) the pressure drop was minimal at lower flow rates and lower pulsatile frequencies, but was significant when either the flow rate or the pulsatile frequency was increased.

Conclusions:

The Medos Deltastream DP3 System can provide non-pulsatile flow and physiologic quality pulsatile flow for pediatric ECLS. When the Medos DP3 pediatric ECLS system is used with pulsatile flow, there is more surplus hemodynamic energy and total hemodynamic energy than non-pulsatile flow.

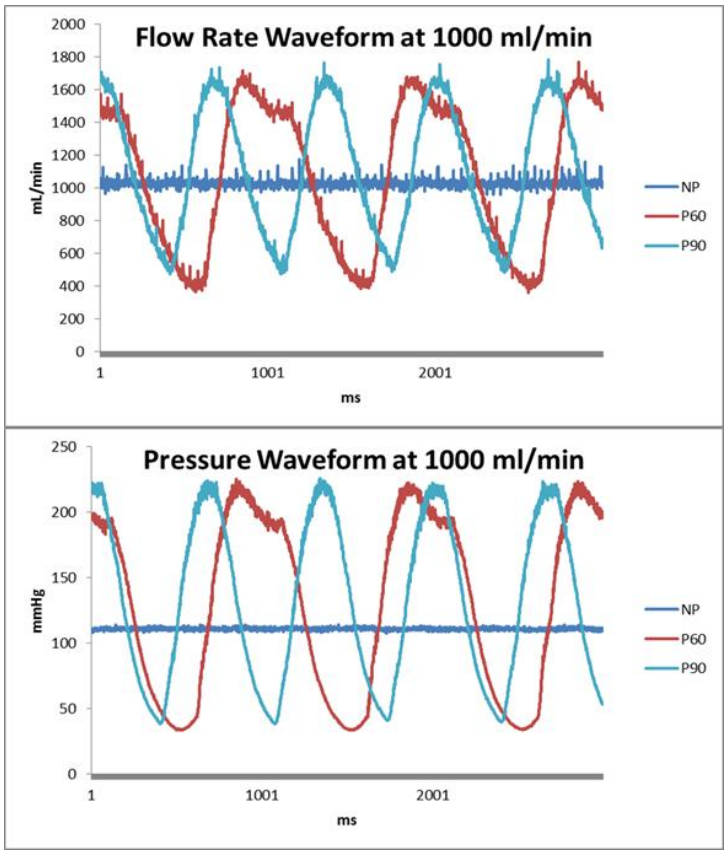


Figure 1: Pre-oxygenator flow and pressure waveforms at flow rate of 1000 ml/min.

S4. NeonatOx II – 12 Hour Pumpless Extracorporeal Lung Support on Premature Lambs

Jutta Arens[1ǂ]; Mark Schoberer[2ǂ]; Aileen Erben[2]; Thorsten Orlikowsky[2]; Daan Ophelders; Reint K. Jellema[3]; Boris W. Kramer[3]; Jan L. Bruse[1]; Petra De Brouwer[1]; Thomas Schmitz-Rode[1]; Ulrich Steinseifer[1]

[1] *Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany*
[2] *Section Neonatology of the Department of Paediatric and Adolescent Medicine, University Hospital, RWTH Aachen University, Aachen, Germany*
[3] *Department of Paediatrics, School of Mental Health and Neuroscience; School of Oncology and Developmental Biology; Maastricht University Medical Center, Maastricht, The Netherlands*
[ǂ] *Both Authors contributed equally to this manuscript*

Background: Impressive progress has been made over the past three decades in the treatment of respiratory failure at the beginning of live. Survival and therapy related morbidity are constantly improving even in premature children as little as 23 weeks of gestational age. Structural and functional pulmonary immaturity however mark an insuperable barrier in the treatment of the smallest children. Mechanical lung substitutes experience a renaissance in basic research. Simple pumpless circuits are currently in the focus of interest. We report our experience with an updated version of NeonatOx, a tailored membrane oxygenator for the treatment of newborn respiratory failure. Improvements in design have allowed us to extend the operating duration to 12 hours.

Methods: We designed a second version of the NeonatOx, optimized regarding gas exchange area (0.116 m²), priming volume (14 ml (21 ml incl. tubing)), and handling. This extracorporeal lung support system was tested on premature Texel lambs (n = 6, 2.600 g ± 460, 127 days ± 0 gestational age (term: 150 days)) with an aimed test duration of 12 h. Animals were born by cesarian section. Cannulation with modified 14 Ga catheters was performed directly after birth as EXIT procedure. Animals were mechanically ventilated as bridging during cannulation and connection to the extracorporeal circuit. Weaning from mechanical ventilation for controlled transition from pulmonary to extracorporeal gas exchange was performed according to protocol: when central venous $pC0_2$ was below 50 mmHg on CPAP (without spontaneous ventilation), Lactate was below 4 mmol/l, and pH > 7.2 the endotracheal tube was clamped.

Results: 3 animals survived the aimed 12 h test duration with a mean tube clamping time of (634 ± 36) min. One animal died after 4 h two after 7 h. Mean blood flow through the extracorporeal circuit was (115 ± 25) ml/min, mean arterial pressure (31 ± 8) mmHg and mean heart rate (204 ± 6) beats per minute (n = 6). The oxygenator increased the mean pO_2 from (21 ± 6) mmHg post oxy to (344 ± 121) mmHg and decreased the mean pCO_2 from (77 ± 10) mmHg to (45 ± 12) mmHg (n = 6).

Conclusions: The improvement in survival between the first and the second developmental stage of NeonatOx is considerable. The oxygenator is originally not meant to be a full lung substitute but rather an assist device. The full elimination of spontaneous or mechanical pulmonary ventilation had to be chosen for experimental requirements in our experiment: The oxygenator performance can only be correctly estimated in-vivo if a pulmonary contribution to the gas exchange is ruled out. The ability of the device to maintain gas exchange even without a pulmonary contribution over such a long period must be regarded as an impressive proof of its properties.

S5. Novel Inflow Cannula for Mechanical Circulatory Support in Patients with Total Caval Pulmonary Connection

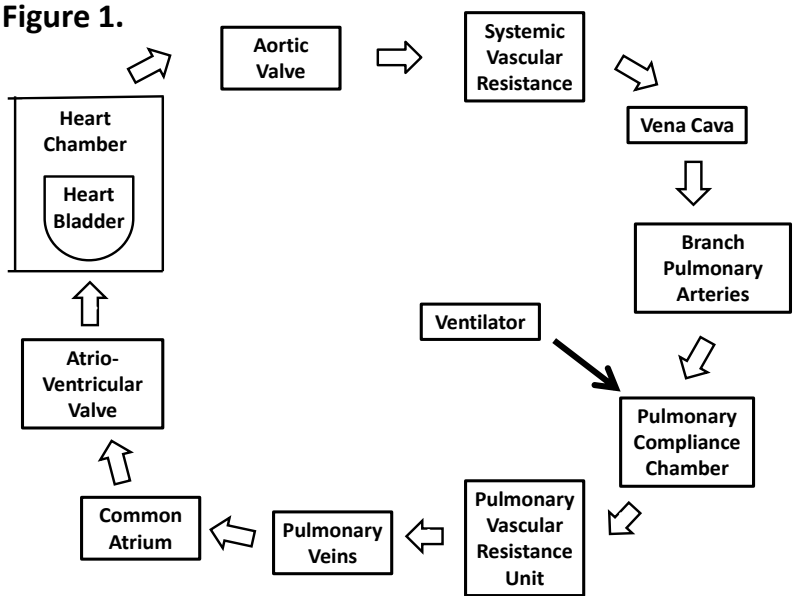
Michael F Swartz, PhD, Doran Mix, BS, Christopher Cistrone, BS, Andrew Hagar, BS, Alexander Kotelsky, BS, Ron Angona, CCP, Karl Schwarz, MD, George M. Alfieris, MD
University of Rochester, Strong Memorial Hospital, Rochester, N.Y. USA

Background:
There are limited options to augment systemic venous and pulmonary arterial flow in patients with total caval pulmonary connection (TCPC). A Veno-Pulmonary Assist Device (VPAD) to augment flow is limited because of the potential for re-circulation, which exists because of the absence of valves in TCPC anatomy. We hypothesized that an inflow cannula that incorporates caval occlusion at the TCPC connection would eliminate re-circulation and maintain PA forward flow.

Methods:
A TCPC model was constructed using a bored acrylic block as the TCPC intersection, and tygon tubing to represent the cava and PA. A pulmonary compliance chamber and pulmonary vascular resistance unit (PVR) unit resulted in venous flow with respiratory variation with physiologic resistance. The remaining circuit consisted of a common atrium and ventricle ejecting blood mimicking fluid into the systemic arterial system (Figure 1). An 18 French inflow cannula, with two external caval occlusion balloons and a right PA outflow graft were connected to a Biomedicus pump at 3,000 rpm's. Pressures and flows were measured at baseline, after VPAD initiation without balloon inflation, and after balloon occlusion of the cava. The shunt fraction was defined as the percentage of flow from the PA into the inflow cannula.

Flow Diagram For TCPC Model

Figure 1.



Results:
At baseline using a fluid volume of 5 liters, the arterial and venous pressures were 111/63 and 6 mmHg respectively, and the PVR was 1.6 woods units. After initiation of the VPAD, distal PA flow was 1.7±0.01 liters/minute with 55±1.0 % re-circulation. However, after caval occlusion, pump flow increased to 2.7 ± 0.1 liters/minute ($p<0.01$), eliminating re-circulation and maintaining PA forward flow.

Conclusions:
This provides evidence that an inflow cannula with caval balloon occlusion can eliminate re-circulation while providing circulatory support in a model of the TCPC circulation.

S6. Incidence and Outcome of Pediatric Patients with Intracranial Hemorrhage while Supported on Ventricular Assist Devices

[1]Robert A. Niebler, MD, [2]Sean Lew, MD, [1]Steven D Zangwill, MD, [3] Ronald K Woods, MD, [3]Michael E Mitchell, MD, [3]James S Tweddell, MD, and [1]Nancy S Ghanayem, MD

Departments of [1]Pediatrics, [2]Neurosurgery and [3]Cardiothoracic Surgery, Medical College of Wisconsin; Milwaukee, WI USA

Background:
Pediatric patients supported on ventricular assist devices (VAD) require systemic anticoagulation and are at risk for complications of intracranial hemorrhage (ICH). Little is known about the incidence or outcome of pediatric patients with ICH while supported on a VAD.

Methods:
A retrospective chart review of all patients receiving VAD support was completed. Patients diagnosed with ICH while supported on a VAD were identified. Significant factors prior to diagnosis of ICH, medical/surgical treatment of ICH, and patient outcomes were assessed.

Results:
Five of thirty (17%) patients supported on a VAD from 1/2000 to present were diagnosed with an ICH. Four patients had an identified cerebral thrombo-embolic injury prior to the ICH. Four patients required significant interruptions in their anticoagulation regimen due to other bleeding concerns prior to ICH. Neurosurgical intervention consisted of evacuation of hemorrhage in one while two others required management of hydrocephalus with external ventricular drainage. Three of the five patients died on VAD support. Two deaths were directly related to ICH, while the third was unrelated. Two patients were successfully transplanted; one remains with a significant neurological impairment and the other has recovered with minimal residual impairment**.**

Table 1: Patients with Intracranial Hemorrhage while on a Ventricular Assist Device

Patient	Age/ Diagnosis	VAD type	Anticoagulants	INR	aPTT (sec)	Platelet Count (K/μL)	Anti-Xa level (IU/mL)
1	10 yo CHD	Thoratec LVAD	Heparin	1.10	64	136	N/A
2	14 yo CHD	Thoratec LVAD	Heparin, Aspirin, Coumadin	1.94	164	262	0.32
3	20 yo CHD	Thoratec BiVAD	Heparin	1.61	33	82	<0.1
4	10 yo CHD	Berlin LVAD	Coumadin, Aspirin, Dipyrimadole	3.63	60	294	N/A
5	12 yo DCM	Berlin LVAD	Enoxaparin, Aspirin, Dipyrimadole	1.13	43	278	0.98

Congenital Heart Disease (CHD), Dilated Cardiomyopathy (DCM)

Conclusions:
ICH is a devastating complication of VAD support. Prior ischemic infarcts and interruptions to anticoagulation may put a patient at risk for ICH. Prompt neurosurgical evaluation/intervention can result in positive outcomes.

S7. Five-year Experience with Mini-Volume Priming in Infants ≤5 kg: Safety of Significantly Less Transfusion Volume

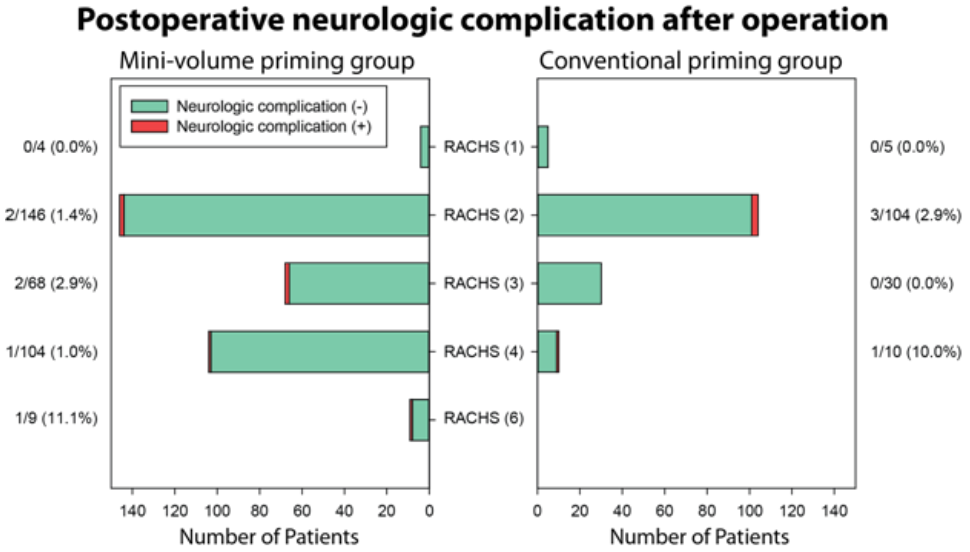
Hyoung Woo Chang, MD, Jinhae Nam, MD, Jae-Hee Cho, Woo Sung Jang, MD, Kwangho Choi, MD, Jeong-Ryul Lee, MD, PhD, Yong-Jin Kim, MD, PhD, Woong-Han Kim, MD, PhD*

Department of Thoracic and Cardiovascular Surgery
Seoul National University Children's Hospital, Seoul, Republic of Korea
**Corresponding author*

Background: Reducing cardiopulmonary bypass (CPB) priming volume in congenital cardiac surgery is important because it is related to less transfusion. This retrospective study was designed to compare safety and transfusion volume between the mini-volume priming (MP) and conventional priming (CP) methods.

