

CONFERENCE PROCEEDINGS

Volume 7, May 2011



The Proceedings of the Seventh International Conference on

Pediatric Mechanical Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion

Akif Ündar, PhD, Editor

May 5-7, 2011, The Hall of Flags, University of Pennsylvania & The Children's Hospital of Philadelphia, Philadelphia, PA, USA

Planning /Scientific Committee:

Conference Founder
Akif Ündar, PhD

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

**The Children's Hospital of
Philadelphia**

Chitra Ravishankar, MD (Chair)
William J. Gaynor, MD (Co-Chair)
Gil Wernovsky, MD (Co-Chair)

**Penn State Hershey Pediatric
Cardiovascular Research Center**

Larry D. Baer, CCP (Co-Chair)
J. Brian Clark, MD (Co-Chair)
John L. Myers, MD (Co-Chair)
Akif Ündar, PhD (Co-Chair)



TABLE OF CONTENTS

Welcome.....	2
Facts and Myths Surrounding Pediatric MCS Research.....	4
International Faculty, Moderators & Wet Lab Instructors.....	8
Conference Supporters.....	9
Final Scientific Program.....	10
International Scientific Committee.....	28
Abstracts.....	32
Index of Authors.....	118

Welcome to the Seventh Annual Event

Akif Ündar, PhD,¹ Chitra Ravishankar, MD,² William J. Gaynor, MD,³ Larry D. Baer, CCP,¹ Joseph Brian Clark, MD,¹ Gil Wernowsky, MD,² John L. Myers, MD¹

¹Penn State Hershey Pediatric Cardiovascular Research Center, Department of Pediatrics, Department of Surgery, and Department of Bioengineering, Penn State Milton S. Hershey Medical Center, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

²Division of Pediatric Cardiology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

³Division of Pediatric Cardiothoracic Surgery, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

On behalf of the organizing committee, we are pleased to welcome you to the *Seventh International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion at the Hall of Flags at University of Pennsylvania and Children's Hospital of Philadelphia* in Philadelphia, Pennsylvania. Chitra Ravishankar, MD will be the scientific chair of the conference. The scientific co-chairs of the pediatric event will be Larry D. Baer, CCP, Joseph Brian Clark, MD, William J. Gaynor, MD, John L. Myers, MD, Akif Ündar, PhD, and Gil Wernowsky, MD.

This year's meeting will commence with registration on Wednesday, May 4, 2011. Formal presentations including a keynote lecture, invited lectures, and slide and poster presentations will begin on Thursday morning May 5, 2011 and continue through Saturday evening May 7, 2011. This year, conference participants will have the distinct pleasure of hearing Dr. Leonard L. Bailey, Surgeon-in-Chief at Loma Linda University Children's Hospital, deliver the keynote speech. Platform presentations will take place in two-hour blocks during the morning and afternoon sessions on Thursday, Friday, and Saturday. Additional slide and poster presentations will be chosen from submitted abstracts.

Plenary sessions will be held throughout the conference focusing on topics including *Pediatric VAD support: unique features and outcomes* (led by Co-Chairs Nancy Ghanayem, MD and Chitra Ravishankar, MD), *Anticoagulation: challenges in*

neonates and children (led by Co-Chairs David R. Jobes, MD and Leslie Raffini, MD, *E-CPR* (led by Vinay M. Nadkarni, MD), *Challenges at the bedside with ECMO and VAD* (led by Sarah Tabbutt, MD, PhD, and James T. Connelly, MD), *Outcomes of pediatric cardiac surgery* (led by John L. Myers, MD), *Pediatric Perfusion* (led by Talya Frey, CCP and Larry Baer, CCP), and *Bioengineering approaches in pediatric cardiovascular medicine* (led by Akif Ündar, PhD).

Two additional special sessions on Friday afternoon at the Children's Hospital of Philadelphia will be added to this year's program:

1) ECLS Simulation (led by Stacie B. Peddy, MD and Marc A. Priest, CCRN): This session is for ICU physicians, CT surgeons, nurses, and perfusionists involved in ECMO cannulation and management. It will use the ECMO simulator to teach hands on training for ECPR. In addition, the session will focus on training residents/fellows and nurses for a successful ECMO program as well as techniques to build a simulator program.

2) Tour of CHOP and ICU Rounds (led by Gil Wernowsky, MD, Antonio Mott, MD and Roxanne Kirsch, MD): This session will be suitable for all staff involved in the management of critically ill children with heart disease. It will include a tour of the unit and discussions regarding resources and staffing requirements. Each interactive session will welcome active participation from attendees regarding all aspects of management and outcomes.

This year's meeting will also include "hands-on" perfusion sessions (led by Larry Baer, CCP, David Palanzo, CCP and Talya Frey, CCP) on Friday afternoon, May 6, 2011.

The Children's Hospital of Philadelphia designates this live activity for a maximum of 21.0 AMA PRA Category 1 Credits T. This program has been approved for 21.0 Category 1 CEU hours by the California Board of Registered Nursing and 25.2 Category 1 CEU hours by the American Board of Cardiovascular Perfusion.

The seventh event will comprise over 95 presentations, including invited lectures, slides, and posters. This year, we have the opportunity to once again publish all of the conference abstracts in the April 2011 issue of the peer-reviewed journal **Artificial Organs**. In addition, the November 2011 issue of **Artificial Organs** will be dedicated to manuscripts to be collected from the regular slide and poster presentations and peer-reviewed during the Seventh Conference. Our special thanks to Angela T. Hadsell, *Executive Editor*, and Paul S. Malchesky, DEng, *Editor-in-Chief*, for making this special issue possible.

Conference Awards

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

Second Annual Meeting of the Society

The second annual meeting of the International Society for Pediatric Mechanical Cardiopulmonary Support will be held in the Houston Hall at the University of Pennsylvania on May 6, 2011. This meeting will be for society members only.

All of the details regarding the Seventh Conference and Second Annual Meeting of the Society can be found at our conference website: <http://www.hmc.psu.edu/childrens/pedscpb/>

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. In addition, we received funds from the following companies (as of April 4, 2011):

Platinum Level:

Maquet Cardiovascular

Bronze Level:

Bellco S.r.l., Italy

Circulite, Inc.

Covidien

Impulse Monitoring, Inc.

Sorin Group USA

SnyCardia Systems, Inc.

St. Jude Medical

Terumo Cardiovascular Systems

Wiley-Blackwell

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

Acknowledgements

The authors personally thank Heather Stokes, Jennifer Stokes, RN, Jessica Beiler, MPH, Julie Vallati, Amy Shelly, RN and Erlee Meyers from the Pediatric Clinical Research Office of the Penn State Hershey Milton S. Medical Center for their assistance in coordination and management of this event. Special thanks go to Ann Hagan and Christina Mannices from the Department of Continuing Medical Education of the Children's Hospital of Philadelphia for their invaluable help for CME issues.

Facts And Myths Surrounding Pediatric Mechanical Cardiovascular Circulatory Support Research: A Personal Perspective – Part I

Akif Ündar, PhD

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

Introduction

The objective of this article is to inform the PUBLIC, the pediatric cardiovascular research community, and the members of the International Society for Pediatric Mechanical Cardiopulmonary Support (ISPMCS) on recent developments in translational research, new devices for chronic support, and the impact of industry on this underserved research area.

The following are well-known facts about congenital heart defects in our small but dedicated research community: 1) approximately one out of 100 babies are born with a congenital heart defect in the United States, 2) early detection with intervention result in increased survival and improved quality of life for these fragile patients, and 3) the annual cost for inpatient services is over \$2.2 billion (1). But, the following facts may be unknown not only to the public, but also to our community: [these facts are extracted via www.itsmyheart.org] (1)

Fact #1: *In the US, twice as many children die from congenital heart defects each year than from all forms of childhood cancers combined. Yet, funding for pediatric cancer research is five times higher than for congenital heart defects (source; Children's Heart Foundation) (1)*

Fact #2: *For every dollar provided by the National Institutes of Health, only one penny is allocated towards pediatric research. This means that only a fraction of that one penny will be directed towards congenital heart defect research (source; Children's Heart Foundation) (1)*

Based on these two lesser known facts, the focus of this article is to share my personal experiences with the academia, the industry, and the government on pediatric mechanical cardiopulmonary support research.

Although there are much better devices for acute and chronic cardiovascular patients compared to 5 to 10 years ago, morbidity and mortality for high-risk patients are still serious problems that clinicians face daily (2). Since the problem is multi-factorial, then the solution should be multi-disciplinary as well. This was the main reason why we have built an international multi-disciplinary research center, international conference, and finally an international society (2-6).

Translational Research

Our philosophy at Penn State Hershey Children's Hospital is that if there is more than one device for the same procedure, we should compare them and make our selection based on the scientific evidence. Every component of our cardiopulmonary bypass or extracorporeal life support circuitry has been evaluated in our center prior to using them in our patients (7, 8). We also share our clinical and experimental protocols with other centers (9, 10). During the past 10 months, members of our clinical team have trained 139 clinicians from 9 outside centers with our custom-made Penn State Hershey pediatric ECLS system using a piglet model (11). The results of this particular project made significant impacts on education and training of clinicians as well as cost savings for the hospital. Simply changing the disposable centrifugal pump head to a lower priced pump head with better hemodynamic

performance saved our institution over \$144,000 in nine months (12, 13). The end of this year's cash savings for the hospital will increase to approximately \$350,000 solely due to this project. Therefore, I believe that translational research not only helps to minimize the injury to these fragile high-risk patients, but also creates significant savings for hospitals and institutions around the globe.

Common Myth

The most common myth surrounding new pediatric circulatory devices is that the industry has very limited interest for pediatric devices due to the small population of pediatric cardiac patients compared to adult patients and the low profit potential. What I see every day is in direct contradiction to this myth that is unfortunately supported by some companies. Figure 1 shows the components of custom-made designs manufactured by the industry and several other companies who have reasonable R&D to improve upon their pediatric CPB, ECLS, and VAD products.

I will never forget the discussion between two industry representatives that took place at our first international conference in 2005 (<http://pennstatehershey.org/web/pedscpb/home>).

One representative justified the myth by simply stating that it was impossible to build a pediatric device (neonatal/infantile) because of the market size, etc. The other representative (at this time, I will use his name) was Johannes Müller, CEO from Berlin Heart. He not only displayed his company's final products comprised of pumps in all sizes for each pediatric population, but he also included the limitations of his devices in Europe. As everyone knows today, the wide use of Berlin Heart in the United States and other parts of the world has led to significant improvements in the outcomes of pediatric cardiac patients (14). Although issues with the device and with management of these patients continue to exist, it was the mentality of Johannes Müller and Berlin Heart that made this huge impact on pediatric cardiac patients for chronic support possible. On the contrary, instead of working on improving their devices, individuals including the other company representative continue to attack our international conference and international society with every possible means including "dictating letters" to clinicians who have significant financial interests with his company.

Government Support

Based on Facts #1 and #2, the first question that should be asked is: why do pediatric patients with worse outcomes receive less research funds from the government? I have no answer to that question, but I would personally ask how these limited funds from tax payers are used for pediatric cardiac patients. It is my opinion that every new device developed using government funds must show clear objectives how these devices will be better than what we currently use every day. If an investigator would develop a new oxygenator, a new ECLS system, or a new VAD comparisons should be made with the state-of-art devices we use every day (Figure 1) rather than making comparisons to outdated examples without any scientific rationale.

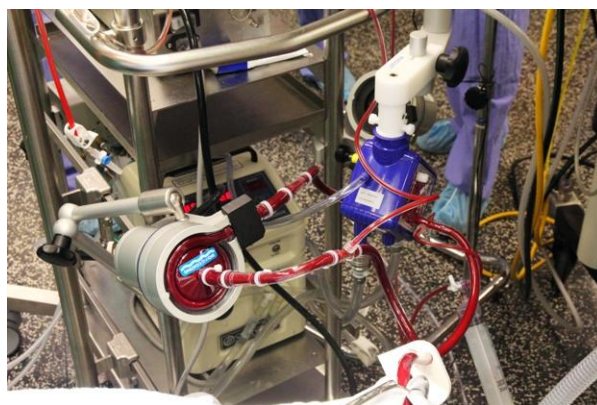


Figure 1. Penn State Hershey ECLS circuit using a piglet model

Below are a few of my personal experiences regarding how some of these funds have been used.

Example #1: One clinician approached me to collaborate on the development of a pediatric device with an industry partner. Although the offer was attractive, he could not respond to any of my basic questions concerning the device including scientific data, size, flow rates, perfusion modes, etc. At the end of our discussion, he told me that even though my questions were important, they were irrelevant for this matter; we will get this award because the company CEO is a long time friend of an individual who works for the government on this project. The following day, I declined his offer because I found no information about this company in the US, and I had another offer from a well-known research center with outstanding preliminary data.

What happened to the outcome of their grant? It was declined, and both the CEO and the clinician blamed me for their unsuccessful and unethical attempt because they thought I was one of the reviewers who rejected their grant. A few months later in a closed-door meeting, the same CEO approached me and asked if I was involved with their grant in any way. My answer was "how could I?" I was a collaborating investigator for another grant in the same project, and I had direct conflict of interest.

Example #2: A government employee once told me "universities just do research, but these companies (he mentioned the names of both companies) must get this funding for survival." It was obvious that this employee's understanding of research was way below his position and power. I tried explaining to him that his job is to support projects with the best potential of reaching clinical settings rather than rescuing companies. I clearly illustrated to him how the CPB and ECLS projects in our institution alone have made significant impacts on dozens of practices in pediatric heart centers throughout the US and around the globe. What was the result of this particular funding? As the employee stated, both companies received the funding.

Example #3: During a government sponsored "internal" grant competition, a CEO of the company utilized all his staff resources and scientific advisory board to help an employee of the government win the grant. This was unfair for the other participants who worked hard and competed for the grant in an ethical and honest approach without inappropriate influences from third parties. After this employee received the prestigious grant, the CEO proceeded to spread the word that his scientific committee had helped this employee with the internal application. What is going to happen if this company's product comes for approval at that particular agency? How will this employee's decision be affected; for the interest of the PUBLIC or for the interest of the company who unethically supported the preparation of the "internal" grant application?

Example #4: What I described earlier of a CEO's dictating letters to academicians was not a joke. When academicians cross the line from being independent investigators to company representatives or sales person, it is unfortunate that they can also write impartial letters to other

investigators solely for their own profit and financial interest.

As a researcher on pulsatile vs. non-pulsatile flow for the past 15 years, I have tried to follow the developments of new devices, especially those for pediatric cardiac patients. I had an opportunity to attend a lecture on pulsatile flow given by a well-known investigator when he visited an institution that has designed more pulsatile devices than any other institution. Although I have not read any publications regarding pulsatile flow from this investigator to that date, I was eager to see his results on the latest research. Contrary to my expectation, this investigator conveyed several stories about the benefits of pulsatile perfusion without showing any scientific evidence. I thought perhaps he did not wish to share his results prior to publication, but to this date he has not published a single article on the benefits of pulsatility. A few weeks later at another conference, I listened to this investigator give a lecture on the same topic but arguing the opposite side. He was now openly stating that non-pulsatile flow is much better, patients can live without a pulse, and he sees these patients in his hospital every day. At the end of his talk, he invited those in the audience who would like to see a patient on a non-pulsatile flow device to his institution. Several well-known company representatives also voiced their support for this investigator and his idea on patients leaving with "no pulse". Immediately after the session, I was in the hallway speaking with a friend about this issue when a gentleman approached us and start talking. After a few words, we noticed that he was not attending the conference. In fact, he was one of the patients with the continuous pump that we had just discussed in the lecture. Both my friend and I asked him the same question at the same time, "Can I check your pulse?" With his permission, we checked his pulse and we were in shock. This "pulseless" patient had a stronger pulse than mine and my older friend's! We thanked him for saving us a trip to the institution to which we were both invited a few minutes ago. I remember saying: "Thank God, these investigators only deal with adult patients." Unfortunately, this is no longer the case.

Summary

As a scientist, it is my obligation to be 100% independent, to search for the truth, and to share the results of our investigations with other investigators

around the globe. I do research for the PUBLIC. In order to achieve the best possible outcome for pediatric cardiac patients, research must be supported by the academia, the government, and the industry. I have no doubt that an overwhelming majority of these three entities do their best everyday to improve the lives of future pediatric cardiac patients. It is unfortunate that a few “bad apples” can damage a significant amount of research using inappropriate and unethical tactics. Sooner or later, everyone will see the facts. These individuals are only here today; they were not here in the past nor will they be here in the future. Only time will tell.

Thank you,

Corresponding Author: Akif Ündar, Ph.D.
Professor of Pediatrics, Surgery, and Bioengineering
Penn State Hershey College of Medicine,
Department of Pediatrics—H085
500 University Drive, P.O. Box 850; Hershey, PA
17033-0850
Phone: (717) 531-6706; fax (717) 531-0355;
e-mail: aundar@psu.edu

References

1. www.itsmyheart.org
2. Ündar A. *Proceedings of the Penn State Hershey Pediatric Cardiovascular Research Center : 2011 Update [Editor] 2011; Volume 1:1-218.*
3. Ündar A, Pauliks L, Clark JB, *et al.* Penn State Hershey – Center for Pediatric Cardiovascular Research. *Artificial Organs* 2009; 33: 883-887.
4. Ündar A, Ravishankar C, Gaynor WJ, Baer LD, Clark JB, Wernowsky G, Myers, JL. Seventh international conference on pediatric mechanical circulatory support systems and pediatric cardiopulmonary perfusion [Invited Editorial]. *Artificial Organs* 2011 (in press).
5. Ündar A. International Society for Pediatric Mechanical cardiopulmonary Support. *Artificial Organs* 2010; 34(4): 279.
6. Ündar A. Penn State Hershey Pediatric Cardiovascular Research Center: 2011 Update [Invited Editorial]. *Artificial Organs* 2011 (in press).
7. Qiu F, Zahn J, Pauliks L. *et al.* Translational Research in Pediatric Extracorporeal Life Support System and Cardiopulmonary Bypass Procedure: 2011 Update. *World Journal for Pediatric and Congenital Heart Surgery* 2011 (in press).
8. Vasavada R, Qiu, Ündar A. Current Status of Pediatric/Neonatal Extracorporeal Life Support: Clinical Outcomes, Circuit Evolution, and Translational Research. *Perfusion* 2011 Feb 28. [Epub ahead of print]
9. Palanzo D, Qiu F, Baer L, Clark JB, Myers JL and Ündar A. Evolution of the Extracorporeal Life Support Circuitry. *Artificial Organs* 2010; 34(11): 869–873.
10. Khan S, Vasavada R, Qiu, Kunselman A, Ündar A. Extracorporeal membrane oxygenation: a comparison of oxygenators and circuits. *Perfusion* 2011 Jan 12. [Epub ahead of print]
11. McCoach R, Weaver B, Carney E, Clark JB, Pauliks L, Guan Y, Qiu F, Chang D, Reed-Thurston D, Myers JL and Ündar A. Pediatric Extracorporeal Life Support Systems: Education and Training at Penn State Hershey Children's Hospital. *Artificial Organs* 2010; 34(11): 1023–1026.
12. Clark JB, Guan Y, McCoach R, Kunselman AR, Myers JL, Ündar A. An investigational study of minimum rotational pump speed to avoid retrograde flow in three centrifugal pumps in a pediatric extracorporeal life support model. *Perfusion* 2011 Jan 12. [Epub ahead of print]
13. Guan Y, Su X, McCoach R, Kunselman A, El-Banayosy A, Ündar A. Mechanical performance comparison between rotaflow and centrimag centrifugal pumps in an adult ECLS model. *Perfusion* 2010; 25(2):71-76.
14. Morales DLS, Almond CSD, Jacquiss RDB, *et al.* Bridging children of all sizes to cardiac transplantation: the initial multicenter North American experience with the Berlin Heart EXCOR ventricular assist device. *J Heart Lung Transplant* 2011; 30; 1-8.

International Faculty, Moderators & Wet Lab Instructors

Atif Akçevin, MD
Tijen Alkan-Bozkaya, MD
Emile A. Bacha, MD
Larry Baer, CCP
Leonard Bailey, MD
Mollie L. Barnes, CNIM
Christopher D. Beaty, RN
Lance Becker, MD
Geoffrey L. Bird, MD
J. Brian Clark, MD
James T. Connelly, BS, RRT-NPS
Yves Durandy, MD
Talya Frey, CCP
Stephanie Fuller, MD
Nancy Ganayem, MD
William J. Gaynor, MD
Colleen E. Gruenwald, RN, CCP
David Hehir, MD
Robert D.B. Jaquiss, MD
David R. Jobes, MD
Beth D. Kaufman, MD
David Kinsel, PE
Roxanne E. Kirsch, MD
Jinfen Liu, MD
Giovanni Luciani, MD
Meredith McDonough, MS
Richard Melchior, CCP

Antonio R Mott, MD
John L. Myers, MD
Vinay M. Nadkarni, MD
Maryam Y. Naim, MD
Susan C. Nicolson, MD
Vincent Olshove, CCP
David Palanzo, CCP
Linda B. Pauliks, MD
Stacie B. Peddy, MD
Kerem Pekkan, PhD
Marc A. Priest, CCRN
Leslie Raffini, MD
Chitra Ravishankar, MD
Arlindo Riso, MD
Tami Rosenthal, CCP, MBA
Eugen Sandica, MD
Amanda Seelhorst, RN
Thomas L. Spray, MD
Ulrich Steinseifer, PhD
Sarah Tabbutt, MD, PhD
Alexis Topjian, MD
James S. Tweddell, MD
Akif Ündar, PhD
Bonnie Weaver, RN, MSN, CCRN
Gil Wernovsky, MD
Sung Yang, PhD
Jeffrey D. Zahn, PhD

Conference Supporters

Educational Grants:

Penn State Hershey Pediatric Cardiovascular Research Center, Hershey, PA

Penn State Hershey Children's Hospital, Hershey, PA

International Society For Pediatric Mechanical Cardiopulmonary Support

Conference Exhibitors:

Platinum level supporters:

MAQUET Cardiovascular

Bronze level supporters:

Bellco S.r.l., Italy

Circulite, Inc.

Covidien

Impulse Monitoring, Inc.

SnyCardia Systems, Inc.

Sorin Group USA

St. Jude Medical

Terumo Cardiovascular Systems

Wiley-Blackwell

Final Scientific Program

Wednesday, May 4, 2011

1:00pm – 5:00pm Registration

Thursday, May 5, 2011

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

8:00am – 10:00am **PLENARY SESSION #1 – Pediatric VAD support: unique features and outcome.**
Moderators: Nancy Ghanayem, MD and Chitra Ravishankar (20 min each)

1. VAD implantation in infants and children: Surgical Challenges (Stephanie Fuller, MD).
 2. ICU management of children supported with VAD (David Hehir, MD)
 3. The Berlin Heart experience (Eugen Sandica, MD)
 4. Ventricular assist device-associated anti-human leukocyte antigen antibody sensitization in pediatric patients (Beth D. Kaufman, MD)
 5. Pediatric VADs: The Future (as of 2011) (Robert D.B. Jaquiss, MD)
- Discussion – 20 minutes

10:00am – 11:00am Break/ Posters

11:00am – noon **Key Note Lecture:**
Introduction: John L. Myers, MD
6. Evolution and Current Status of Infant Heart Transplantation.
(Leonard L. Bailey, MD)

12:00pm – 1:00pm LUNCH

12:00pm – 1:00pm **Young Investigators' Lunch (Class of '49 auditorium)**
(Jutta Arens and Onur Dur, Co-chairs of the Young Investigator's Committee)

1:00pm – 3:00pm **PLENARY SESSION #2 – Topic: Anticoagulation: challenges in neonates and children. Moderators: David R. Jobes, MD and Leslie Raffini, MD (25 min each)**

7. Monitoring of Anticoagulation for Pediatric Cardiopulmonary Bypass

(David R. Jobes, MD)

8. Management of Post-Operative Bleeding in Neonates Undergoing Cardiac Surgery (Colleen E. Gruenwald, RN, CCP)

9. Use of Aprotinin in Cardiac Surgery: Lessons Learned

(James S. Tweddell, MD)

10. Anticoagulation during VAD Support in Infants and Children

(Leslie Raffini, MD)

Discussion: (20 minutes)

3:00pm – 3:45pm

Break/ Posters

3:45pm – 5:00pm

Mini-symposium #1: E-CPR and related topics. Moderator: Vinay M. Nadkarni, MD (20 min each)

11. To cool or not to cool during CPR (Alexis Topjian, MD)

12. Therapeutic hypothermia: the cellular basis (Lance Becker, MD)

13. CPR and E-CPR: what's new? (Maryam Y. Naim, MD)

Discussion (15 minutes)

5:00pm – 6:30pm

Regular Slide Presentations #1

(13 min each—8 min. presentation and 5 min discussion)

Moderators: Atif Akçevin, MD and Joseph B. Clark, MD

S1. Ventricular Assist Device Use: A Single Pediatric Center Experience

Aaron Eckhauser MD¹, Matthew J. O'Connor MD², Chitra Ravishankar MD², Lisa M. Montenegro MD³, Susan C. Nicolson MD³, Peter J. Gruber MD, PhD¹, Thomas L. Spray MD¹, J. William Gaynor MD¹, Beth D. Kaufman MD², Stephanie Fuller MD¹.

Division of Cardiothoracic Surgery¹, Divisions of Pediatric Cardiology², Division of Cardiothoracic Anesthesiology and Critical Care³ at the Children's Hospital of Philadelphia, Philadelphia, PA, USA.

S2. Ventricular Assist Device Support in Children & Adolescents with Heart Failure: The Children's Medical Center of Dallas Experience

Mahesh S. Sharma, MD, Joseph M. Forbess, MD, and Kristine J. Guleserian, MD.

The University of Texas-Southwestern School of Medicine and Children's Medical Center of Dallas, Dallas, Texas, USA.

S3. Anticoagulation for Children on Mechanical Circulatory Support

Hannah Copeland, MD*, Paul E Nolan, PharmD[^], Diane Covington[°], RN, Richard Smith, MSEE[°] and Jack G Copeland, MD*.

**University of California San Diego Department of Surgery – San Diego, CA;*

^University of Arizona College of Pharmacy - Tucson, AZ; °University Medical Center – Tucson, AZ

S4. The impact of extracorporeal membrane oxygenation on survival in pediatric patients with respiratory and heart failure: review of our experience

Takeshi Goto,CCP, Yuta Suzuki,CCP, Ai Osanai,CCP, Kaori Aoki,CCP, Akio Yamazaki,CCP, Kazuyuki Daitoku,MD, Yasuyuki Suzuki,MD, Ikuo Fukuda,MD.

Department of Clinical Engineering, Hirosaki University School of Medicine and Hospital. Department of Thoracic Cardiovascular Surgery, Hirosaki University School of Medicine.

53 Honcho, Hirosaki, Aomori, 036-8563, Japan. 5 Zaifucho, Hirosaki, Aomori, 036-8562, Japan.

S5. NeoNatOx – A Pumpless Extracorporeal Lung Support for Premature Neonates

Jutta Arens^{1†}; Mark Schoberer^{2†}, MD; Anne Lohr², MD; Thorsten Orlikowsky², MD; Matthias Seehase³, MD; Reint K. Jellema³, MD; Jennifer J. Collins³; Boris W. Kramer³, MD, PhD; Thomas Schmitz-Rode¹, MD; Ulrich Steinseifer¹, PhD.

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 Dept. of Paediatrics, School of Mental Health and Neuroscience; School of Oncology and Developmental Biology; Maastricht University Medical Center, Maastricht, The Netherlands. † Both Authors contributed equally to this manuscript.

S6. Development of a Newly Designed Circulatory Assist Device For Fontan Circulation by using Shape Memory Alloy Fiber

Yasuyuki Shiraishi, PhD¹, Akihiro Yamada, BS¹, Telma K. Sugai, MS¹, Hidekazu Miura, PhD¹, Shunichi Mochizuki, MD, PhD¹, Tomoyuki Yambe, MD, PhD¹, Dai Homma, PhD², Masaaki Yamagishi, MD, PhD³.

1 Institute of Development, Aging and Cancer, Department of Medical Engineering and Cardiology, Tohoku University, Sendai, Japan; 2 Toki

Corporation, Tokyo, Japan; 3 Department of Pediatric Cardiovascular Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan.

S7. I³-Assist: Individual, Interactive and Integrated Cardiopulmonary Assist – A Concept

Georg Wagner¹; Peter Schlanstein¹; Jutta Arens¹; Rüdger Kopp², MD; Ralf Bensberg², MD; Rolf Rossaint², MD; Thomas Schmitz-Rode¹, MD; Ulrich Steinseifer¹, PhD

¹Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, ²Dept. of Intensive Care Medicine, University Hospital Aachen, RWTH Aachen University, Germany

6:30pm – 8:30pm

Reception: Wine & Cheese (Class of '49 Auditorium)

Poster Presentation #1

8:00 am – 6:30 pm

Moderator: Tijen Alkan-Bozkaya, MD

P1. In vitro performance of the InCor pediatric VAD

Idágene A. Cestari, PhD; Sérgio A. Hayashida; Helena T. T. Oyama; Simão Bacht ; Arlindo Riso, MD. PhD; Ismar N. Cestari MD. PhD; Marcelo Jatene, MD. PhD; Noedir A.G. Stolf, MD. PhD.

Departments of Bioengineering, Pediatrics and Surgery, Heart Institute, (InCor) University of Sao Paulo Medical School, Sao Paulo, Brazil.

P2. Development of a magnetic bearing system for a new 3rd generation blood pump

Jung Joo Lee¹, PhD, MBA, Chi Bum Ahn^{1,2}, PhD, Jaesoon Choi^{1,2}, PhD, Jun Woo Park¹, PhD, Seung-Joon Song^{1,2}, MS, Kyung Sun^{1,2,3}, MD, PhD, MBA.

¹ Korea Artificial Organ Center, Korea University, ² Biomedical Science of Brain Korea 21, College of Medicine, Korea University, ³ Department of Thoracic and Cardiovascular Surgery, Korea University Medical College, Seoul, Korea.

P3. Scanning electron microscopic investigations to investigate the role of the endocardium in the origin of Dilated Cardiomyopathy (DCM)

Jan D. Schmitt¹, Michael Schultz², Peter Schwartz², Kasim O. Coskun¹, Florian Heidrich¹, Sheila Fatehpur^{1,3}, Samuel Sossalla⁴, Christian Sohns⁴, Friedrich Schöndube¹, Masoud Mirzaie^{1,3}

¹Department of Thoracic, Heart and Vascular Surgery, Göttingen University, Germany

²*Institute for Anatomy, Göttingen University, Germany;* ³*Department of Vascular Surgery, Lippe-Lemgo-Hospital, Lemgo, Germany;* ⁴*Department of Cardiology, Göttingen University, Germany;* ⁵*Department of Cardiac-, Thoracic-, Transplantation- and Vascular Surgery, Hannover Medical School, Hannover, Germany.*

P4. Influence of Mild Metabolic Acidosis on Catecholamine Response in Isolated Myocardium of Non-failing Sheep Hearts

Hanna Schotola¹, MD, Samuel Sossalla², MD, Taufiek K. Rajab³, MD, Karl Toischer², MD, Aron F. Popov⁴, MD, Suyog A. Mokashi³, MD, Michael Quintel¹, MD, Martin Bauer¹, MD, Frederick Y. Chen³, MD, Jan D. Schmitto^{3,5}, MD

¹*Department of Anesthesiologie, Emergency and Intensive Care Medicine, University Hospital Goettingen, Germany;* ²*Division of Cardiology and Pneumology, University Hospital Goettingen, Germany;* ³*Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA;* ⁴*Department of Cardiothoracic Transplantation & Mechanical Support, Royal Brompton & Harefield Hospitals, London, UK;* ⁵*Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany.*

P5. Cardiopulmonary bypass and its effects on neonatal kidney morphology

Theodor Tirilomis, Martin Friedrich, K. Oguz Coskun, Tasso Tempes, Aron-Frederik Popov, Jan D. Schmitto, Friedrich A. Schoendube
Dept. for Thoracic, Cardiac, and Vascular Surgery, University of Goettingen, Germany.

P6. Aggressive Zero-balance Ultrafiltration on Hemostasis: Analysis of Different Volume Used in Deep Hypothermic Circulatory Arrest Surgery

Yongli Cui, MD, Cun Long, MD, Shilei Wang, MD, Chun Zhou, MD, Jinping Liu, MD.
Department of Cardiopulmonary Bypass, Cardiovascular Institute and Fuwai Hospital, CAMS and PUMS, Beijing, China.

P7. Numerical investigation of the influence of pulsatile flow on gas exchange inside an oxygenator

Ralf Borchardt; Marcus Hormes; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD
Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany.

P8. In vitro evaluation of the hemodynamic performance of the electro-pneumatic ventricular assist device according to the fluid viscosity variation

Chi Bum Ahn, PhD, Jung Joo Lee, PhD, Jeasoon Choi, PhD, Jun Woo Park, PhD, Seung Joon Song, MS, Kuk Hei Son, MD, Ho Sung, Son, MD, Sung Ho, Lee, MD, Kyung Sun, MD.

Korea Artificial Organ Center, Brain Korea 21 Project for Medical Science, Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea.

P9. Haptic Virtual Fixture for Robotic Cardiac Catheter Manipulator

^{1,3}Jun Woo Park, PhD, ^{1,2}Jaesoon Choi, PhD, ^{1,2}Seung Joon Song, MS, ^{1,2,3}Yongdoo Park, PhD, ^{1,2,4}Kyung Sun, MD, PhD, MBA

¹Korea Artificial Organ Center, ²Brain Korea 21 Project for Biomedical Science, ³Department of Biomedical Engineering, ⁴Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Korea.

P10. Microfiltration Platform for Continuous Blood Plasma Protein Extraction from Whole Blood during Cardiac Surgery

Kiana Aran, Alex Fok, Larwence A. Sasso, Neal Kamdar, Yulong Guan, Qi Sun, Akif Ündar and Jeffrey D. Zahn.

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

Friday, May 6, 2011

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

**8:00am – 10:00am PLENARY SESSION #3 – Challenges at the bedside with ECMO and VAD
Moderators: Sarah Tabbutt, MD, PhD and James T. Connelly, BS-RRT-NPS**

- 14. Challenges at the Bedside with ECLS, “Where the Rubber Meets the Road”:
Nursing Education (Bonnie Weaver, RN, MSN, CCRN)**
- 15. ECMO activation (Amanda Seelhorst, RN)**
- 16. Role of the ECMO technician (Christopher D. Beaty, RN)**
- 17. Role of child life (Meredith McDonough, MS)**
- 18. Transporting children on ECMO or VAD (Susan C. Nicolson, MD)**

Discussion (30 minutes)

10:00am – 10:45am Break/ Posters

**10:45am – noon Mini Symposium # 2 – Outcome of Pediatric Cardiac Surgery (20 min each).
Moderator: John L. Myers, MD**

- 19. The Norwood operation: the past, the present, and the future
(Thomas L. Spray, MD)**
- 20. Hybrid Stage I for HLHS (Emile A. Bacha, MD)**
- 21. Aortic Valve Surgery (Giovanni Luciani, MD)**

Discussion (15 minutes)

12:00pm – 12:15pm YOUNG INVESTIGATOR AWARDS RECOGNITION

12:15pm – 1:15pm LUNCH

**12:20pm – 1:10pm SECOND ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR PEDIATRIC
MECHANICAL CARDIOPULMONARY SUPPORT (223 Golkin Room)
(MEMBERS ONLY)**

Parallel Session

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

Cardiac ICU Rounds and Case Presentations: These sessions will be held in the CICU at The Children's Hospital of Philadelphia and lead by CICU staff. Each session will be interactive during which active discussion from attendees is invited regarding all aspects of management and outcomes. There will be 2 sessions, each of 90 minutes duration, and space is restricted to 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.

1:15 - 3:00 pm

- **Hospital Tour (CHOP)**
Group #1: ECLS Simulation (Stacie B. Peddy, MD & Marc A. Priest, CCRN)
Group #2: Tour of CHOP and CICU rounds (Gil Wernovsky, MD, Geoffrey L. Bird, MD)

3:15- 5:00 pm

- **Hospital Tour (CHOP)**
Group #1: ECLS Simulation (Stacie B. Peddy, MD & Marc A. Priest, CCRN)
Group #2: Tour of CHOP and CICU rounds (Gil Wernovsky, MD, Antonio Mott, MD, and Roxanne Kirsch, MD)

Parallel Session

1:30pm – 5:00pm Wet-Labs (Larry Baer, CCP, David Palanzo, CCP, and Talya Frey, CCP)

**PSH Pediatric ECLS (David Palanzo, CCP)
Neuromonitoring (J. Brian Clark, MD /Mollie Barnes, CNIM)
Sorin S5- Mini-CPB Circuit (Talya Frey, CCP)
Maquet-HL-20 Pulsatile flow (Larry Baer, CCP)**

Parallel Session

1:15pm – 3:00pm

Invited Lectures (15 min each)

Moderators: Ulrich Steinseifer, PhD and Yves Durandy, MD

22. Myocardial Protection of the Right Ventricle during Cardiopulmonary Bypass.

(Linda B. Pauliks, MD)

23. Measurement of Blood Physical Properties in Microfluidic Environment.

(Sung Yang, PhD)

Regular Slide Presentations #2

(13 min each—8 min. presentation and 5 min discussion)

S8. 50 years of research on the artificial placenta: can we turn a toy into a treasure?

Mark Schoberer^{2‡}, Jutta Arens^{1‡}, MD; Anne Lohr², MD; Matthias Seehase³, MD; Reint K. Jellema³, MD; Jennifer J. Collins³; Boris W. Kramer³, MD, PhD; Thomas Schmitz-Rode¹, MD; Ulrich Steinseifer¹, PhD; Thorsten Orlikowsky², MD

¹Department 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;

³Dept. of Paediatrics, School of Mental Health and Neuroscience; School of Oncology and Developmental Biology; Maastricht University Medical Center,

Maastricht, The Netherlands. [‡]Both Authors contributed equally to this manuscript.

S9. Initial chronic animal experiment with the InCor Pediatric VAD

Arlindo Riso, MD, Idágene A. Cestari, Ph.D, Marcelo Jatene, MD, Carla Tanamati, MD, Luis Fernando Caneo, MD, Juliano Penha, MD, Vera Aiello, MD, Noedir Stolf, MD.

Heart Institute (INCOR), University of Sao Paulo Medical School, Sao Paulo, Brazil.