Methods: Between 2007 and 2012, congenital heart surgery using CPB was performed on 480 infants (≤5 kg): the MP method on 331 infants (MP group, 69.0%) and the CP method on 149 infants (CP group, 31.0%). In the MP group, narrow caliber (3/16") tubes were used and pump heads were vertically aligned in order to shorten the tube lengths. The smallest oxygenators and hemofilters were used and vacuum drainage was applied. Ultrafiltration was vigorously applied during CPB in order to avoid excessive hemodilution.

Results: The mean age and body weight of the patients were 48±41 (0-306) days and 3.8±0.8 (1.3-5.0) kg, respectively. Total priming and transfusion volumes during CPB were lower in the MP group than in the CP group (141±24ml vs. 292±50ml, p<0.001 and 82±40ml vs. 162±82ml, p<0.001, respectively). In the MP group, the smallest priming volume was 110ml. However, there was no significant difference in the lowest hematocrit level during CPB between the 2 groups (22%±3% vs. 22%±3%, p=0.724). The incidence of postoperative neurologic complications was not significantly different between the MP and CP groups (1.8% vs. 2.7%, p=0.509). After adjustment for the RACHS score, BSA, and age, MP was not an independent risk factor of postoperative neurologic complications or early mortality (p=0.213 and p=0.467, respectively).



Conclusions: The MP method reduced priming volume to about 140mL without increased risk of morbidity or mortality in infants ≤5 kg. Total transfusion volume during CPB was reduced by 50% without compromising hematocrit levels. We recommend the use of mini-volume priming which is a safe and efficacious method for reducing transfusion volume.

S8. The Influence of Lower Body Circulatory Arrest on the Acute Kidney Injury after Surgery for Congenital Heart Disease in Neonate

Ko Yoshizumi, MD, Shingo Kasahara, MD, Atsushi Tateishi, MD, Takuya Kawabata, MD, Yosuke Kuroko, MD, Sadahiko Arai, MD, Shunji Sano, MD

Department of Cardiovascular Surgery, Okayama University Graduate School of Medicine, Dentistry and pharmaceutical Sciences, Okayama, Japan

Background:
Acute kidney injury (AKI) is common in children undergoing complex cardiac surgery for congenital heart disease. Cardiopulmonary bypass–associated acute kidney injury in neonates is still poorly understood. The purpose of this study was to investigate the risk factors associated with acute kidney injury after surgery for complex congenital heart disease in these patients with a special focus on the using the lower body circulatory arrest.

Methods:
Between January 2006 and April 2012, cohorts of one hundred eighteen neonates who underwent complex cardiac repair under cardiopulmonary bypass with lower body circulatory arrest were reviewed. AKI was defined based on the Acute Dialysis Quality Initiative's modified for children RIFLE (pRIFLE) definitions for acute kidney risk or injury (AKI-RI) and kidney failure.

Results:
Postoperative acute kidney injury occurred in 59 patients (50%): 30 patients (25%) reached maximum acute kidney injury stage I, 4 (3%) reached stage II, and 25 (21%) reached stage III, and 20.3% required renal replacement therapy within 3 postoperative days. Independent risk factors for acute kidney injury were surgical procedure (palliative or collective), duration of lower body circulatory arrest and cardiopulmonary bypass.

Conclusions:
The duration of lower body circulatory arrest is associated with high incidence of AKI in neonates who underwent cardiac surgery under cardiopulmonary bypass and lower body circulatory arrest time may be a marker for case complexity.

S9. Is There a Difference between Pulsatile and Nonpulsatile Perfusion Mode According to the Regional Brain Perfusion via Using NIRS in Patients which Underwent to Pediatric Cardiac Surgery with CPB?

Alkan-Bozkaya T., Karacı AR.*, Sasmazel A.*, Ersoy C., Türkoğlu H., Akçevin A., Karaaslan P**., Gökay Vural B**.,Ündar A.***

*Istanbul Medipol University, Dept. of Cardiovascular Surgery and Anestesiology**, Istanbul, TURKEY and Istanbul Siami Ersek Hospital, Dept. of Cardiovascular Surgery* and Penn State University, Children's Hospital, Hershey, PA, USA****

Objective:

Despite of all of the improvements in Pediatric heart surgery, postoperative neurological problems still remain. We explored that is there a difference of NIRS values between pulsatile (Group P) and nonpulsatile group (Group NP) at a clinical setting in this study.

Methods:

Using patient data pools from 2 different centers, we created a homogeneous group who had ventricular septal defect (VSD). Each group had 20 patients. Their demographic data (age, BSA, weight) and their perioperative parameters (X-clamp, CPB time and flow rate) were identical statistically.

We measured regional cerebral oxygen saturation index (rSO2i) in 5 perioperative stages (Stage 1: induction, stage 2: X-clamping, stage 3: CPB, stage 4: off CPB and stage 4: postop 2nd hour) with near-infrared spectroscopy (NIRS) in the 2 groups. We compared to our results according to the perfusion modes (Group P vs. Group NP).

A NIRS sensor (5100 C, INVOS, MI, USA) was placed on the right forehead of patients for 48 hours postoperatively. rSO2i was recorded in one minute intervals by computerized data collection system. Data from all patients in each group were pooled and analyzed using t-test and chi-square for between groups comparisons ($p<0.05$ significant).

Results:

We found that there was no difference in NIRS values between 2 groups (Group P vs. Group NP) according to the operation stages (Stage 1-4) but there was a significant difference at Stage 5 (postop 2nd hour). The NIRS-stage5 value was 75.9±7.74 (SEM 1.73) in Group P and NIRS-stage5 value was 71.45±6.85 (SEM 1.53) in the nonpulsatile group. $p=0.0024$. We found also that the lactate levels (stage 5, postoperative 2nd h) were significantly higher ($p=0.0071$) in nonpulsatile group (3.8±1.7) vs. in Group P (2.7±1.1).

All patients survived to hospital discharge, and they were uneventful neurologically at early postoperative period.

Conclusions:

The threshold for low rSO2i values associated with neurological dysfunction is estimated to be 40-50%. Patients may have low NIRS values perioperatively according to the complex cardiac defects. Postoperative follow up for 48 hours is necessary for these cases. Although there was no neurologic problems in the 2 groups we found that lower NIRS values ($p=0.0024$) and higher lactate values ($p=0.0071$) were seen in nonpulsatile group significantly. We need further clinical studies to confirm this data.

S10. Cardiac Surgery in Neonates with Body Weight Less Than 2500 Gram

Jeng-Wei Chen,MD; Shu-Chien Huang, MD; Yih-Sharng Chen, MD; Chung-I Chang, MD; Ing-Sh Chiu, MD, Nai-Kuan Chou, MD

Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan

Background:
Low body weight is a risk factor of mortality in cardiac surgery. Whether the surgery should be delayed till body weight increase or performed despite low body weight is still not clear. We review our experience in cardiac surgery for neonates and infants weighing less than 2500 g and their cardiopulmonary bypass management and outcome.

Methods:
The registration data of cardiac surgery in our institute was reviewed. The patients received cardiac surgery, except simple ligation of patent ductus arteriosus, were included in this study. The patients with their body weight less than 2500gm at the operation was included in this study.

Results:
Between January 2008 and December 2012, there were 53 patients with body weight less than 2500gm underwent early surgical treatment of congenital heart malformations at our hospital. Fifty-one patients were operated under cardiopulmonary bypass, deep hypothermia with circulatory arrest was used in twenty-eight patients (52.8%). The mean age at operation was 17.0 days (range 0–61 days) and the mean body weight was 2232 g (range 1320–2500 g). Sixteen patients were premature (born before 37 weeks of gestation).

Indications for surgery were: Extreme TOF or pulmonary atresia, n=13, coarctation complex, n= 10, total anomalous pulmonary venous return, n= 8, transposition of great arteries, n= 5, hypoplastic left heart syndrome, n= 6, truncus arteriosus, n= 1, and 10 other procedures. Perioperative ECMO was needed in six patients. The hospital mortality rate was16.98% (9/53).

Conclusions:
Cardiac surgery for congenital defect can be performed in low body weight infants were generally complex procedures. The early survival rate was acceptable giving the poor nature course of the complex congenital anomalies. .

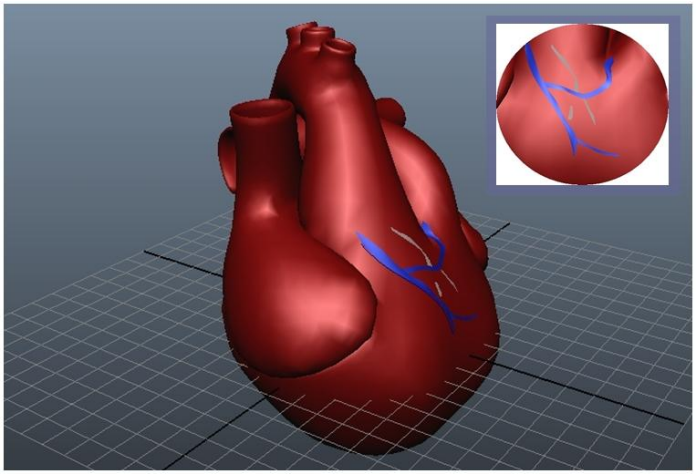
S11. An Implementation of Computer Graphic Simulator Framework for the Training of Congenital Heart Disease Surgery with Interactive Virtual Vessel Re-configuration

Duck Hee Lee, MS, Song E Choi, BA, Seoung Joon Song, PhD, Song Cheol Kim, MD, PhD, Jaesoon Choi, PhD
Medical Engineering R&D Center, Asan Institute for Life Science, Asan Medical Center, Seoul, Korea

Background:
Congenital heart disease (CHD) occurs in various forms of structural and functional problems in the heart and it is a fatal disease that causes more than 50% of children's death [1]. Also, in most cases of the CHD, drug treatment is hardly applicable because of the problem of the circulation and surgical treatment is needed [2]. In this study, a framework for computer simulator for training the CHD surgery has been developed.

Methods:
The heart 3D model used in this study was based on an open source 3D model and the surface structure of which to target specific disease was emphasized by redrawing using computer graphics design software (MAYA, Autodesk, Inc.). The target heart disease was Transposition of Great Arteries (TGA). The framework is composed of various hardware and software modules for 3D deformable model handling, haptic and graphic rendering, and interface to displays and haptic devices. The 3D heart model can be interactively manipulated by the surgeon user during the simulated operation. The haptic rendering provides virtual force feedback experience to the surgeon. The modified blood vessel in the heart model can be interactively deformed, cut, and connected with modified cutting angle.

Results:
The simulation framework has been implemented on a PC and a stereo-enabled display. The haptic feedback function was tested in a system with two commercial haptic devices (PHANToM Omni, Sensable Inc., U.S.A.) for both hand interaction and on the custom-developed 3D heart model as shown below.



Conclusions:
A CHD surgery simulator framework has been developed and the preliminary test has shown the feasibility successfully. Future work includes its extension to more CHD surgery training contents such as septal defects, patent ductus arteriosus, and to various types of mechanical circulatory assist device implantation surgeries.

Acknowledgments:
This study was supported by the Core Medical Device Commercialization Technology Development Program 10043070 funded by the Ministry of Knowledge Economy, Korea.

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S12. Valsartan Improves Myocardial Cardioplegic Protection and Oxidative Stress Tollerance During Ischemia/Reperfusion In Isolated Neonatal Rat Heart.

Gianluca Lucchese, MD, PhD, Giulia Elisa Cambi*, ScD, Rocco Tabbi, CP, Stiljan Hoxha, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Pietro Amedeo Modesti*, MD, PhD, Giovanni Battista Luciani, MD.

*Pediatric Cardiac Surgery Unit, University of Verona, Italy. *Department of Medical and Surgical Critical Care, University of Florence, Italy*

Background:
Signal transducers and activators of transcription(STATs) play an important role in the modulation of inflammation and apoptosis after ischemia/reperfusion. Selective inhibition of Angiotension II type 1(AT1) receptor could represent an adjunctive protective mechanism during cardioplegic arrest in neonatal rat myocytes.

Methods:
Isolated neonatal rat's hearts (n=8 per group) were perfused aerobically (4°C) for 15 min in the Langendorff mode with modified St. Thomas' Hospital no. 2 cardioplegia(MSTH2)(Group 1) and MSTH2+Valsartan 1 μm/L (Group 2). After reperfusion with oxygenated modified Krebs-Henseleit buffer(KHB) until a cardiac rhythm occurred, hearts were again arrested for 10 min. Thus, myocytes were isolated, and STAT2, STAT3, STAT5 and calcium/calmodulin-dependent protein kinase-II(CaMK II) were investigated by Western blot analysis both in basal condition and after stimolation with reactive oxygen species(ROS).

Results:
Times to arrest following initial dose of cardioplegia were 6-14 sec for both groups. Total delivery volume was about 320 mL for a total time of 25 min (in two times). During reperfusion with modified KHB, an indeterminate cardiac rhythm was visualized after 2.5 - 4.7 min in Group 1 and 3.2 - 5.9 min in Group 2 ($p>0.05$). Following the second dose of cardioplegia, times to arrest were comparable. Perfusion with Valsartan supplemented cardioplegia (Group 2) induced a significant reduction in STAT2 and STAT5 phosphorylation (- 48 and -56%, respectively, vs. Group 1, $P < 0.05$) and after stimolation with ROS (-65% and -73% respectively vs. Group 1). Decreased activation of STAT2 and STAT5 was accompanied by reduction of interleukin-1β ($P<0.05$). Valsartan significantly affected even phosphorylation of CaMK II in our study (- 32% vs. Group 1, $P < 0.05$).

Conclusions:
Valsartan added to cardioplegia decreases the inflammatory response of the neonatal rat cardiomyocytes during ischemia/reperfusion and increases oxidative tollerance stress without affecting antiapoptotic and cardioprotective influence provided by activation of STAT3. Furthermore Valsartan improves myocardial protection down-regulating activated CaMK II expression, which is associated with increased apoptosis, and could contribute to optimize both ischemia tolerance and preservation of the neonatal heart.

S13. Carotid Artery Doppler Flow Pattern after Deep Hypothermic Circulatory Arrest in Neonatal Piglets

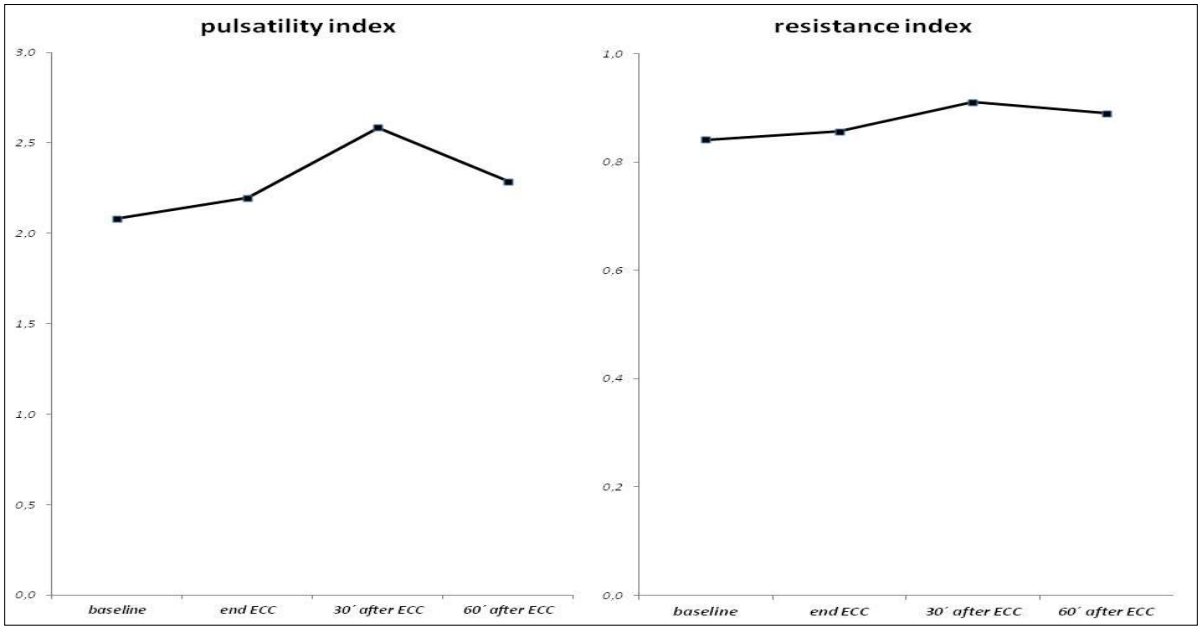
Theodor Tirilomis[1], MD, PhD, Stella Malliarou[2], MD, K. Oguz Coskun[1], MD, Friedrich A. Schoendube[1], MD, PhD

[1]Dept. for Thoracic, Cardiac, and Vascular Surgery, University of Goettingen, and [2]Dept. for Neurology and Neurological Rehabilitation, Asklepios Clinics Schildautal Seesen, Germany

Background: Alterations in blood flow after open-heart surgery may lead to cerebral injury. The mechanisms of neurological disorders after cardiac surgery in neonates are not clear. The aim of the study was the analysis of flow changes in the carotid artery of neonatal piglets after deep hypothermic circulatory arrest (DHCA).

Methods: Eight neonatal piglets (younger than 7 days) were connected to the cardiopulmonary bypass (CPB) and underwent (1) cooling to 18°C core temperature within 30 minutes, (2) circulatory arrest for 90 minutes and finally, (3) re-warming to 37°C after cross-clamp release (60 minutes of reperfusion). The blood flow was measured in the left carotid artery by an ultrasonic flow probe; before CPB (baseline), immediately after termination of reperfusion on CPB, 30 minutes, and 60 minutes later. Additionally, the pulsatility index and the resistance index were calculated and compared. Finally, the relation of the carotid artery flow data with the corresponding pressure data at each time-point was compared.

Results: After DHCA and termination of the reperfusion on CPB the carotid artery mean flow was reduced from 45.26 ± 2.58 ml/min at baseline to 23.29 ± 2.58 ml/min ($p<0.001$) and remained reduced 30 and 60 minutes later ($p<0.001$ vs. baseline). both, the pulsatility index and the resistance index were increased immediately after termination of reperfusion (figure).



Conclusions: The Doppler flow of the carotid artery in neonatal piglets after DHCA reduced and the indices of pulsatility and resistance increased.

S14. Near Infrared Spectroscopy Monitoring in the Pediatric Cardiac Catheterization Laboratory

Ibrahim Cansaran Tanidir[1], Erkut Ozturk[1], Isa Ozyilmaz[1], Murat Saygi[1], Neslihan Kiplapinar[1], Sertac Haydin[2], Alper Guzeltas[1], Ender Odemis[1]

[1] Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Education and Research Hospital, Dept. Of Pediatric Cardiology, Istanbul, Turkey

[2] Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Education and Research Hospital, Dept. of Cardiovascular Surgery, Istanbul, Turkey

Objective:

Near infrared spectroscopy (NIRS) is a non-invazive technique used for determining tissue oxygenation and perfusion. In this study, we aimed to evaluate the relation between cerebral, renal NIRS values and complications in pediatric cardiac patients who underwent catheterization procedures.

Methods:

Between January and June 2012, 123 patients who underwent cardiac catheterization were analyzed. Cerebral and renal NIRS values, electrocardiographic changes, non-invasive blood pressure measurements, pulse oximetry and blood lactate levels were recorded. A hundred twenty-three cerebral and 103 renal NIRS monitoring were performed. INVOS 5100c (Somanetics, Troy, MI, USA) was used for NIRS monitoring.

Results:

Interventional procedures were performed in 73 (60%) patients. Forty-two complications were seen in 33 patients. These were desaturation, arrhythmia, respiratory problems and cardiopulmonary resuscitation. Twenty percent change of NIRS values from baseline was considered significant. Cranial and renal NIRS values decreased significantly in 12 (12/123, 9.8%) and 13 patients (13/103, 12.6%), respectively, compared with baseline values. The specificity and the sensitivity of cranial and renal NIRS values has been found 85% and 63%, 90% and 67%, respectively. NIRS values changed simultaneously with ECG changes during arrhythmia. NIRS values decreased and increased 10-15 seconds before pulse oximetry during desaturation and recovery, respectively. Also, NIRS alerted us in terms of low cardiac output without pulse oximetry and ECG changes in a patient who had a pacemaker generator.

Conclusions:

NIRS monitoring during pediatric cardiac catheterization procedures may provide more information about hemodynamics and can alert for serious complications before other monitoring tools.

S15. A Computerized Mock Circulatory Loop System Using Servo Control Flow Regulator for Time-varying Hemodynamic Characteristics Simulation

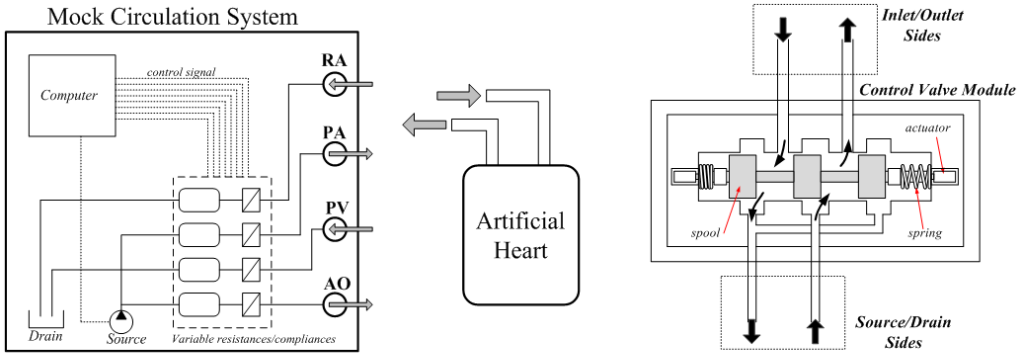
[1]Youngjin Moon, PhD, [1]Jaesoon Choi, PhD

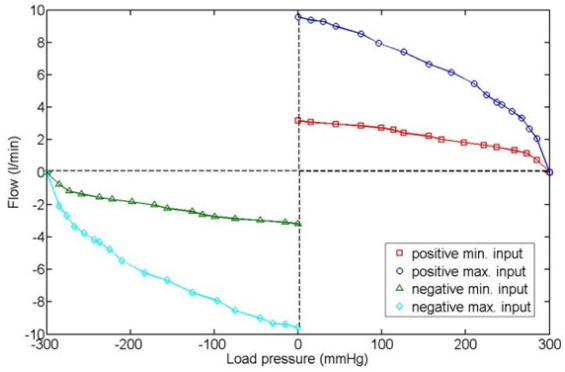
[1]Medical Engineering Research and Development Center, Asan Institute of Life Sciences, Asan Medical Center and University of Ulsan College of Medicine, Seoul, Korea

Background:
To construct a simulator for trainees in cardiopulmonary bypass systems or to simulate a test environment for cardiac assist devices, mock circulatory loop systems and various types of simulators have been developed. In this study, a computerized mock circulatory loop system whose input and output nodes are modularized using servo control flow regulator to simulate dynamic change of hemodynamic status at the nodes, and the rest of the circulatory system is simulated in computer model, is proposed.

Methods:
To implement the time-varying hemodynamics, the proposed system 1) implements the hemodynamic properties at each node components such as resistance and compliance as nonlinear and time-varying ones using servo control flow regulator module, and 2) replaces the cardiopulmonary circulatory mechanism with a computer simulation software. The values of resistance and compliance can be adjusted by using a servo control valve or proportional control valve and buffer chambers. Hemodynamics is modeled as governing equations including nonlinear terms, and a computer in the mock system solves it by numerical methods. The variables controlled by a computer could have a benefit in simulating diversity of the system dynamics, as compared with time invariant ones implemented in fixed property passive mechanical components. As shown in the figures below, this system can simulate various conditions such as time-varying vasoconstriction, connecting with an artificial heart and etc.

Results:
The characteristics of pressure load and flow rate for selected inputs, given the regulator control inputs as 2 and 8 mA when the actuator is a solenoid, were obtained in simulation as below.





Conclusions:
The results demonstrate that the developed mock system can simulate time-varying circulatory conditions effectively utilizing advantages of both mechanical components and computer software.

S16. Quantitation of Fetal Heart Function with Tissue Doppler Velocity Imaging – Reference Values for Color Doppler Velocities and Comparison with Pulsed Wave Doppler Imaging

Ashish P. Saini[1], MD, Serdar Ural, MD[2], Linda B. Pauliks[1], MD, MPH
[1]Pediatric Cardiology, [2]Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Penn Hershey State College of Medicine, Hershey, PA

Background: Quantitation of fetal heart function by echocardiography is challenging. Pulsed wave tissue Doppler imaging (PW) helps but is limited to sampling single regions. Color tissue Doppler imaging (CTDI) permits sampling the entire heart in one heart beat. There are no reference values for CTDI yet.

Methods: The study included 91 fetuses (gestational age 28.6±6.6 weeks). From apical 4-chamber views, tricuspid ring (RV), lateral and septal mitral ring were sampled with PW and CTDI tissue Doppler with a Vivid Q (GE, Madison, WI). During off-line analysis, peak S velocities were determined from 3 beats each.

Results: S velocities correlated with gestational age (R=0.5; p<0.01). PW were significantly higher than CTDI (Table 1). PW and CTDI S velocities correlated (Table 1). There was a systematic bias towards higher velocities with PW v. CTDI (Figure 1).

Table 1: Comparison of PW and CTDI S velocities in 91 fetuses

Sample site	S velocity PW (cm/s)	S velocity CTDI (cm/s)	P value	R value PW vs. CTDI	P value
Mitral ring (lateral LV)	6.1±2.4	4.9±2.2	P<0.01	0.871	P<0.01
Interventricular septum	4.6±1.5	4.2±1.7	P<0.01	0.578	P<0.01
Right ventricle (RV)	7.5±2.8	6.3±2.5	P<0.01	0.698	P<0.01

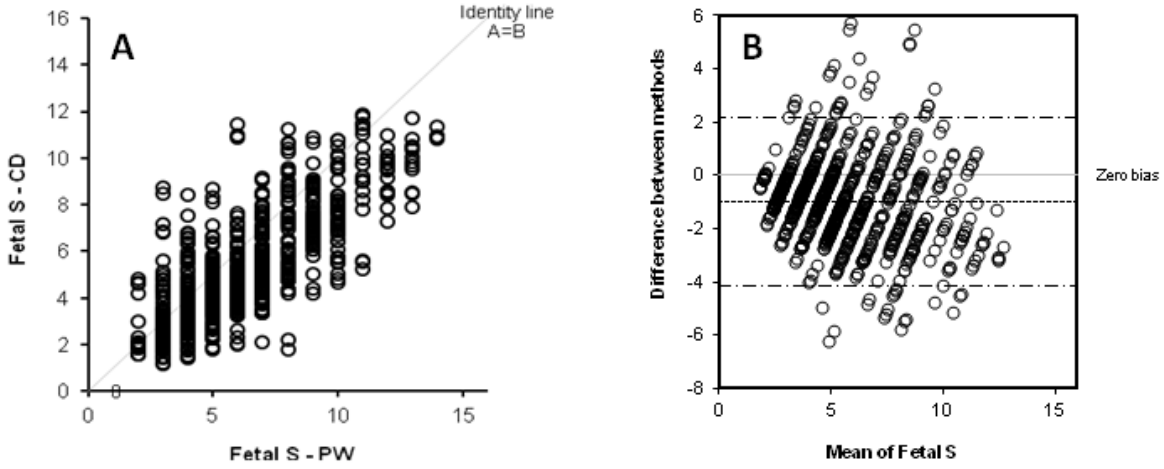


Figure 1: Bland Altman plot for PW Doppler vs. CTDI in 91 fetuses. There was a 0.96 cm/s bias towards higher velocities with PW vs. CTDI.

Conclusions: During fetal echocardiography, color tissue Doppler velocities can be used instead of PW velocities but different reference values should be applied. PW velocities are always higher than CTDI velocities.