S10. Optimization of the Impella Pediatric Anatomic Fit

Scott C. Corbett, PhD, Caitlyn J. Bosecker, MS, Francis Fynn-Thompson, MD
ABIOMED, Inc. Research and Development; Children's Hospital Boston, Department of Cardiac Surgery.

S11. Mechanical Cavopulmonary Assistance of a Patient-Specific Fontan Physiology: Numerical Simulations, Lumped Parameter Modeling, and Suction Experiments

Amy L. Throckmorton PhD¹, James P. Carr¹, Sharjeel A. Tahir¹, Ryan D. Tate¹, Emily A. Downs BS¹, Sonya S. Bhavsar MS¹, Yi Wu PhD², John D. Grizzard MD³, and William B. Moskowitz MD⁴

Mechanical Engineering¹, School of Engineering, Virginia Commonwealth University, Richmond, VA; Mechanical Engineering², School of Engineering, Behrend College, The Pennsylvania State University; Radiology³ and Pediatric Cardiology⁴, Children's Hospital of Richmond and School of Medicine, Virginia Commonwealth University, Richmond, VA.

S12. Comparison of numeric approaches for blood damage predictions and application to the bearing gaps of rotary blood pumps

Roland Graefe, Dipl.-Ing.; Andreas Ding, Cand.-Ing.; Fiete Böhning, Dipl.-Ing.; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD

Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany

3:00pm – 3:45pm

Break/ Posters

3:45pm – 6:30pm

Invited Lecture (15 min)

Moderators: Giovanni Battista Luciani, MD, Eugen Sandica, MD and Chitra Ravishankar, MD

24. Multi-modality Neuromonitoring for Pediatric Cardiac Surgery: The Approach at Penn State Hershey, and a Critical Appraisal of the Available Evidence.

(Joseph B. Clark, MD)

Regular Slide Presentations #3

(13 min each—8 min. presentation and 5 min discussion)

S13. Pre and Post-operative Magnetic Resonance Imaging In Neonatal Arterial Switch Operation Using Warm Perfusion

Y. Durandy*, M. Rubatti**, R. Couturier**, A.*** Rohnean.

* Perfusion and Intensive Care, Institut J. Cartier; ** Anesthesiology, Institut J. Cartier and Centre Chirurgial Marie Lannelongue; *** Radiology, Centre Chirurgial Marie Lannelongue.

S14. Selective cerebro-myocardial perfusion in complex or recurrent aortic arch pathology: a novel technique

Fabrizio De Rita, MD, Gianluca Lucchese, MD, Luca Barozzi, MD, Tiziano Menon, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Giovanni Battista Luciani, MD

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

S15. Clinical Application of a Single-dose HTK Cardioplegic Solution for Pediatric Myocardial Protection in Beijing Fuwai Hospital

Shigang Wang, MD, Shuyi Lv, MD, Guodong Gao, MD, Yulong Guan, PhD, Jinping Liu, MD, Feilong Hei, MD, and Cun Long, MD

Department of Cardiopulmonary Bypass, Cardiovascular Institute and Fuwai Hospital, CAMS and PUMC, Beijing 100037, China

S16. Continuous Warm Perfusion Reduces Renal Injury During Norwood Operation

James M. Hammel, MD, Haili Lang, MS, and Kim F. Duncan, MD

Division of Pediatric Cardiothoracic Surgery, Children's Hospital and Medical Center

Department of Surgery, University of Nebraska Medical Center, Omaha, Nebraska, USA

S17. Incidence of Healthcare-Associated Infections in a pediatric population with extracorporeal ventricular assist device

Tiziana Fragasso, MD, Giorgia Grutter, MD, Zaccaria Ricci, MD, Sonia Albanese, MD, Carmelita Varano, MD, Antonio Amodeo, MD, Paola Cogo MD.

Department of Cardiac Surgery, Children's Hospital and Research Institute "Bambino Gesù" Rome, Italy

S18. Management of Single Ventricle Patients with Berlin Heart EXCOR Ventricular Assist Device: Single Center Experience

Tracey Mackling, RN, CPNP-PC/AC, Tejas Shah, MD, Vivian Dimas, MD, Kristine Guleserian, MD, Monica Ardura, DO, Jami Gross-Toalson, PhD, Ying Lee, PharmD, Janna Journeycake, MD, Aliessa Barnes, MD

Departments of Pediatric Cardiology, Solid Organ Transplant, Pediatric Infectious Disease, Pediatric Hematology, Pharmacy, Psychiatry, and Pediatric Cardiothoracic Surgery, University of Texas Southwestern Medical Center and Children's Medical Center Dallas, Dallas, Texas, USA

S19. Alternative Anticoagulation for Extracorporeal Membrane Oxygenation

Hayden Dando¹; Martin Gill¹; John Dittmer¹; Killian O'Shaughnessy¹; Jenny Lei¹; James McCauley²

¹ *Perfusion Department, Heart Centre for Kids, The Children's Hospital at Westmead, Sydney, Australia;* ² *Biomedical Engineering Department, The Children's Hospital at Westmead, Sydney, Australia*

S20. Antithrombin Replacement during Extracorporeal Membrane Oxygenation

Robert A. Niebler MD; Melissa Christensen BS, Heidi Wellner RN, BSN; Richard Berens MD.

Department of Pediatrics and Anesthesia, Section of Critical Care, Medical College of Wisconsin, and Children's Hospital of Wisconsin; Milwaukee, WI USA

S21. Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome associated with Pneumonia in Children

Shye-Jao Wu, MD.

Division of Cardiovascular Surgery, Departments of Surgery, Mackay Memorial Hospital, Taipei, Taiwan

S22. Shuntless Hemofiltration During Pediatric ECMO: Simple, Safe, and Accurate Management of the Fluid Overloaded Patient.

Daniel R Duncan, BS CCP, Paul J Kerins, BS CCP, Pizarro, Christian, MD.

The Nemours Cardiac Center. A.I. DuPont Hospital for Children, Wilmington, Delaware, USA.

S23. Extracorporeal Life Support (ECLS) Technology Survey: Recent changes in 2011

Deborah Reed-Thurston, MD, Akif Ündar, PhD, Kim Kopenhaver Haidet, PhD, NNP-BC and Jeffrey Shenberger, MD

Department of Pediatrics, Division of Newborn Medicine, Pediatric Cardiovascular Research Center, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Poster Presentation #2:

8:00 am – 6:30 pm

Moderator: Tijen Alkan-Bozkaya, MD

P11. Procalcitonin Predicts Outcome but Not Infection in Pediatric Veno-Arterial ECMO

Alessio Rungatscher, MD, PhD, Fabrizio De Rita, MD, Alberto Merlini, MD, Gianluca Lucchese, MD, Luca Barozzi, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Giovanni Battista Luciani, MD.

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

P12. 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, MS^{*}, Akif Ündar, PhD^{*,†,‡,§}, John L. Myers, MD^{†,‡}

**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*

P13. Extracorporeal Life Support Systems: Alternative vs. Conventional Circuits

Sameer Khan, BS, Rahul Vasavada, MS, Feng Qiu, MD, Allen R. Kunselman, MS, Akif Ündar, PhD

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

P14. Evaluation of two pediatric polymethyl pentene membrane oxygenators with pulsatile and non-pulsatile perfusion

Feng Qiu, MD, Sameer Khan, BS, Jonathan Talor, BSE, Allan R. Kunselman, MS, Akif Ündar, PhD.

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

P15. Multiplexed Real-Time Monitoring of Systemic Inflammation during Mechanical Circulatory Support

Lawrence A Sasso¹, Akif Ündar², Jeffrey D. Zahn¹

¹BioMEMS Laboratory, Department of Biomedical Engineering, Rutgers University, Piscataway, NJ; ²Pediatric Cardiovascular Research Center, Departments of Surgery, Pediatrics, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, PA, USA

P16. Aorticopulmonary window : Surgical Correction of in Neonatal period and results

Alkan-Bozkaya T., Akçevin A., Türkoğlu H., Paker T., Ersoy C*, Ündar A.
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Penn State Hershey Children's Hospital, Hershey, PA, USA

P17. Surgery For Coronary Arterio-Venous Fistula : Indication In Childhood, Treatment and Results

Alkan-Bozkaya T, Turkoğlu H, Akçevin A, Paker T, Ersoy C*, Bayer V*, Aytac A*
Istanbul Bilim University, Dept. of Cardiovascular Surgery, and
V.K.V. American Hospital, Dept. of Cardiovascular Surgery.

P18. Corrected Transposition of the Great Arteries: Surgical Approach – a review

Alkan-Bozkaya T, Turkoğlu H, Akçevin A, Paker T, Aytac A*, Undar A**.
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Dept. of Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Penn State Hershey, Children's Hospital, Hershey, PA, USA

P19. Surgical approach to the primary heart tumors and the results: 36 cases

Alkan-Bozkaya T., Akçevin A., Türkoğlu H., Paker T., Ersoy C*, Ünder A**.
Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Depts. of Neonatology, Pediatric Cardiology, Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Penn State Hershey Children's Hospital, Hershey, PA, USA

P20. Case: Rhabdomyoma in an Infantile Child with No Tuberous Sclerosis Definition, Clinical Presentation and Surgical Approach

Turkoglu H, Alkan-Bozkaya T, Akalin F*.
Istanbul Bilim University, Dept. of Cardiovascular Surgery and Marmara University,
Dept of Pediatric Cardiology, Istanbul, Turkey.*

P21. Hemodynamic Evaluation of the Avalon Elite™ Bi-Caval Dual Lumen Cannulae

Feng Qiu, MD¹, Chiajung K. Lu, BA¹, David Palanzo, CCP¹, Larry D. Baer, CCP¹, John L. Myers, MD^{1,2}, Akif Ünder, PhD^{1,2,3}.
¹*Pediatric Cardiovascular Research Center, Departments of* ²*Surgery, and*
³*Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA*

Saturday, May 7, 2011

7:00am – 8:00am Breakfast

8:00am – 10:00am PLENARY SESSION #4 – Topic- PEDIATRIC CPB
Moderators: Talya Frey, CCP and Larry Baer, CCP (25 min each)

25. An In Vitro Comparison of The Ability of Three Commonly Used Pediatric Cardiopulmonary Bypass Circuits to Filter Gaseous Microemboli. (Richard Melchior, CCP)

26. Bloodless Approach to Pediatric Open Heart Surgery for Repair of Atrial and Ventricular Septal Defects (Vincent Olshove, CCP)

27. ABCs of Pulsatile CPB in Infants and Children: The Penn State Hershey Approach (Larry Baer, CCP)

28. Regulatory Requirements for Medical Device Development (David Kinsel, PE)

Discussion (20 minutes)

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

10:45am – noon Mini Symposium # 3 – Bioengineering Approaches in Pediatric Cardiovascular Medicine
Moderator: Akif Ündar, PhD (20 min each)

29. Real Time Monitoring of Inflammation Biomarkers with Extracorporeal Life Support (ECLS) Intervention (Jeffrey D. Zahn, PhD)

30. Computational fluid dynamics to improve hemodynamics of congenital aortic cannulation (Kerem Pekkan, PhD)

31. Translational Research in Pediatric ECLS Systems: 2011 Update (Akif Ündar, PhD)

Discussion (15 minutes)

12:00pm – 1:00pm LUNCH

1:00pm – 3:30pm Regular Slide Presentations #4
Moderators: Jinfen Liu, MD, Arlindo Riso, MD and Jeffrey D. Zahn, PhD
(13 min each—8 min. presentation and 5 min discussion)

S24. How mechanical circulatory support helps not to need it

U. Schweigmann

Pediatrics III, Cardiology, University Hospital Innsbruck

S25. Acute Right Heart Failure Induced by Multiple Coronary Ligations in a Novel Animal Model

Jan D. Schmitto¹, Suyog A. Mokashi¹, Lawrence S. Lee¹, Otavio Coelho-Filho², Aron F. Popov³, Kasim O. Coskun³, Raymond Kwong², Martin Strüber³, Axel Haverich³, Lawrence H. Cohn¹, R. Morton Bolman III¹, Frederick Y. Chen¹

¹*Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, USA;* ²*Division of Cardiology, BWH, Harvard Medical School, Boston, USA*

³*Department of Cardiac-, Thoracic-, Transplantation- and Vascular-Surgery, Hannover Medical School, Hannover, Germany*

S26. The Crucial Role of MMP and TIMP in the Regulation of Reverse Remodeling in

Sheep Heart Failure

Tobias Vorkamp¹, Florian Heidrich¹, Philipp Ortmann¹, Samuel Sossalla², Kasim O. Coskun¹, Aron F. Popov¹, Christian Sohns², Suyog A. Mokashi³, Masoud Mirzaie¹, Michael Quintel⁴, Martin Bauer⁴, Friedrich A. Schoendube¹, Jan D. Schmitto^{1,3,5}

¹*Department of Cardiac, Thoracic and Vascular Surgery, University Hospital Goettingen, Germany;* ²*Division of Cardiology and Pneumology, University Hospital Goettingen, Germany;* ³*Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA;* ⁴*Department of Anesthesiologie, Emergency and Intensive Care Medicine, University Hospital Goettingen, Germany;* ⁵*Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany*

S27. Cardioplegia and Angiotensin-I Receptor Antagonist Modulate STATs Activation in Neonatal Rat Myocardium.

Gianluca Lucchese, MD, Fabrizio De Rita, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Giovanni Battista Luciani, MD.

Division of Cardiac Surgery, University of Verona, Italy.

S28. Balanced ultrafiltration: inflammatory mediator removal capacity

Yulong Guan, MD, Shigang Wang, MD, Cun Long MD.

Department of Extracorporeal Circulation, Cardiovascular Institute and Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100037, P. R. China

S29. Results of surgical treatment of residual congenital aortic stenosis: Balloon valvuloplasty versus open commissurotomy

Coskun KO¹, Tirilomis T¹, Schmitto JD^{1,2}, Popov AF^{1,3}, Hinz J⁴, Ruschewski W¹
¹Department of Cardiac, Thoracic and Vascular Surgery, University Hospital Goettingen, Germany; ²Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany; ³Department of Cardiac Transplantation and Mechanical Support, Royal Brompton & Harefield Hospitals, UK; ⁴Department of Anesthesiology, Emergency and Intensive Care Medicine, University Hospital Goettingen, Germany

S30. Experimental evaluation of an oxygenator with integrated pulsatile pump for pediatric applications

Ralf Borchardt; Peter Schlanstein; Ilona Mager; Jutta Arens; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD
Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

S31. Analysis of pulsatile and nonpulsatile blood flow effects in different degrees of stenotic vasculature

Jae Seung Jung¹², MD, Kuk Hui Son¹², MD, Chi Bum Ahn², PhD, Ho Sung Son¹², MD, Kyung Sun¹², MD
¹Department of Thoracic and Cardiovascular surgery, Anam Hospital, Korea University Medical Center. ²Korea Artificial Organ Center

S32. Numerical Modeling of Anisotropic Fiber Bundle Behavior in Oxygenators

Sonya S. Bhavsar, MS; Marco Seiwert; Ralf Borchardt, Dipl.-Ing.; Roland Graefe, Dipl.-Ing.; Peter Schlanstein, Dipl.-Ing.; Jutta Arens, Dipl.-Ing.; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, Dr.-Ing.
Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

S33. Sodium Alginate Hydrogel Based Bioprinting Using a Novel Multi-Nozzle Bioprinting System

^{1,2}Seung Joon Song, MS, ^{1,2}Jaesoon Choi, PhD, ^{1,2}Yong Doo Park, PhD, ^{1,2}So Young Hong, MS, ¹Jung Joo Lee, PhD, ¹Chi Bum Ahn, PhD, ^{1,3}Kyung Sun, MD, PhD, MBA
¹Korea Artificial Organ Center, ²Brain Korea 21 Project for Biomedical Science, ³Department of Biomedical Engineering, ³Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea

S34. Evaluation of The Quadrox-i Neonatal Oxygenator with An Integrated Arterial Filter

Arash Salavitabar, BS¹, Feng Qiu, MD¹, Allen Kunselman, MA², Akif Ündar, PhD^{1,3,4}.

¹*Pediatric Cardiovascular Research Center, Departments of* ²*Public Health and Sciences, Departments of* ³*Surgery, and* ⁴*Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA*

3:30 pm

Closing remarks

International Scientific Committee

Chi Bum Ahn, PhD	Richard Berens, MD	Scott C. Corbett, PhD
Vera Aiello, MD	Sonya S. Bhavsar MS	Kasim O. Coskun
Akalın F	Geoffrey L. Bird, MD	R. Couturier
Atif Akçevin, MD	Fiete Böhning, Dipl.-Ing.	Diane Covington, RN
Sonia Albanese, MD	R. Morton Bolman III	Yongli Cui, MD
Tijen Alkan-Bozkaya, MD	Ralf Borchardt	Kazuyuki Daitoku, MD
Antonio Amodeo, MD	Caitlyn J. Bosecker, MS	Hayden Dando
Alexis Antunez	Luis Fernando Caneo, MD	Fabrizio De Rita, MD
Kaori Aoki, CCP	Elizabeth Carney, DVM	Vivian Dimas, MD
Kiana Aran, BS	James P. Carr	Andreas Ding, Cand.-Ing.
Monica Ardura, DO	Gary Ceneviva, MD	John Dittmer
Jutta Arens, Dipl.-Ing.	Idágene A. Cestari, PhD	Emily A. Downs, BS
Aytac A	Ismar N. Cestari MD, PhD	Daniel R Duncan, BS, CCP
Emile Bacha, MD	Frederick Y. Chen, MD	Kim F. Duncan, MD
Simão Bacht	Jaesoon Choi, PhD	Yves Durandy, MD
Larry Baer, CCP	Maryanne R. K. Chrisant, MD	Aaron Eckhauser MD
Leonard L. Bailey, MD	Melissa Christensen, BS	Ersoy C
Aliessa Barnes, MD	Joseph B. Clark, MD	Giuseppe Faggian, MD
Mollie L. Barnes, CNIM	Otavio Coelho-Filho	Sheila Fatehpur
Luca Barozzi, MD	Paola Cogo MD	Alex Fok
Martin Bauer, MD	Lawrence H. Cohn	Joseph M. Forbess, MD
Bayer V	Jennifer J. Collins	Tiziana Fragasso, MD
Christopher D. Beaty, BSN, RN	James T. Connelly, BS, RRT-NPS	Talya Frey, CCP
Lance Becker, MD	Hannah Copeland, MD	Martin Friedrich
Ralf Bensberg, MD	Jack G Copeland, MD	Ikuo Fukuda, MD

Stephanie Fuller, MD	Florian Heidrich	Sung Ho Lee, MD
Francis Fynn-Thompson, MD	Hinz J	Ying Lee, PharmD
Mark Galantowicz, MD	Dai Homma, PhD	Jenny Lei
Nancy Ganayem, MD	So Young Hong, MS	Selena Levine, BA
Guodong Gao, MD	Marcus Hormes	Curt Lind, CHS, MT
J. William Gaynor, MD	Marcelo Jatene, MD, PhD	Jinfen Liu, MD
Martin Gill	R.D.B. Jaquiss, MD	Jinping Liu, MD
Andrew C. Glatz, MD	Reint K. Jellema, MD	Andrew J Lodge, MD
Daniel Gomez, CCP	David R. Jobes MD	Cun Long, MD
Takeshi Goto, CCP	Janna Journeycake, MD	Chiajung K. Lu, BA
Roland Graefe, Dipl.-Ing	Jae Seung Jung, MD	Gianluca Lucchese, MD
John D. Grizzard, MD	Neal Kamdar	Giovanni Battista Luciani, MD
Jami Gross-Toalson, PhD	Beth D. Kaufman, MD	Shuyi Lv, MD
Peter J. Gruber, MD, PhD	Paul J Kerins, BS, CCP	Tracey Mackling, RN
Colleen E. Gruenwald, RN, CCP	Sameer Khan, BS	Ilona Mager
Kristine J. Guleserian, MD	Byung Jun Kim, BS	Alessandro Mazzucco, MD
Giorgia Grutter, MD	Myounggon Kim, MS	James McCauley
Yulong Guan, MD	David Kinsel, PE	Robert McCoach, RN, CCP
Kristine Guleserian, MD	Roxanne E. Kirsch, MD	Meredith McDonough, MS, CCLS
Kim Kopenhaver Haidet, PhD	Rüdger Kopp, MD	Pamela Meinert, RN, PhD
James M. Hammel, MD	Boris W. Kramer, MD, PhD	Richard W. Melchior MPS, CCP
Brian D. Hanna, MD, PhD	Allen R. Kunselman, MS	Tiziano Menon, MD
Axel Haverich	Raymond Kwong	JonDavid Menteer, MD
Sérgio A. Hayashida	Haili Lang, MS	Alberto Merlini, MD
David Hehir, MD	Jung Joo Lee, PhD, MBA	Masoud Mirzaie
Feilong Hei, MD	Lawrence S. Lee	Hidekazu Miura, PhD

Shunichi Mochizuki, MD, PhD	Linda B. Pauliks, MD, MPH	Peter Schlanstein, Dipl.-Ing.
Suyog A. Mokashi, MD	Stacie B. Peddy, MD	Jan D. Schmitto, MD
Dimitrios Monos, PhD	Kerem Pekkan, PhD	Thomas Schmitz-Rode, MD
Lisa M. Montenegro, MD	Juliano Penha, MD	Mark Schoberer, MD
William B. Moskowitz, MD	Alistair Phillips, MD	Friedrich A. Schöndube
Antonio R. Mott, MD	Christian Pizarro, MD	Hanna Schotola, MD
John L. Myers, MD	Aron-Frederik Popov	Michael Schultz
Vinay M. Nadkarni, MD	Thomas Preston, CCP	Peter Schwartz
Aymen Naguib, MD	Marc A. Priest, CCRN	U. Schweigmann
Maryam Y. Naim, MD	Feng Qiu, MD	Matthias Seehase, MD
Susan C. Nicolson, MD	Michael Quintel, MD	Amanda Seelhorst, BSN, RN
Robert A. Niebler, MD	Leslie Raffini, MD, MSCE	Marco Seiwert
Paul E Nolan, PharmD	Taufiek K. Rajab, MD	Tejas Shah, MD
Matthew J. O'Connor, MD	Chitra Ravishankar, MD	Mahesh S. Sharma, MD
Vincent Olshove, CCP	Deborah Reed-Thurston, MD	Jeffrey Shenberger, MD
Thorsten Orlikowsky, MD	Zaccaria Ricci, MD	Yasuyuki Shiraishi, PhD
Philipp Ortmann	Arlindo Riso, MD, PhD	Richard Smith, MSEE
Ai Osanai, CCP	A. Rohnean	Christian Sohns
Killian O'Shaughnessy	Tami Rosenthal, MBA, CCP	Ho Sung Son, MD
Helena T. T. Oyama	Rolf Rossaint, MD	Kuk Hui Son, MD
Paker T.	M. Rubatti	Seung-Joon Song, MS
David Palanzo, CCP	Alessio Rungatscher, MD, PhD	Samuel Sossalla, MD
Stephen M. Paridon, MD	Ruschewski W	Thomas L. Spray, MD
Jaeseong Park, BS	Arash Salavitar, BS	Ulrich Steinseifer, PhD
Jun Woo Park, PhD	Eugen Sandica, MD	Noedir A.G. Stolf, MD, PhD
Yong doo Park, PhD	Larwence A. Sasso, BS	Martin Strüßer

Telma K. Sugai, MS	Karl Toischer, MD	Heidi Wellner, RN, BSN
Kyung Sun, MD, PhD, MBA	Alexis Topjian, MD	Gil Wernovsky, MD
Qi Sun	Türkoğlu H	Robert Wise, CCP
Yasuyuki Suzuki, MD	James S. Tweddell, MD	Karl Woitas, CCP
Yuta Suzuki, CCP	Mehmet C. Uluer, ScM	Shye-Jao Wu, MD
Sarah Tabbutt, MD, PhD	Akif Ündar, PhD	Yi Wu, PhD
Sharjeel A. Tahir	Carmelita Varano, MD	Akihiro Yamada, BS
Jonathan Talor, BSE	Rahul Vasavada, MS	Masaaki Yamagishi, MD, PhD
Carla Tanamati, MD	Tobias Vorkamp	Akio Yamazaki, CCP
Ryan D. Tate	George Wagner	Tomoyuki Yambe, MD, PhD
Tasso Tempes	Shigang Wang, MD	Sung Yang, PhD
Amy L. Throckmorton, PhD	Shilei Wang, MD	Jeffrey D. Zahn, PhD
Theodor Tirilomis	Bonnie L. Weaver, RN, CCRN	Chun Zhou, MD

ICU MANAGEMENT OF CHILDREN SUPPORTED WITH VAD

David Hehir, MD

Children's Hospital of Wisconsin, Milwaukee, WI 53226, USA.

The use of ventricular assist devices (VAD) in children is increasing, as is the complexity of patients supported. Morbidity and mortality remains high despite advances in device engineering and medical management. Improving our knowledge of perioperative physiology and potential morbidities will improve critical care of patients with VAD, which requires coordination of a multidisciplinary team to ensure the best possible outcomes.

Review of the literature on perioperative management of pediatric VAD as well as the experience at the Children's Hospital of Wisconsin was performed in order to summarize the indications and contraindications for VAD implantation, and the patient and device variables which affect ICU management strategies. We describe current post-implant management practices, and present examples of management challenges for consideration.

In the pediatric population, VADs are used as a bridge to transplant or recovery for acute and chronic pump failure in the setting of congenital and acquired heart disease. Commonly, patients who require VADs have pre-existing extra-cardiac organ dysfunction that will affect the peri-operative management strategies and may contribute to post-implant complications. Prior to VAD placement, risk factors for poor outcomes and contraindications for VAD use are poorly defined, and are evaluated on a case-by-case basis. Pre-implant severe neurological injury or acute intracranial bleed, active infection, severe coagulopathy, irreversible renal failure, and unfavorable cardiac anatomy may be considered as possible contraindications.

Critical care in the immediate post-operative period focuses on achieving hemostasis and establishing optimal cardiac output through management of right heart failure, preload, and pulmonary and systemic vascular resistance. In addition, prevention and management of extra-cardiac organ dysfunction such as neurologic injury and renal failure are important variables for a successful VAD run. Once hemostasis is achieved, the focus is shifted to prevention of thrombosis through anticoagulation. As soon as is feasible, patients should be de-intensified in order to limit hospital-acquired complications such as infection. Intensive nutritional and physical rehabilitation should commence soon after implant in order to improve a patient's candidacy for transplant or recovery. Pediatric patients with VADs continue to experience significant mid-term morbidity and mortality particularly related to bleeding, clotting, and neurologic injury and generally require close monitoring throughout the VAD run. Therefore, the use of VAD as destination therapy in pediatrics remains controversial.

In summary, the use of VADs in pediatrics is a potentially life-saving therapy as a bridge to recovery or transplantation, but is associated with high morbidity and mortality. Understanding the post-operative physiology and associated morbidities will help improve post-implant outcomes in the ICU.

The Berlin Heart Experience

Eugen Sandica, MD

Department of Surgery for Congenital Heart Defects, Center for Congenital Heart Defects,
Heart and Diabetes Center NRW, Bad Oeyhausen, Germany

Background:

The Berlin Heart EXCOR Pediatrics is utilized at our center for bridging pediatric patients to cardiac transplantation or myocardial recovery. This retrospective study reviews our results regarding long term support and outcome.

Methods:

Between January 2008 and December 2010 twelve patients (6 female and 6 male) with end-stage heart failure (cardiomyopathy or myocarditis) underwent implantation of a VAD. The median weight was 14,2 kg (range 4.2 – 51.6 kg) and median age was 4.1 years (range 0.25 – 11.8 years). Seven patients were on inotropes and five patients required mechanical ventilation and inotropes before BH implantation. Three patients experienced cardiopulmonary resuscitation before VAD implantation.

Results:

Eight patients received a L-VAD and four patients were supported with a Bi-VAD. Of the 12 patients, 8 were bridge to heart transplantation, one was explanted following myocardial recovery and one died on support. The median support time for this 10 patients was 193 days (range 4 - 488 days). Two patients continued to receive support. One patient presented neurological symptoms but finally was successfully explanted. In six patients a total of six blood pumps were exchanged due to thrombus formation. Three patients had local signs of infection around the cannulae. There was no mediastinitis but two patients required antibiotics therapy. Two patients developed pericardial fluid collection but no surgical exploration or drain insertion was necessary. There was no death after heart transplantation or after explantation of the device.

Conclusions:

The ventricular assist device (VAD) Berlin Heart EXCOR Pediatrics provides an effective means of bridging children of almost all ages and sizes to cardiac transplantation or myocardial recovery. Long term support is possible with a low rate of major complications.

Ventricular Assist Device-associated Anti-Human Leukocyte Antigen Antibody Sensitization in Pediatric Patients

Matthew J. O'Connor, MD, JonDavid Menteer, MD, Maryanne R. K. Chrisant, MD,,Dimitrios Monos, PhD,Curt Lind, CHS, MT, Selena Levine, BA,J. William Gaynor, MD, Brian D. Hanna, MD, PhD,Stephen M. Paridon, MD, Chitra Ravishankar, MD, and Beth D. Kaufman, MD

Children's Hospital of Philadelphia, Philadelphia, PA, USA

Background: Ventricular assist devices (VAD) are associated with the formation of antibodies to anti-human leukocyte antigens (HLA) or sensitization. This has been well described in the adult VAD population. While HLA sensitization may lead to increased risk of rejection and decreased graft function and survival following heart transplant, recent reports have been reassuring regarding adverse impact on OHT outcomes in adults. The incidence and effects of VAD-associated anti-HLA sensitization have not been well studied in the pediatric population.

Methods: A retrospective review of all patients undergoing VAD implant at our institution from 1998 to 2008 was performed. Panel reactive antibody (PRA) results before VAD implant, after VAD implant, and after orthotopic heart transplantation (OHT) were recorded. Patients who became sensitized (PRA for class I and/or II immunoglobulin G antibodies $\geq 10\%$) on VAD support were compared with non-sensitized patients with regard to demographics, diagnosis, device type, and blood product exposure on VAD support. Outcomes after OHT were also compared between groups.

Results: VAD support was initiated in 20 patients (median age, 14.4 years), with 75% survival to OHT or recovery. PRA data before and after VAD implant were available for 17 patients. VAD-associated sensitization developed in 35% of recipients. There were no differences between those sensitized in association with VAD support and non-sensitized patients with regard to age, gender, diagnosis, device type, extracorporeal membrane oxygenation use, or blood product exposure on VAD support. Black race predicted sensitization on VAD ($p = 0.02$). There were no differences in survival or rejection between groups.

Conclusions: VAD therapy was associated with the development of anti-HLA sensitization in 35% of recipients. Black race predicted sensitization, but there were no differences in overall survival or outcomes after OHT. J Heart Lung Transplant 2010;29:109–116.

Pediatric VADs: The Future (as of 2011)

R.D.B. Jaquiss, MD, Andrew J Lodge, MD, Alexis Antunez
Section of Pediatric Cardiothoracic Surgery,
Duke University School of Medicine, Duke Children's Hospital, Durham, North Carolina, USA

Background:

Until recently, the only practical type of mechanical circulatory support (MCS) for small children with severe heart failure was extracorporeal membrane oxygenation. However in the past several years, there has been increasing and favorable experience with the use of paracorporeal ventricular assist devices (VADs) specifically designed for children. These devices have greatly extended the period of circulatory support, whether as bridge to recovery or as bridge to transplant. There remain several challenges associated with MCS in children. Some of these challenges may be addressed with novel devices, some may be addressed with novel medications, and some of which may require alteration in current pre-MCS management, particularly in children with congenital heart disease.

Topics:

- 1 – Pulsatile vs. Continuous Flow: This question seems to have been settled in adult MCS practice, in favor of continuous flow devices, but remains an area of uncertainty in pediatric MCS.
- 2 – Anticoagulation: The incidence of stroke and thromboembolism in pediatric MCS seems higher in adult MCS, and current anti-coagulant therapy is difficult to manage.
- 3 – Single Ventricle Physiology: An important subset of pediatric heart transplant candidates have complex single ventricle malformations and may not be optimally supported by current MCS technology.
- 4 – The Untransplantable: Some pediatric patients are so pre-sensitized to HLA antigens that they are not candidates for transplantation. Can this circumstance be prevented or treated?
- 5 – Destination Therapy for Children: Would patients in the “Untransplantable” category be served by DT?

Conclusion:

Despite recent advances in the field of pediatric MCS/VAD therapy, there remain important challenges and unresolved questions. Some of these issues will be reviewed in this presentation, and speculations about future investigations and directions will be provided.

EVOLUTION AND CURRENT STATUS OF INFANT HEART TRANSPLANTATION

LEONARD L. BAILEY, MD

Loma Linda University Medical Center, CA, USA

Clinical heart transplantation was first accomplished by Christiaan Barnard on December 3, 1967. Newborn heart transplantation was first attempted by Adrian Kantrowitz, just three days later in New York. Sixteen years lapsed before neonatal transplantation was again attempted, first in London, and then in Loma Linda, California in the summer and fall of 1984, respectively. The latter infant, whose xeno-donor was a baboon, became known as "Baby Fae." Neither infant survived a month, but both produced an important impact, through media exposure, on the public consciousness. The first successful neonatal heart transplant occurred in Loma Linda on November 15, 1985. That recipient, born with hypoplastic left heart syndrome, is now 25 years old and living with his original allograft.

The idea of infant organ donation gradually took hold, and the incidence of infant heart transplantation increased. Today, 350-450 pediatric heart transplant procedures are reported annually to the Registry of the International Society for Heart and Lung Transplantation, 25% of which are still in young infants. That number of transplants appears to reflect the contemporary limits of our organ recovery systems.

Fortunately, outcomes of Norwood's staged-reconstruction for complex univentricular heart disease have dramatically improved during the past two decades. This readily available surgical pathway has now largely replaced transplantation as primary therapy for structural heart disease. Indeed, heart transplantation for congenital anomalies has become an avenue of last resort; a form of salvage therapy. It is done in recipients who have failed to respond suitably to one or another of the stages of univentricular reconstruction, or less frequently, for those whose heart failure has followed one or more conventional operations for complex biventricular heart disease. And, it is done for those in need of re-transplantation.

Beyond the first month of two of life, primary transplantation is limited, with few exceptions, to the management of severe cardiomyopathy and the occasional benign, yet clinically complicated tumor. A few of these potential recipients will decompensate and require mechanical circulatory support for survival during their wait for a donor organ. Circulatory support devices are now available for use in infants as small as 10 kilograms in body weight with reasonable outcomes, and for even smaller infants with less predictable outcomes.

MONITORING OF ANTICOAGULATION FOR PEDIATRIC CARDIOPULMONARY BYPASS

David R. Jobes MD.

Professor of Anesthesiology and Critical Care, The Children's Hospital of Philadelphia and the University Of Pennsylvania School Of Medicine.

Background:

Pediatric patients were among the first to have cardiac surgery using cardiopulmonary bypass where heparin was used for anticoagulation. Yet the reports characterizing the evolution of heparin monitoring were largely based in adult patients and extrapolated to the progressively younger pediatric patient population until very recently. The focus of monitoring has shifted from heparin effect that assured no gross fibrin or clot formation to suppression of precursors in the coagulation pathway leading to fibrin formation. A current goal is to prevent activation/consumption of coagulation proteins within the limits imposed by the pharmacologic properties of unfractionated heparin and to minimize the adverse effects of heparin and protamine on hemostasis.

Special Considerations for Pediatric Patients:

The patient population spans the maturation of coagulation protein synthesis where some values at birth are less than 50% of adult normal values and gradually progress reaching adult values after puberty. The protein elements necessary for heparin effect are present in lesser quantity and vary in proportion than in adults resulting in more variable sensitivity. In addition plasma volume is less in cyanotic, polycythemic patients. Dilutional effects during surgery are thereby accentuated and hypothermia alters heparin half-life. Many younger patients receive varying quantities of adult plasma adding to the variability of heparin effect. Laboratory and point of care tests will differ in exhibiting age-related effects on reference ranges.

Evidence of Effective Monitoring in Pediatric Patients:

There is significant heterogeneity in anticoagulation management across institutions indicating inadequate evidence to establish a best practice. Monitoring heparin effect (ACT) is virtually universal and may be accompanied by the addition of heparin level (protamine titration). Point of care tests may be more efficient when linked to values of FXa inhibition, or limiting TAT formation and F1.2 production. Individualized dosing of both heparin and protamine based on in vitro testing appears advantageous in pediatric patients as well as adults. However protocols must be adjusted for the very young patients due to variation in test methods, heparin sensitivity, and dilutional effects. Before adopting published protocols it is advisable to carefully examine the test methods in use, population studied, transfusion strategy, circuit specifications (especially priming elements) and use of adjunctive drugs affecting end points and outcome. A consistent management strategy for anticoagulation across institutions will be difficult to establish until these background practices become more uniform.

Management of Post-operative Bleeding in Neonates undergoing Cardiac Surgery

Colleen Gruenwald, MHSc, RN, CCP, CPP

The Labatt Family Heart Centre, The Hospital for Sick Children, Toronto, Canada

Background:

Cardiac surgery using cardiopulmonary bypass (CPB) is associated with a level of bleeding that is exacerbated in the neonatal patient compared to older children and adults. The causes of increased risk of bleeding in neonates are multifactorial in nature. The bypass system and the techniques more commonly employed during CPB in this population produce exaggerated derangements in an immature hemostatic system. The imbalance of the small patient blood volume and the relatively large circuit volume generally requires an obligatory need for a blood prime, which already represents a major transfusion volume. The challenges presented during neonatal cardiac surgery cannot be solved by a single approach.

Method:

Since the cause of post-operative bleeding in neonates undergoing CPB is multifactorial so must be the approach to its amelioration. Pre-operative iron therapy should be considered if time allows. In the peri-operative forum, bypass prime should be minimized to reduce the effects of dilution. The composition of the priming solution should be optimized to reduce exposure to allogeneic donors but also to supplement necessary coagulation factors to an immature hemostatic system. The use of the cell saver may also be considered to collect any shed blood from the surgical site prior to heparinization and following protamine administration in addition to salvaging any residual blood from the bypass circuit.

Individualized heparin and protamine management during bypass has been found to reduce the need for transfusion and improve clinical outcomes in this population. In addition, very high levels as well as low levels of heparin concentration lead to worse clinical outcomes.

It is generally accepted that neonatal cardiac surgery is associated with the need for blood transfusion. However, both quantity and quality of allogeneic transfusion is associated with increased morbidity and mortality. Furthermore, when transfusion is required, the use of fresh blood has been shown to improve clinical outcomes. Transfusion guidelines throughout the peri-operative period have also been shown to reduce transfusion.