S17. Could ECMO Be Weaned Off for a Child with Acute Fulminant Myocarditis under the Status of Low Left Ventricular Ejection Fraction?

Shye-Jao Wu, MD
Division of Cardiovascular Surgery, Departments of Surgery,
MacKay Memorial Hospital, Taipei, TAIWAN

Background:
ECMO is the last resort to save the lives of children with acute fulminant myocarditis and circulatory collapse. It is usual to wean off ECMO when the patient's hemodynamics is stabilized and left ventricular ejection fraction (LVEF) is improved. However, after one-week run of ECMO support, if the LVEF was still around 20%, but the hemodynamics is stable with low doses of inotropic agents, should we just keep ECMO support or try to wean off ECMO? How could we make a decision? Here I reported a pediatric case successfully weaned off ECMO with recovered cardiac function (adequate cardiac output) but impaired LVEF. After ECMO removal, his LVEF improved to the normal level gradually.

Methods:
The 6-year-old boy suffered from intermittent fever up to 39 ℃, cough with sputum, rhinorrhea, and nasal congestion for a week. Chest x ray showed increased infiltration of bilateral lung fields. At first, he was treated as bronchopneumonia. He also had vomiting, poor appetite and decrease activity. Shortness of breath with retraction was noted. However, symptoms did not improve after medications. He was brought to our hospital. Because his respiratory condition was downhill to impending respiratory failure, endotracheal tube was inserted on the second day of admission. General condition deteriorated persistently. Because of hypotension (SBP around 80mmHg, HR 170-180/min), blood pressure was maintained with dopamine 20mcg/kg/min and dobutamine 20mcg/kg/min and epinephrine 0.5mcg/kg/min. Besides, high CVP level (20-25mmHg) was also found. Elevated cardiac enzyme (CK: 2868IU/L, CKMB: 30.2IU/L, Tropinin-I: 4.95ng/ml) was noted and myocarditis was suspected. Echocardiography showed LVEF 20%-30%. High BNP level (2980pg/mL) was also found. VA-ECMO was set up with Fr15 cannula into right carotid artery and Fr19 cannula into right jugular vein. Initial ECMO blood flow was 1.6-1.8L/min (80-90mL/kg/min).

Results:
After ECMO was set up (ECMO pump speed 2300rpm, ECMO blood flow 1.8L/min, ECMO FiO2 80%, ventilator FiO2 40%), SBP increased to 100-110mmHg, HR decrease to 130-140/min, and CVP level decreased to 12mmHg. The doses of inotropic agents were tapered gradually. After 5-day ECMO run, the ECMO blood flow was weaned down to 0.65L/min, the inotropic agent were nearly totally tapered off, vital signs were also stable and urine output was also adequate (3.4cc/kg/hr). Under these circumstances, I would like to remove ECMO for this patient. However, echocardiography showed LVEF was only 20-25%. At that moment, I used measurement of cardiac output (Edwads Lifesciences, USA) to make sure this patient's cardiac function. Under ECMO blood flow 0.65L/min, the cardiac output was measured 3.2L/min. So I believed the patient's cardiac function could support himself adequately. I remove the ECMO for him at that time, and the patient recovered uneventfully. Total ECMO supporting time was 114 hours. The endotracheal tube was removed 6 days after ECMO removal. The echocardiography done 3 weeks after ECMO removal showed LVEF was 50%. He was discharged home 24 days after ECMO removal.

Conclusions:
Good LVEF usually convinces doctors that ECMO can be removed. Poor LVEF usually disappoints doctors, not mention to removal of ECMO. However, if everything (except for the poor LVEF) is fine, such as stable blood pressure, normal central venous pressure, use of low doses of inotropic agents which are tapering, adequate oxygenation, adequate venous oxygen saturation, adequate urine output, and so on, what is the next step? At this moment, for larger children, measurement of cardiac output might offer us another scientific evidence to make sure whether ECMO can be removed or not.

S18. The Dynamic Observation of Plasma Concentration of Antimicrobial Agents during Balanced Ultrafiltration in Vitro

Yulong Guan, MD, Zhida Fu, MD, Ju Zhao, MD, Peng Sun, MD, Cun Long, MD

Department of Extracorporeal Circulation, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, P.R. China

Background: Routine perioperative intravenous antimicrobial agents, was administered as surgical prophylaxis. However, whether balanced ultrafiltration during extracorporeal circulation has substantial effect on the concentration of antimicrobial agents remains unclear. The concentrations of antimicrobial agents in plasma and ultrafiltrate samples were measured in this pseudo-extracorporeal circulation model.

Methods: Extracorporeal circulation consisted of cardiotomy reservoir (Ningbo Fly Medical Healthcare CO., LTD. Ningbo, China), D902 Lilliput 2 membrane oxygenator (Sorin Group Asia Pte Ltd, Beijing, China) and Capiox® AF02 pediatric arterial line filter (Terumo Corporation, Beijing, China). HEMOCONCENTRATOR BC 20 plus (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) was placed between arterial purge line and oxygenator venous reservoir. Fresh donor human whole blood was added into the circuit and mixed with Ringer's solution to obtain a final hematocrit of 24 – 28%. Two kinds of antimicrobial agents, cefotiam (320 mg) and cefmetazole (160 mg), were bonus added into the circuit. After 30 minutes of extracorporeal circulation, zero-balanced ultrafiltration was initiated and arterial line pressure was maintained at approximately 100mmHg with Hoffman clamp. The rate of ultrafiltration (12 mL/min) was controlled by ultrafiltrate outlet pressure. Identical volume of Plasmaslyte A was dripped into the circuit to maintain stable hematocrit during 45 minutes of experiment. Plasma and ultrafiltrate samples were drawn every 5 minutes and concentrations of antimicrobial agent (including cefotiam and cefmetazole) were measured with high performance liquid chromatography.

Results: All these two antimicrobial agents were detected in ultrafiltrate, demonstrating hemoconcentration may remove antimicrobial agent. The concentrations of plasma antimicrobial agent decreased lineally with the increase of ultrafiltrate volume. At end of balanced ultrafiltration, the concentrations of plasma cefotiam was 104.96 ± 44.36 mg/l, which is about 44.38% ± 7.42% of the initial concentration (238.95 ± 101.12 mg/l) ($p < 0.001$); the concentration of plasma cefmetazole decreased linearly to 25.76 ± 14.78 mg/l, which is about 49.69% ± 10.49% of the initial concentration (51.49 ± 28.03 mg/l) ($p < 0.001$). The total amount of cefotiam in ultrafiltrate is 27.16% ± 12.17% of the total dose administered, whereas cefmetazole in ultrafiltrate is 7.74% ± 4.17%.

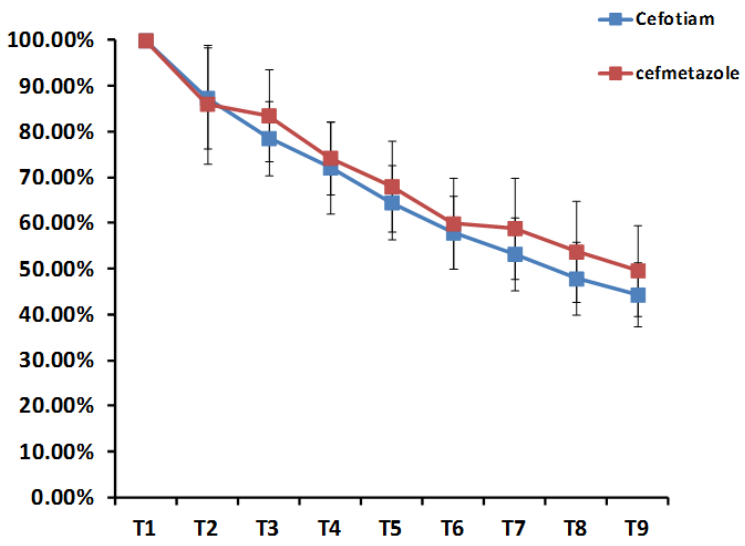


Figure 1 Dynamic percentage changes of concentrations of plasma antimicrobial agents compared to the initial concentrations (T1)

Conclusions:
Balanced ultrafiltration may remove antimicrobial agent from plasma and has prominent influence on plasma concentration of antimicrobial agent. The strategy of surgical prophylaxis should consider this unique technique during extracorporeal circulation.

S19. Universal Method for Object Detection and Tracking in Robot-assisted Laparoscopic Surgery Images

Jiwon Ryu[1], Jaesoon Choi, PhD[2], Hee Chan Kim, PhD[3]

[1]Interdisciplinary Program, Bioengineering Major, Graduate School, Seoul National University, Seoul, Korea, [2]Medical Engineering Research and Development Center, Asan Institute of Life Sciences, Asan Medical Center and University of Ulsan College of Medicine, Seoul, Korea, [3]Department of Biomedical Engineering, College of Medicine and Institute of Medical and Biological Engineering, Medical Research Center, Seoul National University, Seoul, Korea

Objective: In robot-assisted laparoscopic surgery, limited vision through a laparoscope, limitations in agile re-configuration of the surgical instrument setup, or removal of bulky robotic tools, may hinder surgeons from immediate emergency responding. To help surgeons with preventive caution, an advanced universal vision-based technique for object detection and tracking that includes automatic detection of intraoperative hemorrhage and surgical instruments is proposed herein.

Methods: This technique locates the object region of interest by two common processes: feature extraction and tracking. Color and morphological information are used to segment the feature, and a Kalman filter is applied for robust tracking of the object locations with reduced error. Performance for hemorrhage and surgical instrument localization were quantitatively evaluated by root mean square error (RMSE) comparisons and instrument trajectory comparison among results of computerized methods and manual determination, respectively. Hemorrhage area variation analysis using proportionality of area increase and flow are also illustrated.

Results: The average RMSE value for hemorrhage detection using the proposed method was 3.6 pixels. Linearity of a positive slope for increased hemorrhage flow and negative slope for hemorrhage stanching were observed.

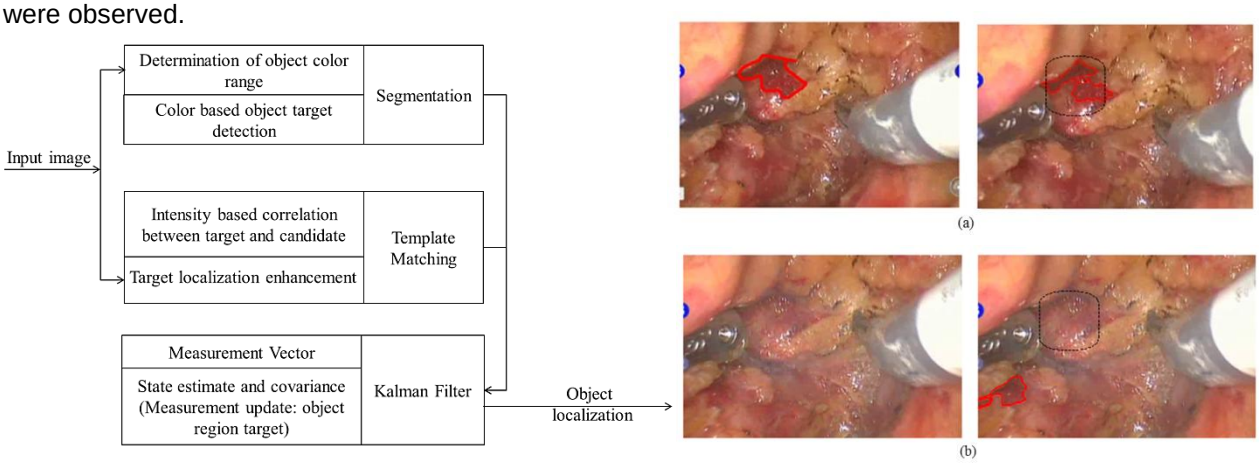


Figure 1. (Left) Block diagram of the computational steps for various object detection including the structure of the proposed Kalman filter for optimal estimation, (Right) Left column: Manually traced hemorrhage region; Right column: Automatically detected region (square) (a) Accurately segmented by segmentation-only method (red boundary) and detected by the proposed technique (b) Manually undetectable, falsely segmented by segmentation-only method, but accurately detected by the proposed technique from previously obtained information

Conclusions: Results show that the proposed technique achieves satisfactory automatic intraoperative object detection and tracking to enhance the surgeon's state-recognition during robot-assisted surgery.

S20. Aortic outflow cannula tip design and orientation impacts cerebral perfusion in pediatric cardiopulmonary bypass

Prahlad G Menon, MS[1], Akif Ündar, PhD[2], Kerem Pekkan, PhD[1,3]

[1]Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania, USA

[2]Penn State Milton S. Hershey Medical Center, Hershey, PA, USA, [3]Koc University, Istanbul, Turkiye

Background: Poor perfusion of the aortic arch is a suspected cause for peri- and post-operative neurological complications associated with cardiopulmonary bypass (CPB). High-speed jets from 8-10Fr pediatric / neonatal cannulae delivering ~1 L/min of blood can accrue sub-lethal hemolytic damage[1] while subjecting the aorta to non-physiologic flow conditions that compromise cerebral perfusion. We emphasize the importance of cannulation strategy and hypothesize engineering better CPB perfusion through a redesigned aortic cannula tip.

Methods: This study employs computational fluid dynamics (CFD) to investigate novel diffuser-tipped aortic cannulae for shape sensitivity to cerebral perfusion, in an *in-silico* cross-clamped aortic arch model with fixed outflow resistances. 17 parametrically altered configurations of an 8FR end-hole and several diffuser cone angled tips in combination with jet incidence angles toward / away from the head-neck vessels were modeled. Experimental pressure-flow characterizations were also conducted.

Results: An 8FR end-hole aortic cannula delivering 1 L/min along the transverse aortic arch was found to give rise to backflow from the brachicephalic artery (BCA), irrespective of angular orientation, for the chosen ascending aortic insertion location. Altering the cannula tip to include a diffuser cone angle (5^0-15^0) eliminated BCA backflow for all angles of jet incidence. Experiments reveal that a 1cm long 10^0 diffuser cone tip demonstrates the best pressure-flow performance improvement in contrast with an end-hole tip, which further improves when preceded by an expanded four-lobe swirl inducer attachment[2].

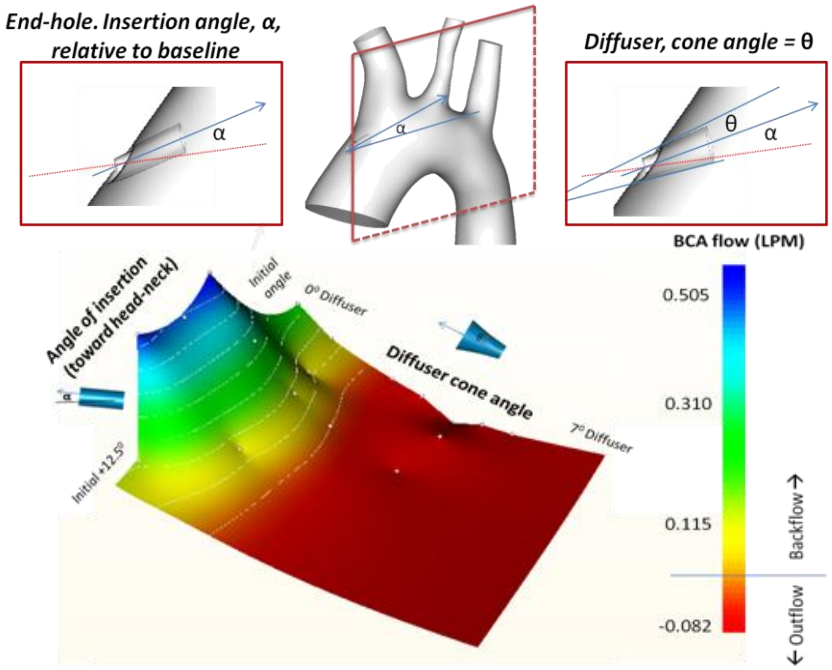


Figure 1. TOP: Parameters employed for shape sensitivity studies are illustrated, along with two sample cannulation configurations. **BOTTOM**: BCA flow direction sensitivity to changes the study parameters.

Conclusions:

Aortic cannula orientation is crucial in determining net head-neck perfusion but precise angulations and insertion-depths are difficult to achieve practically. Altering the cannula tip to include a diffuser cone angle has been shown potential for the first time to ensure a net positive outflow at the BCA. Cannula insertion distanced from the BCA inlet may also avoid backflow due to the Venturi effect.

References:

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2. Menon PG, Undar A, Pekkan K. Computational evaluation and in silico testing of a novel aortic outflow cannula designed for pediatric cardiopulmonary bypass procedures. *BMES Annual Meeting*. Atlanta2012.

P1. Handling Ability of Gaseous Microemboli of Two Pediatric Arterial Filters in a Simulated CPB Model

Ashton Strother[1,2], Shigang Wang, MD[2], Allen R. Kunselman, MA[3], Akif Ündar, PhD[2,4]

[1] Huron High School, Ann Arbor Public Schools, Ann Arbor, MI, USA; Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics[2], Public Health and Sciences[3], Surgery, and Bioengineering[4]. Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Background:
The purpose of this experiment was to compare the Sorin KIDS D131 and Terumo Capiox AF02 pediatric arterial filters, in a simulated CPB procedure, to determine which filter is the best for clinical use.

Methods:
The experimental circuit was primed with 800 ml combination of lactated ringer's solution and human blood (HCT 30%). The two filters were tested under flow rates of 500, 1000, and 1500 ml/min, at room temperature, and their purge lines open and closed, as 5cc of air was injected into the circuit.

Results:
As the flow rates increased the number of GME being returned to the pseudo patient increased for both of the pediatric arterial filters. Having an open purge line increased the number of GME removed from the CPB circuit, caused less of a pressure drop, than when closed, and increased the total hemodynamic energy loss, than when closed. Both of the filters performed and reacted similarly in decreasing GME, hemodynamic energy loss, and pressure drop. The only minor difference was that the Capiox AF02 had slightly less stolen blood flow (109.5 ± 1.7 ml/min at 500 ml/min, 114.7 ± 1.1 ml/min at 1000 ml/min and 105.8 ± 4.2 ml/min at 1500ml/min) from the open purge line than the kids d131 (119.5 ± 2.5 ml/min at 500 ml/min, 128.3 ± 1.0 ml/min at 1000 ml/min and 126.3 ± 3.1 ml/min at 1500 ml/min).

Table 1. Total emboli counts at the inlet and outlet of the arterial filters at different flow rates

Flow rate	Purge line	Terumo Capiox AF02			Sorin KIDS D131		
		Inlet	Outlet	Trap (%)	Inlet	Outlet	Trap (%)
500	Closed	4.2±3.8	1.8±2.4	61.1±41.8	2.8±2.1	0.8±1.3	75.0±41.8
ml/min	Open	5.0±6.7	1.8±3.3	80.4±25.4	2.5±2.5	0.5±1.2	85.0±30.0
1000	Closed	222.8±50.1	123.0±24.8	44.0±7.7	227.0±24.9	130.7±15.6	42.1±6.5
ml/min	Open	141.5±29.0	71.8±23.1	49.9±8.4	157.7±26.9	82.2±27.2	48.9±9.1
1500	Closed	2960.7±792.4*	1966.8±504.3*	33.4±0.8	2893.7±293.1*	2000.2±201.3*	30.9±1.6
ml/min	Open	2196.0±228.9	1402.3±163.6	36.2±3.3	2186.2±488.5	1401.7±328.9	36.0±1.8

* P <0.01, the arterial filter purge line: Closed vs. Open.

Conclusions:
Our study confirmed that both the Sorin KIDS D131 and the Terumo Capiox AF02 were equivalent in their ability to remove significant number of GME, the amount of pressure drop and total hemodynamic energy loss across the arterial filters, at the various flow rates. An arterial filter is not an option, but a necessity for removing microemboli delivering to the patient.

P2. Is NIRS (Near infrared spectroscopy) Monitoring Important during Pediatric Aortic Coarctation and/or Arch Repair?

Alkan-Bozkaya T., Akçevin A., Ersoy C., Türkoğlu H., Karaaslan P*., Gökay Vural B*., Ündar A**.

Istanbul Medipol University, Dept. of Cardiovascular Surgery and Anestesiology, Istanbul, TURKEY and Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA***

Objective:

Aortic cross clamping during coarctation repair and complex aortic arch repairs may create an ischemic problem for the distal tissues. NIRS is a noninvasive method used to measure regional tissue oxygenation continuously and may permit assessment of changes in regional cerebral perfusion in real time.

Methods:

Between May 2012 to date, we operated on 19 pediatric patients who had aortic coarctation (n=14), IAA (N=3, 2 of them with VSD-ASD) and DAA (double aortic arch, n=2). We used NIRS monitoring to determine the real-time changes in cerebral regional oxygenation (rSO2) in patients undergoing aortic coarctation repair and/or arch repair routinely. Our data pool allowed us to examine the changes in rSO2 during aortic coarctation or arch repair for three pediatric age groups (neonates ⩽30 days, infants <1 year, and children ⩾2 yrs). The data for rSO2 were analyzed for each age group according to before, during and after cross-clamping. Antegrade cerebral perfusion via innominate artery was used to repair of complex aortic arch pathologies at 20-22° C.

Results:

19 patients were available for analysis (6 neonates, mean: 6.8 days; 9 infants, mean age: 5.7 mos and 4 children, mean age: 5.5 yrs). The regional oxygenation below the cross clamp (rSO2-S) declined significantly in all three age groups, but the decrease in neonates and infants was significantly greater than in the older children ($p<0.05$). Three of cases (including one IAA-VSD case) had low (<35-40) NIRS values during cross clamping. Two of them had mild and one of them had severe seizures with no recurrence at late postoperative period. Following EEG and MRI for these patients, there was no specific brain lesion. The postoperative monitoring period were 3 months on average. During this period, there was no neurologic deficit, no new seizures and no need for antiepileptic therapy (including the patient with the most severe seizures).

Conclusions:

NIRS (rSO2) value provides real-time threshold data of regional cerebral oxygenation during aortic cross-clamping and arch repairs. While the simultaneous SatO2 changes were minimal, the decline in rSO2 during aortic repairs was rapid and large in most neonates and young infants <1 year which suggests impairment of regional cerebral perfusion presumably because of a lack of adequate collateral circulation and was considerable in children >1 year, probably reason of that they had time to develop a more adequate collateral circulation ($p<0.041$). Low NIRS values (<40) may predict neurological morbidity for the early perioperative period especially after cross-clamping. For such complex cases, antegrade cerebral perfusion can safely be used to prevent major brain damages.

P3. In Vitro Comparison of the Delivery of Gaseous Microemboli and Hemodynamic Energy for a Rotary and Roller Pump

Ranjodh Dhami, BS*, Shigang Wang, MD*, Akif Ündar, PhD*†

Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA*

Background: Cardiopulmonary bypass (CPB) is used for a variety of procedures in pediatric patients. Flow settings of the CPB pump have dramatic effects on patient outcome, and formation of gaseous microemboli within the CPB circuit has been linked to neurological complications. To ensure the ongoing improvement of pediatric CPB, consistent evaluation and improvement of the equipment is necessary. In this study we analyze the Jostra HL-20 roller pump and a Medos Deltastream DP3 rotary pump which has not yet received FDA approval.

Methods: An infant CPB model with heparinized human blood is used to quantity the gaseous microemboli formation (via an Emboli Detection and Classification Quantifier), as well as the hemodynamic energy delivered under flow rates of 400 mL/min, 800 mL/min, and 1200 mL/min.

Results: Results show that in most flow settings the DP3 delivers fewer microemboli than the Jostra roller pump at pre-oxygenator site, but it generates more microemboli at pre-oxygenator site at 1200 ml/min under pulsatile mode. The total volume and the number of gaseous microemboli greater than 40 μm in diameter were lower in DP3 group. The HL-20 exhibits less stolen blood flow (except at 1200 ml/min) and oxygenator pressure drop in both pulsatile and non-pulsatile mode. Additionally, under pulsatile flow the DP3 delivers greater surplus hemodynamic energy and total hemodynamic energy to the patient for all flow rates.

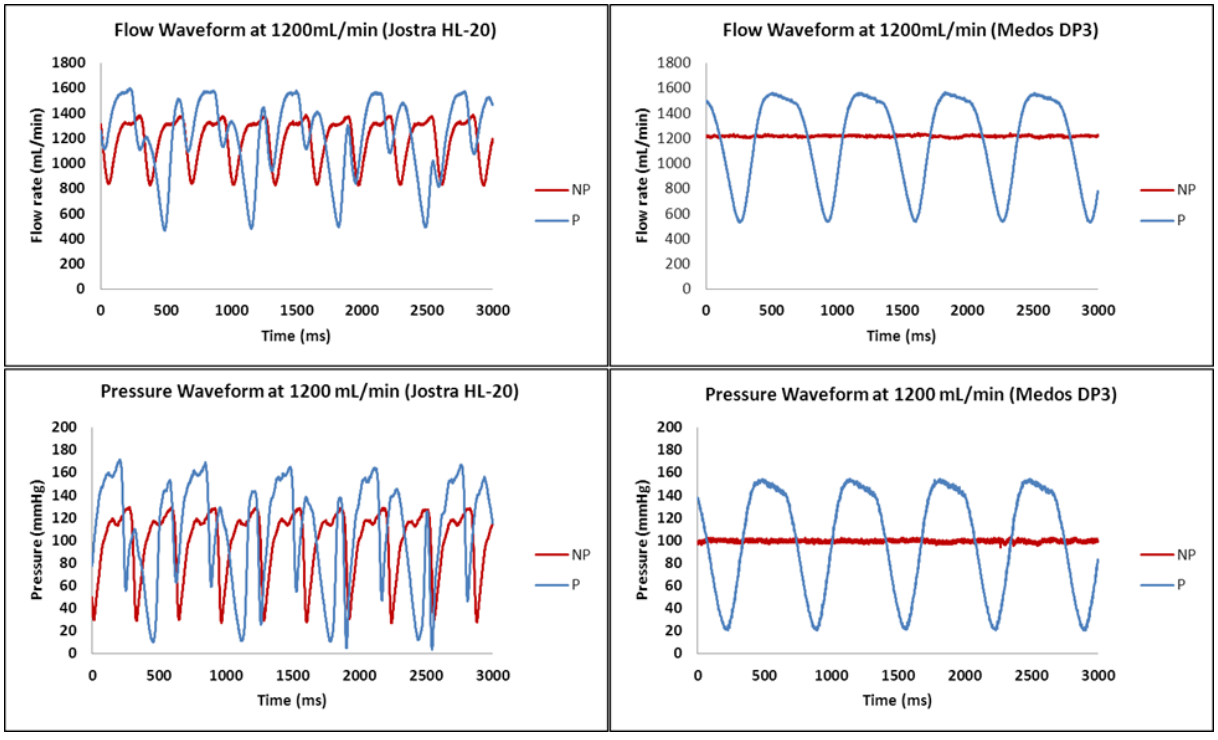


Figure 1: Pressure and flow waveforms under pulsatile (P) and non-pulsatile (NP) mode.

Conclusions: Both pumps produce relatively few microemboli and deliver adequate hemodynamic energy to the pseudo-patient, with the DP3 performing slightly better under most flow settings.

P4. Impacts of Pulsatile Settings on Hemodynamic Energy Output of a Diagonal Pump in a Simulated ECLS System

Shigang Wang, MD[1], Allen R. Kunselman, MD[2], and Akif Ündar, PhD[1,3]

Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics[1], Public Health and Sciences[2], Surgery and Bioengineering[3]. Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Objective: A novel Medos Deltastream DP3 pulsatile ECLS system has been used in clinical practice in Europe. The objective of this study was to evaluate the performance of this system on the hemodynamic energy output and pulsatility in a simulated adolescent ECLS model.

Methods: The experimental ECLS circuit consisted of Medos Deltastream DP3 pump head and console, Medos Hilite 7000 LT oxygenator, 19Fr Bio-Medicus One Piece Femoral Arterial Cannula, 3/8-in ID x 6 feet of venous tubing and 3/8-in ID x 5 feet of arterial tubing, primed with Ringer's Lactate and packed red blood cells (HCT 33%). All trials were conducted at flow rates of 2 - 5 L/min (1 L/min increments) with speed differential values 1000 rpm, frequency 60 - 90 bpm (10 bpm increments) and systolic/diastolic ratio 30%, 50% and 70% at 36°C. Real-time pressure and flow data were recorded using a custom-made data acquisition system and Labview software.