Summary:

The management of post-operative bleeding in neonatal patients undergoing CPB cannot begin at the end of the surgery. Many aspects of care must be considered and optimized at the time of presentation for surgery and performed throughout the peri-operative period. This requires an inter-disciplinary team approach including several modalities of care and techniques employed.

Further research needs to be undertaken that will explore the immature haemostatic system of the neonate and interventions that may improve anticoagulation efficiency during CPB. Finding ways to balance a scarce blood donation resource with the need for quality products continues to be a challenge.

The Use of Aprotinin in Pediatric Cardiac Surgery: Lessons Learned.

James S Tweddell, MD. The Children's Hospital of Wisconsin and the Medical College of Wisconsin

Aprotinin is a serine protease inhibitor that has strong anti-inflammatory and anti-fibrinolytic activities because it inhibits kallikrein and plasmin and preserves platelet function.(1-3) Until recently, aprotinin was used prophylactically to reduce the risk of bleeding and to minimize cardiopulmonary bypass induced inflammation in cardiac surgery patients at high risk for perioperative bleeding. Aprotinin was commonly used "off-label" in children and appeared particularly appealing, because coagulopathic bleeding and a significant inflammatory response are universal among neonates and small infants undergoing cardiac surgery. There are a number of single center retrospective studies and a handful of randomized controlled trials looking at aprotinin in pediatric cardiac surgery.(4-16) The randomized controlled studies are complicated by small numbers of patients, variable aprotinin dosing, use of different stratification strategies and end-points. They generally but not universally show a benefit in terms of decreased bleeding and transfusions. In 2006 and 2007 two studies from the Institute for Ischemia Research and Education Foundation summarized the impact of aprotinin among about 4400 adult patients undergoing cardiac surgery that were part of an international prospective observational data base.(17, 18) These studies suggested an increased in mortality, stroke and renal failure among adult patients receiving aprotinin during open-heart surgery. In 2008 a multicenter, blinded, randomized, controlled study of over 2331 patients comparing amicar, tranexamic acid and aprotinin among adult patients undergoing cardiac surgery found a trend towards increased thirty day mortality among the patients randomized to aprotinin.(19) As a result of these studies the availability of aprotinin was severely curtailed and it is no longer available for pediatric use. Recently an analysis of over 30,000 pediatric heart surgery patients contained within the Pediatric Health System Database, a large multi-institutional database, was performed looking at the impact of aprotinin in congenital heart surgery.(20) This study found that aprotinin use was not associated with increased mortality or renal failure and that among patients undergoing reoperations, ICU and hospital length of stay were reduced. This analysis suggests a potential role for aprotinin among high-risk pediatric cardiac surgical patients. The analysis of multi-center databases is ongoing and may provide additional insight into the impact of aprotinin in pediatric cardiac surgery. Perhaps these studies could justify the initiation of a multi-center randomized trial of aprotinin in pediatric cardiac surgery although the willingness of the manufacturer to supply the drug remains unknown. As pediatric specialists we are all too commonly in the position of using drugs for "off label" indications. What is the lesson to be learned from the experience with aprotinin? In the future we cannot be complacent and assume that once a drug is approved it will continue to be available for "off label" use. We will need to be involved in systematic clinical investigation of critically valuable drugs borrowed for pediatric practice in order to make certain we have proper indications and safety profiles that can be used to define specific indications for our patients.

References:

1. van Oeveren W, Harder MP, Roozendaal KJ, Eijssman L, Wildevuur CR. Aprotinin protects platelets against the initial effect of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990 May;99(5):788-96; discussion 96-7.
2. Dietrich W. Reducing thrombin formation during cardiopulmonary bypass: is there a benefit of the additional anticoagulant action of aprotinin? J Cardiovasc Pharmacol 1996;27 Suppl 1:S50-7.
3. Mojcik CF, Levy JH. Aprotinin and the systemic inflammatory response after cardiopulmonary bypass. Ann Thorac Surg 2001 Feb;71(2):745-54.
4. Backer CL, Kelle AM, Stewart RD, Suresh SC, Ali FN, Cohn RA, et al. Aprotinin is safe in pediatric patients undergoing cardiac surgery. J Thorac Cardiovasc Surg 2007 Dec;134(6):1421-6; discussion 6-8.
5. Chauhan S, Kumar BA, Rao BH, Rao MS, Dubey B, Saxena N, et al. Efficacy of aprotinin, epsilon aminocaproic acid, or combination in cyanotic heart disease. Ann Thorac Surg 2000 Oct;70(4):1308-12.
6. D'Errico CC, Shayevitz JR, Martindale SJ, Mosca RS, Bove EL. The efficacy and cost of aprotinin in children undergoing reoperative open heart surgery. Anesth Analg 1996 Dec;83(6):1193-9.

7. Davies MJ, Allen A, Kort H, Weerasena NA, Rocco D, Paul CL, et al. Prospective, randomized, double-blind study of high-dose aprotinin in pediatric cardiac operations. *Ann Thorac Surg* 1997 Feb;63(2):497-503.
8. Dietrich W, Mossinger H, Spannagl M, Jochum M, Wendt P, Barankay A, et al. Hemostatic activation during cardiopulmonary bypass with different aprotinin dosages in pediatric patients having cardiac operations. *J Thorac Cardiovasc Surg* 1993 Apr;105(4):712-20.
9. Herynkopf F, Lucchese F, Pereira E, Kalil R, Prates P, Nesralla IA. Aprotinin in children undergoing correction of congenital heart defects. A double-blind pilot study. *J Thorac Cardiovasc Surg* 1994 Sep;108(3):517-21.
10. Murugesan C, Banakal SK, Garg R, Keshavamurthy S, Muralidhar K. The efficacy of aprotinin in arterial switch operations in infants. *Anesth Analg* 2008 Sep;107(3):783-7.
11. Seghaye MC, Duchateau J, Grabitz RG, Jablonka K, Wenzl T, Marcus C, et al. Influence of low-dose aprotinin on the inflammatory reaction due to cardiopulmonary bypass in children. *Ann Thorac Surg* 1996 Apr;61(4):1205-11.
12. Williams GD, Ramamoorthy C, Pentcheva K, Boltz MG, Kamra K, Reddy VM. A randomized, controlled trial of aprotinin in neonates undergoing open-heart surgery. *Paediatr Anaesth* 2008 Sep;18(9):812-9.
13. Arnold DM, Fergusson DA, Chan AK, Cook RJ, Fraser GA, Lim W, et al. Avoiding transfusions in children undergoing cardiac surgery: a meta-analysis of randomized trials of aprotinin. *Anesth Analg* 2006 Mar;102(3):731-7.
14. Jaquiss RD, Ghanayem NS, Zacharisen MC, Mussatto KA, Tweddell JS, Litwin SB. Safety of aprotinin use and re-use in pediatric cardiothoracic surgery. *Circulation* 2002 Sep 24;106(12 Suppl 1):I90-4.
15. Siehr S, Stuth E, Tweddell J, Hoffman G, Troshynski T, Jones D, et al. Hypersensitivity reactions to aprotinin re-exposure in paediatric surgery. *Eur J Cardiothorac Surg* Feb;37(2):307-11.
16. Carrel TP, Schwanda M, Vogt PR, Turina MI. Aprotinin in pediatric cardiac operations: a benefit in complex malformations and with high-dose regimen only. *Ann Thorac Surg* 1998 Jul;66(1):153-8.
17. Mangano DT, Tudor IC, Dietzel C. The risk associated with aprotinin in cardiac surgery. *N Engl J Med* 2006 Jan 26;354(4):353-65.
18. Mangano DT, Miao Y, Vuylsteke A, Tudor IC, Juneja R, Filipescu D, et al. Mortality associated with aprotinin during 5 years following coronary artery bypass graft surgery. *JAMA* 2007 Feb 7;297(5):471-9.
19. Fergusson DA, Hebert PC, Mazer CD, Fremes S, MacAdams C, Murkin JM, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med* 2008 May 29;358(22):2319-31.
20. Pasquali SK, Hall M, Li JS, Peterson ED, Jaggars J, Lodge AJ, et al. Safety of aprotinin in congenital heart operations: results from a large multicenter database. *Ann Thorac Surg* Jul;90(1):14-21.

Anticoagulation during VAD Support in Infants and Children

Leslie Raffini MD, MSCE, Division of Hematology, Department of Pediatrics, Children's Hospital of Pediatrics, University of Pennsylvania

Background:

Ventricular assist devices as a bridge to cardiac transplant are increasingly utilized in neonates and children with heart failure. Complications are common, and neurologic events, both hemorrhagic and thromboembolic, are a significant source of morbidity and mortality.

Methods:

Currently available evidence regarding anticoagulation during VAD support was reviewed.

Results:

1. High quality evidence regarding how best to manage anticoagulation in pediatric VAD patients is lacking.
2. Pro-thrombotic risk factors include coagulation activation due to the foreign surface of the device, altered flow dynamics, venous stasis, and acute infection.
3. Anticoagulation is a critical component of the management of patients with ventricular assist devices, and is generally achieved using a combination of anticoagulant drugs (unfractionated heparin, low molecular weight heparin and warfarin) and anti-platelet agents (aspirin, dipyridole and plavix).
4. There are numerous diagnostic assays that can be performed to help assess the level of anticoagulation including prothrombin time, partial thromboplastin time, anti-Xa level, thromboelastography, thromboelastography with platelet mapping, PFA-100 and other platelet function studies.
5. Use of standardized protocols, with individualized titration of anticoagulation based on interpretation of extensive coagulation assays is becoming more common and complicated. These protocols will need to be refined based upon close evaluation of the clinical outcomes (hemorrhage or thrombosis) of patients.
6. Data from the recently completed Berlin Heart EXCOR Pediatric IDE study may help improve anticoagulation management of patients in the future.

Conclusions:

Life-threatening hemorrhagic and thrombotic events are common in infants and children during VAD support. Clinical studies focused on understanding how best to individualize anticoagulation management using current diagnostic assays are required to reduce these complications.

To Cool or Not To Cool During CPR

Alexis Topjian, MD,

The Pediatric Intensive Care Unit, The Children's Hospital of Philadelphia. Philadelphia, PA, USA.

Therapeutic hypothermia following cardiac arrest improves neurologic outcome in select populations. Following adult ventricular fibrillation arrest and perinatal hypoxic ischemic encephalopathy, hypothermia improves morbidity and mortality when compared to usual care.

Evaluation of therapeutic hypothermia in the pediatric cardiac arrest population has been limited thus far to retrospective evaluations and to date there have been no published prospective trials. Doherty et al. performed a multicenter retrospective cohort study across 5 centers, of which only three utilized hypothermia. 88% of the study population were children with underlying heart disease and 94% of the arrests were in-hospital.¹ In contrast, Fink et al. evaluated a single center's retrospective experience with induced therapeutic hypothermia for primarily asphyxia-associated cardiac arrests. Only 8% of patients had underlying heart disease and only 9% suffered in-hospital arrests. Both studies showed no outcome benefit from therapeutic hypothermia when controlling for multiple variables.² Systematic evaluation of the feasibility of a standard algorithm for induction and maintenance of therapeutic hypothermia following pediatric cardiac arrest using surface cooling showed that overshoot hypothermia <32°C, hypokalemia and bradycardia (< 2%ile for age in 58%) were common.³ Despite this, there were no episodes of bleeding or ventricular tachyarrhythmia that required treatment. A recent study of therapeutic hypothermia to treat patients with traumatic brain injury showed more hypotension in hypothermia subjects and a trend for higher mortality.⁴ The American Heart Association's current recommendation is "Therapeutic hypothermia (32°C to 34°C) may be considered for children who remain comatose after resuscitation from cardiac arrest. It is reasonable for adolescents resuscitated from sudden, witnessed, out-of-hospital VF cardiac arrest."⁵

To date, therapeutic hypothermia during or following pediatric cardiac arrest has not been clinically proven to improve neurologic outcome. To address whether therapeutic hypothermia improves outcomes following pediatric cardiac arrest, a multicenter randomized clinical trial comparing therapeutic hypothermia (32-34°C) to therapeutic normothermia (36-37.5) (Therapeutic Hypothermia After Pediatric Cardiac Arrest (THAPCA, www.thapca.org) is currently underway.

References:

1. Doherty DR, Parshuram CS, Gaboury I, et al. Hypothermia therapy after pediatric cardiac arrest. *Circulation* 2009;119:1492-500.
2. Fink EL, Clark RS, Kochanek PM, Bell MJ, Watson RS. A tertiary care center's experience with therapeutic hypothermia after pediatric cardiac arrest. *Pediatr Crit Care Med* 2009.
3. Topjian A, Hutchins L, Diliberto MA, et al. Induction and maintenance of therapeutic hypothermia after pediatric cardiac arrest: Efficacy of a surface cooling protocol. *Pediatr Crit Care Med* 2010.
4. Hutchison JS, Ward RE, Lacroix J, et al. Hypothermia therapy after traumatic brain injury in children. *N Engl J Med* 2008;358:2447-56.
5. Kleinman ME, Chameides L, Schexnayder SM, et al. Part 14: pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122:S876-908.

CPR and E-CPR: what's new?

Maryam Y. Naim, M.D.

Department of Anesthesiology and Critical Care,
The Children's Hospital of Philadelphia, Philadelphia PA 19104

In October 2010, the American Heart Association released updated guidelines for cardiopulmonary resuscitation (CPR), and emergency cardiovascular care. Major changes in the pediatric basic life support guidelines [1] include initiation of CPR with chest compressions rather than rescue breaths (C-A-B versus A-B-C), compression depth to one-third of the anterior-posterior diameter of the chest, and recommendations for automatic external defibrillator to extend to infants if manual defibrillators are not available. Key additions in the pediatric advanced life support guidelines [2] include guidance on management of cardiac arrest in children with single-ventricle physiology and pulmonary hypertension. Post cardiac arrest care recommendations now include avoidance of hyperoxemia in the post resuscitation phase, and consideration of therapeutic hypothermia in comatose survivors of pediatric cardiac arrest. A post mortem evaluation is also recommended for children with sudden unexplained cardiac death. The guidelines also recommend consideration of early activation of extracorporeal life support for cardiac arrest (E-CPR) in highly supervised environments for children with a potentially reversible cause of arrest.

Two recent large studies on E-CPR from the Extracorporeal Life Support Organization (ELSO) database [3] and National Registry of CardioPulmonary Resuscitation (NRCPR) [4] showed increased use of E-CPR in children, with no increase in survival over time. Survival rates to hospital discharge in series looking at mixed pediatric populations range from 33-47.5% [3-6]. Patients who require E-CPR for primary cardiac disease continue to have superior outcomes compared to patients with non-cardiac disease, with a reported 42-51% [7-8] survival to hospital discharge. Increasing information is also emerging on neurologic outcomes in the E-CPR pediatric population. There is a broad range of reported neurologic injury [4-5, 8-9], favorable neurologic outcomes at hospital discharge in some reports range from 75-94.9% [4, 8]. However, these high percentages most likely do not represent true long-term neurologic injury, as the majority of survivors are young infants. The future of E-CPR research includes assessment of long term-neurologic outcomes of E-CPR survivors [10], quality of life assessments, evaluation of cost-effectiveness of rapid deployment teams [11], and development of new techniques for safe and rapid cannulation.

1. Berg, M.D., et al., *Part 13: pediatric basic life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care*. Circulation, 2010. **122**(18 Suppl 3): p. S862-75.
2. Kleinman, M.E., et al., *Part 14: pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care*. Circulation, 2010. **122**(18 Suppl 3): p. S876-908.
3. Thiagarajan, R.R., et al., *Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children*. Circulation, 2007. **116**(15): p. 1693-700.
4. Raymond, T.T., et al., *Outcomes among neonates, infants, and children after extracorporeal cardiopulmonary resuscitation for refractory in-hospital pediatric cardiac arrest: a report from the National Registry of Cardiopulmonary Resuscitation*. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies, 2010. **11**(3): p. 362-71.

-
5. Morris, M.C., G. Wernovsky, and V.M. Nadkarni, *Survival outcomes after extracorporeal cardiopulmonary resuscitation instituted during active chest compressions following refractory in-hospital pediatric cardiac arrest*. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies, 2004. **5**(5): p. 440-6.
 6. Tajik, M. and M.G. Cardarelli, *Extracorporeal membrane oxygenation after cardiac arrest in children: what do we know?* European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery, 2008. **33**(3): p. 409-17.
 7. Chan, T., et al., *Survival after extracorporeal cardiopulmonary resuscitation in infants and children with heart disease*. The Journal of thoracic and cardiovascular surgery, 2008. **136**(4): p. 984-92.
 8. Kane, D.A., et al., *Rapid-response extracorporeal membrane oxygenation to support cardiopulmonary resuscitation in children with cardiac disease*. Circulation, 2010. **122**(11 Suppl): p. S241-8.
 9. Barrett, C.S., et al., *Neurological injury after extracorporeal membrane oxygenation use to aid pediatric cardiopulmonary resuscitation*. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies, 2009. **10**(4): p. 445-51.
 10. Lequier, L., et al., *Two-year survival, mental, and motor outcomes after cardiac extracorporeal life support at less than five years of age*. The Journal of thoracic and cardiovascular surgery, 2008. **136**(4): p. 976-983.e3.
 11. Mahle, W.T., et al., *Cost-utility analysis of salvage cardiac extracorporeal membrane oxygenation in children*. The Journal of thoracic and cardiovascular surgery, 2005. **129**(5): p. 1084-90.

Ventricular Assist Device Use: A Single Pediatric Center Experience

Aaron Eckhauser MD1, Matthew J. O'Connor MD2, Chitra Ravishankar MD2, Lisa M. Montenegro MD3, Susan C. Nicolson MD3, Peter J. Gruber MD, PhD1, Thomas L. Spray MD1, J. William Gaynor MD1, Beth D. Kaufman MD2, Stephanie Fuller MD1.

Division of Cardiothoracic Surgery¹, Divisions of Pediatric Cardiology², Division of Cardiothoracic Anesthesiology and Critical Care³ at the Children's Hospital of Philadelphia, Philadelphia, PA, USA

Background:

Assess outcomes of ventricular assist devices (VADs) as a bridge to heart transplantation (HT) or recovery in young patients with congenital heart defects (CHD) and cardiomyopathy (CM).

Methods:

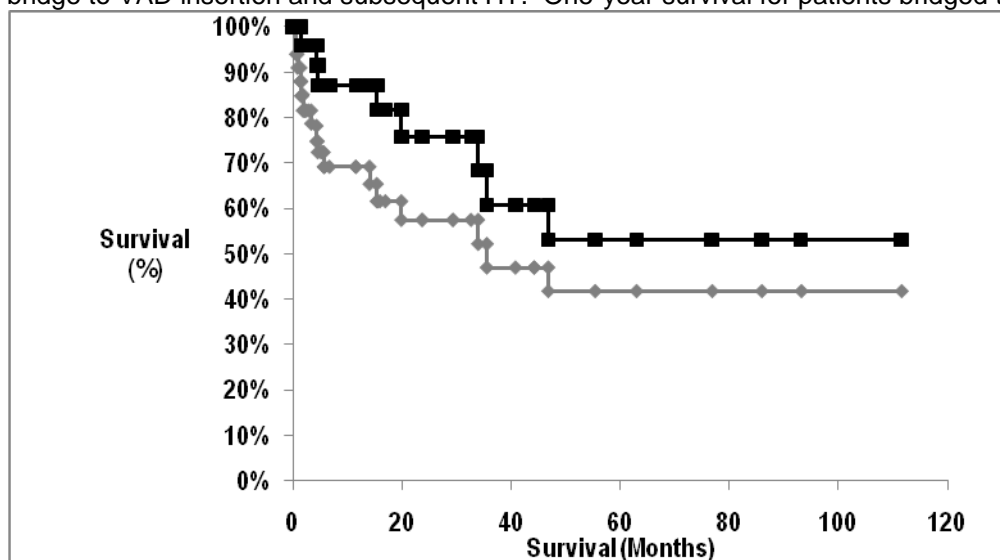
Retrospective analysis of patients undergoing VAD insertion from October 1998 to December 2010. Survival estimates were calculated using the Kaplan-Meier method.

Results:

Paracorporeal pneumatic VADs were used in 33 patients. Median age was 13.6 years (2.2 months to 25 years). Median weight was 47.5 kg (4 to 110 kg). Diagnoses were dilated CM in 23 patients (72%), CHD in 8 (22%) and restrictive CM in 2 (6%). Extracorporeal membrane oxygenation (ECMO) was used as a bridge to VAD in 8 (24%). Median duration of VAD support was 86 (8 to 423) days. Post-VAD complications included bleeding requiring reexploration in 10 (31%), neurologic events in 8 (24%), infection in 17 (52%), and respiratory failure requiring tracheostomy in 4 (12%). Twenty-four (75%) patients were bridged to HT including 5/8 bridged to VAD with ECMO and one recovered. Causes of death prior to HT were neurologic in 3 patients, sepsis in 2, and multiorgan failure in 3 patients. Overall 1-year survival after VAD was 68±8%. For patients bridged to HT with VAD, 1-year survival was 81±9%. All patients requiring ECMO prior to VAD who underwent HT survived to hospital discharge. Figure 1 shows Kaplan-Meier survival estimates.

Conclusions:

VAD can be used successfully as a bridge to HT in young patients with CHD and CM. ECMO is an effective bridge to VAD insertion and subsequent HT. One-year survival for patients bridged to HT is excellent.



Ventricular Assist Device Support in Children & Adolescents with Heart Failure: The Children's Medical Center of Dallas Experience

Mahesh S. Sharma, MD, Joseph M. Forbess, MD, and Kristine J. Guleserian, MD

The University of Texas-Southwestern School of Medicine and Children's Medical Center of Dallas, Dallas, Texas USA

Background:

Children with heart failure unresponsive to medical therapy are left with few options for survival. Ventricular assist devices are life-saving options for such patients, allowing for bridge to transplantation or cardiac recovery.

Method:

Retrospective review from May 2006 to October 2010. Fourteen patients underwent implantation of ventricular assist devices for refractory heart failure.

Results:

Median age was 9 years (range 1–17 years), weight 42 kg (range 9.7-71 kg). Indications for support: end-stage cardiomyopathy (n =8), myocarditis (n=3), univentricular failure (n=2), and postcardiotomy heart failure (n =1). Level of limitation at time of implant included critical cardiogenic shock in 6 (43%) and progressive decline in 8 (57%). ECMO was used as a bridge to VAD in 5 (36%) of patients. Preimplant variables: 86% of patients requiring mechanical ventilation (median 4.5 days), hyperbilirubinemia in 75%, and acute renal insufficiency in 79%. Device selection was systemic VAD in 11 (79%) and BiVAD in 3 (21%). Berlin Heart EXCOR was used in 8 patients while 6 patients received a Thoratec iVAD or pVAD. Median duration of support was 87 days (range 8–313 days). Overall survival was 86%. 64% were successfully bridged to transplantation, 21% continue on support, 14% died while on a device, and no patients were weaned from VAD. Children supported for single ventricle heart failure had a 67% survival with none currently bridged to transplantation. Complications included bleeding requiring reoperation in 21% (n = 3), stroke in 29% (n =4), driveline infections in 7% (n=1). In two patients, a total of six pump exchanges were performed for thrombus formation.

Conclusions:

Survival for pediatric patients of all ages is excellent using current device technology with a majority of patient's being successfully bridged to transplantation. Morbidity is acceptably low considering the severity of illness. Significant challenges exist with long-term extracorporeal support due lack of donor availability and the high incidence of preformed alloantibodies.

Anticoagulation for Children on Mechanical Circulatory Support

Hannah Copeland, MD*, Paul E Nolan, PharmD[^], Diane Covington, RN[°], Richard Smith, MSEE[°] and Jack G Copeland, MD*

*University of California San Diego Department of Surgery – San Diego, CA

[^]University of Arizona College of Pharmacy - Tucson, AZ

[°]University Medical Center – Tucson, AZ

Background:

Anticoagulation of children on mechanical circulatory support presents a challenge. We implanted more than 350 devices in using a consistent anticoagulation protocol.

Methods:

We performed a retrospective review of all children implanted with mechanical assist devices since 1997. Infants under 2 years were titrated to normal AT III levels. Patients received dipyridamole immediately after device implantation, with IV infusion - 0.1 mg/kg/hour or in older children with a dose of 50 to 100mg per NG tube every 6 hours. ASA 2 - 10 mg/kg IV daily was started after chest tube bleeding minimized and the platelet count was $\geq 150,000$. Once chest tube bleeding was $< 1 \text{ ml/kg/H}$, heparin was started at 5-10 units/kg/hour targeting normocoagulability by TEG. Coagulation monitoring included TEG, platelet aggregation studies, INR, PTT and platelet count.

Results:

28 children, ages 1 month to 16 years, were implanted for 3-107 days (mean 27). Eighteen received LVADs, 7 BiVADs, and 3 TAHs. Adverse events during the 756 days of device support, included: 7 (25%) takebacks for bleeding, 8 strokes (29%): 3 fatal, 2 with a mild residual deficit, and 3 without deficit, and 4(14%) visceral emboli: 2 fatal and 2 non-fatal (both longterm survivors). There were 8 deaths (29%). Causes of death were embolic (5), graft failure (1), pre-implant anoxic brain damage (1), and post-explant heart failure (1). Mortality while on device support was 7/28 (25%) leaving 21/28 (75%) surviving to transplantation or weaning from device. 20/28 (71%) discharged, 10 after transplantation and 10 after native heart recovery from the hospital surviving for 2 months - 9 years.

Conclusions:

We describe an anticoagulation protocol based upon TEG and platelet aggregation studies and using heparin, ASA, and dipyridamole. Adequate anticoagulation is more difficult in children. However, 71% of the patients survived long term.

The Impact of Extracorporeal Membrane Oxygenation on Survival in Pediatric Patients with Respiratory and Heart Failure: Review of Our Experience

Takeshi Goto,CCP, Yuta Suzuki,CCP, Ai Osanai,CCP, Kaori Aoki,CCP, Akio Yamazaki,CCP, Kazuyuki Daitoku,MD, Yasuyuki Suzuki,MD, Ikuo Fukuda,MD

Department of Clinical Engineering, Hirosaki University School of Medicine and Hospital.
Department of Thoracic Cardiovascular Surgery, Hirosaki University School of Medicine.

53 Honcho, Hirosaki, Aomori, 036-8563, Japan. 5 Zaifucho, Hirosaki, Aomori, 036-8562, Japan

Background:

Extracorporeal membrane oxygenation (ECMO) is widely used for circulatory support in pediatric cardiac patients with low cardiac output and hypoxemia. We retrospectively evaluate the efficacy of ECMO support for respiratory and heart failure in infants and children.

Methods:

From April 2002 to February 2011, 14 patients aged 19 days to 20 years old (average 44 months), bodyweight 2.6 kg to 62 kg (median 14.1kg) underwent ECMO support for failing cardiac function, hypoxemia and low cardiac output syndrome. In 12 patients, ECMO was introduced after operation for congenital heart disease (6 complete repair including Fontan circulation and 6 palliative repair). In one patient, ECMO was introduced after partial pulmonary resection for congenital cystic adenomatoid malformation because of respiratory failure. One who had fulminant myocarditis caused severe heart failure. Patients' demographics, duration of extracorporeal membrane oxygenation, additional support and outcomes were analyzed.

Result:

Ten patients (71%) were successfully weaned from ECMO and eight patients (57%) discharged from the hospital. The mean duration of ECMO support was 585 hours (range 11-2029 hours). Although management of the ECMO circuit, including anticoagulation (ACT:150-250), was conducted following the institutional practice guidelines, it was difficult to control the bleeding. Seven patients required renal replacement therapy during ECMO support using peritoneal dialysis or continuous hemodiafiltration. Five patients had additional operative procedures; systemic-pulmonary shunt in three and Fontan takedown in two. A patient who had longest ECMO support for respiratory failure due to ARDS after lung surgery was successfully weaned from ECMO because HFO (high frequency oscillation) improved respiratory function.

Conclusions:

ECMO for heart and respiratory failure in infant and children is effective and allows time for recovery of cardiac dysfunction and acute hypoxic insult. The long term ECMO support over 2000 hours was very rare, but it was possible to wean from ECMO using HFO.

NeoNatOx – A Pumpless Extracorporeal Lung Support for Premature Neonates

Jutta Arens^{1†}; Mark Schoberer^{2†}, MD; Anne Lohr², MD; Thorsten Orlikowsky², MD; Matthias Seehase³, MD; Reint K. Jellema³, MD; Jennifer J. Collins³; Boris W. Kramer³, MD, PhD; Thomas Schmitz-Rode¹, MD; Ulrich Steinseifer¹, PhD

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 Dept. of Paediatrics, School of Mental Health and Neuroscience; School of Oncology and Developmental Biology; Maastricht University Medical Center, Maastricht, The Netherlands

† Both Authors contributed equally to this manuscript

Background: Gas exchange in premature neonates is regularly impaired by structural and functional immaturity of the lung. Mechanical ventilation, which is vitally important to sustain oxygenation and CO₂-elimination causes at the same time mechanical and inflammatory destruction of lung tissue. To date extracorporeal oxygenation is no treatment option, one reason among others being the size of available oxygenators and cannulas.

We hypothesized that, by maintenance of the fetal cardiopulmonary bypass and interposition of a suitable passively (arterio-venous) driven membrane oxygenator, a substantial improvement in gas exchange can be achieved. In close cooperation between engineers and neonatologists we developed a miniaturized oxygenator and adapted cannulas to be used as a pumpless extracorporeal lung support which is connected to the circulation via cannulation of the umbilical cord vessels.

Methods: From a range of commercially available catheters we chose a 14 Ga. One-Lumen-Central-Venous-Catheter (Arrow Deutschland GmbH, Erding, Germany) for cannulation. To evaluate the ideal insertion depth we shortened these catheters from their original length (200 mm) to 40, 60, 80, 100 and 120 mm (four catheters each). This selection of catheterlengths was investigated on premature Texel lambs (n = 6, 2452 g ± 1054, 134 days ± 2.7 gestational age (term = 150 days)) for maximum flow, pressure drop and viability. Experiments were carried out by use of a short extracorporeal circuit with flow and pressure monitoring. The collected data were used to generate a requirement specification for the extracorporeal circuit including an oxygenator (in sense of an “artificial placenta”).

Results: Max. extracorporeal flows were achieved with L=80 and 60 mm catheters (148 resp. 130 ml/min). Hence, for the following in vivo test series 70 mm catheterlength was chosen. An oxygenator with 0.09 m² gas exchange surface area and 12 ml priming volume (19 ml incl. tubing) was designed, produced and tested in vitro and in vivo. In vitro tests showed a typical gas exchange of 47 ml_{CO₂}/l_{blood} and 53 ml_{O₂}/l_{blood} at 80 ml/min blood flow and 160 ml oxygen flow. In vivo (fig. 1) a mean pCO₂ (pO₂) at the oxygenators inlet of 54 ± 21 mmHg (49 ± 26 mmHg) and at the oxygenators outlet of 34 ± 7 mmHg (160 ± 64 mmHg) at mean blood flow of 91 ± 35 ml/min resp. 33 ml/Kg/min was found. The animals were hemodynamically stable.

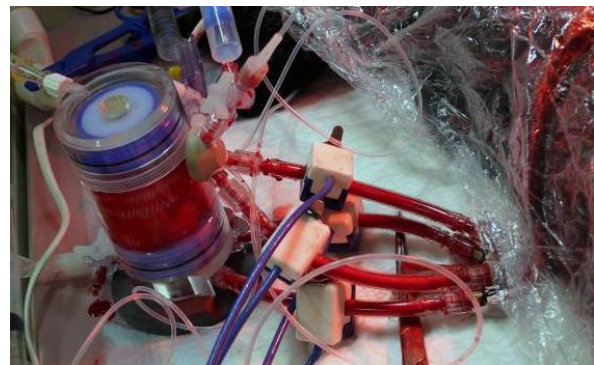


Fig. 1: NeoNatOx connected to the navel vessels of a premature lamb

Conclusions: We have developed a small oxygenator and extracorporeal circuit which is suitable to establish a pumpless extracorporeal lung support for premature lambs. We regard this as one step on the way to clinical application of the artificial placenta.

Development of a Newly Designed Circulatory Assist Device For Fontan Circulation by using Shape Memory Alloy Fiber

Yasuyuki Shiraishi, PhD¹, Akihiro Yamada, BS¹, Telma K. Sugai, MS¹, Hidekazu Miura, PhD¹, Shunichi Mochizuki, MD, PhD¹, Tomoyuki Yambe, MD, PhD¹, Dai Homma, PhD², Masaaki Yamagishi, MD, PhD³

¹ Institute of Development, Aging and Cancer, Department of Medical Engineering and Cardiology, Tohoku University, Sendai, Japan

² Toki Corporation, Tokyo, Japan

³ Department of Pediatric Cardiovascular Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan

Background:

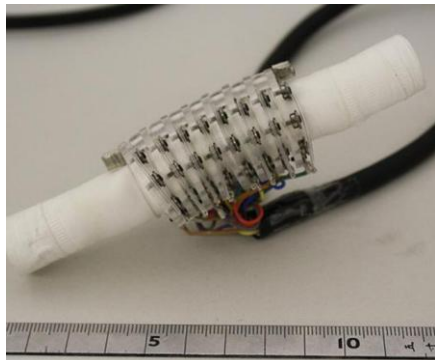
Total cavopulmonary connection (TCPC) is commonly applied for the surgical treatment of congenital heart disease such as single ventricle in pediatric patients. Patients with no ventricle in pulmonary circulation are treated along with Fontan algorithm, in which the systemic venous return is diverted directly to the pulmonary artery without passing through subpulmonary ventricle. In order to promote the pulmonary circulation after Fontan procedure, we developed a newly designed pulmonary circulatory assist device by using shape memory alloy fibers.

Methods:

We developed a pulmonary circulatory assist device as a non-blood contacting mechanical support system in pediatric patients with TCPC. The device has been designed to be installed like a cuff around the ePTFE TCPC conduit, which can contract from outside. We employed a covalent type functional anisotropic shape memory alloy fiber (Biometal, Toki Corporation, Tokyo Japan) as a servo actuator of the pulmonary circulatory assist device. The diameter of this fiber was 100 μm , and its contractile frequency was 2-3 Hz. Heat generation with electric current contracts these fibers and the conduit. The maximum contraction ratio of this fiber is about 7% in length. In order to extend its contractile ratio, we fabricated and installed mechanical structural units to control the length of fibers. In this study, we examined basic contractile functions of the device in the mock system.

Results:

Figure 1 shows a prototype model of the mechanical TCPC assist device developed in this study, which is attached onto the ePTFE conduit of 18mm in diameter. The internal pressure of the conduit increased to 62 mmHg by the mechanical contraction under the condition of 400 msec-current supply in the mock examination with the overflow tank of 10mmHg loading.



Conclusion:

A prototype model of the pulmonary circulatory assist device for TCPC was developed.

I³-Assist: Individual, Interactive and Integrated Cardiopulmonary Assist – A Concept

George Wagner¹; Peter Schlanstein¹; Jutta Arens¹; Rüdger Kopp², MD; Ralf Bensberg², MD; Rolf Rossaint², MD; Thomas Schmitz-Rode¹, MD; Ulrich Steinseifer¹, PhD

¹ Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany

²Dept.of Intensive Care Medicine, University Hospital Aachen, RWTH Aachen University, Germany

Background:

Current heart-lung-machines (HLMs) and extracorporeal life support (ECLS) are available in a few, often only three, sizes of components like oxygenators and heat exchangers. Considering the body weight range from neonates to adults, suitable adaptations for patients' needs are mostly impossible. Additionally, if components have to be replaced, e.g. due to failure, the entire system needs to be stopped. As the components of HLMs and ECLS are identical only in parts, another extracorporeal system must be installed when changing over from HLM to ECLS, unavoidably causing haemodilution.

In order to diminish these known limitations we designed an entirely new concept conjoining HLM and ECLS.

Methods:

I³-Assist aims at developing a highly integrated and modular extracorporeal system which can be adapted to individual treatment needs of the patient. To achieve an optimized priming volume and contact surface, oxygenator and heat exchanger modules in only one size will be provided. These modules can be combined by the user to achieve the gas/heat exchange area suitable for the individual patient (e.g. one for a neonate, five for a small or eight for a tall adult). Additionally, all modules of an HLM/ECLS system will be exchangeable under operating conditions. Thus, an immediate and seamless transition between operation modes can be carried out and the system can be modified according to changing individual needs during surgery and therapy. Due to the highly integrated design the system can be placed near the operating table and can be used for inter- and intrahospital transport. The key feature of the design is the development of a safe and easy connection of the different modules. First in vitro experiments (fig. 1) demonstrate the feasibility of the modular design regarding flow regulation and pressure build-up.

Results:

Using flows from 100-800 ml/min the pressure loss over each module was determined. The total loss was equal to conventional oxygenators with integrated heat exchangers. The oxygenators represented 2/3, the heat exchanger 1/3 of the loss. Due to the passive custom made dividing and collection units, each line was equally exposed to the systems flow within a range of $\pm 3\%$.

Conclusions:

The I³-Assist project is focused on developing a highly integrated and modular system of life-supporting functional units. This system can be used as a heart-lung-machine (HLM), but also as an extracorporeal life support (ECLS), and for inter- plus intrahospital transportation. Furthermore, the system can be adapted to the individual and varying requirements of patients.

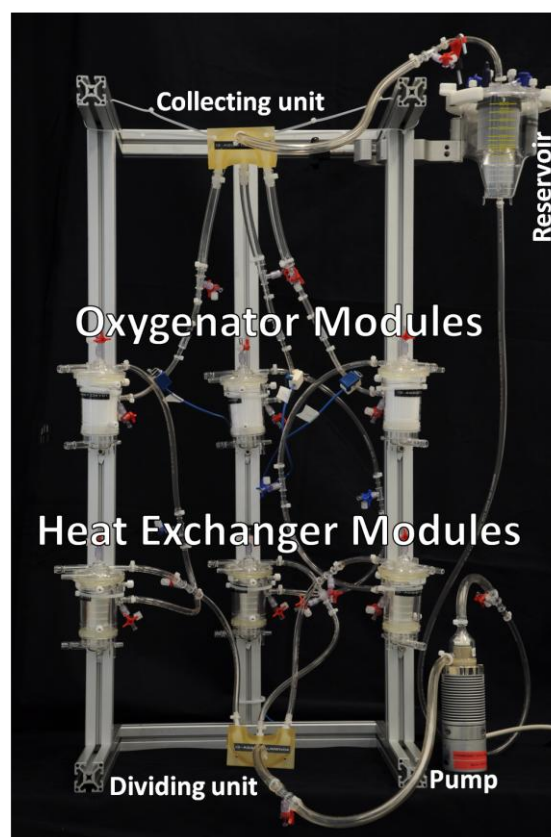


Figure 1: Setup of a modular parallel test-bench

In vitro performance of the InCor pediatric VAD

Idágene A. Cestari, PhD; Sérgio A. Hayashida; Helena T. T. Oyama; Simão Bacht ; Arlindo Riso, MD PhD; Ismar N. Cestari MD. PhD; Marcelo Jatene, MD. PhD; Noedir A.G. Stolf, MD. PhD.
Departments of Bioengineering, Pediatrics and Surgery, Heart Institute, (InCor) University of Sao Paulo Medical School, Sao Paulo, Brazil.

Background:

A 15 mL pulsatile pump for pediatric patients was designed based on the adult-size pump developed and clinically evaluated in our Institution. The pump consists of a blood and a pneumatic chamber separated by a polyurethane diaphragm and it is fitted with 2 trileaflet bovine pericardial valves. Blood contacting surfaces are heparin-coated. A pneumatic actuator allows adjustment of pump output flow through the control of full-to-empty cycle and filling pressure.

Methods:

A closed loop hydraulic simulator of pediatric circulation was designed to evaluated pump hydrodynamic performance. The simulator combines a fluid reservoir and a compliance chamber to which the pump inflow and outflow valved orifices are connected. A clamp downstream the pump is used to adjust afterload pressure. Hemolysis was evaluated using fresh bovine blood on a dual loop recirculating flow system were the InCor pediatric pump was compared side-to-side with a pediatric pump of similar volume available for clinical use.

Results:

Under test conditions of 100 mmHg afterload and preload pressures up to 18 mm Hg, using control modes of fixed frequency (40-100 bpm) or full-to-empty the pump achieved flows varying from 0,5 to 1.5 L/min. Maximum flow was obtained with the use of negative pressure in the pneumatic chamber during filling phase. The normalized index of hemolysis determined by measuring plasma free hemoglobin was $0,08 \pm 0,03$ g/100L. No statistical difference was found between the hemolysis of the InCor and the commercially available pump.

Conclusions:

These results suggest that the InCor pediatric VAD may be suitable for clinical use. Further evaluation of its long term performance is warranted.

Development of a magnetic bearing system for a new 3rd generation blood pump

Jung Joo Lee¹, PhD, MBA, Chi Bum Ahn^{1,2}, PhD, Jaesoon Choi^{1,2}, PhD, Jun Woo Park¹, PhD, Seung-Joon Song^{1,2}, MS, Kyung Sun^{1,2,3}, MD, PhD, MBA

¹. Korea Artificial Organ Center, Korea University,

². Biomedical Science of Brain Korea 21, College of Medicine, Korea University,

³. Department of Thoracic and Cardiovascular Surgery, Korea University Medical College, Seoul, Korea

Background:

The magnetic bearing system is an important factor in the 3rd generation blood pump for the matter of durability, hemocompatibility, and so on. However, it has important issues, such as efficiency, volume and hemodynamic stability of flow path as well as mechanical stability, stiffness and so on, for the blood pump to be more safe and efficacious. There were many studies for these matters. In this study, a new magnetic bearing system including motor for a new 3rd generation blood pump was developed and evaluated.

Methods:

The magnetic bearing system consists of a magnetic levitation system and a BLDC motor system. The entire control degree of freedom is one and is for the axial levitation. The radial levitation is solved with passive radial magnetic levitation system. For the purpose of obtaining of improved efficiency of the entire system, the magnetic circuit for the axial levitation was separated with the magnetic circuit for the drive of motor, and each magnetic circuit was designed to have a minimum gap with placing parts, as impeller blade, outside the circuit. For this design, non-contact gap sensor was manufactured to have smallest volume.

Finally, the integrated system of magnetic levitation system, motor system and the gap sensor was manufactured and the performance was evaluated with MATLAB xPC Target system.

Results:

An eddy current gap sensor was developed to have a dimension of 2.38 mm outside diameter and 0.88 mm thickness, and a resolution of 5 μ m. A BLDC motor system was developed to have a dimension of 20 mm outside diameter and 28.75 mm length, and a power of 4.5W. It showed the torque of 8.6mNm at 5,000 rpm. The entire system was developed to have a dimension of 22 mm outer diameter and 97 mm length, including the motor and the sensor.

It showed sufficient levitation performance in the stop state and the rotation state with a gap of 0.3 mm. It showed the steady position error of 0.01 μ m in the stop state and position error of 0.02 μ m in the rotational speed of 5,000 rpm and current consumption was 0.15A and 0.17A, respectively.

Conclusions:

A new magnetic bearing system with a unique design was developed and evaluated. It would be an important step in the further development of a new 3rd generation blood pump.

Scanning electron microscopic investigations to investigate the role of the endocardium in the origin of Dilated Cardiomyopathy (DCM)

Jan D. Schmitto¹, Michael Schultz², Peter Schwartz², Kasim O. Coskun¹, Florian Heidrich¹, Sheila Fatehpur^{1,3}, Samuel Sossalla⁴, Christian Sohns⁴, Friedrich Schöndube¹, Masoud Mirzaie^{1,3}

¹Department of Thoracic, Heart and Vascular Surgery, Göttingen University, Germany

²Institute for Anatomy, Göttingen University, Germany

³Department of Vascular Surgery, Lippe-Lemgo-Hospital, Lemgo, Germany

⁴Department of Cardiology, Göttingen University, Germany

⁵Department of Cardiac-, Thoracic-, Transplantation- and Vascular Surgery, Hannover Medical School, Hannover, Germany

Background:

Dilated cardiomyopathy (DCM) is a cardiac disease multifactorial etiology and increasing incidence. During recent years, genetics and the pathophysiology of DCM have been intensively investigated, and thereby the knowledge of DCM has increased rapidly. However, the pathophysiological mechanisms, by which morphological modifications eventually result in clinical heart failure, are complex and yet not totally understood.

Methods:

We aimed to investigate the pathophysiological origin of DCM from a morphological point of view. Therefore, scanning-electron and polarized-light-microscopic-investigations on explanted DCM-hearts were performed. Tissue samples were taken from 4 male (72±2 years) and 2 females (63±1 years). The study population included DCM-patients who were listed on transplant waiting-list while being clinically categorized in NYHA III-IV. Hearts were explanted for cardiac transplantation and explanted hearts were examined by scanning-electron-microscopy and polarized-light-microscopic-investigations.

Results:

The endocardial layer is partially desquamated from basement membrane and showed isolated island-like cell-formations. Endothelial island areas lost cell-connection to each other as well as to basement membrane. Additionally, abrasion of the endothelial cells, formation of filiform and lamellar Lambl's excrescences, locally-well-defined elevations above the intact endothelium, calcium deposits and hyperplasia of collagen fibers could be detected.

Conclusion:

In this study of explanted DCM-hearts, several morphological modifications of the endocardium and extracellular-matrix were identified by scanning-electronical and polarized-microscopic-investigations. Our results lead to the suggestion that collagen-synthesis disturbances may play an important role for the etiological origin of the development of DCM.

Influence of Mild Metabolic Acidosis on Catecholamine Response in Isolated Myocardium of Non-failing Sheep Hearts

Hanna Schotola¹, MD, Samuel Sossalla², MD, Taufiek K. Rajab³, MD, Karl Toischer², MD, MD, Suyog A. Mokashi³, MD, Michael Quintel¹, MD, Martin Bauer¹, MD, Frederick Y. Chen³, MD, Jan D. Schmitto^{3,5}, MD

¹Department of Anesthesiologie, Emergency and Intensive Care Medicine, University Hospital Goettingen, Germany

²Division of Cardiology and Pneumology, University Hospital Goettingen, Germany

³Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

⁴Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany

Background:

Congenital Cardiac Surgery is postoperatively often associated with acute metabolic changes leading to hemodynamic disturbances necessitating the need for inotropic treatment. Within the cardiac community, there is still controversial discussion about standardized medical therapy to treat postoperative acidosis e.g. by buffering and hence improving catecholaminergic response of the heart.

The aim of this study was to investigate the influence of mild (and thus clinical relevant) acidosis on cardiac contractility and catecholamine response in intact trabeculae.

Methods:

Intact trabeculae (n=24) were isolated from the right ventricle of healthy sheep hearts. Two different groups (Group1:pH=7.40,n=9;Group2:pH=7.20,n=13) were investigated and force amplitudes were measured at frequencies between 30-180bpm and increasing catecholamine concentrations (isoprenaline 0 to 3*10⁻⁶mM).

Results:

The present study shows that mild metabolic acidosis of pH=7.20 has no significant negative inotropic and lusitropic effects on isometrically-contracting sheep trabeculae. Additionally, there was no difference in force-frequency-relation-experiments, in force amplitude as well as in relaxation kinetics compared to physiological pH=7.40. Furthermore, no differences in catecholamine response were experimentally observed. In both pH-groups, relative force amplitude was equal after maximum isoprenaline concentration. Additionally, relaxation kinetics did not show differences after catecholamine stimulation.

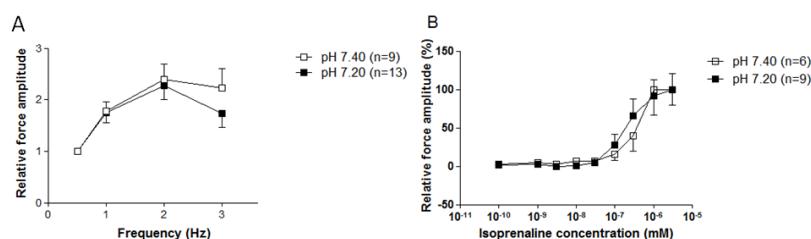


Fig. 1: A - Influence of mild acidosis on contractility of trabeculae during increasing stimulation frequencies: Mean force amplitudes normalized to the lowest frequency showing no significant differences in force development between 0.5 and 3 Hz (n=9 vs. 13, P=ns) [0.5 Hz absolute values 3.1±2.6 for pH 7.4 vs. 3.8±2.6 mN/mm² for pH 7.2, P=ns]; **B - Influence of mild acidosis on contractility of trabeculae during increasing isoprenaline concentrations:** Mean force amplitudes normalized to baseline and maximum force showing no significant differences in force development between baseline and maximum isoprenaline concentrations (n=6 vs. 9, P=ns) [baseline absolute values 4.3±4.0 for pH 7.4 vs. 3.9±1.2 mN/mm² for pH 7.2, P=ns]

Conclusion:

In this study, we revealed that mild metabolic acidosis (pH=7.20) has no significant negative inotropic effects on isometrically-contracting sheep trabeculae compared to a physiological pH of 7.40. Additionally, each pH-group showed similar effects in the magnitude of catecholamine responses. The presented investigations underline the suggestion that buffering of mild acidosis has no beneficial impact to improve catecholaminergic response in healthy isolated trabeculae.

Further investigations in vivo and/or in failing hearts with known reduced compensatory reserves will be necessary to examine optimal medical treatment for metabolic abnormalities after cardiac surgery.

Cardiopulmonary Bypass and Its Effects on Neonatal Kidney Morphology

Theodor Tirilomis, Martin Friedrich, K. Oguz Coskun, Tasso Tempes, Aron-Frederik Popov, Jan D. Schmitto, Friedrich A. Schoendube
Dept. for Thoracic, Cardiac, and Vascular Surgery, University of Goettingen, Germany

Background:

Renal failure after open-heart surgery is even in neonatal age a serious complication with high morbidity and mortality. The aim of the study was to find out the influence of cardiopulmonary bypass (CPB) on renal morphology in a neonatal animal model.

Methods:

The kidneys of newborn piglets were examined after cardiopulmonary bypass in mild hypothermia of 32°C (CPB; n=4) regarding tubular dilatation, vacuole formation, leucocytic infiltration, epithelial destruction, and interstitial edema. Thereafter, the findings were compared with the morphology of normal neonatal kidneys (control; n=4).

Results:

All but the interstitial edema were significant altered if compared to the normal renal tissue; tubular dilatation (CPB vs. control p <0.05), vacuole formation (CPB vs. control p <0.05), leucocytic infiltration (CPB vs. control p<0.05), and epithelial destruction (CPB vs. control p<0.001).

Conclusions:

In comparison to the morphology of normal neonatal kidneys significant alterations were found after CPB in neonatal piglets.

Aggressive Zero-balance Ultrafiltration on Hemostasis: Analysis of Different Volume Used in Deep Hypothermic Circulatory Arrest Surgery

Yongli Cui, MD, Cun Long, MD, Shilei Wang, MD, Chun Zhou, MD, Jinping Liu, MD.
Department of Cardiopulmonary Bypass, Cardiovascular Institute and Fuwai Hospital, CAMS and PUMS, Beijing, China

Background:

The purpose of this study is to compare the effect of zero-balance ultrafiltration (ZBUF) on hemostasis. This technique is thought to be effective on removal inflammatory mediators. It is seemed that the greater ultrafiltration volume is used, the better outcome the patients will have. And ZBUF is widely used in deep hypothermic circulatory arrest (DHCA) operations, due to its strong inflammatory response. But whether the good outcome is also for hemostatic function is should be further evaluated. In this investigation we compared concentrations of some important hemostatic components between three groups with different ZBUF volumes.

Methods:

Twenty Chinese laboratory miniature piglets (4.12 ± 0.12 kg) underwent cardiopulmonary bypass (CPB) with DHCA were randomly divided into 4 groups: one control group and three ZBUF groups. The piglets in control group received no ZBUF, those in three ZBUF groups received 50ml/kg, 100ml/kg, 150ml/kg zero-balance volume respectively, and the ZBUF started after rewarming. Plasma level of FVII, FIII, FIX, FX, FII were measured before CPB (T1), 5min after the start of CPB (T2), after the ZBUF finished (T3), and 1hour after CPB (T4). The T3 in control group was chosen at rewarming to 36°C, because all of other three groups finished ZBUF at this temperature.

Results:

The result showed that all of these coagulatory factors have no difference at T1, T2, and T4, the FIX, FX, FII had no statistical differences at all time points in all of the four groups. FVII, FIII in 150ml/kg group, compared with control group, had relative low concentrations ($P=0.029$, $P=0.024$ respectively), but there were no significant difference between the three ZBUF groups.

Conclusions:

We supposed that the aggressive ZBUF (more than 150ml/kg) might lead to some coagulatory factors loss.

Numerical investigation of the influence of pulsatile flow on gas exchange inside an oxygenator

Ralf Borchardt; Marcus Hormes; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD
Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

Background:

The gas exchange within a hollow fiber membrane oxygenator is highly dependent on fiber arrangement and flow conditions. To investigate these influences on a microscopic scale, numerical simulation can be used. The intention of this study is to use a validated numerical model to describe the influence of pulsatile blood flow on gas exchange inside a membrane oxygenator on a microscopic scale.

Methods:

A rectangular cross section of an oxygenator including four fibers in a cross flow arrangement calculated (fig. 1). 45 % of the fibers surface were defined as pores according to commercial propylene fibers.

Non-Newtonian behavior of blood was calculated by using the Ballyk model, gas exchange of O₂ and CO₂ by using the Hormes model, which is validated for blood inside a cross oxygenator. The Hormes model uses partial pressures at the pores surfaces to calculate diffusive as well as convective gas exchange. Besides the physical and chemical properties of and CO₂ it also includes diffusion resistance of red blood cells.

Pulsatile flow was defined at the blood inlet means of sinusoidal functions varying the mean volume as well as the frequency (50 - 80 1/min) the amplitude (20 - 80 % of mean flow). To ensure comparability, corresponding constant flows were simulated as well.

Results:

Time-averaged O₂ partial pressure difference for a sinusoidal blood flow is up to 7.2 % higher than for a corresponding constant flow. In contrast time-averaged O₂ mass flow difference is up to 4.5 % lower for a sinusoidal flow. For CO₂ the partial pressure difference is slightly increased by up to 0.7 % while the CO₂ mass flow difference is reduced by up to 3.1 %. This opposed conclusion is due to a time shift between the maximum blood flow and maximum partial pressure curve.

Conclusions:

There is an influence of pulsatility on gas exchange on a microscopic scale. The different conclusions for partial pressures and mass flows indicate the importance of accurate measuring techniques during in vitro tests of pulsatile blood flows. Here the time averaged mass flow should be investigated.

General conclusions about the influence of pulsatile flows in oxygenators cannot be made from these results as only a small cross section was investigated. Non sinusoidal flows have to be calculated in the future as well.

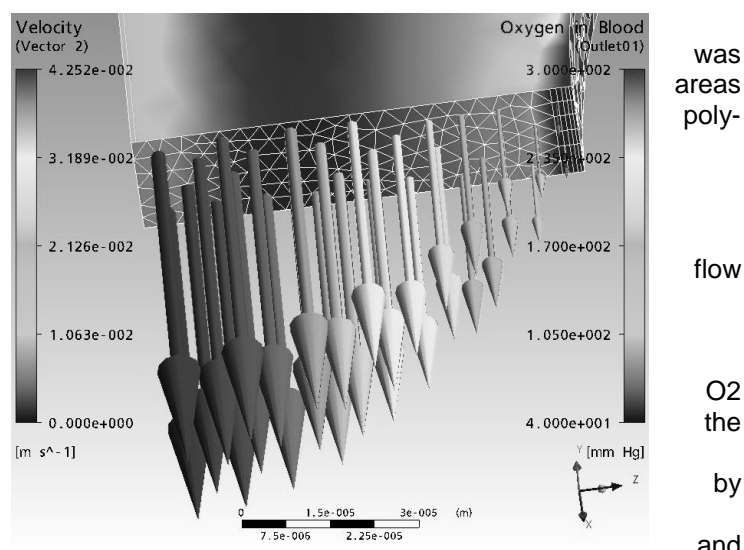


Fig. 1: Blood velocity vectors at the cross sections outlet

In Vitro Evaluation of the Hemodynamic Performance of the Electro-pneumatic Ventricular Assist Device According to the Fluid Viscosity Variation

Chi Bum Ahn, PhD, Jung Joo Lee, PhD, Jeasoon Choi, PhD, Jun Woo Park, PhD, Seung-Joon Song, MS, Kuk Hei Son, MD, Ho Sung, Son, MD, Sung Ho, Lee, MD, Kyung Sun, MD.
Korea Artificial Organ Center,
Brain Korea 21 Project for Medical Science,
Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea.

Background:

The blood viscosity of the patient who equipped with a mechanical circulatory support device can be changed by various conditions during long-term operation. It is known generally that the blood viscosity can affect the hemodynamic performances of the blood pump and therefore, quantitative evaluation of the effect of blood viscosity variation on the pump performance is important. In this study, the effect of fluid viscosity variation on the performance of the pulsatile blood pump developed by the Korea Artificial Organ Center (KH-VAD) was evaluated *in vitro*.

Methods:

Three solutions have been used for experiments which were composed of a normal saline and a glycerin and have different viscosities of 1.87, 2.76, and 3.44 cP, respectively. The hemodynamic energy was generated using a Donovan-type mock circulatory system and the KH-VAD, measured using an ultrasonic flow meter and a pressure sensor, and recorded on a monitoring computer in real-time manner for statistical processes.

Results:

Experimental results showed that mean pressure values were increased in accordance with the viscosity increase. When the viscosity increased 25%, 50%, and 85% compared to the normal saline, the mean pressure was increased 4.5, 6.65, and 11.2 mmHg respectively, and the pump output was decreased according to the viscosity increase. Energy equivalent pressure (EEP) value was increased according to the viscosity-induced pressure rise; however, surplus hemodynamic energy (SHE) value did not show any apparent changing trend.

Conclusions:

The hemodynamic performance of the KH-VAD was affected by the viscosity of the circulating fluid. Therefore, further study on the relationship between the blood viscosity and pump performance is needed to enhance long-term feasibility of the KH-VAD.

Haptic Virtual Fixture for Robotic Cardiac Catheter Manipulator

^{1,3}Jun Woo Park, PhD, ^{1,2}Jaesoon Choi, PhD, ^{1,2}Seung Joon Song, MS, ^{1,2,3}Yong doo Park, PhD, ^{1,2,4}Kyung Sun, MD, PhD, MBA

¹Korea Artificial Organ Center, ²Brain Korea 21 Project for Biomedical Science, ³Department of Biomedical Engineering, ⁴Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Korea

Background:

In manual or robot-assisted catheter intervention, excessive manipulation force may cause tissue perforation. To prevent collision of catheter tip and the vessel wall, we developed forbidden-region virtual fixture. Using images acquired routinely for catheter interventions, structure and size of blood vessel and the relative position of the catheter tip inside the vessel can be obtained.

Methods:

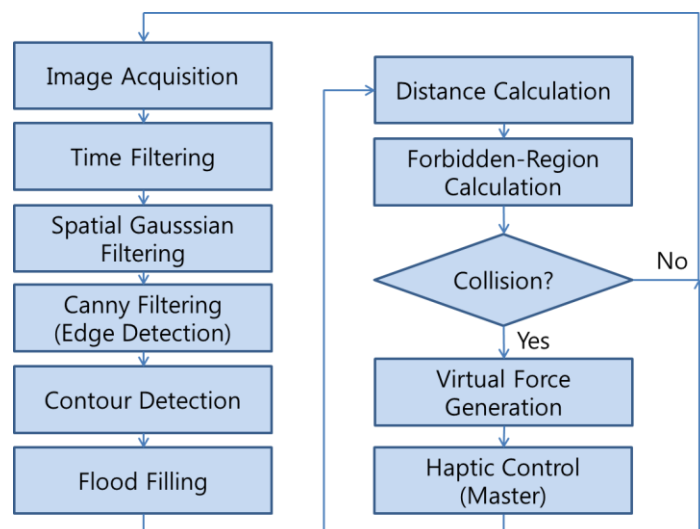
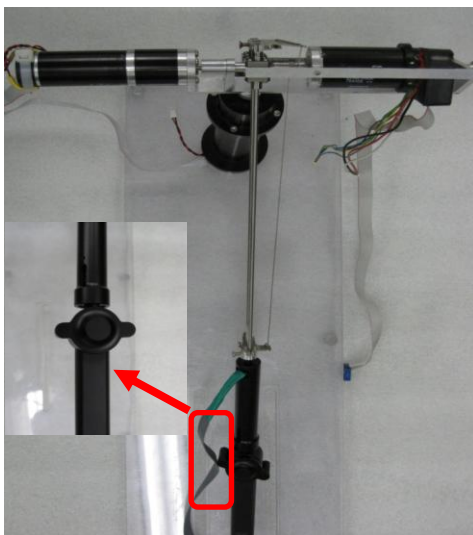
A master-slave configured robotic platform for cardiac catheter was used for this study. The robotic master handle can provide multi-degree-of-freedom haptic rendering. A testbed mimicking human vasculature in the shape and the inner radii was built for simulated intervention tests. A digital optical camera was used for image acquisition. After vessels and the catheter tip were segmented, distance between the vessel inner wall and the catheter tip was calculated and forbidden-region that catheter tip should keep away from was set for safe catheter manipulation. Virtual force generation algorithm was developed for feeding the catheter tip's penetration into the forbidden-region back to the user by the haptic master. To validate the suggested method, *in-vitro* experiments were conducted.

Results:

Through edge detection and a chain of image filtering, catheter tip and vessel wall were segmented well. Virtual force generator worked appropriately. Compared with the conventional manipulation without forbidden-region virtual fixture, suggested method diminished frequency of wall collision and raised safety of the manipulation.

Conclusions:

A robotic catheter manipulation method implementing forbidden-region virtual fixture with image analysis was developed. We think this is helpful for safe manipulation of cardiac catheters.



Microfiltration Platform for Continuous Blood Plasma Protein Extraction from Whole Blood during Cardiac Surgery

Kiana Aran, Alex Fok, Larwence A. Sasso, Neal Kamdar, Yulong Guan, Qi Sun, Akif Ündar and Jeffrey D. Zahn

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

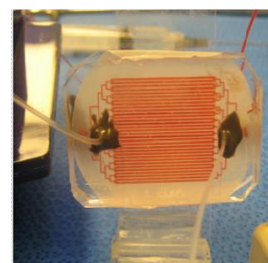
Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

In the past few years, there have been many reports on plasma separation from whole blood using a variety of microfluidic devices yet none of the reported blood separation microdevices have been tested under clinically relevant conditions. This report describes the design and fabrication of a membrane based blood microfiltration device which can operate at high flow rates with a very high recovery (>80%) of protein biomarkers used in clinical diagnosis. The system developed in this study is intended to be used as a platform to track the concentrations of inflammatory biomarkers (complements and cytokines) within human blood during cardiac surgeries, especially when extracorporeal circulatory support also known as cardiopulmonary bypass (CPB) is used. Although CPB revolutionized how cardiac surgeries are performed by allowing complicated valve replacement and cardiac repairs, especially of congenital defects in pediatric patients, coronary artery bypass grafts (CABG) and even heart transplants, the use of CPB is not without risks and adverse effects. The ultimate goal of these studies are to allow continuous patient inflammation monitoring during surgical procedures to allow physicians to anticipate surgical and postoperative complications and to better understand patient morbidity related to inflammation associated with the CPB procedure.

Methods:

The microfiltration system consists of a two-compartment mass exchanger with two aligned sets of PDMS microchannels, separated by a porous polycarbonate (PCTE) membrane. Blood flows through the channels on one side of the device (reservoir channels) and blood plasma is filtered through the membrane and into the channels on other side of the membrane (filtrate channels). The microfiltration device has been tested using a simulated CPB circulation loop primed with donor human blood, in a manner identical to a clinical surgical setup. A small portion of the blood was redirected the arterial port of the membrane oxygenator to the microfiltration device without further modification. The fluid fractions from both microdevice outlets of the reservoir and filtration channels were collected in 20 minute intervals for a total circulation time of 4 hours. Discrete blood samples of 1 ml volume were also collected from the arterial port of the membrane oxygenator as a control sample. concentration of inflammatory cytokines (TNF- α , IL-1 β , IL-6, and IL-8) were measured using immunofluorocytometry.

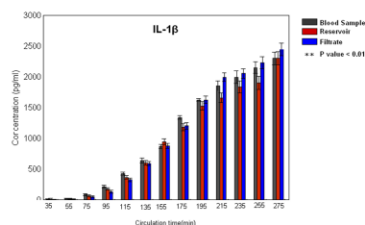


from
any

The

Results:

The results tracked cytokine concentrations collected from both the reservoir and filtrate samples which were comparable to those from direct blood draws, indicating very high protein recovery of the microdevice.



Additionally, the cytokine concentration increased significantly compared to baseline values over the circulation time for all cytokines analyzed. The high plasma protein recovery, absence of hemolysis and low level of biofouling on the membrane surface during the experimental period (over 4 hours) were all indications of effective and reliable device performance for future clinical applications.

Challenges at the Bedside with ECLS “Where the rubber meets the road”: Nursing Education

Bonnie L. Weaver, RN, MSN, CCRN, Akif Ündar, PhD, Feng Qiu, MD, Larry Baer, John L. Myers, MD, J. Brian Clark, MD, Linda Pauliks, MD, Gary Ceneviva, MD, Pamela Meinert, RN, PhD

Nursing Education & Professional Development, Pediatric Cardiovascular Research Center, Department of Perfusion, Departments of Surgery, Pediatrics, Pediatric Critical Care Medicine, Department of Nursing Education & Professional Development, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

The design of the Penn State Hershey Pediatric ECLS circuit composed of a Rotaflow centrifugal pump, a Quadrox-iD Pediatric PMP HFMO, two Bio-Medicus ECLS cannulae (arterial and venous), and 3 feet of ¼ inch tubing for both the arterial and venous. In January 2009, the circuit was established as the standard of care for children requiring ECLS in the PICU. With the changes in the circuitry, the model of care for patient delivery was also redesigned. This initiative translated to an educational endeavor for all members of the ECLS clinical team. The following is a report of our experience @ the bedside with the conversion of the new circuit & care delivery model.

Historically 2 clinicians, 1 ECLS trained specialist (Respiratory Therapist, RN, or Perfusionist) & 1 ECLS trained PICU nurse, managed the patient's care. With the new circuit, the management of care was directed by the PICU nurse with the support of ECLS trained specialists,

Methods:

The training consisted of both didactic & hands on experience to develop the appropriate skill set & develop critical thinking. During the didactic part of the course, the circuit was demonstrated as a wet lab. The final part the course was a voluntary visit to the animal research facility. Both normal operation and emergency procedures were reviewed. The session concluded with clinical case scenarios to reinforce the education and training.

Results:

The fall of 2009, our first patient was cared for following the training initiative. At present we report a 44% survival rate for patient's requiring ECLS. A spectrum of clinical questions remain with this change in therapy. We report our experience along with the clinical realities during this presentation.

1. Qiu F, Clark JB, Myers JL, Ündar A, et al. Translational Research in Pediatric Extracorporeal Life Support System and Cardiopulmonary Bypass Procedure: 2011 Update. *World Journal for Pediatric and Congenital Heart Surgery* 2011 (in press).
2. Palanzo D, Qiu F, Baer L, Clark JB, Myers JL, Ündar A. Evolution of the ECLS circuitry [Guest Editorial]. *Artif Organs* 2010;34: 869-873.
3. Qiu F, Uluer MC, Kunselman A, Clark JB, Myers JL, Ündar A. Impact of the length of the tubing on hemodynamics in a simulated neonatal ECLS circuit. *Artif Organs* 2010;34: 1003-1009.
4. Khan S, Vasavada R, Qiu F, Kunselman AR, Ündar A. Extracorporeal Life Support Systems: Alternate vs. Conventional Circuits. *Perfusion*. 2011. (in press)
5. Clark JB, Guan Y, McCoach R, Kunselman AR, Myers JL, Ündar A. An investigational study of minimum rotational pump speed to avoid retrograde flow in three centrifugal blood pumps in a pediatric extracorporeal life support model. *Perfusion* 2011. (in press)
6. McCoach R, Weaver B, Carney E, et al. Pediatric extracorporeal life support systems: education and training at Penn State Hershey Children's Hospital. *Artificial Organs* 2010;34:1023-1026.

Challenges at the Bedside with ECMO and VAD

Amanda Seelhorst BSN, RN^{*}; Christopher D. Beaty, BSN, RN[^]; Meredith McDonough, MS, CCLS IV[#]

^{*}Cardiac Center Clinical Level IV; [^]ECMO Program Core Specialist; [#]Child Life, Education and Creative Arts Therapy Department, all at The Children's Hospital of Philadelphia.

Background:

Any institution that provides extracorporeal support must be capable of providing that service quickly and efficiently. Mobilization of the cannulation team requires a system of notification to the providers that is effective and reliable. Through a process involving investigation, trial and evaluation, a system was developed at the Children's Hospital of Philadelphia that provides all the required elements for effective information transfer to mobilize the personnel for an emergency ECMO cannulation.

Once on extracorporeal life support, the ECMO Specialist must constantly evaluate the clinical situation in order to make appropriate technical adjustments and to communicate effectively with the management team of the patient ongoing clinical status.

During extracorporeal support, the patient and family have special needs requiring specific attention. The Child Life Specialist interacts with the patient, if possible, and the families, to support, educate and often provide comfort to them during this very stressful process throughout the hospitalization.

Results:

The ECMO Program at the Children's Hospital of Philadelphia has provided this level of support since 1990. Over 900 patients have been supported, with an average of 40-60 patients annually over the last five years. Approximately 30 patients have been supported by VAD. A relatively new category of ECMO support is called ECPR (Extracorporeal Cardiopulmonary Resuscitation), in which ECMO is the rescue from a cardiopulmonary arrest or other emergent clinical scenario. Most often this is seen in the Cardiac Center of the hospital, and required an emergency notification system to be used to notify all members of the cannulation almost simultaneously. An effective system is currently in use now.

Ongoing support of the patient requires continuous monitoring of the patient by the ECMO specialist in conjunction with the bedside nurse and the medical/surgical team. Decisions must be made regarding care and management, and the specialist is important to the effective integration of the plans. Often, this may require the transport of the patient on extracorporeal support to diagnostic/therapeutic venues such as the cardiac catheterization lab, operating room or radiology for continuing care.

Concurrently, the Child Life Specialist is vital in the support of the family members during the most critical phase of the support process, oftentimes consulting with the family members to inform them of what they will be seeing as they approach the bedside for the first time after cannulation, and supporting the family members, such as siblings throughout the hospitalization. Patients on long-term support such as the VAD also require the specialized knowledge of the Child Life Specialist in providing support with age appropriate developmental educational strategies with the disease process and treatment.

Conclusions:

The Nursing Department, the ECMO Program, the Child Life Department, and the Cardiac Center physicians are part of an effective system to provide excellent support to both the patients and their families during the hospitalization. Continual evaluation and refinements to the many processes involved are necessary to provide this level of support.

TRANSPORTING CHILDREN ON ECMO OR VAD

Susan C. Nicolson M.D.

Division Chief, Cardiothoracic Anesthesia Medical Director, The Cardiac Center at The Children's Hospital of Philadelphia; Professor of Anesthesiology and Critical Care Medicine, University of Pennsylvania School of Medicine

Background

Since the 1990s almost no pediatric patient has been deemed too young, too small or too sick to be a candidate for any known medical or surgical treatment. This care philosophy results in a small percentage of these high risk patients, as well as an occasional low risk patient, requiring cardiovascular and/or respiratory support consisting of ECMO or VAD. An increasing number of practitioners place a child with impending cardiopulmonary failure on support preemptively to minimize the potential for other organ system dysfunction. An increasing number of assist devices are available for pediatric patients with options available for younger, smaller patients, including infants. ECMO is used as a bridge to VAD, transplant or recovery and VAD as a bridge to transplant or recovery. Improvements in technology coupled with practitioners understanding of how to safely care for patients on support systems have made it possible for children to remain on either ECMO and/or VAD for extended periods of time, weeks to months. These children may require transport for diagnostic studies or interventions, not feasible at bedside, which result in changes in management.

Transport

The increased use of support, expanded support options and longer support times results in more patients requiring transport on ECMO or VAD. Transporting these children is not without risk. The potential benefits of diagnosis or treatment made possible via transport need to be weighed against the potential risks. Transport of these patients can be safely accomplished by a highly skilled multidisciplinary flexible team executing a well thought out, effectively communicated plan with readily available redundant equipment and supplies.

References:

1. Prodhan P et al.: Intrahospital Transport Of Children On Extracorporeal Membrane Oxygenation: Indication, Process, Interventions and Effectiveness. *Pediatr Crit Care Med* 11: 227-233, 2010.

Hybrid Stage I for HLHS

Emile Bacha, MD
Morgan Stanley Children's Hospital of NewYork-Presbyterian (CHONY)
Columbia University
NY, NY

Hybrid pediatric cardiac surgery is an emerging field that combines skills and techniques traditionally used by congenital heart surgeons and interventional pediatric cardiologists. A key paradigm shift for surgeons is the extensive use of indirect imaging techniques (as opposed to direct visualization in the field), such as fluoroscopy or transesophageal echocardiography, used on the beating heart while performing a given task, as opposed to working on an arrested flaccid heart. Hybrid techniques are especially useful when surgery alone or catheter-based interventions alone are not achieving a satisfactory result for a given problem, or when the combination of the two fields results in less invasiveness and less trauma to the patient.

Hybrid procedures can be performed in an OR, cath lab, or hybrid room. The key conditions for any location is to have enough space and outlets available to use a CPB machine or ECMO, an echo machine, good lighting for surgery, stocked equipment nearby, and a fluoroscopy-friendly table that can move side to side. A biplane cath lab is not typically required, but can be very useful for ductal stenting. Hybrid procedures are now employed in several areas of congenital heart surgery.

In the most common version, the hybrid stage I procedure is performed in the catheterization lab or a specially designed "hybrid room". Via median sternotomy, bilateral branch PA bands are placed using 1.5-2 mm wide rings cut from the usual 3.5mm Goretex shunt. A clip should be applied to each band, so that it can be seen on fluoroscopy. Next, a 5-0 prolene purse-string is placed at the sinotubular junction of the main PA and a wire is passed into the descending aorta under fluoroscopy. A 6 or 7 Fr introducer is positioned with a few mm's of the tip inside the vessel. An angiogram is shot to delineate the aortic arch and exclude any possible narrow areas at the isthmus, transverse arch or ascending aorta-arch junction that would preclude a hybrid approach (risk of retrograde CoA). The band position and tightness is verified by selective branch PA angiograms, using a Judkins-Right catheter if necessary. If all the above conditions are met, a ductal stent (either self-inflatable or balloon dilated) is placed under fluoroscopic guidance.

Creating a non-restrictive atrial septum remains difficult. If the atrial septum is non restrictive, it is left alone. If it is restrictive, balloon dilation or stenting can be performed. This can be done peratrially (via purse-string on right atrial free wall), or via an umbilical venous line, or percutaneously in a delayed fashion (preferred).

Some centers prefer to band the PA's in the OR first, and follow by ductal stent placement (with or without atrial stent) in the cath lab. If the bands have to be revised, the patient has to undergo a second operation.

The 2d stage consists of aortic arch reconstruction, removal of ductal stent, atrial septectomy, cavopulmonary shunt and PA plasty.

Advantages of this strategy include complete avoidance of neonatal CPB, avoidance of sensitization to homograft tissue in case transplantation is planned, less use of hospital resources and the possibility of stabilizing sick neonates with non-CPB intervention.

Disadvantages include the possibility of retrograde aortic coarctation with subsequent cerebral or coronary malperfusion (in aortic atresia patients), antegrade coarctation from ductal shrinkage if the stent does not cover

the entire duct, ductal stent dislodgement or embolization, branch PA distortion and the difficulty of achieving a non-restrictive atrial septum. A retrograde shunt from main PA to innominate artery has been described to bypass any isthmus obstruction, but this does not bypass an obstruction between ascending aorta and aortic arch.