Results: In this ECLS system, non-pulsatile did not create surplus hemodynamic energy (**SHE**). Higher SHE was recorded at the pre-oxygenator site under the pulsatile mode with varying frequencies and systolic/diastolic ratios (**Figure 1**). Pulsatile flow generated more total hemodynamic energy (**THE**) at the pre-oxygenator and the pre-cannula sites and at all flow rates, regardless of pulsatile settings. Pulsatile settings of frequency and systolic/diastolic ratio did not affect oxygenator and arterial cannula pressure drops.

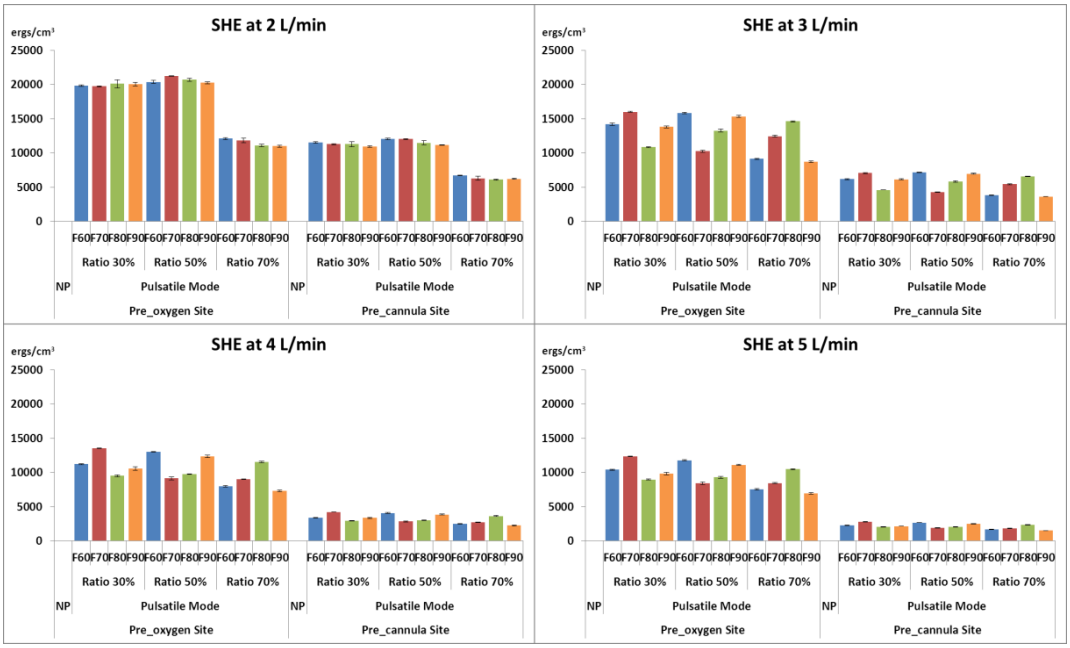


Figure 1. SHE at different pulsatile settings and flow rates.

Conclusions: The novel Medos Deltastream DP3 diagonal pump can generate non-pulsatile and pulsatile flow without backflow in a simulated adolescent ECLS model. Pulsatile flow provided more SHE and THE. The pulsatile settings of frequency and systolic/diastolic ratio could affect SHE.

P5. Hemodynamic Energy Change Depends on Position of Patients during Extracorporeal Circulation

[1]Chi Bum Ahn, PhD, [3]Kuk Hui Son, MD, [1,2]Sung Ho Lee, MD, [1,2]Ho Sung Son, MD, [1,2]Jae Seung Jung, MD, [1,2]Kyung Sun, MD.

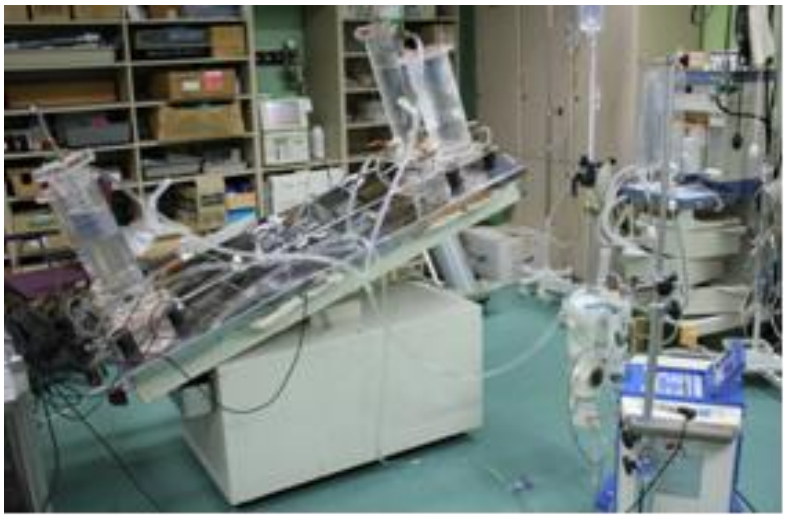
1. Korea Artificial Organ Center; 2. Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea; 3. Department of Thoracic and Cardiovascular Surgery, College of Medicine, Gachon University, Incheon, Korea.

Objective:

Most patients in the intensive care unit assisted with the extracorporeal circulation (ECC) are nursed in the semi-recumbent position, resting at an angle of 30–45°. This choice of resting position helps prevent of ventilator-associated pneumonia. We evaluated that this semi-recumbent position could affect hemodynamic energy.

Methods:

Extracorporeal circulation was constructed for Donovan mockup system using a pulsatile pump (Twin-Pulse Life Support). The pump flow was set as 2, 3, 4 L/min. The mean arterial pressure (MAP, mmHg), mean arterial flow (MAF, L/min), energy equivalent pressure (EEP, mmHg), percent EEP, and surplus plus hemodynamic energy (SHE, ergs/cm^3) at the descending thoracic aorta were measured on supine position and semi-recumbent (Semi-) position (20° of head up position).



Results:

MAP and MAP of the aorta were increased at semi-recumbent position (**Table 1**). EEP was increased at semi-recumbent position, though %EEP was decreased. SHE was also decreased at semi-recumbent position.

Table 1. Change of the hemodynamic energy depend on position.

	Head-up position					Head-down position				
	MAP	MAF	EEP	%EEP	SHE	MAP	MAF	EEP	%EEP	SHE
2L	101.702	1.267	103.865	2.127	2880.963	101.313	1.225	103.327	1.988	2682.543
Semi-	93.273	1.183	95.515	2.404	2987.015	106.310	1.311	108.214	1.790	2535.252
3L	100.897	1.719	104.145	3.220	4327.421	100.291	1.678	103.121	2.822	3769.566
Semi-	93.905	1.625	97.265	3.578	4475.813	104.302	1.803	106.919	2.509	3485.218
4L	100.460	2.283	105.014	4.534	6066.406	99.842	2.219	104.568	4.734	6295.170
Semi-	93.275	2.140	98.131	5.207	6469.054	108.633	2.318	113.463	4.446	6433.943

Conclusions:

Position change could effect on hemodynamic energy. For proper delivery of hemodynamic energy, position change should be considered during ECC.

P6. In Vitro Performance Analysis of Novel Pulsatile Diagonal Pump in Simulated Pediatric Mechanical Circulatory Support System

Shigang Wang, MD* and Akif Ündar, PhD*†

Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA*

Background: The objective of this study was to evaluate the pump performance of the third-generation Medos Deltastream DP3 on hemodynamic profile and pulsatility in a simulated pediatric mechanical circulatory support system.

Methods: The experimental circuit consisted of a Medos Deltastream DP3 pump head and console (MEDOS Medizintechnik AG, Stolberg, Germany), a 14Fr Terumo TenderFlow Pediatric arterial cannula, a 20Fr Terumo TenderFlow Pediatric venous return cannula, 1/4-in ID x 3 feet tubing plus 1/4-in x 8 in connection tubing for both arterial and venous lines. Trials were conducted at flow rates ranging from 250 ml/min to 1000 ml/min (250 ml/min increments) and rotational speeds ranging from 1000 rpm to 4000 rpm (1000 rpm increments) using human blood (HCT 40%). The post-cannula pressure was maintained at 60 mmHg by a Hoffman clamp. Real-time pressure and flow data were recorded using a Labview-based acquisition system.

Results: The pump could provide adequate non-pulsatile and pulsatile flow, create more hemodynamic energy under pulsatile mode, and generate higher positive and negative pressures when clamping both sides of the pump head, respectively. After the conversion from non-pulsatile to pulsatile mode, the flow rates and the rotational speeds also increased.

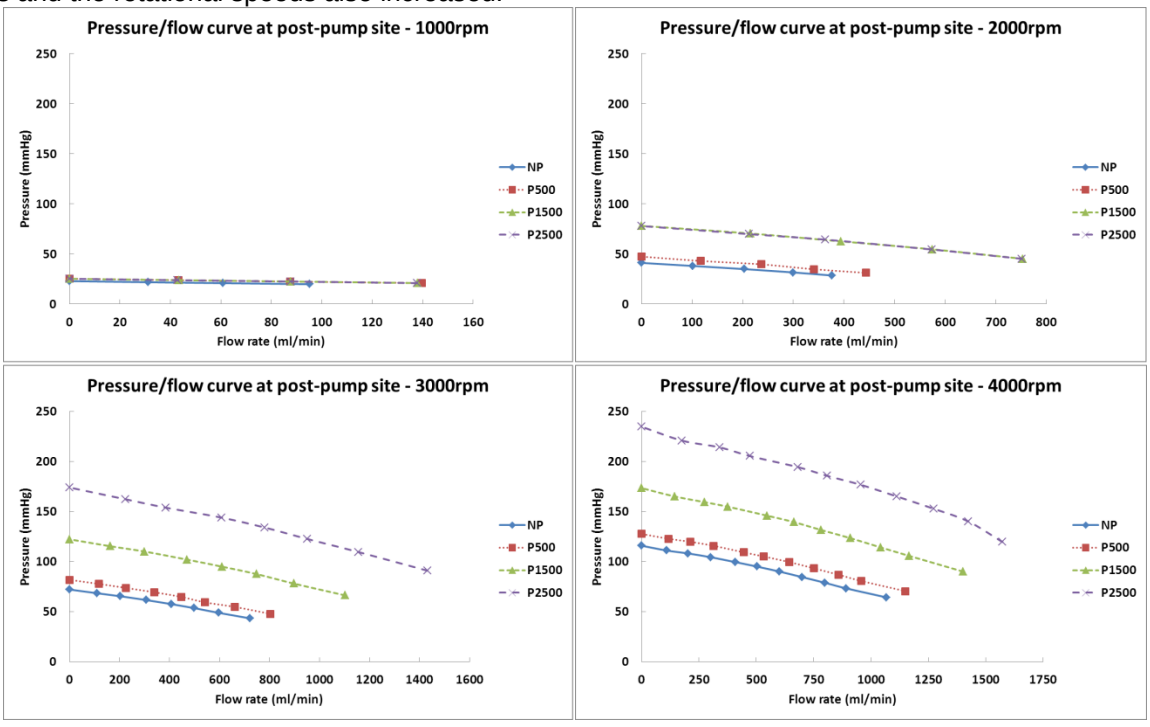


Figure 1. Pressure/flow curves (Post-pump site) under pulsatile (P) and nonpulsatile (NP) modes.

Conclusions: The novel Medos Deltastream DP3 diagonal pump is able to supply the required flow rate for pediatric MCS, generate adequate quality of pulsatility without backflow, and provide extra surplus hemodynamic energy output in a simulated pediatric MCS system.

P7. Impact of Pulsatile Flow Settings on Hemodynamic Energy Levels Using the Novel Diagonal Medos DP3 Pump in a Simulated Pediatric ECLS System

Pelumi Adedayo, MS*, Shigang Wang, MD* and Akif Ündar, PhD*†

Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA*

Background: The objective of this study was to evaluate the pump performance of the novel diagonal Medos Deltastream DP3 pump under non-pulsatile to pulsatile mode with varying differential speed values in a simulated pediatric Extracorporeal Life Support (ECLS) System.

Methods: The experimental circuit consisted of a Medos Deltastream DP3 pump head and console, a Medos Hilite 2400 LT hollow fiber membrane oxygenator, a 14Fr Medtronic DLP arterial cannula and a 20Fr Terumo TenderFlow Pediatric venous return cannula. Trials were conducted at flow rates ranging from 500 ml/min to 2000 ml/min (500 ml/min increments) and differential speed values ranging from 500 rpm to 2500 rpm (500 rpm increments) using human blood (HCT 35%). The post-cannula pressure was maintained constantly at 60 mmHg. Real-time pressure and flow data were recorded using a custom-made data acquisition system and Labview software.

Results: Under all experimental conditions, pulsatile flow generated significantly greater energy equivalent pressure (EEP), surplus hemodynamic energy (SHE) and total hemodynamic energy (THE) compared to non-pulsatile flow. Under non-pulsatile flow, she was zero. Higher differential speed values generated greater EEP, she and the values. There was little variation in the oxygenator pressure drop and the cannula pressure drop in pulsatile flow, compared to non-pulsatile flow.

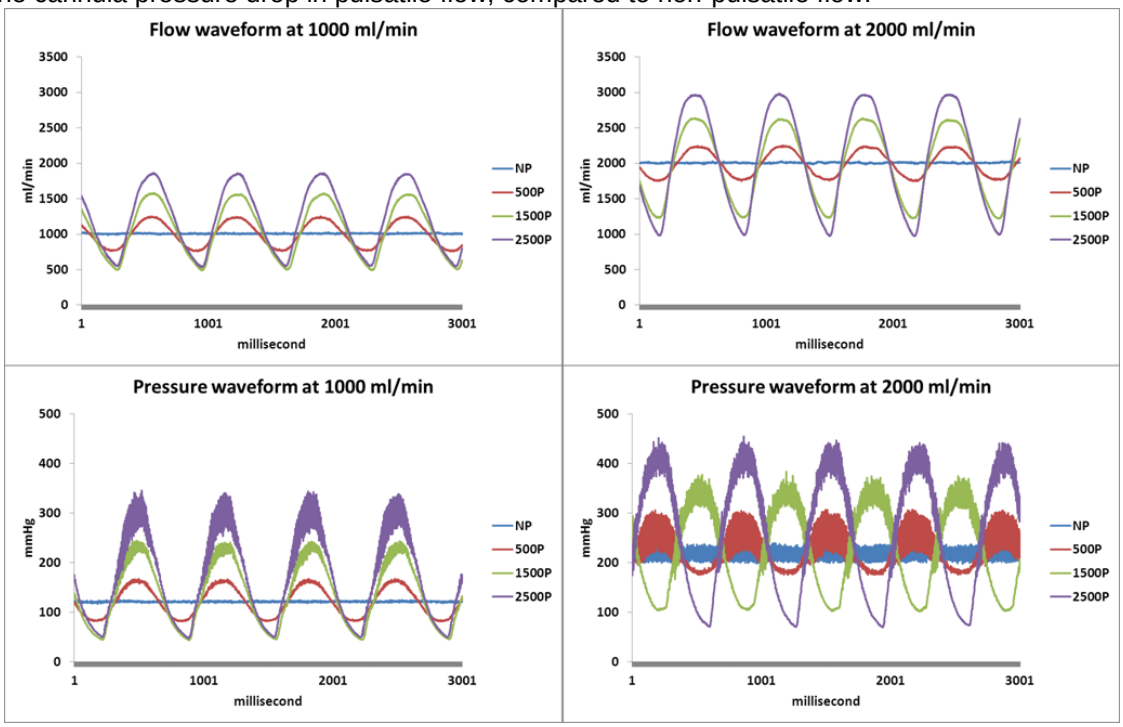


Figure 1. Flow and pressure waveforms at pre-oxygenator site.

Conclusions: The novel Medos Deltastream DP3 diagonal pump is able to generate physiological quality of pulsatile flow, without backflow. With increased differential rpm, the pump generated greater EEP, SHE and THE.

P8. A Rare Reason of Right Ventricular Failure: The Decortication Requiring because of Constructive Pleuritis at Redo Case who had Tetralogy of Fallot

Turkoglu H., Sarıtas T*., Alkan-Bozkaya T., Gunluoglu MZ**., Oktem S., Ersoy C., Karaaslan P[a]., Gökay Vural B[a]., Akcevin A.***

Istanbul Medipol University Hospital, Dept. of Cardiovascular Surgery, Pediatric Cardiology, Thoracic Surgery**, Dept. of Pediatric Pulmonology***, Dept. of Anestesiology[a], Istanbul, TURKEY*

Constrictive pleuritis is rare reason of pulmonary hypertension and right ventricular failure after cardiac surgery.

9-year-old boy with Down's syndrome on whom total correction operation of TOF had been performed in another country 8 months ago was referred to our clinic for the correction of residual VSD, complete AV block and left- sided massive pleurisy

After insertion a temporary pacemaker, in diagnostic cardiac catheterization, it was seen that the left lung was not expanded.

Residual VSD was closed with a patch through the right atrium with CPB on the patient whose mean pulmonary artery pressure was 30 mmHg, and the mean systemic pressure was 70 mmHg.

Septate massive pleural septas were drained by being cut in the case during which simultaneously dual-chamber pacemaker implantation of epicardial lesion was performed.

It was seen in cardiac catheterization of the patient whose certain signs of heart failure continues according to the echocardiographic examination and findings of tachypnea and edema continues that left lung still could not be expanded, therefore divisions of the left pulmonary artery especially in the upper and middle parts were not filled with opaque material.

On the patient of whom the average pulmonary artery pressure was 35 mmHg and average systematic pressure was 62 mmHg it was decided to do decortication by the council.

After the decortication it was found that the echocardiographic signs of right congestive heart failure and edema decreased significantly.

As a result, the constrictive pleuritis is a rare cause of pulmonary hypertension and right congestive heart failure. The clinic may improve dramatically after the effective surgical lung decortication.

P9. In Vitro Evaluation of Medos Deltastream DP3 Pulsatile ECLS System

Shigang Wang, MD[1], Allen R. Kunselman, MD[2], and Akif Ündar, PhD[1,3]

Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics[1], Public Health and Sciences[2], Surgery and Bioengineering[3]. Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Background: A novel Medos Deltastream DP3 pulsatile ECLS system has been used in clinical practice in Europe. The objective of this study was to evaluate the performance of this system on hemodynamic efficiency and pulsatility in a simulated ECLS model for adolescent patients.

Methods: The experimental ECLS circuit consisted of Medos Deltastream DP3 pump head and console, Medos Hilite 7000 LT oxygenator, 19Fr Bio-Medicus One Piece Femoral Arterial Cannula, 21Fr Bio-Medicus One Piece Femoral Venous Cannula, 3/8-in ID x 6 feet of venous tubing and 3/8-in ID x 5 feet of arterial tubing, primed with Ringer's Lactate and packed red blood cells (HCT 35%). All trials were conducted at flow rates of 2 - 5 L/min (1 L/min increments) with speed differential values 500 rpm, 1000 rpm and 1500 rpm at 36°C. Real-time pressure and flow data were recorded using a custom-made data acquisition system and Labview software.

Results: Under pulsatile mode, Medos DP3 generated significantly greater energy equivalent pressure (EEP), surplus hemodynamic energy (SHE) and total hemodynamic energy (THE) than non-pulsatile mode. Under nonpulsatile mode, SHE was zero. Higher differential speed values created greater EEP, SHE and THE values. The flow rates, revolution speeds and oxygenator pressure drops did not change with increasing speed differential values. Figure 1 presents flow and pressure waveforms.

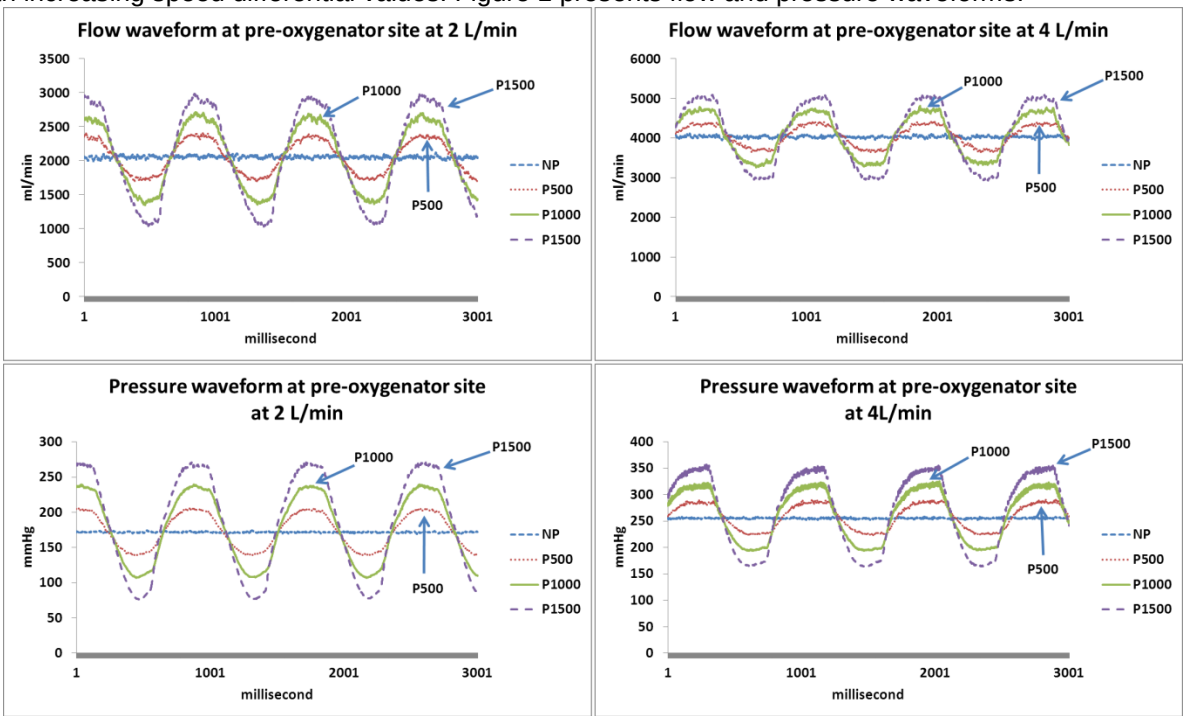


Figure 1. Flow and pressure waveforms at different pulsatile settings.

Conclusions: The Medos Deltastream DP3 diagonal pump can provide nonpulsatile flow and physiologic quality pulsatile flow without backflow in a simulated ECLS system for adolescents. Medos Hilite 7000 LT performed exceptionally well with regards to trans-membrane pressure gradient and hemodynamic energy delivery. The Medos Deltastream DP3 ECLS system is capable of clinical needs for adolescent heart and lung circulatory supports.

P10. Evaluation of Capiox and Quadrox-i Hollow Fiber Membrane Oxygenator in a Simulated CPB Circuit for Adolescents

Shigang Wang, MD[1], Allen R. Kunselman, MD[2], and Akif Ündar, PhD[1, 3]

Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics[1], Public Health and Sciences[2], Surgery and Bioengineering[3]. Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Background: The Capiox RX25 and Quadrox-i Adult oxygenators are commonly used in clinical CPB circuits. This study was designed to test the effectiveness of two oxygenators in order to evaluate gaseous microemboli (GME) trapping capability and hemodynamic performance for adolescent patients.

Methods: A simulated CPB circuit was used and primed with Ringer's Lactate and packed red blood cells (HCT 25%). All trials were conducted at flow rates of 2 - 5 L/min (1 L/min increments) with a closed and open arterial filter purge line at 36°C. The post-cannula pressure was maintained at 100 mmHg. After 5 cc of bolus air was introduced into the venous line, an Emboli Detection and Classification (EDAC) system was used to detect and classify GME at the pre-oxygenator, post-oxygenator and pre-cannula sites. At the same time, real-time pressure and flow data were recorded and hemodynamic energy was calculated using a custom-made data acquisition system and Labview software.

Results: Our results showed that the Quadrox-i oxygenator pressure drops were lower than Capiox at all flow rates. The Quadrox-i oxygenator retained more hemodynamic energy across the oxygenator. Two oxygenators could trap the majority of GME, but Capiox did better than the Quadrox-i oxygenator. No GME was delivered to the pseudo patient at all flow rates in Capiox group. The Capiox venous reservoir could capture more GME at lower flow rates, while Quadrox-i venous reservoir performed better at higher flow rates. An open arterial filter purge line reduced slightly GME in Capiox group, but GME increased in Quadrox group.

Table 1. GME counts under a closed or open arterial filter purge line at different sites.

Flow rate	Oxygenator	Purge line	Pre-oxygenator		Post-oxygenator		Pre-cannula	
			Total	>40μm	Total	>40μm	Total	>40μm
2L/min	Capiox	Closed	3±2	0±0	1±1	0±0	0±0	0±0
		Open	3±0	0±0	0±0	0±0	0±0	0±0
	Quadrox-i	Closed	104±13	7±3	3±2	0±0	0±0	0±0
		Open	111±16	6±2	10±5	0±1	0±0	0±0
3L/min	Capiox	Closed	84±6	1±1	0±0	0±0	0±0	0±0
		Open	61±7	1±1	0±0	0±0	0±0	0±0
	Quadrox-i	Closed	209±38	26±6	36±12	2±2	4±2	0±0
		Open	305±37	39±14	64±19	3±1	5±2	0±0
4L/min	Capiox	Closed	234±24	5±3	0±0	0±0	0±0	0±0
		Open	181±11	3±2	0±0	0±0	0±0	0±0
	Quadrox-i	Closed	95±19	12±4	26±10	2±1	2±1	0±0
		Open	152±33	17±4	27±5	2±1	5±2	0±0
5L/min	Capiox	Closed	388±21	15±5	0±0	0±0	0±0	0±0
		Open	327±11	8±3	0±0	0±0	0±0	0±0
	Quadrox-i	Closed	95±15	14±4	37±11	4±3	8±3	0±0
		Open	109±18	12±5	28±14	3±1	5±2	0±0

Conclusions: Quadrox-i Adult oxygenator is a low-resistance, high-compliant oxygenator. The GME handling ability of Capiox RX25 performed well in our simulated CPB model for adolescent patients. Further optimized design for the venous/cardiotomy reservoir is needed.

P11. MIFS (Minimal Incision Full Sternotomy) in Pediatric Cardiac Surgery Indications, Technique and Results

Ersoy C., Alkan-Bozkaya T., Akcevin A., Türkoğlu H.

Istanbul Medipol University, Dept. of Cardiovascular Surgery, Istanbul, TURKIYE

Objective:
The size of incision in the cardiac surgery was decreased with the new techniques especially video-assisted operations and robotic surgery. Alternative operative approaches also became widely used with improved cosmetic results and high degree of safety.

Methods:
Between January 2000 to January 2013, we operated 318 pediatric patients who had cardiac surgery using cardiopulmonary bypass via MIFS, in 2 clinics; VKV American Hospital and Medipol University Hospital. Age range: 4 months to 15 years (median age: 6yrs). Cases were: ASD (n=171), VSD (n=98), AVSD (n=21) and others (n=28). Mean X-Clamp time was 21 min 815-61 min). Range of ICU and hospital stay were 1-2 and 2-4 days. Incision sizes were 3-8 cm (mean 4 cm). Average follow up time was 48 months.

Results and Conclusions:
There was no serious intraoperative complication regarding to cannulation, bleeding or exposure. There was no hospital morbidity, except one case who was taken to reoperation because of recurrent VSD via conventional full sternotomy. MIFS seems to be provides less pain, excellent cosmetic results and much more comfortable hospitalization for the pediatric patients without any special instruments. Durations of ICU and hospital stay were shorter according to who had operated with conventional methods ($p<0.05$).

P12. Postoperative Cerebral Perfusion Monitoring with NIRS in Pediatric Patients Undergoing Cardiac Surgery

Alkan-Bozkaya T., Karaaslan P*., Gökay Vural B*., Türkoğlu H., Akçevin A., Ersoy C., Ündar A**.

Istanbul Medipol University, Dept. of Cardiovascular Surgery and Anestesiology, Istanbul, TURKEY and Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA***

Objective: Although there are improvements in mortality, postoperative neurological morbidity remains a significant problem after neonatal cardiac surgery with cardiopulmonary bypass (CPB) because of cyanosis, increased cerebral vascular resistance and low cardiac output. We followed regional cerebral oxygen saturation index (rSO2i) with near-infrared spectroscopy (NIRS) in a heterogeneous group of pediatrics for the possible cerebral desaturation in the postoperative period and determined if this places them at risk for adverse outcomes.