Hybrid palliation is very beneficial in the following single ventricle patients:

- Major non-cardiac defects
- Cerebral hemorrhage
- Late presentation
- Non-resolving end-organ damage from shock at presentation
- Sepsis

Hybrid palliation is possibly beneficial in the following patients with single ventricle:

- Very high-risk patients such as
 - HLHS/Intact or highly restrictive atrial septum
 - HLHS(AA/MS), with LV-coronary fistulae
- Additional cardiac defects
- Poor ventricular function and TR

The role of hybrid palliation is debatable in:

- “Straightforward” HLHS or other SV anomalies such as single LV’s (because of improved outcomes in this category)
- Aortic atresia with narrow distal arch (because of the strong likelihood of retrograde aortic coarctation)

Further developments will depend on new technologies such as therapeutic ultrasound for percutaneous ASD creation, bioabsorbable stents, injectable gene therapy to keep the ductus open, percutaneous flow occluders for all-percutaneous approach, miniaturized adjustable PA bands, or stable oral version of PGE.

Selected References:

- 1.Akintuerk H, Michael-Behnke I, Valeske K, et al. Stenting of the arterial duct and banding of the pulmonary arteries. Basis for combined Norwood stage 1 and 2 repair in hypoplastic left heart. Circulation 105:1099-1103, 2002
- 2.Bacha EA, Daves S, Hardin J, et al. Single Ventricle Palliation for High-Risk Neonates: The Emergence of an Alternative Hybrid Stage I Strategy. JTCVS 131:163-171, 2006
- 3.Stoica SC, Philips AB, Egan M, et al. The retrograde aortic arch in the hybrid approach to hypoplastic left heart syndrome. Ann Thorac Surg. 2009;88:1939-46
- 4.Galantowicz M, Cheatham JP, Phillips A, et al. Hybrid approach for hypoplastic left heart syndrome: intermediate results after the learning curve. Ann Thorac Surg. 2008;85:2063-70

Aortic Valve Surgery

Giovanni Battista Luciani, MD

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

Aortic valve disease is the by far the most common native and postoperative cardiac valve lesion presenting in children and adults with congenital heart defects. Aside from native valve dysplasia, primarily in the form of bicuspid or unicuspid disease, the population of patients with systemic semilunar valve dysfunction after repair of cono-truncal lesion is steadily growing. Given the young, sometime neonatal, age at onset therapeutic solutions are destined to be palliative in nature. For the very same reason, survival and functional outcome are expected to accommodate growth, education, employment, pregnancy and physical activity. Catheter-based solutions represent the mainstay for obstructive aortic or semilunar valve lesions in the very young. Application of trans-catheter prosthetic valve implantation in the grown-up or adult, however, remains to be validated. Surgical management of aortic valve disease, native or recurrent, has clearly shifted from replacement to reparative strategies. Due to improved understanding of systemic semilunar valve pathophysiology and to progress in applied research, repair techniques have matured into reproducible and dependable therapies in aortic regurgitation and in select cases of stenosis or mixed disease. Institutional experience over the last 8 years shows that repair is associated with negligible early and late mortality and satisfactory freedom from cardiac reintervention. Considering the physiological quality of life and the preservation of subsequent replacement strategies (surgical, catheter-based), repair should be considered the gold standard for management of young patients with congenital aortic valve disease.

Myocardial protection of the right ventricle during cardiopulmonary bypass

Linda B Pauliks, MD, MPH, Department of Pediatrics, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background: Tissue Doppler echocardiography (TD) permits noninvasive assessment of regional myocardial function. Right ventricular (RV) dysfunction post open heart surgery is a recognized complication in adults where a tissue Doppler marker, isovolumic contraction acceleration (IVA) in the RV predicted functional class 6 months after coronary bypass surgery. Young children have an immature calcium metabolism but there is little knowledge about their RV recovery after open heart surgery.

Methods: Transthoracic tissue Doppler echocardiographic images were acquired preoperatively in the operating room and on postoperative day 1 from standard views in form of digital TD raw data. During off-line analysis (Echopac, GE, Madison, WI) myocardial velocities and IVA were studied in the RV and LV near the mitral and tricuspid ring. Strain rate was measured the mid-wall segment.

Results: The pilot study included 31 children aged 3.6 ± 4.4 y (0.1- 16y). At 24 hours, LV markers had recovered but RV was depressed (Table). A second study involved 53 infants aged 0.39 ± 0.23 years (0.2-0.9 y) including 10 with RV incision. There were no significant differences for RV tissue Doppler parameters between infants with and without surgical RV incision: RV IVA was 3.6 ± 1.2 vs. 3.4 ± 1.2 m/s² in group 1 and 2 at baseline (NS) and post RV IVA declined to 1.5 ± 0.8 vs. 1.5 ± 0.7 m/s² (NS). RV peak systolic strain rate at baseline was -2.7 ± 0.7 vs. -3.1 ± 0.9 /s in group 1 and 2 and at the post study it declined to -1.6 ± 0.6 vs. -1.6 ± 0.5 /s (NS).

Conclusions: Our results suggest suboptimal protection of the right ventricle during open heart surgery in children. Subclinical RV dysfunction was seen regardless of RV incision. Findings are consistent with prior studies in adult populations. Tissue Doppler imaging is a sensitive tool for the study of myocardial function and may serve as an outcome marker for studies on myocardial protection during cardiopulmonary bypass.

Table: Systolic (S) velocities and strain rate (SR) pre and post open heart surgery in 31 children

Parameter	OR PRE	24 hours POST	P value
LV longitudinal (mitral ring)			
S (cm/s)	5.3 ± 1.7	4.8 ± 1.4	0.059
SR (1/s)	-2.2 ± 0.7	1.9 ± 0.7	0.062
RV longitudinal (tricuspid ring)			
S (cm/s)	7.4 ± 3.0	4.6 ± 1.6	<0.001
SR (1/s)	-3.1 ± 1.0	-2.1 ± 0.9	<0.001

Measurement of Blood Physical Properties in Microfluidic Environment

¹Myounggon Kim, MS, ¹Jaeseong Park, BS, ²Byung Jun Kim, BS, and ^{*123}Sung Yang, PhD

¹School of Mechatronics, ²Graduate-program of Medical System Engineering, and ³Department of Nanobio Materials and Electronics, Gwangju Institute of Science and Technology, Gwangju, Republic of Korea, *Email: syang@gist.ac.kr

Background:

Blood is one of the most important clinical samples, which is used to determine physiological state of a patient. Most blood tests conducted in the clinical laboratory are biochemical tests executed on plasma or serum. Recently, it is revealed that biophysical properties of blood including blood viscosity, RBC aggregation index, are closely related with physiological state of a patient, especially who is suffering from cardiovascular diseases (CVDs). Current technology provides enough information of biophysical properties of blood. However, it does have a lack of cost-effective and convenient methods for providing them. In this study, three independent micro devices for the measurement of biophysical properties (Hct, RBCs aggregation index, viscosity) of the blood are introduced.

Methods:

For all experiments, blood samples were either purchased from a blood bank or drawn from the antecubital vein and collected in vacutainers (6 ml, BD, Franklin Lakes, NJ, USA), which contained (K2) Ethylenediaminetetraacetic acid (EDTA) as the anti-coagulant. Then, blood sample was modified in order to intentionally change the resistivity (dilution of blood in saline) or osmolality (dilution with mannitol). All devices were prepared by following conventional soft lithography process. In micro-hemocytometer and micro-aggregometer experiments, once a drop of blood is placed in the well of the device, either electrical impedance or conductivity was measured by using a commercially available impedance analyzer (4294A, Agilent) and compared with the ones measured by conventional methods. In micro-viscometer experiments, blood sample was precisely infused to the device by using a commercial syringe pump.

Results:

In Hct measurement, the Hcts estimated from the impedance modeling for a variety of the blood plasma resistivity and the blood plasma osmolality were only less than 4.5% and 2.5% differences in maximum respectively, compared with the one measured by a gold standard. In aggregation experiments, as soon as dropped the blood sample into a chamber, the conductivity increases and became a steady state because of the aggregation. Once the aggregation is finished, the erythrocyte start to sediment and the conductivity decreases in time course. In addition, the proposed method displayed clearly different slopes and amplitudes of aggregation and ESR with respect to protein-concentrations. In micro-viscometer experiments, the device has been modified from the previously reported one in last year so that the device is now able to measure blood viscosity in different shear rate at the same time. Then it was found that the proposed device is able to measure blood viscosities in various shear rates at the same time.

Conclusions:

Three microdevices have been developed and tested using blood sample in order to measure blood Hct, viscosity, RBC aggregation index, and ESR. All devices show the promising evidences that these devices are applicable to measure biophysical properties of blood, although the additional optimization study should be conducted.

Acknowledgement:

This research was partially funded by grants from the National Research Foundation of Korea (No. 2010-0012897), the Ministry of Education, Science and Technology (WCU Program, No. R31-2008-000-10026-0), and the institute of Medical System Engineering (*iMSE*) in the GIST, Republic of Korea.

50 years of research on the artificial placenta: Can we turn a toy into a treasure?

Mark Schoberer^{2†}, Jutta Arens^{1†}; MD; Anne Lohr², MD; Matthias Seehase³, MD; Reint K. Jellema³, MD; Jennifer J. Collins³; Boris W. Kramer³, MD, PhD; Thomas Schmitz-Rode¹, MD; Ulrich Steinseifer¹, PhD; Thorsten Orlikowsky², MD

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 Dept. of Paediatrics, School of Mental Health and Neuroscience; School of Oncology and Developmental Biology; Maastricht University Medical Center, Maastricht, The Netherlands

† Both Authors contributed equally to this manuscript

Background: Viability of the premature newborn is determined by the immaturity of the lung. Progress in Neonatology has shifted the border to a gestational age as little as 22 to 24 weeks. This limitation is marked and apparently frozen by a milestone in fetal development: the beginning transformation of pulmonary parenchyma from the saccular to the alveolar phase.

The need for collateral concepts of gas exchange for any further leap forward in the treatment of extremely premature born children is evident. The idea of extracorporeal gas exchange is especially appealing for this group of patients because fetal oxygenation happens extracorporeally. The young organism is prepared for this procedure through a number of unique physiological characteristics: Navel vessels provide a natural interface to the central circulation. The high oxygen-affinity of fetal haemoglobin allows high oxygen saturation at low partial pressures. Finally the fetal shuntways allow an adaption to varying demands of pressure and perfusion in pulmonary vs. systemic plus extracorporeal circulation.

Review: The concept of an artificial placenta meaning the connection of an extracorporeal oxygenator to the organism via the navel vessels has been subject of experimental research since the early 1960's. For three decades, dimensioning of the devices required pump-driven circuits. Initially, the critical shunt flow was mitigated by reverse perfusion of the navel vessels. Anterograde, arteriovenous, but still pump driven perfusion of the extracorporeal circuit was later allowed by use of complex flow-control systems.

Perspective: Miniaturisation now enables us to follow the most simple, physiologic and to our view the most promising concept of a passive, arteriovenous oxygenation. Our own oxygenator (Fig. 1) has a filling volume of 12 ml (19 ml incl. tubing) and has been successfully used in a lamb of less than 2000 g bodyweight.

We give an overview over the history of extracorporeal membrane oxygenation of the newborn against the context of current and future clinical treatment concepts of pulmonary immaturity. Key problems which need to be solved to make mechanical gas exchange a clinical treatment option of prematurity related lung failure are specified.



Fig. 1: Pumpless Extracorporeal Lung Support for Premature Neonates

Initial chronic animal experiment with the InCor Pediatric VAD

Arlindo Riso, MD, Idágene A. Cestari, Ph.D, Marcelo Jatene, MD, Carla Tanamati, MD, Luis Fernando Caneo, MD, Juliano Penha, MD, Vera Aiello, MD, Noedir Stolf, MD.
Heart Institute (INCOR), University of Sao Paulo Medical School, Sao Paulo, Brazil.

Background:

A pediatric VAD is under development in our Institution. The VAD is pneumatically actuated and utilizes bovine pericardial valves. Hemodynamic performance of the device has been acutely evaluated in 7 piglets (10 to 12 kg bd wt) undergoing left ventricular assistance (2 h) with Cardiac Index maintained in clinical acceptable ranges. To date thrombogenesis and hemolysis have been chronically evaluated in one adult female sheep for 29 days.

Methods:

Following Penn State protocol we studied the performance of a 15 ml pediatric VAD in an adult sheep (24 Kg bd wt). After anesthesia and full heparinization the LV and descending aorta were cannulated and both cannulas were connected to the VAD placed on a silicone sack in a pocket created in the abdominal wall. The drive line was exteriorized and pumping was initiated. Antibiotic therapy and analgesia were maintained during the post-operative (PO) period. ACT was measured daily and intravenously heparin was administered to maintain ACT > 200 s. In the 29th PO day, the animal was euthanized under full anesthesia and complete necropsy was performed.

Results:

The animal was extubated 3 hours after the end of the operation. Free hemoglobin levels were maintained near baseline values. The pump operation was set in the full-to-empty mode which was maintained throughout the assistance. At study termination, the abdominal pocket and the drive line subcutaneous tunnel were filled with purulent secretion. The anatomic-pathological findings consisted of organizing thrombi restricted to the LV cannulation site with no signs of systemic thromboembolism.

Conclusions:

Operation of the pedVAD was stable and no adverse effects such as bleeding, hemolysis or important thromboembolism were observed. These results suggest the applicability of the experimental protocol utilized ensuring the continuation of chronic animal evaluation of the pedVAD under development.

Optimization of the Impella Pediatric Anatomic Fit

Scott C. Corbett, PhD, Caitlyn J. Bosecker, MS, Francis Fynn-Thompson, MD
ABIOMED, Inc. Research and Development
Children's Hospital Boston, Department of Cardiac Surgery

Background:

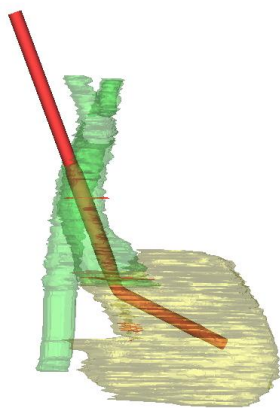
The Impella Pediatric is a catheter-based percutaneous ventricular assist device (VAD) for treatment of acute right heart failure. The device is based on the Impella 2.5, provides flows of up to 2.0 L/min and up to 7 days of support. The device inlet resides in the left ventricle; a flexible cannula traverses the aortic valve, while the device outlet resides in the ascending aorta.

Methods:

A fit study was initiated to determine the optimal cannula geometry and evaluate fit of the device. CT scans from seventeen pediatric patients (7 x 4-5 kg, 6 x 6-10 kg, 4 x 11-15 kg) were used. Only one acceptable single ventricle CT scan was available. Lengths and angles between the ascending aorta, aortic valve and left ventricle were measured using Mimics software (Materialise NV, Belgium) and used to define an 'average' cannula. Additionally, preserved aorta and left ventricle specimens from 5-25 kg patients were used to evaluate the fit of the 'average' cannula (2 x 5 kg, 2 x 10 kg, 2 x 15 kg, 2 x 25 kg).

Results:

Fit of this device was acceptable in scans of patients ≥ 10 kg (4/4 fit), was marginal in patients 6-10 kg (4/6 fit), and did not fit in patients < 5 kg (3/7 fit) due to the 30 mm rigid length of the motor in the ascending aorta. The device fit in the one single ventricle scan in the 6-10 kg range. Evaluation in preserved specimens showed that the lengths and angles fit well in the ventricle in all cases, while the motor was too long in the 5 kg specimens. Motor length was acceptable in all other specimens. Acceptable fit was demonstrated in preserved single ventricle specimens (1 x 5 kg, 1 x 10 kg, 1 x 15 kg). Both the Mimics and specimen fits showed that the addition of a short pigtail was accommodated and this will help to stabilize the device in the ventricle.



Conclusions:

The results generated by Mimics and the preserved specimen fit studies were in agreement: 1) the 'average' cannula geometry and positions of inlet and outlet cages are a good fit and do not threaten aortic or mitral structures, and 2) the rigid length of the motor is too long for 5-10 kg patients. The proposed target population for this device is 10-25 kg ($0.5-1.0 \text{ m}^2$ BSA); carotid insertion appears feasible for 15+ kg patients, while 10 kg patients may require direct aortic insertion. Direct insertion may be possible for 5 kg hypoplastic left heart patients.

Mechanical Cavopulmonary Assistance of a Patient-Specific Fontan Physiology: Numerical Simulations, Lumped Parameter Modeling, and Suction Experiments

Amy L. Throckmorton PhD¹, James P. Carr¹, Sharjeel A. Tahir¹, Ryan D. Tate¹, Emily A. Downs BS¹, Sonya S. Bhavsar MS¹, Yi Wu PhD², John D. Grizzard MD³, and William B. Moskowitz MD⁴

Mechanical Engineering¹, School of Engineering, Virginia Commonwealth University, Richmond, VA; Mechanical Engineering², School of Engineering, Behrend College, The Pennsylvania State University; Radiology³ and Pediatric Cardiology⁴, Children's Hospital of Richmond and School of Medicine, Virginia Commonwealth University, Richmond, VA.

Background: The implementation of mechanical cavopulmonary assistance offers a possible therapeutic option for Fontan patients until a donor heart becomes available or hemodynamic stability can be achieved. This study investigated the performance of an intravascular axial flow blood pump to support the Fontan circulation.

Methods: Four models of the extra-cardiac, total cavopulmonary connection (TCPC) Fontan configuration were evaluated to formulate numerical predictions: an idealized TCPC with a 1-diameter inferior vena cava (IVC) offset, a patient-specific TCPC generated from MRI data, and each of these two models having a blood pump in the IVC. A lumped parameter model of the Fontan physiology was used to specify boundary conditions. Pressure-flow characteristics, energy gain calculations, scalar stress levels, and blood damage estimations were determined. Suction limitation experiments using Sylgard elastomer tubing to mimic vein compliance were also conducted.

Results: The pump produced pressures of 1-16 mmHg for 2000-6000 RPM and flow rates of 0.5-4.5 L/min. Maximum scalar stress estimations were 3 Pa for the non-pump models and 290 Pa for the pump-supported cases. The blood residence times for the pump-supported cases were considerably shorter (0.9 seconds) as compared to the non-supported configurations (2.5 seconds). However, the blood damage indices were higher, reaching 1.5% for the anatomic model with pump-support. The pump successfully augmented pressure in the TCPC junction and increased the hydraulic energy of the TCPC as a function of flow rate and rotational speed. The suction experiments revealed minimal deformation (<3%) in the tubing at a pump speed of 9000 RPM.

Conclusions: These results indicate that the blood pump successfully augmented pressure in the TCPC junction and increased the hydraulic energy of the TCPC as a function of flow rate and rotational speed. Scalar stress levels, blood damage indices, particle residence times, and suction limits were found to be at acceptable levels.

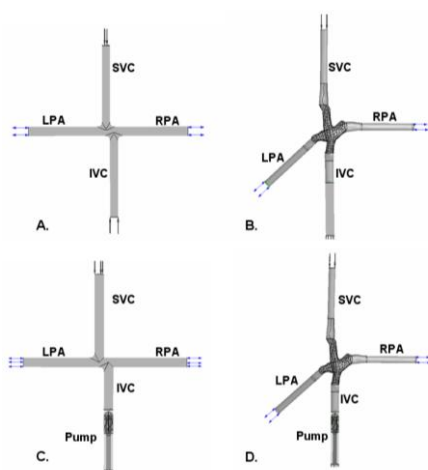


Figure 1. Four Numerical Models.

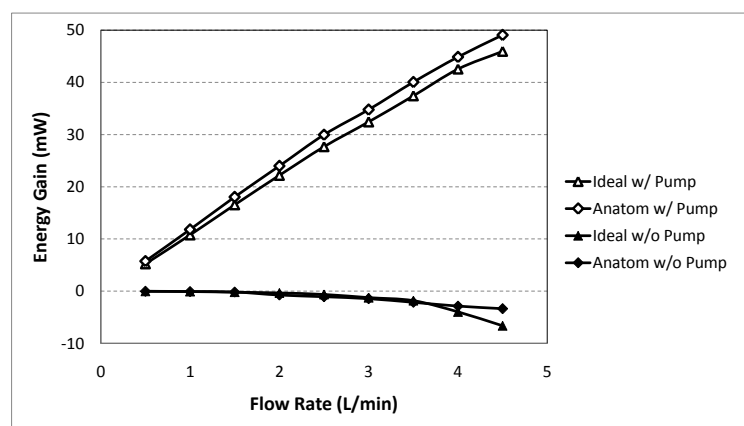


Figure 2. Energy Gain due to Mechanical Assistance of the TCPC Junction.

Comparison of numeric approaches for blood damage predictions and application to the bearing gaps of rotary blood pumps

Roland Graefe, Dipl.-Ing.; Andreas Ding, Cand.-Ing.; Fiete Böhning, Dipl.-Ing.; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD

Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Germany

Purpose:

For all cardiovascular devices, it is desirable to assess potential flow induced blood damage as soon as possible in the development process. Experimental blood tests are indispensable but also tedious and results may vary significantly depending on the blood, deficient surface treatment, material selection, minor changes in the procedure or conditions. The purpose of this study is to compare the numerous existing numeric approaches to predict mechanical blood damage and apply them to the bearing gap of a research rotary blood pump.

Methods:

Methods to predict blood damage with CFD can be distinguished into Eulerian or Lagrangian approaches or combinations thereof. No model has been accepted as applicable for all types of blood flows referring to turbulence, residence times of blood cells, more-dimensional stress, and stationary versus transient flows. An experimental test rig, see Figure 1, has been

designed to test the effect of bearing parameters such as gap width, gap length, rotational speed, eccentricity of the rotor, diameter and pressure difference. This test rig defined the investigated flow volume to allow for a comparison of numerical and experimental results. Examples of all basic types of blood damage models were applied to compare a total number of 18 bearing gap configurations.

Results:

The results varied significantly for different gap configurations and also for different models. Only trends were consistent for all models. Simple approaches, e.g. the evaluation of the wall shear stress, produced quick results but lacked an objective basis for design decisions. Eulerian approaches, see Figure 2, proved to improve understanding of the amount of stress to which blood is exposed. Lagrangian predictions successfully connected the stress level to residence times.

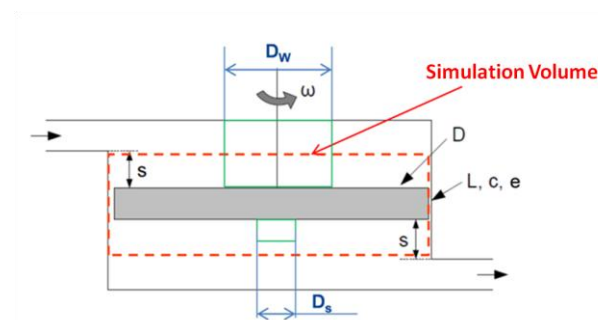


Figure 1: Definition of simulation volume

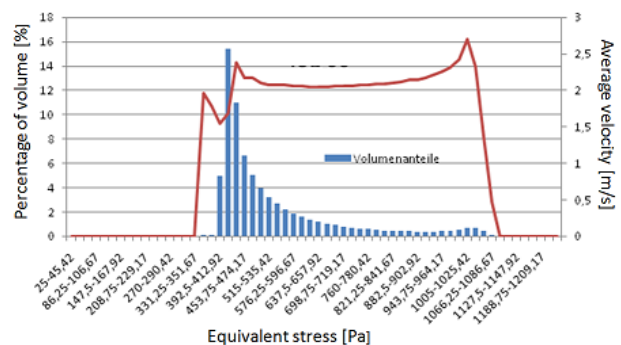


Figure 2: Eulerian blood damage prediction

Conclusions:

Depending on the demand for accuracy and for speed of result production, different approaches to correlate flow simulation results to expected blood damage exist. These approaches differ in complexity and care must be taken when conducting blood damage predictions. A Lagrangian approach promises to yield the most accurate results. Experimental blood test results remain indispensable but this study warrants the use of CFD to speed up and improve the development process.

Multi-modality Neuromonitoring for Pediatric Cardiac Surgery: The Approach at Penn State Hershey and a Critical Appraisal of the Available Evidence

Joseph B. Clark, MD, Mollie L. Barnes, CNIM, Akif Ündar, PhD, and John L. Myers, MD
Pediatric Cardiovascular Research Center, Departments of Surgery and Pediatrics
Penn State College of Medicine, Penn State Hershey Children's Hospital, Hershey, PA, USA

Background: Brain injury remains an unfortunate source of morbidity associated with congenital heart surgery. Intraoperative neuromonitoring is used by many centers, and may help to minimize neurologic injury and improve outcomes. In this report, our protocol for multi-modality intraoperative neuromonitoring is described, and the relevant available evidence in the literature is reviewed.

Methods: Neuromonitoring during congenital heart surgery at our institution is performed using a combination of near-infrared spectroscopy (NIRS), transcranial Doppler ultrasound (TCD), and electroencephalography (EEG). Monitoring devices are positioned on the patient by a dedicated neurophysiologist. NIRS data is routinely available to the entire operating room team. Surveillance of TCD and EEG data is continuously provided by a neurophysiologist stationed in the room, who provides feedback to the surgeon and team regarding cerebral blood flow velocity, embolic signals in the head and arterial bypass tubing, and status of the EEG signals. Adverse or concerning parameters typically instigate attempts at corrective intervention, such as cannula repositioning, increase in pump flow, red blood cell transfusion, further deairing, change in anesthetic technique, or other maneuvers.

Results: The influence of neuromonitoring on the rate of adverse neurologic events in our patient population is currently under review and will be the subject of a future report. A review of the literature regarding neuromonitoring studies in cardiac surgery was performed. Reports were categorized as NIRS, TCD, EEG, or multi-modality. Among the monitoring tools, NIRS appears to be the most widely used, although its precise clinical value remains the subject of ongoing debate. One recent comprehensive review concluded that NIRS use in pediatric cardiac surgery has not been associated with improved outcomes. Since this review, multiple studies regarding NIRS and congenital heart surgery have been published, with mixed results. Although there is an abundance of literature regarding TCD and cerebral emboli in adult cardiac surgery, there are very few such studies pertaining to the pediatric population. One guideline offered a positive recommendation for TCD use in cardiac surgery, but was not specific to congenital heart surgery. Nevertheless, no definitive conclusions from the literature can be drawn for this modality. Reports of EEG use have more often focused on pre- and postoperative studies rather than intraoperative monitoring. The few reports of pediatric intraoperative EEG have not clearly shown a correlation between EEG findings and neurologic outcomes, and have not evaluated EEG use as a guide to real-time corrective intervention. A recent guideline offered no recommendation for EEG during cardiac surgery. Finally, for multi-modality neuromonitoring, one retrospective pediatric study showed compelling evidence that intervention based on neuromonitoring was associated with decreased adverse neurologic events and decreased hospital stay. Although this landmark report likely encouraged the practice of neuromonitoring for pediatric cardiac surgery, this study has not been repeated, and a randomized trial may not be feasible due to ethical concerns.

Conclusions:

Limited evidence is available to demonstrate that intraoperative neuromonitoring is associated with improved neurologic outcomes in congenital heart surgery. Although additional positive findings are available in the adult literature, it may not be appropriate to extrapolate these results to the pediatric population. Further clinical outcomes research is needed to assess the utility and cost-effectiveness of intraoperative neuromonitoring for pediatric heart surgery.

Pre and Post-operative Magnetic Resonance Imaging In Neonatal Arterial Switch Operation Using Warm Perfusion

Y. Durandy*, M. Rubatti**, R. Couturier**, A. Rohnean***

* Perfusion and Intensive Care, Institut J. Cartier

** Anesthesiology, Institut J. Cartier and Centre Chirurgical Marie Lannelongue

*** Radiology, Centre Chirurgical Marie Lannelongue

Introduction:

Neurological morbidity is a major concern in pediatric cardiac surgery. Cardiopulmonary bypass is one of the few modifiable factors affecting the patient neurodevelopmental outcome. This study is to measure the incidence of MRI abnormalities after neonatal arterial switch operation using warm surgery.

Patients and Method:

The neonates admitted for a transposition of the great arteries had, whenever possible, a pre-operative and a post-operative brain MRI. Data collected were: prenatal diagnosis, in-hospital birth, Raskind procedure, prostine continuous infusion, pre-operative inotropic support, and pre-operative mechanical ventilation, age the operative day, weight, pre and post-operative brain MRI abnormalities. All the MRI were interpreted by the same senior specialist in pediatric neuroimaging.

Results:

MRI were performed preoperatively in 11 patients and postoperatively in 14 patients.

Prenatal diagnosis 7/15, In-hospital birth 7/15, Raskind procedure 10/15, Prostine infusion 12/15, Pre-operative Inotropic support 2/15, Pre-operative mechanical ventilation 7/15

Age the operative day: median 7 d (5 d - 22 d), Weight: median 3.5 kg (2.9 kg to - 4.1 kg)

	Normal	Abnormal	Stroke	White matter injury
Pre-operative MRI	5/11 - 45%	6/11 - 55%	5/11 - 45%	1/11 - 9%
Post-operative MRI	8/14 - 57%	6/14 - 43%	5/11 45%	1/14 - 7%

There was one new lesion in a patient who had pre-operative abnormalities, but no worsening of preoperative lesions was observed.

Discussion:

To our knowledge no study assessing the quality of brain protection with brain MRI following warm pediatric surgery was previously published. In this study the incidence of preoperative brain abnormalities is 55% in a range previously published but the incidence of new lesion or of worsening of pre-existing lesion following surgical cure is low compared to data from the literature. The results obtained in this small group of patient are encouraging and are the basis of a larger study which is underway.

Selective Cerebro-myocardial Perfusion in Complex or Recurrent Aortic Arch Pathology: A Novel Technique

Fabrizio De Rita, MD, Gianluca Lucchese, MD, Luca Barozzi, MD, Tiziano Menon, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Giovanni Battista Luciani, MD
Division of Cardiac Surgery, University of Verona, Verona, Italy

Background:

Simultaneous cerebro-myocardial perfusion has been described in neonatal and infant arch surgery, suggesting reduction in cardiac morbidity. Here described is a novel technique for selective cerebral perfusion combined with controlled and independent myocardial perfusion during surgery for complex or recurrent aortic arch lesions.

Methods:

From April 2008 to December 2010, 9 patients with arch pathology underwent surgery (2 HLHS, 4 recurrent arch obstruction, 2 aortic arch hypoplasia+VSD, 1 single ventricle+TGA+arch hypoplasia). Median age was 105 days (6 days-36 years) and median weight 4.4 kg (1.6 kg-52 kg). Via midline sternotomy, an arterial cannula (6 or 8 Fr. for infants) was directly inserted into the innominate artery or through a PTFE graft (for neonates <2.0 kg). A cardioplegia delivery system was inserted into the aortic root (or into the ductus arteriosus in cases of ductal-dependent circulation, and then relocated into the aortic root). Under moderate hypothermia, ascending and descending aorta were cross-clamped and "beating heart and brain" aortic arch repair performed. Mean blood pressure was maintained between 20-25 mmHg, cerebral blood flow rate regulated at 30-40 ml/kg/min, while myocardial at 15-20 ml/kg/min.

Results:

Average cardiopulmonary bypass time was 160±68 min. (71-310). Average time of splanchnic ischemia during cerebro-myocardial perfusion was 41±18 min. (17-69). No intraoperative technical complications occurred. Weaning from cardiopulmonary bypass was achieved without inotropic support in 5 and with low dose in 4. Three patients, body weight <2.5 kg, needed delayed sternal closure. No neurologic dysfunction was noted. Renal function proved satisfactory in all.

Conclusions:

The present experience suggests that selective and independent cerebro-myocardial perfusion is feasible in patients with complex or recurrent aortic arch disease, starting from premature newborn less than 2.0 kg of body weight to grown-ups. The technique is as safe as previously reported methods of cerebro-myocardial perfusion and possibly more versatile.

Clinical Application of a Single-dose HTK Cardioplegic Solution for Pediatric Myocardial Protection in Beijing Fuwai Hospital

Shigang Wang, MD, Shuyi Lv, MD, Guodong Gao, MD, Yulong Guan, PhD, Jinping Liu, MD, Feilong Hei, MD, and Cun Long, MD

Department of Cardiopulmonary Bypass, Cardiovascular Institute and Fuwai Hospital, CAMS and PUMC, Beijing 100037, China

Objectives: To summarize our clinical perfusion experiences and outcomes in pediatric myocardial protection with a single-dose HTK cardioplegic solution in Beijing Fuwai hospital in 2010.

Methods: We retrospectively reviewed clinical perfusion data of 518 pediatric patients with complex CHD using a single-dose HTK solution in 2010, and summed up our clinical experiences.

Results: 518 pediatric patients included 336 males, 182 females aged 3 days to 11 years (1.7+/-2.1 years) and body weight 3 to 32.5 Kg (9.6+/-4.7 Kg). Mean CPB time was 141.4+/- 53.7 min (52 - 360 min), and mean aortic cross-clamping time was 94.3+/-38.7 min (20 - 264 min). The mean perfusion volume of HTK solution was 410.6 +/- 176.9 ml (150 - 1000 ml) and 45.1 +/- 10.3 ml/kg. 31 cases need 2 or more times perfusion due to re-aortic cross clamp, restarting CPB and operation. Spontaneous defibrillation occurred in 498 cases (96.1%) (More details see Table 1). 1 case need ECMO support after CPB and weaned from ECMO successfully.

Conclusions: Pediatric myocardial protection with a single-dose HTK cardioplegic solution is a safe and effective cardioplegic method in complicated cardiac surgery with prolonged aortic cross-clamping time without increasing the operation risk.

Table 1. Clinical perfusion data of a single-dose HTK solution.

Cross-clamping Group	Cases	CPB Time (min)	X-clamping T (min)	HTK Volume (ml/kg)	Self-recovery (%)	NPT (°C)
≤ 60 min	105	85.7±18.1	50.0±8.5	44.0±10.3	103(98.1%)	28.2±2.2
60 -120 min	310	134.5±26.0	89.8±16.9	44.5±9.9	297(95.8%)	26.7±2.3
120 - 180 min	83	200.8±36.4	139.6±115.4	48.9±10.5	79(95.2%)	25.8±2.5
>180min	20	295.9±40.4	209.2±25.1	45.1±11.4	20(100%)	25.4±2.1

NTP: Nasopharyngeal temperature

Continuous Warm Perfusion Reduces Renal Injury During Norwood Operation

James M. Hammel, MD, Haili Lang, MS, and Kim F. Duncan, MD
Division of Pediatric Cardiothoracic Surgery, Children's Hospital and Medical Center
Department of Surgery, University of Nebraska Medical Center, Omaha, Nebraska, USA

Background:

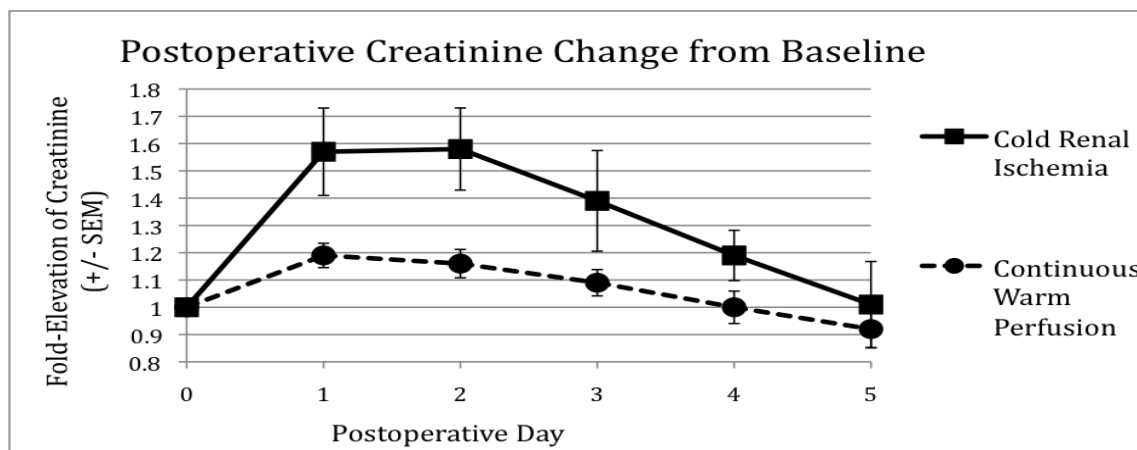
Conventional perfusion approaches for Norwood aortic arch reconstruction include deep hypothermic circulatory arrest and selective cerebral perfusion. Both of these techniques result in a period of cold renal ischemia (CRI). Canulation of both the innominate artery and the descending aorta allows maintenance of continuous warm perfusion (CWP) to the kidney and the entire body during aortic arch reconstruction. Renal dysfunction often complicates recovery after complex neonatal cardiac surgery. This review was undertaken to assess the effect of perfusion technique, CRI or CWP, on postoperative renal function.

Methods:

The records of 46 consecutive neonates undergoing Norwood operation since 2004 were reviewed. The Acute Dialysis Quality Initiative Group RIFLE criteria for renal injury and failure were applied. Incidence of renal injury was compared by Chi squared, and change in creatinine by T test.

Results:

17 patients underwent Norwood with CWP, 29 with CRI. Median bypass time and crossclamp time were significantly shorter in CWP than CRI (100 v. 189 min, $p = 0.005$ and 26 v. 68 min, $p < 0.001$). Creatinine change from baseline was significantly less in CWP than CRI at 24 and 48 hours (1.19 ± 0.24 v. 1.58 ± 0.61 , $p = 0.02$; and 1.58 ± 0.60 v. 1.16 ± 0.28 , $p = 0.01$)(see Chart). 1 of 17 CWP patients had renal injury by urine output criteria at 24 hours, compared to 7 of 29 CRI patients ($p=0.01$). 0 of 17 CWP had renal injury by creatinine change criteria, and 2 of 17 had risk of renal dysfunction, versus 6 of 29 and 12 of 29 CRI respectively ($p = 0.006$ and $p = 0.003$). Median fluid balance at 24 hours was +121 ml. for CWP vs. +252 ml for CRI. Renal dysfunction eventually resolved in all patients.



Conclusions:

Patients undergoing Norwood operation with continuous warm perfusion of the entire body had less transient renal injury. This was reflected in less early positive fluid balance. Early postoperative renal dysfunction prolongs the period of critical illness after Norwood and can be avoided through this alternative perfusion technique.

Incidence of Healthcare-Associated Infections in a pediatric population with extracorporeal ventricular assist device

Tiziana Fragasso, MD, Giorgia Grutter, MD, Zaccaria Ricci, MD, Sonia Albanese, MD, Carmelita Varano, MD, Antonio Amodeo, MD, Paola Cogo MD.
Department of Cardiac Surgery, Children's Hospital and Research Institute "Bambino Gesù" Rome, Italy

Background:

To evaluate Healthcare-Associated Infection (HAI) rates in pediatric patients supported by EXCOR® Pediatric (Berlin Heart, BH) ventricular assist device (VAD).

Setting: Pediatric Cardiosurgical Intensive Care Unit (pCICU).

Methods:

Retrospective analysis of all patients admitted to pCICU for VAD implantation between January 1st, 2009 and December 31st, 2010 (24 months). Diagnoses were made according to Center for Disease Control (CDC).

Results:

Nine patients' charts were reviewed.

Median age was 8 months (6-11 IQR), seven patients had a Left VAD(LVAD), two a Bi-VAD. All patients with LVAD underwent heart transplant after a median of 59 days (37-109 IQR) of support.

All patients with Bi-VAD (2) died after 12 days of assistance. No HAIs were recorded during their admission.

Fifteen HAIs were reported in 5 patients out of 9 (56%). All infected patients had more than one HAI during their admission and, compared to non infected, a longer mechanical support (104 vs 32 days, $p<0,05$) and a longer pCICU Length of Hospital Stay (LOHS, 129 vs 51 days $p<0,05$). The table below summarizes microbiology. Four bacteria were multidrug resistant, 3 carbapenem-resistant *P. Aeruginosa* (50% of all *Pseudomonas* isolated) and 1 Methicillin-Resistant *S.Aureus* (MRSA) .

One patient had an endocarditis on mechanical ventricle caused by *Pseudomonas Aeruginosa* the day of transplant (diagnosed intraoperatively by positive blood culture and swabs). He received appropriate antibiotic therapy perioperatively and no positive cultures in the postoperative period. Two patients with infection on insertion site of BH's cannulas had an uncomplicated post transplantation course. The third patient with infection on cannula's insertion site is still on VAD waiting for transplant.

	ENDOCARDITIS	SSI	CLABSI	CAUTI	VAP	GI	tot (%)
S. aureus			1				1 (6,25)
E.faecalis			2				2 (12,5)
CONS		1,00	2	1			4 (31,25)
Klebsiella			1				1 (6,25)
P.Aeruginosa	1,00	2,00	1		2		6 (37,25)
S.Marcescens					1		1 (6,25)
C.difficile						1	1 (6,25)
TOT	1,00	3,00	7	1	2	1	16
rate x 1000 device days	1,53	4,70	14,6	5	13,5		

Conclusions:

VAD use as a bridge to cardiac transplantation is associated with a large number of device-related infections. Patients with infected VADs wait longer for transplantation than patients with uninfected VADs with no impact on survival.

Management of Single Ventricle Patients with Berlin Heart EXCOR Ventricular Assist Device: Single Center Experience

Tracey Mackling, RN, CPNP-PC/AC, Tejas Shah, MD, Vivian Dimas, MD, Kristine Guleserian, MD, Monica Ardura, DO, Jami Gross-Toalson, PhD, Ying Lee, PharmD, Janna Journeycake, MD, Aliessa Barnes, MD

Departments of Pediatric Cardiology, Solid Organ Transplant, Pediatric Infectious Disease, Pediatric Hematology, Pharmacy, Psychiatry, and Pediatric Cardiothoracic Surgery, University of Texas Southwestern Medical Center and Children's Medical Center Dallas, Dallas, Texas, USA

Background:

There is minimal data regarding chronic management of single ventricle VAD patients.

Purpose:

To describe our center's multidisciplinary team management of single ventricle patients supported with the Berlin Heart EXCOR Pediatric VAD successfully transitioned to the inpatient ward.

Results:

Pt #1 is a 4 year old with double outlet right ventricle with aortic atresia, L-looped ventricles and heart block who developed heart failure 1 year after Fontan. She initially required ECMO support and was transitioned to Berlin Heart systemic VAD. She has been supported for 316 days (ICU 309 days, floor 7 days). The post operative course was complicated by intermittent infection including MRSA, hepatic and renal insufficiencies, and transient antithrombin, protein C and protein S deficiencies resulting in multiple thrombi. She had a total of 5 pump changes over 10 months. Her hepatic and renal functions normalized. Current long-term medical management includes anticoagulation with enoxaparin, platelet inhibition with aspirin and dipyridamole, and antibiotic prophylaxis using trimethoprim/sulfamethoxazole.

Pt #2 is a 4 year old with HLHS who developed heart failure 2 years after bidirectional Glenn shunt. At systemic VAD implantation, he was intubated with renal insufficiency. He is now on the inpatient floor with normalized renal function and supplemental oxygen via nasal cannula during the day and BiPAP at night. He has been supported for 162 days (CICU 114 days, floor 48 days). Long-term medical management includes anticoagulation with warfarin and single agent platelet inhibition using dipyridamole due to aspirin resistance.

Conclusions:

A consistent specialized multidisciplinary team approach to the medical care of our VAD patients, consisting of cardiothoracic surgeons, heart transplant team, hematologist, pharmacist, infectious disease physician, psychiatrist, specialty trained bedside nursing and nurse practitioners has allowed us to effectively manage these patients long term with no significant hemodynamic bleeding, clotting or infectious complications that would preclude transplantation.

Alternative Anticoagulation for Extracorporeal Membrane Oxygenation

Hayden Dando¹; Martin Gill¹; John Dittmer¹; Killian O'Shaughnessy¹; Jenny Lei¹; James McCauley²

¹ Perfusion Department, Heart Centre for Kids, The Children's Hospital at Westmead, Sydney, Australia

² Biomedical Engineering Department, The Children's Hospital at Westmead, Sydney, Australia

Objectives:

To describe the use of prostacyclin and nitric oxide as primary anticoagulation for an extracorporeal membrane oxygenation (ECMO) circuit.

Methods:

A case report of a 5 year old boy who presented with rapidly progressive acute renal failure, and developed pulmonary haemorrhage. Due to acute respiratory failure and failed conventional ventilation, extracorporeal membrane oxygenation (ECMO) was initiated. However it proved impossible to control the pulmonary haemorrhage and the heparin infusion used for anticoagulation was stopped. In an effort to prevent thrombus formation in the circuit nitric oxide, was introduced into the ventilating gas of the oxygenator, and prostacyclin was infused into a port on the blood inlet of the oxygenator.

Discussion:

Traditionally, anticoagulation during ECMO is achieved using a heparin infusion. Heparin-less ECMO can be achieved in adults using a circuit comprised of tubing coated with covalently bonded heparin. Due to the inevitable fibrin build up in the smaller circuits and lower absolute flows used in paediatrics, a move to non heparin bonded tubing has occurred.

Nitric oxide (NO), produced by normal vascular endothelial cells, limits platelet activation, adhesion, and aggregation, preventing the adhesive receptor-ligand interactions that promote thrombus formation and growth^{1,2}.

Prostacyclin exhibits an anti-platelet activation effect due to reduction in Thromboxane A2 and platelet derived growth factor. It may also infer an anti-inflammatory effect by reduction in interleukin production.

Further in vitro work has shown that nitric oxide in the ventilating gas diffuses through a poly-methyl-pentene non-microporous oxygenator.

Conclusions:

Nitric oxide (NO) passes from the gas phase to the blood phase of a PMP oxygenator. Together with prostacyclin, NO appears to exert a powerful but transient, antithrombotic effect on blood in an extracorporeal circuit.

¹ Loscalzo J. Nitric oxide insufficiency, platelet activation, and arterial thrombosis. *Circ Res* 2001;88:756-62.

² Alonso D, Radomski MW. Nitric oxide, platelet function, myocardial infarction and reperfusion therapies. *Heart Fail Rev* 2003;8:47-54.

Antithrombin Replacement during Extracorporeal Membrane Oxygenation

Robert A. Niebler M.D.; Melissa Christensen B.S., Heidi Wellner R.N., B.S.N.; Richard Berens M.D.
Department of Pediatrics and Anesthesia, Section of Critical Care, Medical College of Wisconsin, and
Children's Hospital of Wisconsin; Milwaukee, WI USA

Background:

Heparin remains the predominant anticoagulant during extracorporeal membrane oxygenation (ECMO). Heparin acts by potentiating the anticoagulant effect of antithrombin. Acquired antithrombin deficiency is common in pediatric patients requiring ECMO, and may result in ineffective anticoagulation with heparin. Bleeding complications are common during ECMO and antithrombin replacement may result in worsening of bleeding. Our objective is to determine what effect antithrombin replacement has on the anticoagulant effect of heparin and blood loss during ECMO.

Methods:

A retrospective chart review of all patients at Children's Hospital of Wisconsin supported on ECMO in 2009 that received antithrombin was performed. Antithrombin activity levels, heparin drip rate, and activated clotting times (ACT) were compared before, 4, 8, and 24 hours after antithrombin administration. Chest tube output and pRBC transfusion volume as measures of blood loss were compared from 24 hours before antithrombin administration to 24 hours after.

Results:

Antithrombin was administered as a single bolus dose in 30 patients with a median age of 3 months and a range of 1 day to 19.5 years. Antithrombin activity increased at 8 and 24 hours after administration. The heparin drip rate, ACT levels, chest tube output, and pRBC transfusion volumes did not change after antithrombin administration.

	Prior to Antithrombin	4 hours after	8 hours after	24 hours after
Antithrombin Activity (U/mL, mean +/- SD)	61.5 +/- 13.0	Not Available	96.8 +/- 25.6*	84.4 +/- 26.3*
Heparin Dose (units/kg/hour, mean +/- SD)	24.6 +/- 13.3	23.4 +/- 12.9	24.6 +/- 13.3	25.1 +/- 14.6
Activated Clotting Time (seconds, mean +/- SD)	175 +/- 23	176 +/- 22	170 +/- 18	173 +/- 29

* $p < 0.02$

	24 hours prior to Antithrombin	24 hours after Antithrombin
Chest Tube Output (mL/kg/day, median (range))	37.6 (0-195)	28.7 (0-93)
pRBC Transfusion (mL/kg/day, median (range))	21.3 (0-65)	16.4 (0-99)

Conclusions:

Antithrombin administration resulted in higher activity levels for 24 hours without a significant effect on heparin requirement or ACT. Measures of bleeding did not increase.

Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome associated with Pneumonia in Children

Shye-Jao Wu, MD.

Division of Cardiovascular Surgery, Departments of Surgery,
MacKay Memorial Hospital, Taipei, Taiwan

Background:

Acute respiratory distress syndrome (ARDS) is a condition associated with significant morbidity and mortality in children. Therapeutic modalities include lung protective ventilation strategies, inhaled nitric oxide, surfactant therapy, high frequency oscillation ventilation and so on. Extracorporeal membrane oxygenation (ECMO) may be tried if all the treatment modalities fail to get the patients stabilized. This report is to present our clinical experience of ECMO for ARDS associated with pneumonia unresponsive to conventional treatment in children.

Patients and Methods:

From December 2001 to October 2009, twelve patients of ARDS were treated with ECMO (Medtronic Inc. Anaheim, CA, USA) in our hospital, with mean age of 4.6 years (range 1.9 to 13.3 years) and mean body weight of 19kg (range 11.5 to 40 kg). ECMO was initiated because of failed maximal medical and ventilatory therapy. The criteria for ECMO initiation included high ventilator setting (PIP>35cmH₂O, PEEP >10cmH₂O with FiO₂ 1.0), severe hypoxemia with AaDO₂ (alveolar-arterial oxygen gradient) > 600mmHg or oxygenation index (OI) > 40, severe shock with unstable hemodynamic status. Among the 12 patients, initial symptoms included fever, cough, and dyspnea. The average duration from initial symptoms to the development of ARDS was 6 days (range 0-10 days). All chest X-ray pictures revealed white-out picture before ECMO. Six patients had pleural effusion, and bilateral chest tubes were inserted in 3 patients. All 12 patients had sepsis. T-antigen was positive in 4 of 6 patients with pneumococcal pneumonia. Three developed hemolytic uremic syndrome. Acute renal failure was found in 6 patients, and 3 of them received peritoneal dialysis before ECMO therapy. Two patients received high frequency oscillatory ventilation and two patients received inhaled nitric oxide therapy before ECMO.

Results:

In 8 patients, venoarterial (VA) ECMO were indicated for intractable shock and respiratory failure, 4 received venovenous (VV) ECMO for respiratory failure only. VA ECMO was changed to VV ECMO when the cardiac function recovered but lung function was still impaired in 4 of the 8 patients. The duration of ECMO support was 241.08±194.93 hours, ranged 24~689 hours. The survival rate was 20% (1/5) between 2001 and 2003, but from then on, the survival rate improved significantly. Since 2004, the survival to lung recovery was 100% (7/7) and survival to discharge was 85.7% (6/7). The overall survival to lung recovery was 66.7% (8/12) and the overall survival to discharge was 58.3% (7/12). One patient with leukemia and leucopenia survived to lung recovery, but died of hepatic failure and sepsis 2 months later.

Conclusions:

ECMO may provide the last chance of survival for children with severe ARDS who are not responding to conventional treatment, even in the condition of pneumonia with septic shock.

Shuntless Hemofiltration During Pediatric ECMO: Simple, Safe, and Accurate Management of the Fluid Overloaded Patient.

Daniel R Duncan, BS CCP, Paul J Kerins, BS CCP, Pizarro, Christian, MD. The Nemours Cardiac Center. A.I. DuPont Hospital for Children, Wilmington, Delaware, USA.

Background:

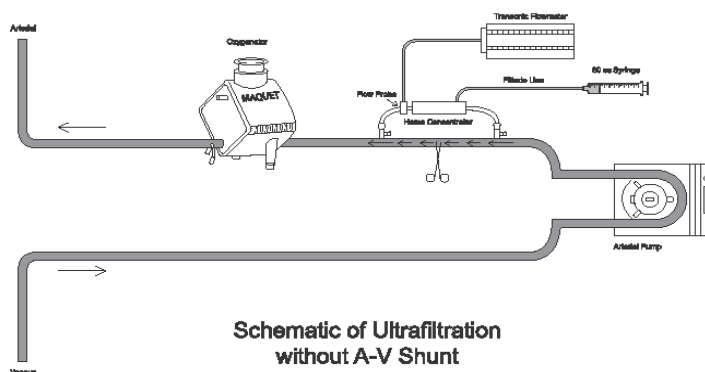
Hemofiltration is commonly performed during pediatric ECMO to remove excess body fluid accumulation secondary to renal insufficiency and systemic inflammation. The obligatory shunt arising from the conventional placement of the hemofilter, with an arterial (post oxygenator) inflow and venous (pre pump) outflow, requires both diligent monitoring of the shunted volume to prevent hypoperfusion, and a compensatory increase in pump flow. Additionally, the volume of filtrate is often difficult to accurately regulate and quantify, resulting in potential undesired fluid shifts, especially in small patients.

Methods:

To eliminate the AV shunt that occurs with conventional placement, both the hemofilter inlet and outlet are connected in parallel to the post pump, preoxygenator leg of the ECMO circuit (Figure 1). A Transonic flow probe is placed on the outlet limb of the hemofilter, and flow through the device is modulated with a tubing clamp placed on the circuit segment between the hemofilter inlet and outlet. The desired hourly filtrate volume is divided by 12 or 6, corresponding to 5 or 10 minute intervals, and this volume is removed via a syringe connected to the filtrate line.

Conclusions:

Placing the hemofilter in parallel with the positive pressure limb of the ECMO circuit eliminates AV shunting without compromising device performance (e.g. filtrate removal rate, device clotting). Simultaneously, circuit operation is simplified: indicated pump flow equals actual circuit flow at the arterial cannula, negating additional calculations or pump flow modifications. Collecting filtrate directly into a syringe rather than relying on an external metering system greatly enhances accuracy and minimizes the risk of excess fluid removal.



Extracorporeal Life Support (ECLS) Technology Survey: Recent changes in 2011

Deborah Reed-Thurston, MD, Akif Ündar, PhD, Kim Kopenhaver Haidet, PhD, NNP-BC and Jeffrey Shenberger, MD, Department of Pediatrics, Division of Newborn Medicine, Pediatric Cardiovascular Research Center, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

Recent FDA approval of a neonatal hollow-fiber membrane oxygenator has sparked interest among clinicians regarding the ECLS technology currently in use throughout the U.S. The principal aim of this study is to survey ECLS centers on the type of ECLS equipment being used in neonates/children. The second aim was to identify the respondents' rationale(s) for changing technology.

Method:

This is a descriptive study utilizing a postal survey to Directors and Coordinators of all 125 U.S. ECLS centers identified from Extracorporeal Life Support Organization (ELSO) as of November 2010. Survey questions included frequency of ECLS, listing of neonatal and pediatric oxygenators and pumps being used and questions regarding clinicians' knowledge base and rationale for changing either oxygenator or pump.

Results:

Questionnaires were sent to all 125 U.S. ECLS Centers. Responses were received from 94 (75%) of the 125 centers. The majority of respondents were ECLS Coordinators (56.5%), followed by Directors (39%). Duplicate surveys (18 centers) were received and results were omitted when discordant. Respiratory diagnosis is still the predominant indication for ECLS at any age. Over half of centers are using a hollow-fiber oxygenator for neonates and for 80% of pediatric patients (Table 1). Roller pumps are used in 70% of neonatal and pediatric ECLS. Forty percent of centers changed the oxygenator type within the past three years while a third changed both the oxygenator and pump. Less than 10% of centers reported problems with either oxygenator or pump in both neonates and pediatric ECLS. More than one third of respondents that changed oxygenators cited the primary reason for changing was "clinical preference/experience", while one third was split between "FDA approval" and "Research results". Cost was not reported as a factor for change by any center. In 45% of centers, a multidisciplinary group made decisions on changing technology.

Table 1. Oxygenators- Neonates and Pediatric Patients

<i>Oxygenator Type</i>	<i>Neonate- Number (%)</i>	<i>Pediatric- Number (%)</i>
Silicone rubber membrane-Medtronic	41 (45)	15 (20)
Hollow-fiber membrane		
Maquet- Quadrox D*	26 (29)	47 (62)
Maquet- Quadrox-iD pediatric	15 (17)	10 (13)
Medtronic Minimax	5 (5.6)	3 (4)
Medos Hilite 800 LT	2 (2)	0
Terumo Capiiox Baby Rx	1 (1)	0
Other- not specified		1 (1)

*This oxygenator is designed for adult use, but many neonatal and pediatric centers have used it prior to approval of Maquet-Quadrox-iD pediatric oxygenator in the United States.

Table 2. Pumps- Neonates and Pediatric Patients

<i>Pump Type</i>	<i>Neonate - Number (%)</i>	<i>Pediatric- Number (%)</i>
Roller-		
Stöckert	36 (40)	25 (33)
Sorin	13 (14)	10 (13)
Maquet Jostra- HL 20	9 (10)	8 (11)
Cobe	7 (7.8)	5 (7)
Other	1 (1)	0
Centrifugal-		
Maquet Jostra-Rotaflow	5 (5.5)	8 (11)
Sorin- Revolution	2 (2)	4 (5)
Biomedicus	1 (1)	5 (7)
Levitronix Centrimag	1 (1)	4 (5)
Terumo	1 (1)	1 (1)
Other- not specified	4(4)	5 (7)

Conclusions:

This survey indicates that close to one half of ECLS centers implemented new technology within the past 3 years. Additionally, over a third of respondents' plan to implement the new FDA-approved oxygenator for neonates in the next six months. Clinical outcomes reported by ELSO do not take into account type of oxygenator/pump used. It will be necessary to evaluate the clinical response of the newest technology and encourage centers to publish their results.

Procalcitonin Predicts Outcome but Not Infection in Pediatric Veno-Aarterial ECMO

Alessio Rungatscher, MD, PhD, Fabrizio De Rita, MD, Alberto Merlini, MD, Gianluca Lucchese, MD, Luca Barozzi, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Giovanni Battista Luciani, MD. Division of Cardiac Surgery, Departments of Surgery, University of Verona, Verona, Italy

Background:

To investigate Procalcitonin (PCT) levels and relative value in diagnosis of infection and in assessment of severity of organ dysfunction in pediatric patients on ECMO after cardiac surgery.

Methods:

PCT and C-reactive protein (CRP) plasma concentrations were measured daily in a total of 94 samples in 14 consecutive pediatric patients treated with veno-arterial ECMO after cardiac surgery. Each patient was examined daily for signs and symptoms of infection and organ failure during the treatment with ECMO. The severity of organ failure was assessed by the sepsis-related organ failure assessment (SOFA) score.

Results:

Median plasma PCT and CRP concentration in non infected versus infected patients were 2.3 versus 2.9 ng/mL ($p=0.07$) and 95.8 and 101.3 mg/L ($p=0.09$), respectively. Area under receiver operating characteristic curve for PCT as predictor of multiple organ failure (SOFA score > 9) and mortality was respectively 0.772 (95 % confidence- interval (CI): 0.651 - 0.894), and 0.861 (95 %-CI: 0.779 - 0.943), compared with 0.580 (95% CI, 0.488-0.672) and 0.677 (95% CI, 0.622-0.733) for CRP ($p<0.01$).

Conclusions:

These results provide the first evidence that neither PCT nor CRP are reliable marker of infection in pediatric patients treated with ECMO. However, PCT is a valuable prognostic marker: high levels of PCT are correlated with mortality and the severity of organ dysfunction.

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, MS*, Akif Ündar, PhD^{*,†,‡,§}, John L. Myers, MD^{†,‡}
*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

Background:

In order to optimize the hemodynamic performance of an extracorporeal life support (ECLS) circuit, each component of the circuit should be rigorously evaluated. In previous studies, we have evaluated the hemodynamic properties of selected oxygenators, roller pumps, and centrifugal pumps. While many cannulae manufacturers may evaluate the flow characteristics of their products using water as the priming solution, we have intentionally used human blood as the priming solution in this study to evaluate the different sizes of arterial and venous cannulae in a simulated neonatal ECLS circuit.

Methods:

The neonatal ECLS circuit was composed of a Capiiox Baby RX05 oxygenator, a Rotaflow centrifugal pump, a blood reservoir and a heater & cooler unit. Seven combinations of Medtronic Bio-Medicus arterial and venous cannulae were tested (8F-10F, 8F-12F, 10F-10F, 10F-12F, 10F-14F, 12F-12F, 12F-14F). Both the length of arterial tubing (1/4 inch) and the venous tubing (3/8inch) were 2 feet. The flow rates and the pressure drops of the arterial cannulae were measured at pump speeds from 2500 to 4000 rpm and pseudo-patient pressures of 40, 60, and 80 mmHg. The system was primed with Lactate Ringer's solution and human blood with a hematocrit of 40% and at a temperature of 37°C. The priming volume of the circuit including all of the components was 135ml. The volume of pseudo patient was 500ml.

Results:

At equivalent pump speeds, an increase in the size of the cannulae was associated with a linear increase in flow rate. The increase in flow rate was effectively greater when incrementally upsizing the arterial cannulae than the venous cannulae. The pressure drops of the arterial cannula were correlated with the flow rates, regardless of the pseudo-patient pressure, and the venous cannula used simultaneously.

Fig 1. Flow ranges of seven cannula combinations at 60mmHg

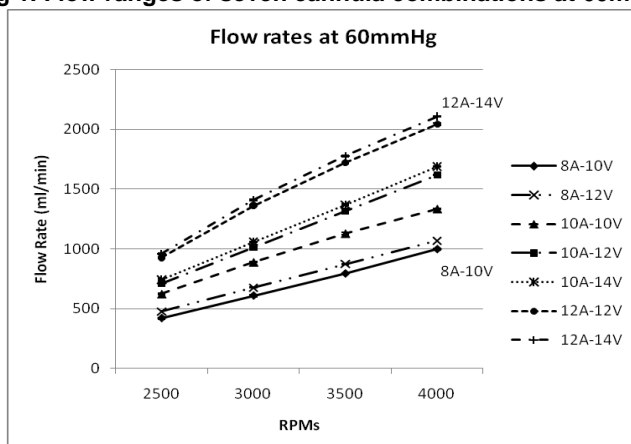
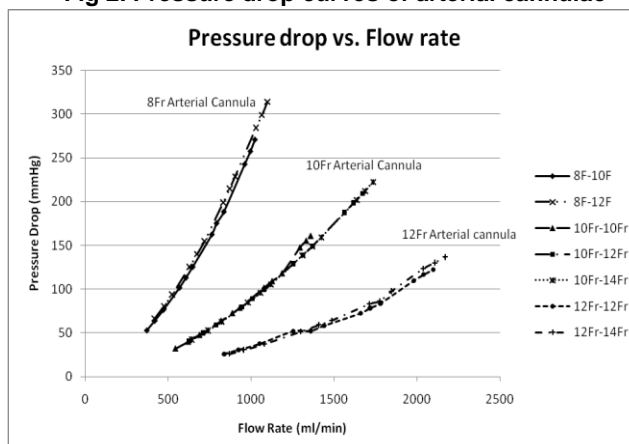


Fig 2. Pressure drop curves of arterial cannulae



Conclusions:

Increasing the size of the cannulae used for neonatal ECLS support permits higher flow rates at equivalent pump speeds and patient pressures. The arterial cannula has greater impact on the maximum achievable flow rate when a centrifugal pump is used in a neonatal ECLS circuit. These results may serve to guide clinicians in the choice of cannulae size to optimize the hemodynamics of pediatric ECLS.

Extracorporeal Life Support Systems: Alternative vs. Conventional Circuits

Sameer Khan, BS, Rahul Vasavada, MS, Feng Qiu, MD, Allen R. Kunselman, MS, Akif Ündar, PhD
Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, and
Public Health and Sciences, Penn State Hershey College of Medicine, Penn State Hershey Children's
Hospital, Hershey, Pennsylvania, USA

Background:

Emerging technologies and practices for pediatric and neonatal extracorporeal life support (ECLS) are promising. This experiment sought to compare the Medtronic 0800 silicon rubber membrane oxygenator to the Quadrox-iD Pediatric oxygenator in the conventional roller pump circuit, as well as comparing the conventional circuit to an alternative circuit.

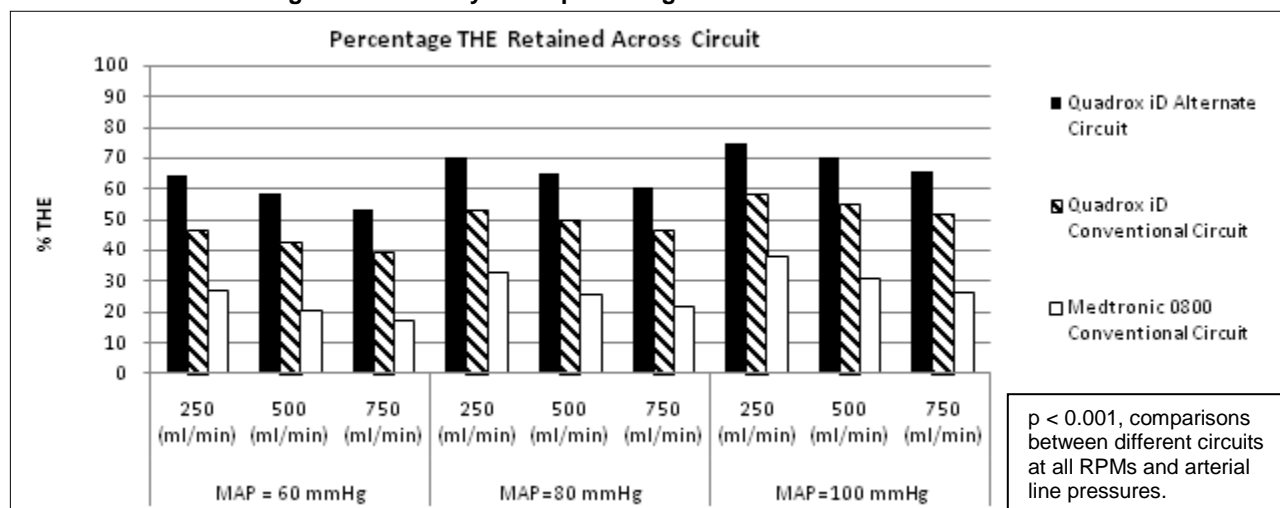
Methods:

Three circuits were set up in the experiment. Two conventional roller pump circuits were used to compare the two oxygenators and an alternative circuit consisting of the Quadrox-iD Pediatric oxygenator and Maquet Rotaflow centrifugal pump system was used to identify differences between circuits. All three circuits were primed with Lactated Ringers' solution and human blood, with an hematocrit of 40%. Testing occurred at flow rates of 250, 500, and 750 ml/min at 37°C for mean arterial line pressures of 60, 80, and 100 mmHg.

Results:

The results of the experiment showed lower pressure drops and greater retention of total hemodynamic energy (THE) across the Quadrox-iD Pediatric oxygenator compared to the Medtronic 0800 oxygenator. Furthermore, the centrifugal pump used in the alternative circuit showed no back flow at flow rates as low as 250 ml/min while, on the other hand, rpm levels were kept below 2200 for flow rates as high as 750 ml/min.

Figure 1. Summary of the percentage of THE retained across the circuits.



Conclusions:

Findings support the usage of the Quadrox-iD Pediatric oxygenator in a circuit utilizing the Rotaflow centrifugal pump system due to lower pressure drops and greater percentage of THE retained across the circuit. Additional advantages of the alternative circuit include rapid set-up time, easy transport, lower priming volumes, and no gravity-dependent venous drainage system so that it can be situated in close proximity to and at the level of the patient. The alternate circuit has been translated into clinical application in our institution.

Evaluation of Two Pediatric Polymethyl Pentene Membrane Oxygenators with Pulsatile and Non-Pulsatile Perfusion

Feng Qiu, MD, Sameer Khan, BS, Jonathan Talor, BSE, Allan R. Kunselman, MS, Akif Ündar, PhD.
Pediatric Cardiovascular Research Center, Departments of Pediatrics, Surgery, Bioengineering, and Public Health and Sciences, Penn State Hershey College of Medicine, Penn State Hershey Children's Hospital, Hershey, Pennsylvania, USA

Background:

Polymethyl pentene (PMP) membrane oxygenators are gaining more and more popularity instead of conventional silicone membrane oxygenators in extracorporeal life support (ECLS) circuit. This experiment sought to compare two PMP hollow-fiber membrane oxygenators: the Medos HILITE 2400LT and the Maquet Quadrox-iD Pediatric in terms of transmembrane pressure gradients and hemodynamic energy preservation under both pulsatile and non-pulsatile conditions.

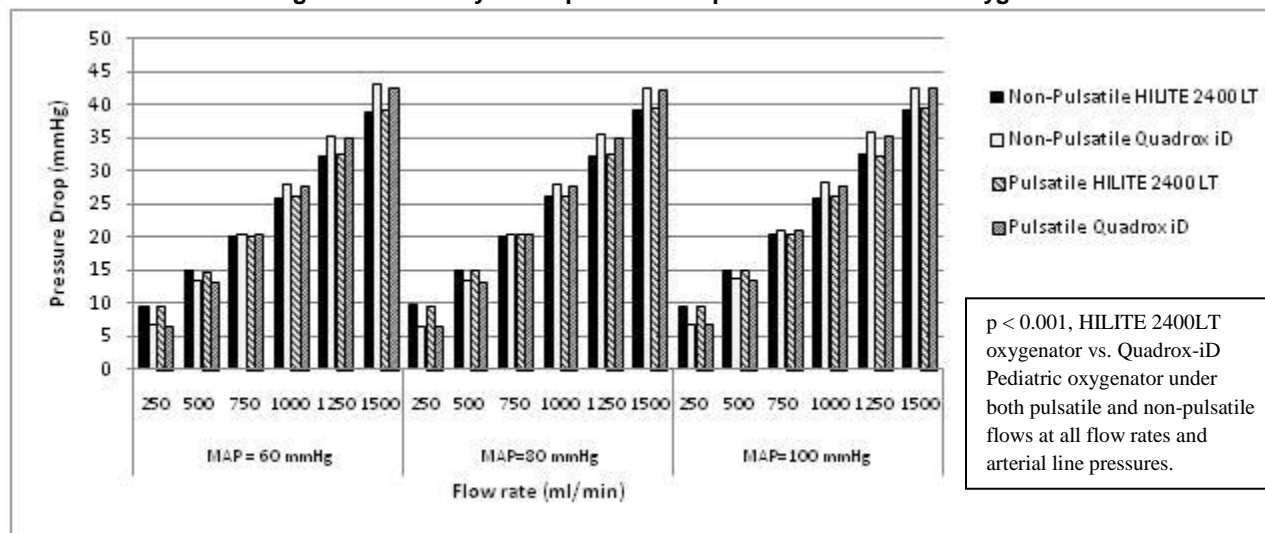
Methods:

A simulated ECLS circuit was used to test these two oxygenators. The circuit consisted of a roller pump, ¼ inch tubing for both arterial and venous line, an oxygenator, and a venous reservoir as a pseudo-patient. Three pressure transducers were placed upstream and downstream of the oxygenator and the distal arterial line. The experimental system was primed with Lactated Ringer's solution and packed human red blood cells to maintain a hematocrit of 40%. The total volume was 600ml, including the 350ml volume of the pseudo-patient. The tests were performed at 37°C, six flow rates (250, 500, 750, 1000, 1250, 1500 ml/min) and three distal arterial line pressures (60, 80, 100 mmHg), under both pulsatile and non-pulsatile perfusions.

Results:

Both oxygenators had adequate performances in pressure drop and hemodynamic energy preservation. There were no significant differences between pre- and post-oxygenators for mean pressure (MP), energy equivalent pressure (EEP) and total hemodynamic energy (THE). During the pulsatile perfusion mode, the HILITE 2400 LT retained a greater percentage of surplus hemodynamic energy (SHE) across the oxygenator.

Figure 1. Summary of the pressure drops of the tested PMP oxygenator



Conclusions:

Both the Quadrox-iD Pediatric and HILITE 2400LT PMP membrane oxygenators are suitable for pediatric ECLS therapy under both non-pulsatile and pulsatile perfusion. An optimized combination of flow rate and MAP should be achieved in order to deliver the maximal pulsatile energy in the extracorporeal circuit.

Multiplexed Real-Time Monitoring of Systemic Inflammation during Mechanical Circulatory Support

Lawrence A Sasso¹, Akif Ündar², Jeffrey D. Zahn¹

¹BioMEMS Laboratory, Department of Biomedical Engineering, Rutgers University, Piscataway, NJ

²Pediatric Cardiovascular Research Center, Departments of Surgery, Pediatrics, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

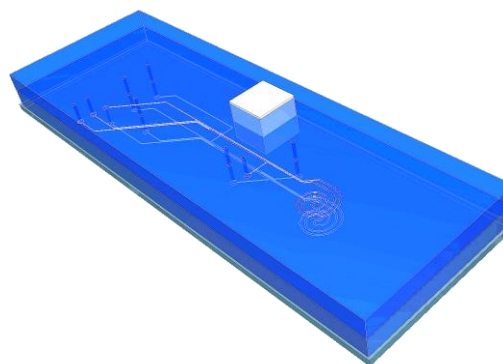
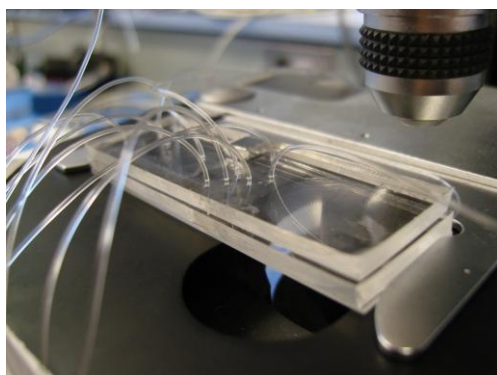
Mechanical circulatory support procedures such as cardiopulmonary bypass and extracorporeal life support are known to cause significant inflammatory responses, which lead to complications and diminished patient outcomes. The ability to thoroughly characterize the systemic inflammatory response is limited by the available assaying techniques, especially due to the limited blood volume available for testing. By combining microfluidic technology with a multiplexed microbead-based cytokine immunoassay, we are developing a system which will monitor and thoroughly characterize the inflammatory response at high sampling rates and with real-time output.

Methods:

A multi-layer microfluidic chip is fabricated by conventional soft lithography. The device is infused with the reagents of the Bio-Rad Bio-Plex kit via syringe pump, which includes antibody coated magnetic microbeads, secondary labeling antibody, and fluorescent tagging solution. The microbead solution is pre-mixed to allow detection of between one and fifty cytokines simultaneously. The blood plasma sample is provided as a continuous stream from a microfiltration device, and a flow controller ensures a steady stream of sample plasma into the immunoassay device. Upon reaching the outlet of the device, the microbeads are fluorescently labeled, having a fluorescence intensity which is proportional to concentration of each analyte in the blood. The incubated beads are currently being collected in fractions and interrogated by flow cytometry, and in future work they will flow directly into a flow cytometer for real-time, continuous measurements.

Results:

Preliminary results have shown that the microfluidic device is able to perform the necessary incubations with continuous flow operation. It has also been shown that the assay incubation times can be reduced from the typical 30 minutes per stage to as low as 2 minutes, although the sensitivity is reduced. A trade-off must be chosen between assay lag time and minimum cytokine concentration sensitivity.



Conclusions:

The fully integrated assay will allow continuous measurement of inflammatory markers during mechanical circulatory support procedures with very high sampling rates and lag times likely below 20 minutes.

Aorticopulmonary Window : Surgical Correction of in Neonatal Period and Results

Alkan-Bozkaya T., Akçevin A., Türkoğlu H., Paker T., Ersoy C*, Ündar A.

Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Penn State Hershey Children's Hospital, Hershey, PA, USA

Introduction:

Aorticopulmonary window (APW), a congenital abnormality, is a rarely seen case. Early diagnosis and surgical intervention is life-saving in such cases. The objective of this study was to discuss our results and management methods of this rare pathology.

Material and method:

Between 2002 to 2011, 12 patients which had APW pathologie with the signs of cardiac failure mainly were operated in our clinic. 6 of them had associated with APW and interrupted aortic arch. All of them were low birth weight (under 1500 grams) and mean wight was 1.34 kg. They were taken to the surgery emergently by echocardiographic diagnosis. In all of the cases, complete correction was successfully achieved in a single session via median sternotomy and with cardiopulmonary bypass (CPB) and total circulatory arrest (TCA, 18oC). Pulsatile perfusion mode was used in all cases during CPB.

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

Results:

Early and late postoperative periods of our 11 cases in the 6-28 monthly follow-up have no problem. Because of these rare cases, we think that surgical correction can be possible and safely applied in neonatal period in such combined arch pathologies. We thought that early intervention and especially pulsatile perfusion mode is more suitable choice in this high risk group pathologies (according to improved patient outcome in maintaining better cardiac, renal and pulmonic function) in the early postoperative period. Short intubation period (8 ± 6.12 hours) and short ICU (1.21 ± 1.03 days) and hospital stay (6.4 ± 1.51 days) were observed in all five patients.