Methods: We began using routine noninvasive cerebral monitoring in the form of near infrared cerebral cortical spectroscopy (NIRS) in pediatric patients who underwent cardiac surgery with CPB and aortic coarctation w/wo aortic arch reconstruction. A NIRS sensor (5100 C, INVOS, MI, USA) was placed on the right forehead of patients for 48 hours postoperatively. rSO2i was recorded in one minute intervals by a computerized data collection system. Patients were classified into those with cyanotic vs. those with acyanotic group who had complete anatomic repair. All of patients were categorized according to the Jenkins risk stratification. Database from all patients in each group were collected and analyzed using t-test and chi-square for between groups comparisons, and Pearson Correlation to test strength of associations within groups of pulse oximeter saturation (SpO2) and rSO2i with $p<0.05$ significant.

Results: Between May 2012 to date, 146 pediatric patients who underwent congenital heart surgery were included into the study. Ages ranged from 2 days to 156 months (median 18 months). NIRS data measured perioperatively; after induction, X-Clamp time, off CPB time, POD1 (first 2 hrs), after extubation time and and POD2 (48 h). Cases were divided into two groups: 51 of them were cyanotic including 15 Single Ventricle (1V) patients and 36 biventricular repair (2V) patients (10 with d-transposition of the great arteries who underwent arterial switch operation). 96 of the patients were acyanotic including aortic arch pathology (14 AoCoA, 3 IAA; 2 of them had also ASD-VSD and 2 Double aortic arch). NIRS database showed that the mean postoperative rSO2i was higher in the two ventricle (2V) group (71%±7 vs. 45%±5, $p<0.001$). 72% of the single ventricle rSO2i values were 50% or below, and 25% of values were 40% or below; versus only 12% of values 50% or less, and only 0.1% below 40% in the two ventricle patients ($p<0.001$) rSO2i exhibited a positive correlation with SpO2 in the SV group (Pearson correlation 0.25, $p<0.001$), and a negative correlation with the 2V group (Pearson –0.20, $p<0.001$). All patients survived to hospital discharge except 3 with HLHS who undergone the Norwood procedure, those 3 patients and 2 of 2V patients had depressed level of consciousness and seizures. There were ischemic changes in basal ganglia and cortex on MRI; all of these patients had low NIRS values (rSO2i <50%) in the 48 hours perioperatively. No neurologic deficit when followed up by Pediatric Neurology. Results were confirmed by the EEG screening perioperatively in all patients who were undergone CPB or arch repair operation. Pulsatile perfusion mode was used to all patients who had undergone CPB.

Conclusions: The threshold for low rSO2i values associated with neurological dysfunction is estimated to be 40%. In cyanotic group with single ventricle pathology, the majority of postoperative rSO2i values was below 50%. Very low rSO2i may be associated with the frequent appearance of new hypoxic-ischemic brain lesions seen on postoperative MRI.

P13. Using a Secondary Reservoir for Pump Suckers to Avoid the Generation of Foam during CPB Procedures in Pediatric Patients

Akif Ündar, PhD[1,2], David Palanzo, CCP[1,3] , Robert Wise, CCP[1,3], Larry Baer, CCP[1,3] and Shigang Wang, MD[1]

Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics[1], Surgery and Bioengineering[2], Perfusion Department, Penn State Heart and Vascular Institute[3], Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Translational research is a must when evaluating different oxygenators, pumps, cannulae, etc. for the safety of pediatric as well as adult cardiopulmonary bypass (CPB) patients (1). The primary goal of "translational research" is to take research from the "bench-to-bedside".

Selection of the components of the circuitry should be based solely on scientific evidence. Translational research must be done at independent institutions with no financial or any other benefit from their research projects other than selecting the safest products for their patients. As a routine practice at Penn State Hershey Children's Hospital, every single new CPB component is evaluated at the Pediatric Cardiovascular Research Center prior to using them in patients (1,2). Direct comparisons are made with current devices in identical clinical settings in order to evaluate new products. Of course, all these devices are approved by the Food and Drug Administration (FDA) for clinical use, but the variability among these devices is not small at all. The cost of an oxygenator or a centrifugal pump-head may play a significant role in the decision-making process, but it is already documented that the price of a device does not "always" correlate well with the performance (3). So, the less expensive disposable device may have better scientific results. Therefore, translational research is a must, not an option, in particular for the safety of neonatal and pediatric cardiac patients undergoing CPB procedures as well as cost savings for the institutions.

Recently, a few pediatric centers found the incidents of foam breaking through from the cardiotomy reservoir in the venous reservoir when using certain types of pediatric oxygenators, when extreme sucker and vent return was required (4). We would suggest an approach that may eliminate this particular problem for neonatal and infantile patients, not just for these particular oxygenators, but for all other oxygenators with similar mismatches of flow rate between the oxygenator and the cardiotomy reservoir. We would suggest incorporating a secondary cardiotomy reservoir for pump suckers to avoid the foam from entering the venous reservoir. There will be a very small additional cost ($100) for a second reservoir, but this may be necessary for the safety of the patient. If the patient weight is below 12 kg, we use a secondary reservoir for pump suckers as a routine practice at Penn State Hershey (**Figure 1**). We started using this secondary reservoir over nine years ago when we noticed the same problem with a different oxygenator. Since then, we have always used a secondary reservoir, in particular for neonates and infants, although we have also changed the oxygenator. We have never seen these types of events after adding the secondary reservoir for pump suckers. We believe that the secondary reservoir is a necessity for minimizing not only microemboli counts, but also systemic inflammation during CPB for neonates and infants.

In summary, it is impossible to eliminate microemboli generation during pediatric and adult CPB, but translational research may significantly help to reduce the microemboli (1,5,6). We strongly recommend using a secondary reservoir, solely for pump suckers, to avoid the generation of foam during CPB procedures.

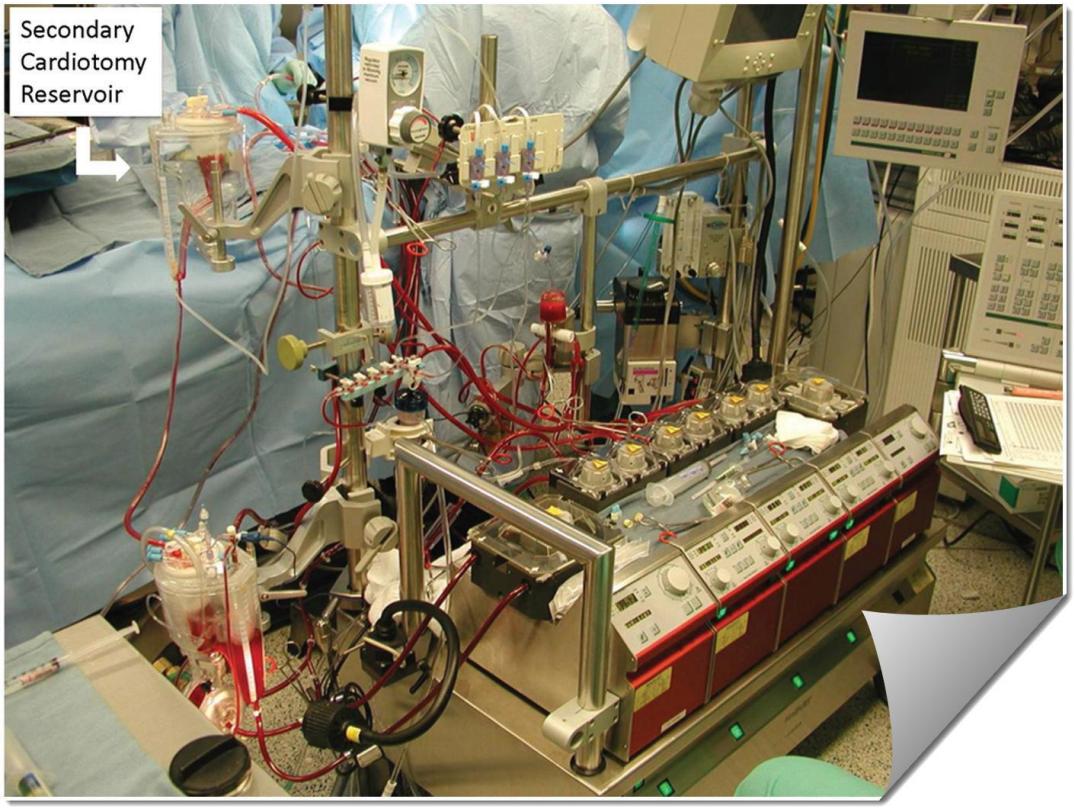


Figure 1. Penn State Hershey clinical CPB circuitry, including secondary cardiotomy reservoir for pump suckers.

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P14. Monitoring Biomarkers after Pediatric Heart Surgery: A New Paradigm on the Horizon

***Mehmet Aĝirbaşli, MD and †Akif Ündar, PhD**

**Department of Cardiology, Marmara University, Istanbul, Turkey; †Penn State Hershey Pediatric Cardiovascular Research Center, Department 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, PA, USA*

Until recently, risk scoring systems for adult patients consisted of only clinical criteria. Currently, we are experiencing an abundant surge of literature integrating a wide range of biomarker arrays to clinical criteria in assessing the risk in an adult (Table 1).

In fact, novel risk scoring systems such as Reynolds criteria have emerged by combining the validated biomarkers to the traditional risk factors. Novel biomarkers potentially improve clinical management of cardiovascular disease, but there are gaps in understanding their role during childhood. The reason might be related to relatively lower prevalence of cardiovascular disease in children compared to the adult population.

One exceptional group is the children with congenital heart disease. Recent studies indicate that novel biomarkers can alert the clinician in a timely manner about neurological and myocardial injury and their inflammatory consequences. Current technologies enable us to measure several biomarkers using only a few microliters of plasma.

The preliminary studies show that novel biomarkers in addition to the traditionally studied biomarkers can help the clinician to identify children at high risk following pediatric heart surgery. Future studies are needed to confirm the role of biomarkers in monitoring children after cardiopulmonary bypass.

TABLE 1. *Examples of biomarkers related to organs and systems*

Early biomarkers of myocardial injury	Heart fatty acid-binding protein (FABP), pregnancy-associated plasma protein A (PAPP-A), myeloperoxidase (MPO)
Conventional biomarkers of myocardial injury	Creatine kinase myocardial band (CK-MB), myoglobin, troponin I, troponin T
Traditional biomarkers of neurological injury	Creatine kinase brain band (CK-BB), neuron-specific enolase (NSE), and S100β protein
Novel biomarkers of neurological injury	Ubiquitin C-terminal hydrolase 1 (UHCL1), phosphorylated axonal neurofilament heavy chain (pNF-H), tissue plasminogen activator (t-PA), plasminogen activator inhibitor 1 (PAI-1) (7,14), glial fibrillary acidic protein (GFAP)
Biomarkers expressed in the vascular wall	Interleukin (IL)-6, monocyte chemotactic protein (MCP-1), tumor necrosis factor (TNF)-α, IL-18, IL-10, C-reactive protein (CRP), serum amyloid A (SAA), complement 3, fibrinogen, matrix metaloproteinase (MMP) 1,2,9, PAPP-A, type III collagen, tissue factor, PAI-1, von Willebrand factor (vWF), D-dimer, sCD40 ligand, IL-8, P-selectin, adhesion molecules, MPO
Biomarkers related to inflammation	CRP, B2 microglobulin, CD40, CD40 ligand, complement 3, EN-RAGE, ferritin, adhesion molecules (ICAM-1, VCAM), immunoglobulin (Ig) A, G, M, IL-1,6,8,12,16,18, MMP, TNF-α
Biomarkers related to thrombosis	PAI-1, factor VII, fibrinogen, tissue factor, vWF
Biomarkers related to oxidative stress	Glutathione S transferase, A-1 antitrypsin, IL-2,4,5,15, haptoglobin
Biomarkers related to heart failure	Brain natriuretic peptide (BNP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), TNF-α, MMP2, 9, tissue inhibitor of metalloproteinase 1 (TIMP1), troponin I, troponin T

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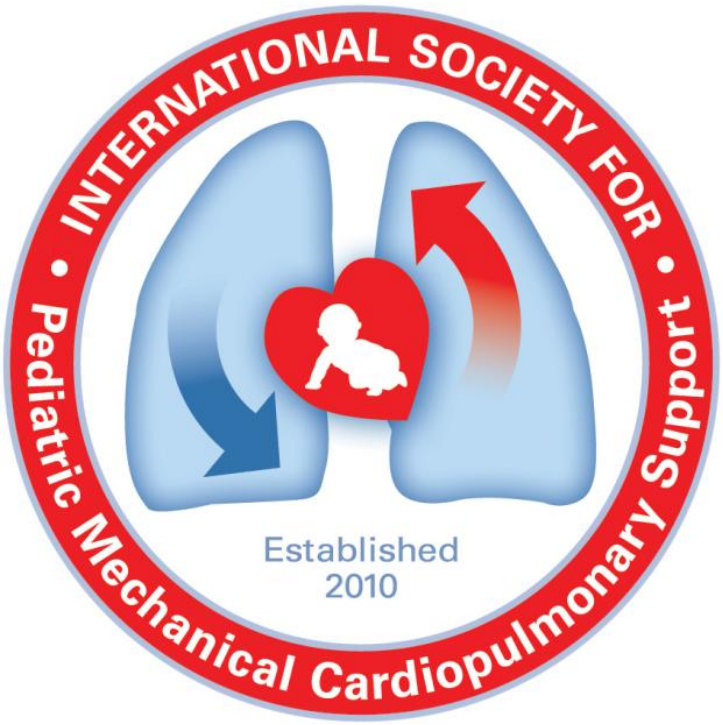

The mission of this society is to focus on the current problems associated with pediatric cardiac patients during and after acute or chronic cardiac support. The society will bring together as many distinguished clinicians, bioengineers, and basic scientists as possible to precisely define current problems and suggest novel approaches and solutions.

Our motto continues to be:

IF THE COURSE OF JUST ONE CHILD'S LIFE IS IMPROVED AS A RESULT OF THIS SOCIETY, WE HAVE REACHED OUR GOAL.

Akif Ündar, PhD, Founder and President

International Society Web Site: http://www.cvent.com/d/7cqc1m