Surgery for Coronary Arterio-Venous Fistula : Indication in Childhood, Treatment and Results

Alkan-Bozkaya T, Turkoğlu H, Akcevin A, Paker T, Ersoy C*, Bayer V*, Aytac A*.

Istanbul Bilim University, Dept. of Cardiovascular Surgery, and
V.K.V. American Hospital, Dept. of Cardiovascular Surgery.

Summary

Coronary artery - venous fistula cases (a-v fistula) are 0,4% of cardiac anomalies. Its prognosis is asymptomatic in childhood and it may also cause cardiac insufficiency findings. Spontaneous healing is possible. In the course of years, angina pectoris and cardiac insufficiency may appear more evidently. In our clinic, eleven patients have been operated due to a-v coronary fistula starting from June ,1988. Patient ages were from 12 months to 19 years (average age is 6,5). 3 of the patients were female children and 8 of them were male children. 5 of the fistulas were originated from LAD, 3 of them from RCA , and 3 of them were originated from Cx artery. 8 of them were drained into right ventricle and 3 of the fistulas were drained into right atrium. Accompanied pathologies were ASD in one patient and mitral cleft in another patient. Both accompanied pathology were recovered by operation. Extracorporeal circulation was applied during surgical operation in all cases. Primary closure of the fistula was applied in 4 cases, pericardial patch repair was used in 5 cases and in 2 cases ligation was applied. In all cases, any postoperative complication was not observed. Tracing terms in patients, under regular control, were from 8 months to 13 years (average term 106,4 months). Functional capacity of all patients were NYHA I, and they had not any problem. If obvious clinical complains is not existing in child patients with a-v coronary fistula, they may be followed for a period. If spontaneous healing does not occur, early repair operations provide successful results and absolute recovery.

Depending on shunt size, congestive cardiac insufficiency, angina pectoris, bacterial endocarditis, dyspnea, fatigue, frequent upper respiratory infections, paroxysmal nocturnal dyspnea, and hemoptysis may appear. It is supposed that, these symptoms occur due to the change in coronary blood. Treatment of coronary artery fistulas is surgical. Surgical technique is modified depending on preoperative or intraoperative findings. In general, ligation of abnormal coronary artery close to its cardiac entrance. However, in most cases, simple ligation is applied, in some cases, open heart technique may be required for surgical closure. Early ligation is indicated in all cases, because it prevents from frequent appearance of late symptoms and complications and eliminates increased mortality and morbidity rates during ligation in aged patients. Surgical operation in coronary arterial-venous fistulas is a safety method, and its mortality and morbidity rate is very low.

Corrected Transposition of the Great Arteries: Surgical Approach – a Review

Alkan-Bozkaya T, Turkoğlu H, Akcevin A, Paker T, Aytac A*, Ündar A**.

Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Dept. of Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Penn State Hershey Children's Hospital, Hershey, PA, USA

Corrected transposition of the Great Arteries (c-TGA) is a rare condition and has been estimated to account for 0.5-1.4% of congenital heart disease. It is frequently associated with dextrocardia (25%). Most of the clinical and surgical retrospective studies have reported a male predominance in corrected transposition and the causes are thought to be multifactorial.

The presence of ventricular inversion (atrioventricular discordance) with ventriculoarterial discordance has been called corrected transposition or physiologically corrected transposition because these 2 anomalies in sequence ensure that blood flow continues in its usual physiologic pathway. Van Praagh et al found that the segmental classification was S,L,L in 94% (S: atrial situs solitus, L :L-looped, L : the position of the aortic valve, which is anterior and to the left of the pulmonic valve), I,D,D in 3%, and S,L,D in 3%. In the normal heart, the aorta is posterior and to the right. In the presence of situs inversus, the nomenclature for corrected transposition is I,D,D.

Pathophysiology is determined by the presence and type of associated lesions. When no other defects are present, the path of the blood flow is physiologic. The most common anatomic associations include the presence of a ventricular septal defect (VSD), which may be observed in almost 80% of cases and the presence of pulmonary stenosis, which has been reported in approximately 50% of cases. Tricuspid valve anomalies (dysplasia, straddling, or Ebsteinlike malformation) are also quite common and are reported in 14-56% of patients. Coarctation and interrupted aortic arch have also been frequently reported, but subvalvar and valvar aortic stenosis are quite uncommon. Conduction abnormalities also are common. The reported incidence of complete atrioventricular (AV) block has ranged from 12-33%.

A multi-institutional study confirmed that congestive cardiac failure is common in patients with or without associated cardiac defects. By age 45 years, 67% of patients with associated anomalies and 25% of patients without associated anomalies were in congestive cardiac failure.

Poor right ventricular function and complete AV canal as risk factors for mortality. Risk factors for progressive right ventricular dysfunction included conventional biventricular repair, complete AV block, and severe tricuspid regurgitation. Knowing the position of the AV node in this defect is extremely important if injury to it during surgery is to be avoided. This anterior position of the AV node is more commonly reported in situs solitus.

For the rare patients who have corrected transposition and no other associated abnormalities, no treatment may be required because their life expectancy has been reported to be near normal.

Recent advances in the technology of Doppler echocardiography make noninvasively diagnosing this condition possible and allows for great accuracy, not only postnatally but also using fetal echocardiography.

Surgical therapy may be palliative, at least initially, or it may involve complete repair. Palliation includes pulmonary artery banding in infancy for moderate VSDs and modified Blalock Taussig shunts for infants with severe pulmonic stenosis. Complete repair may be either a physiologic or an anatomic repair. Pulsatile perfusion mode favorable for these complex pathologies because of positive effects on vital organ recovery recorded. In the former, only the associated defects are addressed, but the right ventricle continues to function as the systemic ventricle.

The prognosis depends on the associated anatomic malformations and the conduction system abnormalities.

Surgical Approach to the Primary Heart Tumors and the Results: 36 Cases

Alkan-Bozkaya T., Akçevin A., Türkoğlu H., Paker T., Ersoy C*, Ündar A**.

Istanbul Bilim University, Dept. of Cardiovascular Surgery and V.K.V. American Hospital, Depts. of Neonatology, Pediatric Cardiology, Cardiovascular Surgery, Istanbul, TURKEY and Penn State University, Penn State Hershey Children's Hospital, Hershey, PA, USA

Introduction:

36 patients underwent surgeries in our clinic between May 1993 and May 2010. The age range of the cases was 1-68 (mean: 31) and % 72 of them were female (25/36).

Material-Method:

The cases were studied in 3 groups. Group I : Atrial myxoma, Group II : non-myxoma benign tumors, Group III : Malign tumors. The cases were all called and invited for clinical control. All living cases (n = 35) came. All patients were evaluated with right atriotomy under the cardiopulmonary bypass and transeptal approaches and operated. Same as specified in the literature,

the most frequent location of the myxomas in our series was left atrium localization (n=21, %67.7) and in one case bi-atrial positioning was noticed. 2 cases had left ventricular location among which 3 had apical localization, while in one case it was located under mitral posterior leaflet. One case showed a very rare localization; on the right ventricular free wall. Right ventricular localization was treated with the transeptal method for all cases except this last one. Myxomas had clung to the interatrial septum (n=21), left atrial ceiling (n=5), inter-ventricular septum (n=4), under the mitral posterior leaflet (n=1) or to the right ventricular free wall (n=1) by a pedicle.

All of the myxomas were resected together with their pedicles and the surrounding tissue. The defect caused after the resection were primarily closed by fresh autologous pericard patch (n=19) or by monofilament non-absorbable suture material (n=12). In one of the cases, mitral valve replacement was conducted in the same session with the operation. Pathological evaluation of the materials extracted from all cases confirmed them as myxomas. While one patient in the myxsoma group lost in the 3rd postoperative day due to pneumonia. All of the other cases had no problem at the clinical and echocardiographic monitoring.

In the non-myxsoma tumor group one of the 3 cases, a female patient of 24; showed Lipoma which is a very rare defect originating from inter-ventricular septum (this is the 7th case in the literature) and the other 2 cases were rhabdomyomase observed in a little girl of age 3 and 18 months old a boy.

In the malign group, 2 cases were operated: one case had angiosarcom (68/E) and the other had fibrosarcom. Widespread cardiac involvement was present in the angiosarcom case and the patient deceased in the early postoperative period due to low heart output.

Conclusion:

Surgical treatment of the primary heart tumors was applied in all cases where resection was possible. Full cure can be achieved after resection in the benign tumor cases. No recurrences were noticed in our series. Screening of all heart ventricles via the postoperative endoscopic camera can contribute to the containment of recurrences. In the malign tumors, there is a better response to active palliation in the tumor load and the subsequent adjuvant chemotherapy and the chance to survive is higher.

Case: Rhabdomyoma in an Infantile Child with No Tuberous Sclerosis Definition, Clinical Presentation and Surgical Approach

Turkoglu H, Alkan-Bozkaya T, Akalın F*.

Istanbul Bilim University, Dept. of Cardiovascular Surgery and Marmara University, Dept of Pediatric Cardiology*, Istanbul, Turkey

Case Report:

Cardiac tumors occur very rarely in infantile age. A 11-months-old male infant referred to our clinic from the pediatric cardiology department for cardiac murmur and tachypnea. After physical examination and echocardiographic evaluation diagnosis was intracardiac mass and the open heart surgery recommended to the child's family. No congenital heart history in his family and there is no signs of Tuberous sclerosis.

Echocardiographic examination showed a big mass measuring 2X2.4 cm at left atrium and right deviation of atrial septum was present.

Patient was operated under cardiopulmonary bypass. Right atrial approach, through the ASD with enlargement, the mass was at the left atrium and atrial septum deviated to right. Mass resected with the capsule and created large ASD and left atrial posterior wall were repaired with a autolog pericardial patch. Postoperative pathologic evaluation confirmed diagnosis.

Postoperative course was uneventful. Postoperative electrocardiogram was sinus.

Postoperative-echocardiogram : Mild mitral regurgitation was present and septum intact.

Conclusions:

Surgical resection, when possible, is the treatment of choice for all primary cardiac tumors. Patients with benign tumors are probably cured by resection and in our experience there was no known tumor recurrence.

Hemodynamic Evaluation of the Avalon Elite™ Bi-Caval Dual Lumen Cannulae

Feng Qiu, MD¹, Chiajung K. Lu, BA¹, David Palanzo, CCP¹, Larry D. Baer, CCP¹, John L. Myers, MD^{1,2}, Akif Ündar, PhD^{1,2,3}.

¹Pediatric Cardiovascular Research Center, Departments of ²Surgery, and ³Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

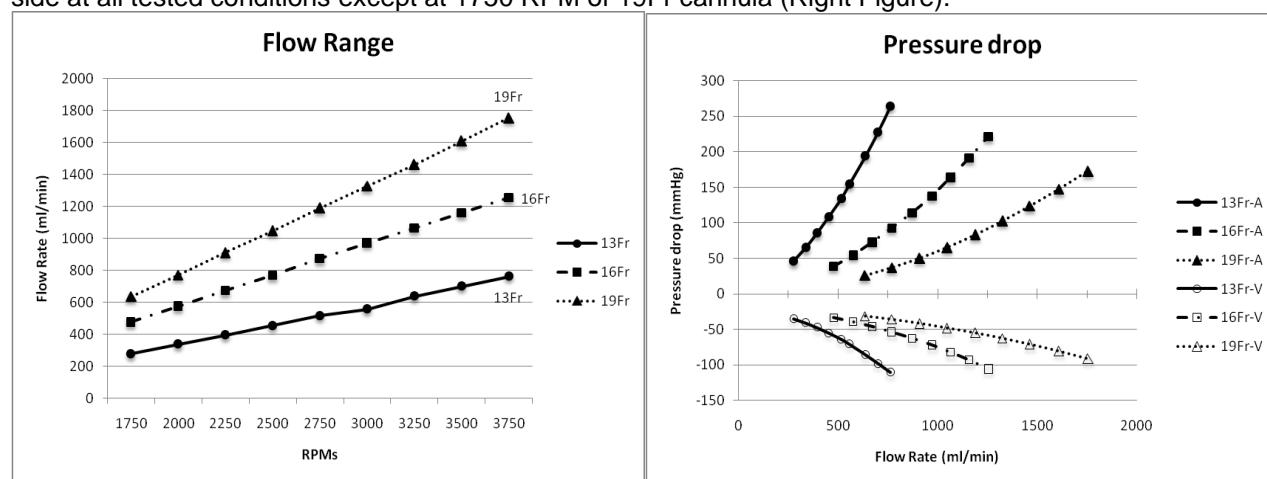
In previous studies, we have evaluated the hemodynamic properties of selected oxygenators, pumps (centrifugal and roller), and single lumen cannulae. Since the dual lumen cannulae are widely used in veno-venous ECLS and are receiving popularity due to their advantages over the single lumen cannulae (simplified cannulation procedure, less injury to the patient, and less impact on the hemodynamic parameters), we evaluated the flow ranges and pressure drops of three different sizes of Avalon Elite™ dual lumen cannulae (13Fr, 16Fr, 19Fr) (Avalon Laboratories, LLC, Rancho Dominguez, CA, USA) in a simulated neonatal ECLS circuit primed with human blood.

Methods:

The experimental ECLS circuit was composed of a Rotaflow centrifugal pump (MAQUET Cardiopulmonary AG, Hirrlingen, Germany), a Capiiox BabyRX05 oxygenator (Terumo Corporation, Tokyo, Japan), three feet of ¼ inch venous and arterial line tubing, an Avalon Elite™ dual lumen cannula, and a soft reservoir as a pseudo-right atrium. The circuit was primed and de-aired with Lactated Ringer's solution, then the LR solution was replaced by human blood to maintain a hematocrit of 36%. The blood pressure in the pseudo-right atrium was continuously monitored and maintained at 4-5 mmHg. Two pressure transducers were inserted into the arterial and venous lines close to the cannulae. One tubing flow probe (Transonic Systems Inc., Ithaca, NY, USA) was attached to the arterial line. For each cannula, pump flow rates and pressures at both the arterial and venous sides were recorded at RPMs from 1750 to 3750 in 250 intervals. For each RPM, six data sets were recorded for a total of 162 data sets. The total volume of the system was 300ml. All the experiments were conducted at 37°C using a HCU 30 heater-cooling unit (MAQUET Cardiopulmonary AG, Hirrlingen, Germany).

Results:

The flow range for the 13Fr, 16Fr, and 19Fr cannulae were from 228 to 762 ml/min, 478 to 1254 ml/min, and 635 to 1754 ml/min, respectively (Left Figure). The pressure drops on the arterial side were higher than the venous side at all tested conditions except at 1750 RPM of 19Fr cannula (Right Figure).



Conclusions:

The results of this study showed the flow range as well as the pressure drops of three dual lumen cannula in different sizes using human blood, which is more applicable in clinical settings compared to the evaluations using water.

An in vitro comparison of the ability of three commonly used pediatric cardiopulmonary bypass circuits to filter gaseous microemboli.

Richard W. Melchior MPS, CCP, Tami Rosenthal, MBA, CCP, Andrew C. Glatz, MD.

Department of Perfusion Services and The Division of Cardiology, Children's Hospital of Philadelphia, The University of Pennsylvania School of Medicine Philadelphia, PA, USA.

Background:

The purpose of this study was to compare the ability of three commonly used pediatric cardiopulmonary bypass (CPB) circuits to filter gaseous microemboli (GME) in an in vitro model.

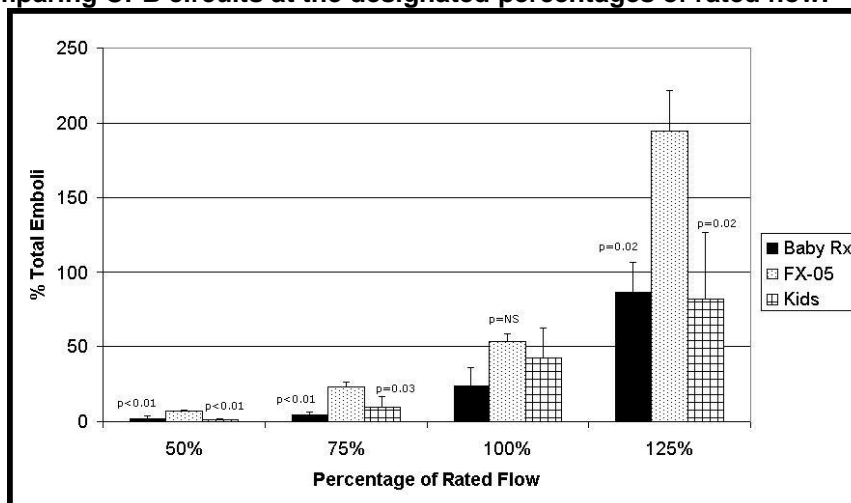
Methods:

Devices were tested at different levels of two specific independent variables: volume of air injected (1, 3 and 5ml) and percentage of each oxygenator's rated flow (50%, 75%, 100% and 125%). The air-handling ability of each CPB circuit was determined by the Emboli Detection and Classification Quantifier (Luna Innovations Inc., Roanoke, VA).

Results:

At all tested conditions, the FX-05 allowed a higher percentage of GME when compared to either one or both of the other two CPB circuits. When comparing oxygenators at similar absolute flow rates, the KIDS D100/D130 CPB circuit performed worse compared to the other two CPB circuits.

**Percentage of total emboli GME at the post-arterial line filter sensor (5ml injection of air).
Comparing CPB circuits at the designated percentages of rated flow.**



Conclusions:

The combination of the Baby RX-05 oxygenator and Capiiox AF02 arterial line filter provides the highest level of protection from air emboli in an in vitro investigation.

Publication: [Perfusion](#). 2010 Jul;25(4):255-63; discussion 265-6. Epub 2010 Jun 21.

Bloodless Approach to Pediatric Open Heart Surgery for Repair of Atrial and Ventricular Septal Defects

Vincent Olshove CCP, Thomas Preston, CCP, Daniel Gomez, CCP, Aymen Naguib, MD, Mark Galantowicz, MD, Alistair Phillips, MD.

The Heart Center @ Nationwide Children's Hospital, Columbus, OH, USA.

Introduction:

In adult cardiac surgery the use of blood has been associated with increased morbidity, mortality, length of stay (LOS) and costs. In pediatric cardiac surgery the amount of hemodilution due to circuit size has made the use of blood commonplace and has been identified as a significant hurdle the pediatric perfusionist and cardiac surgical team must overcome to successfully perform bloodless operations. We performed a retrospective review of blood use for all patients undergoing cardiopulmonary bypass for repair of atrial or ventricular septal defect repair.

Methods:

Chart review of all patients 15 kilograms (kg) or less who underwent cardiopulmonary bypass for repair of ASD or VSD between January 2006 and December 2009. Patients were divided into groups based on whether they received blood.

Discussion:

One hundred eleven patients were included for evaluation. Forty-two percent of procedures (47/111) were performed without blood in the operating room and 31% (34/111) were discharged without administration of blood product. The mean weight of the bloodless group was 10.07 ± 3.5 kg (range 4.78 – 15.2) vs 4.85 ± 1.4 kg (range 2.8 – 10.9), $p < 0.05$. LOS was 3.5 ± 1.0 vs 5.7 ± 3.6 days significantly less for the bloodless OR group vs the blood group. 97% of bloodless group were extubated in the OR compared to 70% for the blood group. Hemoglobin on arrival to the intensive care unit was 9.6 ± 1.3 gm/dL (range 7.4 to 13.6) in the bloodless group versus 12.4 ± 2.6 gm/dL (range 7.0 to 17) in the blood group. Lactates were not significantly different in the OR (1.44 vs 1.46 mmol/L) or CTICU (1.26 vs 1.36 mmol/L) for the bloodless vs blood group. There were no neurologic events or complications in the bloodless group and there was no mortality in either group.

Conclusion:

Bloodless surgery within this patient population is achievable.

ABCs of Pulsatile Cardiopulmonary Bypass in Infants and Children The Penn State Hershey Approach

Larry D. Baer, CCP, John L. Myers, MD, J. Brian Clark, MD, Shigang Wang, MD, Feng Qiu, MD, David Palanzo, CCP, Karl Woitas, CCP, Robert Wise, CCP, and Akif Ündar, PhD
Pediatric Cardiovascular Research Center, Departments of Surgery, Pediatrics, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

Pulsatile flow cardiopulmonary bypass (CPB) versus non-pulsatile flow CPB remains a controversial subject, to this day. Recent clinical evidence suggests that the utilization of pulsatile flow perfusion better preserves pulmonary, cardiac and renal function than a non-pulsatile approach (1). Previous pulse strategies focused primarily on pulse pressure gradients when determining optimal pulsatile flow settings. Generation of pulsatile flow depends on an energy gradient rather than on a pressure gradient so calculation and utilization of hemodynamic energy formulas are necessary for precise quantification (2).

Methods:

When using pulsatile flow during CPB, the settings of the heart-lung machine are important (3). The following settings were used to produce the optimal pulse wave at the Penn State Hershey Children's Hospital: base flow = 10%, start time = 20, stop time = 80 and frequency = 90 bpm for patients > 15 kg; 100 bpm for patients 7-15 kg; 120 bpm for patients < 6.9 kg. When selecting a circuit, each component should be evaluated for its effect on the artificially produced pulsatile waveform by quantifying the difference of pressure-flow waveforms by using the total hemodynamic energy (THE), energy equivalent pressure (EEP) and the surplus hemodynamic energy (SHE). These formulas were used to select the circuit components with the best hemodynamic profiles (2,3).

Results:

When compared to the patients receiving non-pulsatile CPB, the pulsatile group had better clinical outcomes with less inotropic support, shorter intubation times, less time spent in the intensive care unit and shorter hospital length of stay. Other data comparisons showed that the patients receiving pulsatile CPB had higher urine output, lower levels of adrenalin and lactate and higher albumin levels (4,5). To date, we have not seen any adverse effects of pulsatile flow in our pediatric CPB cases.

Conclusions:

Pulsatile flow during CPB maintains a higher level of microcirculation perfusion at physiologic levels, decreases the systemic inflammatory response and improves vital organ recovery leading to better clinical outcomes.

References

- 1 Akçevin A, Alkan-Bozkaya T, Qiu F and Ündar A. Evaluation of Perfusion Modes on Vital Organ Recovery and Thyroid Hormone Homeostasis in Pediatric Patients Undergoing Cardiopulmonary Bypass. *Artificial Organs* 2010; 34(11): 879–884.
- 2 Ündar A. Pulsatile versus non-pulsatile cardiopulmonary bypass procedures in neonates and infants: from bench to clinical practice [Invited Editorial]. *ASAIO Journal* 2005; 51: vi-x.
- 3 Rider AR, Ressler NM, Karkhanis TR, Kunselman AR, Wang S, Ündar A. The impact of pump settings on the quality of pulsatility. *ASAIO Journal* 2009; 55: 100-105.
- 4 Haines N, Wang S, Ündar A, Alkan A, Akçevin A. Clinical outcomes of pulsatile and non-pulsatile mode of perfusion. *Journal of Extracorporeal Technology* 2009 41: P26-P29.
- 5 Rogerson A, Guan Y, Kimatian SJ, Kunselman A, Clark JB, Myers JL, Ündar A. Transcranial Doppler ultrasonography: a reliable method of monitoring pulsatile flow during cardiopulmonary bypass in infants and young children. *Journal of Thoracic and Cardiovascular Surgery* 2010;139 (4):e80-2.

Regulatory Requirements for Medical Device Development

David Kinsel, PE
Product Development Manager for Surgeon Products
Terumo Cardiovascular Systems Corporation, Ann Arbor, Michigan, USA

Background:

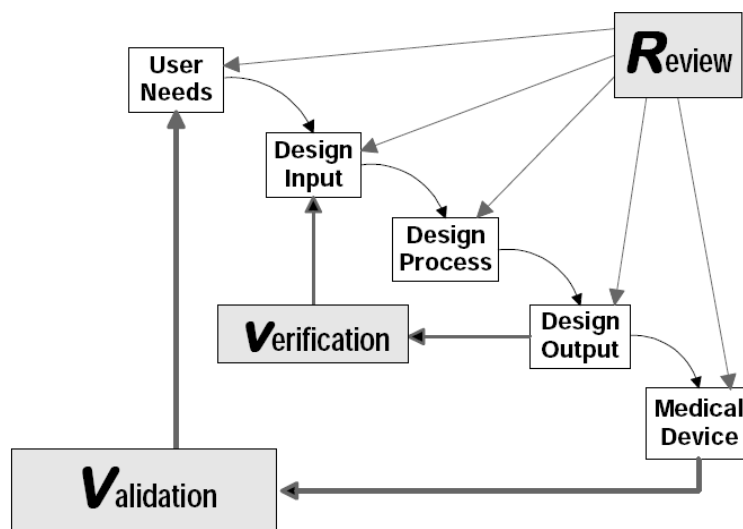
Medical devices used in the United States must comply with federal regulations established to ensure that specified requirements have been met. An overview of these design control requirements is provided to increase awareness of the development process and provide a basis for mutual understanding for continued dialog with end users.

Methods:

Design control requirements were established by the United States Food and Drug Administration (FDA) as an element of the Quality System Regulation (QSR) in 1996. Device manufacturers are required to have a Quality Management System (QMS) to ensure their devices are safe and effective. The QMS is established by writing operating procedures to achieve consistent application of the methods used to meet the regulatory requirements. The FDA has the responsibility to audit device manufacturers for compliance to the regulation.

Results:

The requirements of the QSR and the resulting device design control procedures lend themselves to what is commonly known as the waterfall development process as shown in the diagram below. This iterative process results in documented evidence that is defined in the QSR as the Design History File. This record of development is essential for managing the product life cycle. The elements and purpose of the design control process will be presented to illuminate today's development environment.



Conclusion:

Collaboration between device developers and the practitioner is essential for improving clinical outcomes and reducing time to market of innovative devices.

Real Time Monitoring of Inflammation Biomarkers with Extracorporeal Life Support (ECLS) intervention

Jeffrey D. Zahn¹, PhD, Akif Ündar², PhD, Kiana Aran¹, BS and Lawrence Sasso¹, BS

¹Department of Biomedical Engineering, Rutgers University, Piscataway, New Jersey, USA

²Pediatric Cardiovascular Research Center, Departments of Surgery, Pediatrics, and Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

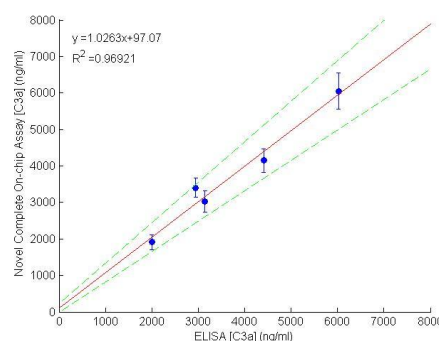
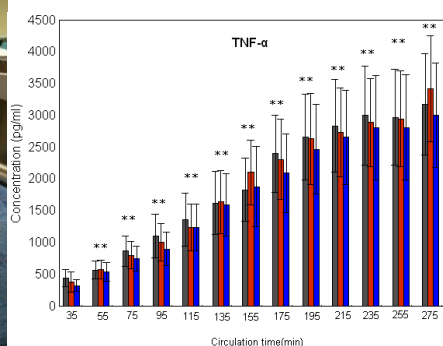
The use of Extracorporeal Life Support (ECLS) has been associated with a pronounced systemic inflammatory response (SIR) with increasing severity with increasing duration of ECLS use and the possibility of ECLS cannulation introducing infection. However, as advances in ECLS circuit design and perfusion protocols have made circuit operation easier and less labor intensive, the use of ECLS has become more common. We believe, that the use of ECLS circuits with continuous monitoring capabilities for inflammatory biomarkers, lactate, toxins and biomolecules directly secreted from bacteria and/or viruses or produced from the body's immune response, coupled with predictive modeling of inflammatory processes will assist in treatment of patients on ECLS.

Methods:

A microfluidic analytical system which can simultaneously measure plasma cytokine and complement concentrations in real-time has been developed. This microanalytical system is designed to continuously filter a circulating blood sample and measure the filtered inflammation markers in a continuous, real-time fashion and device has been tested by filtering whole blood continuously sampled from both a simulated and porcine ECLS model (Figure 1). The designed microimmunoassay is based upon a magnetically controlled incubation process with antibody conjugated paramagnetic beads allowing serial processing steps of the beads to be performed autonomously: from antibody-antigen binding in the antigen stream, bead washing, fluorescently tagged secondary antibody labeling and finally optical detection in a detection area. Since beads are continuously infused and mixed with the analyte solution in a well controlled incubation process, as the analyte concentration changes, the corresponding bead fluorescence also changes allowing continuous tracking of fluctuating analyte concentrations. Through the use of multiplexed immunoassay kits (Bio-Rad Bio-Plex Pro Multiplex Assay), sensing of multiple analytes in parallel with a processing residence time of 10 to 15 minutes from bead introduction to fluorescence quantification is enabled.

Results:

A microfiltration device perfused from a porcine ECLS model was connected to a sampling manifold on the arterial port of the membrane oxygenator. Collected fractions were analyzed showing cytokine concentration increasing significantly over the sampling period for each protein analyzed. The microimmunoassay was validated by comparing C3a measurements made on collected plasma by the μ IA device with those made using a standard ELISA plate.



Conclusions:

This predictive capability enabled by these diagnostic devices will assist in improving ECLS patient care by assisting in determining proper medical treatments and interventions.

Computational Fluid Dynamics to Improve Hemodynamics of Congenital Aortic Cannulation

Kerem Pekkan, PhD

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

Background:

Patients born with congenital heart defects, such as the hypoplastic left heart syndrome (HLHS), require complex arterial cannulation strategies for neonatal aortic arch reconstruction. Optimal cannula performance requires reduced blood and vascular damage, excellent cerebral perfusion and low pulsatile energy dissipation. Particularly the neonatal flow conditions and small dimensions pose unique challenges for the optimal aortic cannula and perfusion waveform design. Computational fluid dynamics is a useful tool to understand the complex flow regimes of the aortic cannulation site that influence performance and further control these flow structures for improved hemodynamics.

Methods:

Three-dimensional (3D) patient-specific, neonatal flow regimes during the typical neonatal aortic cannulation are classified using an experimentally and *in vivo* validated computational fluid dynamics (CFD) model. Hemodynamic performance indices that are critical for cannula design are defined and computed. Building upon an earlier study that classified congenitally defective aortic outflow track templates (Pekkan, et al. JBM, 2007) the impact of different HLHS arterial cannulation locations are studied. Microscopic computed tomography (micro-CT) scans of contemporary neonatal cannulae are performed to obtain the device-specific 3D reconstructions of the tip regions. The pulsatile jet-flow regimes at cannulae exit are investigated using our in-house high-resolution CFD solver utilizing both the *in vivo* and *in vitro* cannulae waveforms (Undar, et al.).

Results:

The cerebral distribution of blood flow and hemodynamic performance is tightly related to the positioning and orientation of the arterial cannula in standard and complex arch configurations. Major differences in the exit jet-flow structures and the wake development of different cannulae tip design resulted in significant changes in pulsatile energy dissipation and blood damage. CFD results are compared with *in vitro* pressure drop measurements from mock-up extracorporeal life support circuit and influenced by the jet structure.

Conclusions:

Patient-specific CFD results indicated that the major flow regimes which influence the hemodynamic performance of aortic cannulation are; (i) internal cannula flow, (ii) exit jet and (iii) wall stagnation flow. In this study the quality and performance of internal and exit jet flow structures are particularly focused and compared using a large number of device-specific microCT scans of neonatal cannulae tips. Exit jet-flow regimes of neonatal cannulae are less than optimum and there is significant room for improvement. The CFD aided predictive design approach as presented in this contribution will also be useful to optimize the hemodynamics of wall stagnation regime and can be applied to other neonatal circuit components.

Translational Research in Pediatric Extracorporeal Life Support Systems: 2011 Update

Akif Ündar, PhD, Feng Qiu, MD, Linda Pauliks, MD, Allen R. Kunselman, MA, David Palanzo, CCP, Larry Baer, CCP, Karl Woitas, CCP, Robert Wise, CCP, Robert McCoach, RN, CCP, Bonnie Weaver, RN, MSN, CCRN, Elizabeth Carney, DVM, Yulong Guan, MD, Mehmet C. Uluer, ScM, J Deborah Reed- Thurston, MD, Joseph Brian Clark, MD, John L. Myers, MD

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

Cardiovascular centers around the globe consider many factors when selecting components of the extracorporeal life support systems (ECLS). Ideally, they should have access to scientific data to guide evidence based choices, in order to optimize patient safety and minimize circuit related morbidity. Translational research is rarely done to evaluate different pump systems (roller vs. centrifugal), oxygenators, and cannulae (1). Three of the major focuses of Penn State Hershey Pediatric Cardiovascular Research Center are 1) to do translational research for selecting the best combination of pumps, oxygenators, cannulae, and tubing length on clinical ELCS, 2) to train clinicians (including clinicians from other centers) with our newest circuits in-vitro-and in-vivo, and 3) to share our clinical protocols with other pediatric centers around the globe. The main objective of this presentation is to share our most recent research results on custom-made ECLS circuitry.

Based on the results of the translational research and input from the entire clinical team including perfusionists, nurses, surgeons, and engineers, we built our Penn State Hershey Pediatric ECLS circuit (Figure 1), which is composed of a Rotaflow centrifugal pump, a Quadrox-iD Pediatric PMP HFMO, two Bio-Medicus ECLS cannulae (arterial and venous), and 3 feet of ¼ inch tubing for both the arterial and venous line.

All of the components in the circuit have been tested in our center before being used in piglet experiments, including the impact of different lengths and diameters of tubing on the hemodynamics of the circuit (1-3).

The priming volume of the circuit is 190 ml, and the inner surface has "tip to tip" biocompatible coating. It not only enables rapid priming (less than 10 minutes), but provides superior safety and portability, as well (2).

When we compared this new circuit with the conventional ECLS circuit, the results showed much lower pressure drops and a greater retention of total hemodynamic energy through the new circuit, and there was no retrograde flow using the centrifugal pump at flow rates as low as 250 ml/min (4, 5).

We have finished the training of the clinical ECLS team including 110 clinicians from five centers and we are now using this new circuit in our clinical settings (6).

Figure 1: Penn State Hershey Pediatric ECLS Circuit (1)



References

1. Qiu F, Clark JB, Myers JL, Ündar A, et al. Translational Research in Pediatric Extracorporeal Life Support System and Cardiopulmonary Bypass Procedure: 2011 Update. *World Journal for Pediatric and Congenital Heart Surgery* 2011 (in press).
2. Palanzo D, Qiu F, Baer L, Clark JB, Myers JL, Ündar A. Evolution of the ECLS circuitry [Guest Editorial]. *Artif Organs* 2010;34: 869-873.
3. Qiu F, Uluer MC, Kunselman A, Clark JB, Myers JL, Ündar A. Impact of the length of the tubing on hemodynamics in a simulated neonatal ECLS circuit. *Artif Organs* 2010;34: 1003-1009.
4. Khan S, Vasavada R, Qiu F, Kunselman AR, Ündar A. Extracorporeal Life Support Systems: Alternate vs. Conventional Circuits. *Perfusion*. 2011. (in press)
5. Clark JB, Guan Y, McCoach R, Kunselman AR, Myers JL, Ündar A. An investigational study of minimum rotational pump speed to avoid retrograde flow in three centrifugal blood pumps in a pediatric extracorporeal life support model. *Perfusion* 2011. (in press)
6. McCoach R, Weaver B, Carney E, et al. Pediatric extracorporeal life support systems: education and training at Penn State Hershey Children's Hospital. *Artificial Organs* 2010;34:1023-1026.

How Mechanical Circulatory Support Helps Not to Need It

U. Schweigmann
Pediatrics III, Cardiology, University Hospital Innsbruck

Background:

During the past three years five potential candidates for mechanical circulatory support (MCS) were treated in our center. Finally, none of them needed MCS despite the fact that all of these patients would have been supported with MCS, when treated five years earlier in our center.

Methods:

Subjects, seen in this period, where two toddlers, suffering from fulminant myocarditis, two adolescents, suffering from post-myocarditis-cardiomyopathy and one adolescent with endocardial fibroelastosis, resulting in severe restrictive left ventricular dysfunction after dilation of critical valvular aortic stenosis in the neonatal period.

All patients presented in acute cardiocirculatory decompensation. All patients were admitted to ICU, sedated and intubated. Use of catecholamines was kept short (<48h) by the standardized use of levosimendan and niteritide. MCS (ECMO, Berlinheart Excor Pediatric®, Heartware®) was always available. Initiation of MCS would have been indicated, in case of progressive multi organ failure (MOF).

The two toddlers recovered completely with normalization of myocardial function within 6 months. The three adolescents were listed for high urgency cardiac transplantation and received a graft within three weeks. None of the patients developed progressive MOF. All five patients were discharged home in NYHA I condition.

Conclusion:

Standardized use of new drugs and short-time availability of MCS allows more cautious indication for MCS. Integration of MCS to a standardized therapy, including modern drugs, results in excellent outcome at lower risk and better cost-effectiveness in pediatric patients with acute heart failure.

Acute Right Heart Failure Induced by Multiple Coronary Ligations in a Novel Animal Model

Jan D. Schmitto¹, Suyog A. Mokashi¹, Lawrence S. Lee¹, Otavio Coelho-Filho², Aron F. Popov³, Kasim O. Coskun³, Raymond Kwong², Martin Strüber³, Axel Haverich³, Lawrence H. Cohn¹, R. Morton Bolman III¹, Frederick Y. Chen¹

¹Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, USA

²Division of Cardiology, BWH, Harvard Medical School, Boston, USA

³Department of Cardiac-, Thoracic-, Transplantation- and Vascular-Surgery, Hannover Medical School, Hannover, Germany

Background:

Heart failure is one of the worldwide fastest growing epidemics in healthcare. Within this growing patient population, acute right heart failure (aRHF) is associated with a high mortality rate. Although a wide variety of left heart failure animal models exist, there are only a few truly successful, reproducible models of aRHF.

Methods:

Six healthy sheep (38±5kg) underwent multiple, strategic coronary artery ligations on the right ventricle (RV). Eight to ten ligations were performed transmurally on 3 of 4 RV-segments: anterior, lateral and posterior. Side branches of LAD and RCA were ligated to create multiple, patchy areas of myocardial infarction. Cardiac function was evaluated using echocardiography and pressure-volume-energetics for 30 minutes following coronary ligations.

Results:

In each sheep, aRHF was induced as visually noted by right ventricular hypo-/akinesis. Hemodynamically, CVP has significantly increased from 8±2mmHg (baseline) to 15±4mmHg (30 min), ($p<0.05$). Average right-ventricular-ejection-fraction (RVEF) has significantly decreased from 65±5% to 29±4% ($p<0.05$); RV-end-systolic-diameter (RVESD) increased significantly from 3.2±0.4cm to 6.0±0.4cm ($p<0.05$), whereas RV-end-diastolic-diameter (RVEDD) increased significantly from 6.4±0.4cm to 7.8±0.5cm (30min, $p<0.05$). Mean RVES-Area increased from 7.8±4cm² to 17.4±2.4cm² (30min) and RVED-Area increased from 12.6±0.8cm² (baseline) to 23.4±0.8cm² (30min), ($p<0.05$).

Conclusions:

We developed a novel model of acute, ischemic right heart failure using multiple coronary ligations clinically and hemodynamically mimicking right heart cardiomyopathy. Our proposed RHF-model is both, highly-effective and stable reproducible, potentially useful for further experimental research on new treatment methods for RHF, e.g. development of new drugs, right ventricular assist devices (RVAD), cardiac transplantation or more.

The Crucial Role of MMP and TIMP in the Regulation of Reverse Remodeling in Sheep Heart Failure

Tobias Vorkamp¹, Florian Heidrich¹, Philipp Ortmann¹, Samuel Sossalla², Kasim O. Coskun¹, Aron F. Popov¹, Christian Sohns², Suyog A. Mokashi³, Masoud Mirzaie¹, Michael Quintel⁴, Martin Bauer⁴, Friedrich A. Schoendube¹, Jan D. Schmitto^{1,3,5}

¹Department of Cardiac, Thoracic and Vascular Surgery, University Hospital Goettingen, Germany

²Division of Cardiology and Pneumology, University Hospital Goettingen, Germany

³Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

⁴Department of Anesthesiology, Emergency and Intensive Care Medicine, University Hospital Goettingen, Germany

⁵Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany

Background:

The following study describes investigations of biomolecular changes in a stable and reproducible animal model of chronic heart failure (CHF) in sheep. Therefore, different types of metalloproteinases (MMP) and tissue inhibitors of metalloproteinase (TIMP) were examined as they play a crucial role in the regulation of reverse remodeling of cardiac extracellular matrix. Additionally, for detection of inflammatory reactions in heart-failing animals expression of interleukin-1 β (Il-1 β) and tumor necrosis factor alpha (TNF- α) were analyzed.

Methods:

CHF was induced by multiple microembolization under fluoroscopic guidance. Therefore, polystyrol microspheres (90 μ m, n=25.000) were injected through cardiac catheter into left main coronary artery via bolus injection. Animals underwent CME up to three times in intervals of 2 to 3 weeks until they started to develop stable signs of CHF. Follow-up period was 3 months.

Expression of mRNA of MMPs (MMP-2, MMP-14), TIMPs (TIMP-1, TIMP-4), Il-1 β and TNF- α were quantitatively measured by real-time polymerase chain reaction. Glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) was used as a reference housekeeping gene. CHF was detected by clinical signs (tachycardia, tachypnoea, lung and peripheral edema), as well as echocardiographic examination (significantly decreased cardiac output, decreased ejection fraction) in all animals of CME group (n=10).

Results:

The presented experiments were performed in 15 juvenile sheep (78 \pm 4kg; control-group, n=3; ShamOP, n=2; coronary microembolization [CME], n=10). Quantitative analysis of biomolecular markers showed a significantly higher expression of Il-1 β and TNF- α in CHF animals compared with control myocardium (p<0.05). Also expression of MMP-14 and TIMP-4 was significantly higher in myocardium of embolized animals compared to control group (p<0.05).

Conclusion:

Multiple sequential intracoronary microembolization can effectively induce myocardial dysfunction with clinical and biomolecular signs of chronic ischemic cardiomyopathy. Quantitative analysis of biomolecular markers showed a significantly higher levels of MMP-2 and MMP-14 in CHF animals compared with control myocardium indicating activated reverse remodeling processes in heart failing animals. The model is well suitable for further experiments on the investigation of chronic heart failure treatment such as cardiac transplantation or left ventricular assist devices.

Cardioplegia and Angiotensin-I Receptor Antagonist Modulate STATs Activation in Neonatal Rat Myocardium.

Gianluca Lucchese, MD, Fabrizio De Rita, MD, Giuseppe Faggian, MD, Alessandro Mazzucco, MD, Giovanni Battista Luciani, MD.

Division of Cardiac Surgery, University of Verona, Italy.

Background:

Previous investigations have shown that the signal transducers and activators of transcription (STATs) signaling pathway plays an important role in the modulation of apoptosis after ischemia and reperfusion. The mechanism for this enhanced cardioprotection is unknown, but we believe that alterations STATs may play a role. To investigate this hypothesis, we examined the effects of Angiotensin I and II receptor antagonist added to cardioplegia on the downstream response of the different STATs, connected with pro-hypertrophic and anti-apoptotic pathways (STAT3) and with pro-inflammatory pathways (STAT2, STAT5).

Methods:

Isolated, non working hearts ($n = 3$ per group) from neonatal rats were perfused aerobically (37°C) for 20 minutes in the Langendorff mode with the modified St. Thomas' Hospital (MSTH) no. 2 cardioplegic solution (group 1), the MSTH no. 2 cardioplegic solution + Angiotensin (Ang)-I receptor antagonist (group 2) and MSTH + Ang-II receptor antagonist (group 3). Thus myocytes were isolated by enzymatic digestion and STAT2, STAT3 and STAT5 were investigated in Western blot studies.

Results:

Times to arrest after cardioplegia were 8-12 seconds for all groups. Total cardioplegia delivery volume was about 300 mL for the 20-minutes. STAT2 and STAT5 phosphorylation respectively +45% and +60% after 20/min were greater in group 1 than group 2 ($p < 0,05$). STAT2 and STAT5 activation was blunted by Ang-I receptor antagonism but not Ang-II. There were no significant differences in STAT3 phosphorylation among all groups.

Conclusions:

Only the addition of Ang-I receptor antagonist to modified St. Thomas' Hospital cardioplegia significantly decreases the inflammatory and the edematous response of the neonatal rat myocardium without affecting anti-apoptotic influence provided by tyrosine phosphorylation of STAT3. Ang-I receptor antagonist added to cardioplegia represents an additional modality for enhancing myocardial protection during cardiac surgery and could contribute to optimize the ischemia tolerance of the pediatric heart .

Balanced ultrafiltration: inflammatory mediator removal capacity

Yulong Guan, MD, Shigang Wang, MD, Cun Long MD.

Department of Extracorporeal Circulation, Cardiovascular Institute and Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100037, P. R. China

Background:

Ultrafiltration with hemoconcentration may remove excess fluid load and alleviate tissue edema, and has been universally adopted in extracorporeal circulation protocols during pediatric cardiac surgery. Balanced ultrafiltration is advocated to remove inflammatory mediators generated during surgery. However, whether balanced ultrafiltration can remove all or a portion of the inflammatory mediator load remains unclear. The inflammatory mediator removal capacity of balanced ultrafiltration was measured during pediatric extracorporeal circulation in vitro.

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 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%. After 2 hours of extracorporeal circulation, balanced ultrafiltration was initiated and arterial line pressure was maintained at approximately 100mmHg with Hoffman clamp. The rate of ultrafiltration (12ml/min) was controlled by ultrafiltrate outlet pressure. Identical volume of plasmalyte 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 inflammatory mediators including Interleukin (IL) 1 β , IL-6, IL-10, tumor necrosis factor (TNF) α , and neutrophil elastase (NE) were measured.

Results:

All assayed inflammatory mediators were detected in ultrafiltrate, demonstrating hemoconcentration may remove inflammatory mediators. However, dynamic observations suggested ultrafiltrate TNF α concentration was higher than IL-1 β , IL-6, IL-10 and NE ($p < 0.05$). Concentrations of all inflammatory mediators in ultrafiltrate were not increased linearly compared to those in plasma. The respective ultrafiltrate to plasma concentration ratios indicates hemoconcentration protocols only remove limited amounts of inflammatory mediators.

Conclusions:

Balanced ultrafiltration may selectively remove inflammatory mediators from serum. Respective ratios of inflammatory mediators in ultrafiltrate compared to plasma as well as total amount of inflammatory mediators in ultrafiltrate suggest balanced ultrafiltration removes a limited portion of total inflammatory mediator load.

Results of surgical treatment of residual congenital aortic stenosis: Balloon valvuloplasty versus open commissurotomy

Coskun KO¹, Tirilomis T¹, Schmitto JD^{1,2}, Popov AF^{1,3}, Hinz J⁴, Ruschewski W¹

¹Department of Cardiac, Thoracic and Vascular Surgery, University Hospital Goettingen, Germany

²Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany

³Department of Cardiac Transplantation and Mechanical Support, Royal Brompton & Harefield Hospitals, UK

⁴Department of Anesthesiology, Emergency and Intensive Care Medicine, University Hospital Goettingen, Germany

Background:

Despite its limited effectiveness in relief of aortic stenosis(AS) and high re-intervention rates, transcatheter balloon aortic valvuloplasty (BVP) still remains the first line treatment for critical AS in neonates. Since we propose that open commissurotomy is a valid option with good results for neonates, we evaluated the outcome of 37 patients after surgical treatment of residual aortic stenosis.

Methods:

Between 2000 and 2008, we retrospectively examined a total of 33 patients 8 female and 25 male neonates with residual aortic valve disease who underwent aortic valve surgery. Aortic dysfunction was congenital in all patients.

Results:

BVP was performed in 16 pts, and valve commisurotomy in 17pts. After the first intervention residual AS or severe aortic regurgitation developed in all patients. 15 patients with severe aortic valve regurgitation after aortic valvuloplasty underwent Ross operation as secondary operation. A total 9 patients required reoperations after commisurotomy, 5 of them had an mechanical aortic valve replacement because of aortic regurgitation. There were 2 in-hospital deaths and no late mortality. 14 of the patients are free from aortic valve surgery after commisurotomy. Survival after 10 years free from aortic valve surgery was 100%.

Conclusion:

Although BVP is the first line treatment in critical AS in neonates, surgical aortic valvuloplasty (Commisurotomy) is a valid option with good results for children with AS. Surgical commisurotomy for aortic valve stenosis can be done with low mortality and morbidity. The risk for early recurrent stenosis or regurgitation is low, and the need for aortic valve replacement can be delayed. Furthermore, cardiac surgeons should always be involved in preoperative therapy strategy to predict clinical benefit and success.

Experimental Evaluation of An Oxygenator with Integrated Pulsatile Pump for Pediatric Applications

Ralf Borchardt; Peter Schlanstein; Ilona Mager; Jutta Arens; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, PhD

Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

Purpose:

Large surface areas and high filling volumes are associated with adverse reactions within cardiopulmonary devices. By combining a pulsatile blood pump and an oxygenator the priming volume of an extracorporeal blood circuit can be reduced.

Methods:

Flexible silicone tubes (\varnothing_i 2 mm, wall thickness 150 μm) were placed in specific positions within the fiber bundle. With this predictable tube arrangement consistency the in-vitro test modules was ensured. The silicone tubes collapse and expand due to pulses. In combination with magnetic pinch valves at the oxygenator in- and outlet they generate a pulsatile flow through the oxygenator (fig1).

The pulsating tubes within the fiber bundle actively distribute blood inside the oxygenator. This could potentially reduce risk of shunt flows and recirculation- or stagnation areas and consequently increase the oxygenators' gas exchange efficiency.

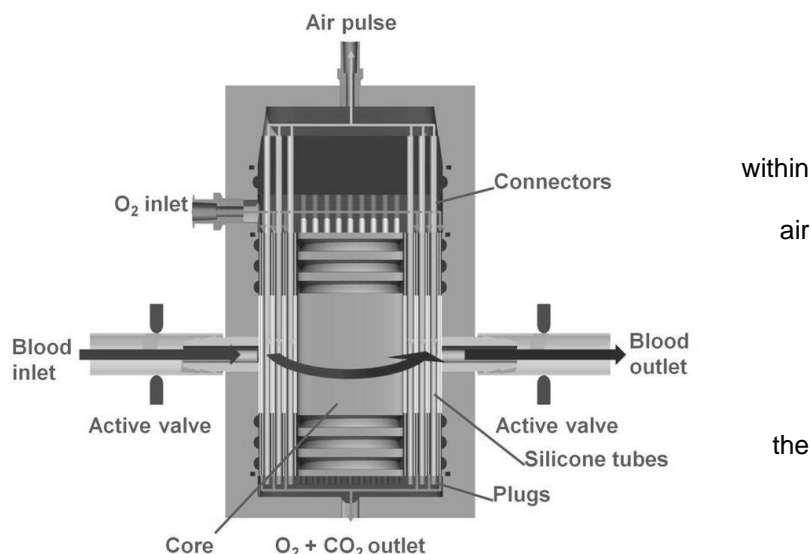


Fig. 2: Sectional view of oxygenator with integrated silicone tubes

Results:

In-vitro tests were done with five modules following the DIN EN 12022/ISO 7199, using heparinized porcine blood. For blood flows up to 500 ml/min the oxygen and carbon dioxide transfer rates were 60-77 $\text{ml}_{\text{O}_2}/\text{l}_{\text{blood}}$ and 45-77 $\text{ml}_{\text{CO}_2}/\text{l}_{\text{blood}}$ respectively.

Priming volume was below 25 ml. Hence, it is smaller than commercially available oxygenators even though it has an integrated pump.

Conclusions:

The results of the in-vitro tests show the feasibility of integrating a pulsatile pump, by means of collapsing and expanding silicone tubes, inside an oxygenator. All modules were able to sustain sufficient gas exchange for the pumped blood flow.

In a future design step these pumping silicone tubes could also be used as a heat exchanger, by using tempered saline solution as a driving fluid. First in-vitro tests that prove the practicability of saline solution as a driving fluid were successfully performed. This additional integration of a heat exchanger would further reduce the priming volume of an extracorporeal blood circuit and potentially expand the range of applications for oxygenators.

Analysis of pulsatile and nonpulsatile blood flow effects in different degrees of stenotic vasculature

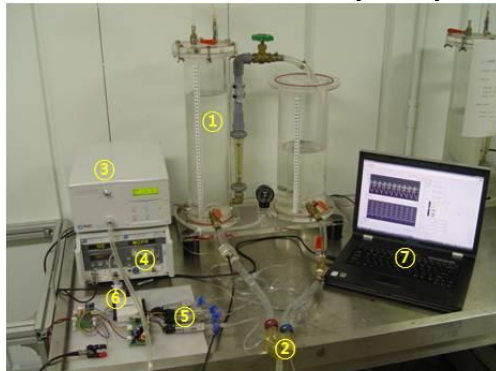
Jae Seung Jung¹², MD, Kuk Hui Son¹², MD, Chi Bum Ahn², PhD, Ho Sung Son¹², MD, Kyung Sun¹², MD
¹Department of Thoracic and Cardiovascular surgery, Anam Hospital, Korea University Medical Center.
²Korea Artificial Organ Center

Background:

A vessel lumen that chronically narrowed by atherosclerosis, should be increased in a flow velocity and intra-stenotic area pressure to maintain a equal flow. It can be followed by a decrease in the Energy Equivalent Pressure(EEP), lead to the reduction in perfusion on peripheral tissue. In this study, we will show the differences of EEP and flow change on the different degrees of stenotic vasculature

Methods:

The cannulae with 25%, 50%, and 75% intra-luminal stenosis of diameter were located to a outlet cannula(Figure 1). Using H-VAD(pulsatile pump: group A and Biopump(non-pulsatile pump: group B), constant flow of 2L/min is maintained then real time flow and velocity in distal part of the stenotic cannula is measured by ultrasonic flow meter and pressure sensor. The obtained values were digitalized by A/D converter and the data is analyzed by MATLAB.



- ① : Mockup system
- ② : Blood pump
- ③ : H-VAD
- ④ : Ultrasonic flow meter sensor
- ⑤ : Pressure sensor
- ⑥ : NI DAQ board
- ⑦ : Data logging computer

Results:

The decreased level of EEP(mmHg) on the 75% stenosis was in both groups much alike. (A: 160.7→67.3[58.2% decrease], B: 174.8→74.3[57.5% decrease]). As the percent EEP(%EEP) fell into below 10%, we found that a pulsatility was disappeared on the 50% stenosis in group A. Surplus Hemodynamic Energy(SHE) in all degrees group B was of course 0, but it was also zero in group A on the 75% stenosis.

Conclusions:

We made certain that a indication for intervention on above 75% stenosis of a diameter was appropriate. In spite of a pulsatile pump, a pulsatility was disappeared on above 50% stenosis of a diameter(X area 75%), but EEP maintained only on pulsatile pump in that conditions. Therefore we also could verify that a pulsatile flow had a advantage on the energy delivery.

Numerical Modeling of Anisotropic Fiber Bundle Behavior in Oxygenators

Sonya S. Bhavsar, MS; Marco Seiwert; Ralf Borchardt, Dipl.-Ing.; Roland Graefe, Dipl.-Ing.; Peter Schlanstein, Dipl.-Ing.; Jutta Arens, Dipl.-Ing.; Thomas Schmitz-Rode, MD; Ulrich Steinseifer, Dr.-Ing.

Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Helmholtz Institute, RWTH Aachen University, Aachen, Germany

Background:

Prediction of flow patterns through oxygenator fiber bundles can allow shape optimization such that efficient gas exchange can occur with minimal thrombus formation and hemolysis. Computational Fluid Dynamic (CFD) simulations can be used to predict three-dimensional flow velocities and flow distribution from spatially dependent variables and allow estimations of erythrocyte residence time within the fiber bundle. This study builds upon previous work to develop an accurate numerical model for oxygenators which would allow for accelerated iterations in oxygenator shape and diffuser plate design optimization.

Methods:

Hollow fiber flow channels were developed to permit experimental calculation of fluid permeability in two directions: main flow along the hollow fiber and perpendicular to the hollow fibers. Two fluid compartments were manufactured to permit one directional flow and hollow fibers were arranged in the axial and transverse directions to measure permeability. Commercial software (ANSYS CFX, Canonsburg, PA) was used to develop a three-dimensional CFD model of an anisotropic porous medium from these experimental results. This model was used to predict pressure loss throughout the device, visualize blood distribution within the fiber bundle, and estimate erythrocyte residence time within the bundle.

Results:

Experimental flow channels measurements produced a streamwise permeability of $1.143\text{e-}08 \text{ m}^2$ and transverse permeability of $2.385\text{e-}09 \text{ m}^2$. These permeabilities, coupled with previous work with volume porosity, were used to develop the numerical model of anisotropic behavior through porous fiber bundles which indicated a more uniform flow field throughout the oxygenator as shown in Figure 1.

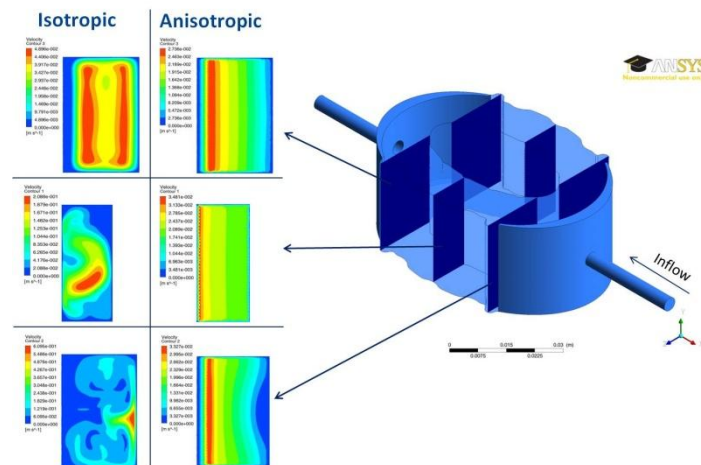


Figure 1: Comparison of isotropic and anisotropic flow distributions in oxygenator fiber bundles.

Conclusions:

Incorporation of known anisotropic fiber bundle behavior in previous numerical models more accurately represents fluid behavior through an oxygenator fiber bundle. CFD coupled with experimental validation can produce a powerful tool for oxygenator design and development.

Sodium Alginate Hydrogel Based Bioprinting Using a Novel Multi-Nozzle Bioprinting System

^{1,2}Seung Joon Song, MS, ^{1,2}Jaesoon Choi, PhD, ^{1,2}Yong Doo Park, PhD, ^{1,2}So Young Hong, MS, ¹Jung Joo Lee, PhD, ¹Chi Bum Ahn, PhD, ^{1,3}Kyung Sun, MD, PhD, MBA

¹Korea Artificial Organ Center, ²Brain Korea 21 Project for Biomedical Science, ³Department of Biomedical Engineering, ³Department of Thoracic and Cardiovascular Surgery, College of Medicine, Korea University, Seoul, Korea

Background: Bioprinting is an emerging technology for constructing bio-artificial tissues or organs of complex 3D structure, which provides with high precision spatial shape forming ability in larger scale than conventional tissue engineering methods and with simultaneous multiple components composition ability. It utilizes computer controlled three-dimensional printer mechanism for the three-dimensional biological structure construction. In this study, sodium alginate hydrogel that can be utilized for large dimension tissue fabrication with its fast gelation property was studied regarding its material-specific printing technique and printing parameter using a multi-nozzle bioprinting system.

Methods: A sodium alginate solution was prepared with concentration of 1.5% (w/v) and 0.5% CaCl₂ solution was used as cross-linker for the gelation. The two materials were loaded in each of two nozzles in the multi-nozzle bioprinting system that has total 4 nozzles of which the printing parameters such as injection speed, nozzle moving speed, and etc., can be separately controlled (Fig.1 Left). A 3D alginate structure was fabricated through a layer-by-layer printing manner. Each layer was formed through 2 phases of printing, one with the sodium alginate solution and the second with the calcium chloride solution, in identical printing pattern and speed condition. The target patterns were lattice shape with 2 mm spacing and two different line widths. The nozzle moving speed was 6.67 mm/sec and the injection head speed was 10 μ m/sec. For the two different line widths, two different injection needles with inner diameters of 260 μ m and 410 μ m were used. The number of layers accumulated was 5 in this experiment. By varying the nozzle moving speed and the injection speed, various pattern widths and pore sizes could also be achieved.

Results: An example of the layered printing results is shown in Fig. 1 (Center). Although the lattice structure could be well formed, the viscous property of the alginate hydrogel made the pattern dragged to slant. Fig. 1 (Right) shows an example of single layer printing with the thicker injection needle setting and comparatively clear right angle shape preservation in the printed pattern can be observed in contrast with layer accumulated test results.

Conclusions: The feasibility of sodium alginate hydrogel freeform formation by alternate printing of alginate solution and sodium chloride solution was confirmed in the developed multi-nozzle bioprinting system.

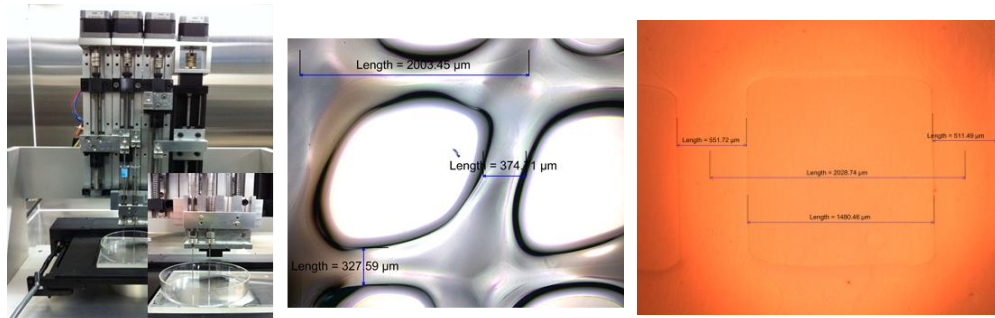


Figure 1. Multi-nozzle bioprinting system (left), layered printing result (center), and single layer example (right)

Evaluation of the Quadrox-i Neonatal Oxygenator with an Integrated Arterial Filter

Arash Salavitarab, BS¹, Feng Qiu, MD¹, Allen Kunselman, MA², Akif Ündar, PhD^{1,3,4}.

¹Pediatric Cardiovascular Research Center, Departments of ²Public Health and Sciences, Departments of ³Surgery, and ⁴Bioengineering, Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

Background:

Cardiopulmonary bypass (CPB) can be a potential cause of morbidity in patients for several reasons, including gaseous microemboli (GME) formation, diverted blood flow from the patient via an open purge line of the arterial filter, and pressure drop across the oxygenator. This study investigated the new QUADROX-i Neonatal Oxygenator (Maquet, D-72145, Hirrlingen, Germany) with an integrated arterial filter in terms of the hemodynamic properties and ability to clear GME in response to hypothermic versus normothermic conditions, open versus closed arterial filter purge line, and varying flow rates in a simulated CPB circuit.

Methods:

The QUADROX-i Neonatal Oxygenator with integrated arterial filter and Venous Hardshell Cardiectomy Reservoir (Maquet, VHK11000, Hirrlingen, Germany) were connected to a HL-20 roller pump (Jostra, Austin, TX), Jostra-30 heat-cooler system (Jostra, Austin, TX), and Capiox CR10 hard shell reservoir (Terumo Corporation, Tokyo, Japan) simulated as the pseudopatient. The purge line was composed of 24-inch-long tubing (1/8-1/32) without a one-way valve and COBE 5 port manifold (Sorin Cardiovascular Inc., Arvada, CO) connecting the oxygenator via the prefilter deairing port to the venous reservoir. A flow probe, pressure transducer, and Emboli Detection and Classification (EDAC) quantifier transducer were placed upstream and downstream to the oxygenator. The circuit was primed with fresh human blood of 26% hematocrit diluted with Lactate Ringer's solution. Five ml of air were injected proximal to the venous cardiectomy reservoir under non-pulsatile perfusion with flow rates of 500 ml/min, 750 ml/min, and 1000 ml/min under two different temperatures (35°C and 25°C). A total of 8 air bolus injections were made at each individual set of conditions for a total of 96 injections.

Results:

The QUADROX-i Neonatal Oxygenator displays extremely low pressure drops and blood flow diverted from the patient, as well as high rates of GME-capturing. A diverted flow less than 5% of the pump flow was observed, and the pressure drop across the oxygenator was not affected by the diverted flow through the purge line.

Table 1. The pressure drop, diverted flow, and GME capturing at different flow rates and temperatures (Mean±SD).

Pump Flow Rate (ml/min)	Purge Line Status	Pressure Drop (mm Hg)		“Stolen” Blood Flow (ml/min)		% GME Count (Post-Oxy/ Pre-Oxy)	
		35°C	25°C	35°C	25°C	35°C	25°C
500	Open	10.4 ± 0.6	12.4 ± 0.1*	20.5 ± 1.1	23.2 ± 1.3	3.9%	6.3%
	Closed	10.5 ± 0.1	12.8 ± 0.1	N/A	N/A	3.2%	9.7%
750	Open	18.3 ± 0.1*	22.8 ± 0.1*	22.8 ± 0.5	24.1 ± 0.9	18.7%	13.9%
	Closed	18.7 ± 0.1	23.1 ± 0.1	N/A	N/A	19.7%	12.4%
1000	Open	28.5 ± 0.1*	34.6 ± 0.1*	25.1 ± 0.8	27.3 ± 1.8	24.7%	42.1%
	Closed	28.9 ± 0.0	35.0 ± 0.1	N/A	N/A	28.6%	41.3%

* p < 0.001, purge line open vs. closed.

Conclusions:

The QUADROX-i Neonatal has excellent hemodynamic properties in terms of showing 1) extremely low pressure drops compared to all previous studies, 2) limiting the “stolen” blood flow caused by an open arterial filter purge line, as well as 3) displaying high rates of GME-capturing. An open purge line does not significantly affect the pressure drop across the oxygenator nor the percentage of total emboli cleared, but does increase the number of emboli detected.

Index of Authors

A

Ahn, CB 15, 28, 53, 59, 114, 116
Aiello, V 18, 28, 71
Akalin, F 28, 97
Akçevin, A 8, 11, 22, 23, 28, 93, 94, 95, 96
Albanese, S 20, 28, 80
Alkan, T 8, 13, 21, 22, 23, 28, 93, 94, 95, 96, 97, 101
Amodeo, A 20, 28, 80
Antunez, A 28, 35
Aoki, K 12, 28, 48
Aran, K 15, 28, 61, 103
Ardura, M 20, 28, 81
Arens, J 10, 26, 28, 49, 51, 70, 113, 115
Aytac, A 23, 28, 94, 95

B

Bacha, EA 8, 16, 28, 65
Bacht, S 13, 28, 52
Baer, LD 2, 3, 8, 17, 23, 24, 28, 62, 98, 101, 105
Bailey, LL 2, 8, 10, 28, 36
Barnes, A 20, 28, 81
Barnes, ML 8, 28, 75
Barozzi, L 20, 21, 28, 77, 88
Bauer, M 28, 55, 109
Bayer, V 23, 28, 94
Beaty, CD 8, 16, 28, 63
Becker, L 8, 11, 28
Bensberg, R 28, 51
Berens, R 21, 28, 83
Bhavsar, SS 19, 26, 28, 73, 115
Bird, GL 8, 17, 28
Böhning, F 19, 28, 74
Bolman, RM 25, 28, 108
Borchardt, R 14, 26, 28, 58, 113, 115
Bosecker, CJ 18, 28, 72

C

Caneo, LF 18, 28, 71
Carney, E 28, 105
Carr, JP 28, 73
Ceneviva, G 28, 62
Cestari, IA 13, 18, 28, 52, 71
Cestari, IN 13, 28, 52
Chen, FY 28, 55, 108
Choi, J 28, 53, 59, 60, 116
Chrisant, MRK 28, 34
Christensen, M 21, 28, 83

Christian, P 85
Clark, JB 2, 8, 11, 17, 19, 22, 28, 62, 75, 89, 101, 105
Coelho-Filho, O 28, 108
Cogo, P 20, 28, 80
Cohn, LH 28, 108
Collins, JJ 28, 49, 70
Connelly, JT 2, 8, 16, 28
Copeland, H 12, 28, 47
Copeland, JG 12, 28, 47
Corbett, SC 18, 28, 72
Coskun, KO 28, 54, 56, 108, 109, 112
Couturier, R 19, 28, 76
Covington, D 12, 28, 47
Cui, Y 14, 28, 57

D

Daitoku, K 12, 28, 48
Dando, H 28, 82
De Rita, F 20, 21, 25, 28, 77, 88, 110
Dimas, V 20, 28, 81
Ding, A 19, 28, 74
Dittmer, J 28, 82
Downs, EA 19, 28, 73
Duncan, DR 21, 28, 85
Duncan, KF 20, 28, 79
Dur, O 10
Durandy, Y 8, 18, 28

E

Eckhauser, A 11, 28, 45
Ersoy, C 22, 23, 28, 93, 94, 96

F

Faggian, G 20, 21, 25, 28, 77, 88, 110
Fatehpur, S 28, 54
Fok, A 15, 28, 61
Forbess, JM 11, 28, 46
Fragasso, T 20, 28, 80
Frey, T 2, 3, 8, 17, 24, 28
Friedrich, M 14, 28, 56
Fukuda, I 12, 28, 48
Fuller, S 8, 10, 11, 29, 45
Fynn-Thompson, F 18, 29, 72

G

Galantowicz, M 29, 100
Ganayem, N 8, 29

Gao, G	20, 29, 78
Gaynor, JW	2, 8, 11, 29, 34, 45
Gill, M	29, 82
Glatz, AC	29, 99
Gomez, D	29, 100
Goto, T	12, 29, 48
Graefe, R	19, 26, 29, 74, 115
Grizzard, JD	19, 29, 73
Gross-Toalson, J	20, 29, 81
Gruber, PJ	11, 29, 45
Gruenwald, CE	8, 11, 29, 38
Gutter, G	20, 29, 80
Guan, Y	15, 20, 25, 29, 61, 78, 105, 111
Guleserian, KJ	11, 20, 29, 46, 81

H

Haidet, KK	21, 29, 86
Hammel, JM	20, 29, 79
Hanna, BD	29, 34
Haverich, A	29, 108
Hayashida, SA	13, 29, 52
Hehir, D	8, 10, 29, 32
Hei, F	20, 29, 78
Heidrich, F	29, 54, 109
Hinz, J	29, 112
Homma, D	12, 29, 50
Hong, SY	29, 116
Hormes, M	14, 29, 58

J

Jaquiss, RDB	8, 10, 29, 35
Jatene, M	13, 18, 29, 52, 71
Jellema, RK	29, 49
Jobes, DR	2, 8, 10, 11, 29, 37
Journeycake, J	20, 29, 81
Jung, JS	29, 114

K

Kamdar, N	15, 29, 61
Kaufman, BD	8, 10, 11, 29, 34, 45
Kerins, PJ	21, 29, 85
Khan, S	22, 29, 90, 91
Kim, BJ	29, 69
Kim, M	29, 69
Kinsel, D	8, 24, 29, 102
Kirsch, RE	8, 29
Kopp, R	29, 51
Kramer, BW	29, 49, 70
Kunselman, AR	22, 29, 89, 90, 91, 105, 117
Kwong, R	29, 108

L

Lang, H	20, 29, 79
Lee, JJ	15, 29, 53, 59, 116
Lee, LS	29, 108
Lee, SH	29, 59
Lee, Y	20, 29, 81
Lei, J	29, 82
Levine, S	29, 34
Lind, C	29, 34
Liu, J	8, 24, 29
Liu, JP	14, 20, 29, 57, 78
Lodge, AJ	29, 35
Lohr, A	49, 70
Long, C	14, 20, 25, 29, 57, 78, 111
Lu, CK	23, 29, 98
Lucchese, G	20, 21, 25, 29, 77, 88, 110
Luciani, GB	8, 16, 19, 20, 21, 25, 29, 67, 77, 88, 110
Lv, S	20, 29, 78

M

Mackling, T	20, 29, 81
Mager, I	26, 29, 113
Mazzucco, A	20, 21, 25, 29, 77, 88, 110
McCauley, J	29, 82
McCoach, R	29, 105
McDonough, M	8, 16, 29, 63
Meinert, P	29, 62
Melchior, RW	29, 99
Menon, T	20, 29, 77
Menteer, J	29, 34
Merlini, A	21, 29, 88
Mirzaie, M	29, 54, 109
Miura, H	12, 29, 50
Mochizuki, S	12, 30, 50
Mokashi, SA	30, 55, 108, 109
Monos, D	30, 34
Montenegro, LM	11, 30, 45
Moskowitz, WB	19, 30, 73
Mott, AR	8, 30
Myers, JL	2, 8, 10, 16, 22, 23, 30, 62, 75, 89, 98, 101, 105

N

Nadkarni, VM	2, 8, 11, 30
Naguib, A	30, 100
Naim, MY	8, 11, 30, 43
Nicolson, SC	8, 11, 16, 30, 45, 64
Niebler, RA	21, 30, 83
Nolan, PE	12, 30, 47

O

O'Connor, MJ	11, 30, 34, 45
O'Shaughnessy, K	30, 82
Olshove, V	8, 24, 30, 100
Orlikowsky, T	30, 49, 70
Ortmann, P	30, 109
Osanai, A	12, 30, 48
Oyama, HTT	13, 30, 52

P

Paker, T	22, 23, 30, 93, 94, 95, 96
Palanzo, D	3, 8, 17, 23, 30, 98, 101, 105
Paridon, SM	30, 34
Park, J	30, 69
Park, JW	15, 30, 53, 59, 60
Park, YD	30, 60, 116
Pauliks, LB	8, 18, 30, 68, 105
Peddy, SB	2, 8, 17, 30
Pekkan, K	8, 24, 30, 104
Penha, J	18, 30, 71
Phillips, A	30, 100
Pizarro, C	30
Popov, AF	14, 30, 56, 108, 109, 112
Preston, T	30, 100
Priest, MA	2, 8, 17, 30

Q

Qiu, F	22, 23, 27, 30, 62, 89, 90, 91, 98, 101, 105, 117
Quintel, M	30, 55, 109

R

Raffini, L	2, 8, 10, 11, 30, 41
Rajab, TK	30, 55
Ravishankar, C	2, 8, 10, 11, 19, 30, 34, 45
Reed-Thurston, D	21, 30, 86, 105
Ricci, Z	20, 30, 80
Riso, A	8, 13, 18, 24, 30, 52, 71
Rohnean, A	30, 76
Rosenthal, T	8, 30, 99
Rossaint, R	30, 51
Rubatti, M	19, 30, 76
Rungatscher, A	21, 30, 88
Ruschewski, W	30, 112

S

Salavitarab, A	27, 30, 117
Sandica, E	8, 10, 19, 30, 33
Sasso, LA	15, 30, 61, 92, 103
Schlanstein, P	26, 30, 51, 113, 115

Schmitto, JD	14, 30, 54, 55, 56, 108, 109, 112
Schmitz-Rode, T	14, 19, 26, 30, 49, 51, 58, 70, 74, 113, 115
Schoberer, M	30, 49, 70
Schöndube, FA	30, 54, 56, 109
Schotola, H	30, 55
Schultz, M	30, 54
Schwartz, P	30, 54
Schweigmann, U	25, 30, 107
Seehase, M	30, 49, 70
Seelhorst, A	8, 16, 30, 63
Seiwert, M	26, 30, 115
Shah, T	20, 30, 81
Sharma, MS	11, 30, 46
Shenberger, J	21, 30, 86
Shiraishi, Y	12, 30, 50
Smith, R	12, 30, 47
Sohns, C	30, 54, 109
Son, HS	30, 59, 114
Son, KH	30, 59, 114
Song, SJ	30, 53, 59, 60, 116
Sossalla, S	30, 54, 55, 109
Spray, TL	8, 11, 16, 30, 45
Steinseifer, U	8, 14, 18, 19, 26, 30, 49, 51, 58, 70, 74, 113, 115
Stolf, NAG	13, 30, 52, 71
Strüber, M	30, 108
Sugai, TK	12, 31, 50
Sun, K	15, 31, 53, 59, 60, 114, 116
Sun, Q	15, 31, 61
Suzuki, Y	12, 31, 48
Suzuki, Yu	12, 31, 48

T

Tabbutt, S	2, 8, 16, 31
Tahir, SA	31, 73
Talor, J	22, 31, 91
Tanamati, C	18, 31, 71
Tate, RD	31, 73
Tempes, T	14, 31, 56
Throckmorton, AL	19, 31, 73
Tirilomis, T	14, 31, 56, 112
Toischer, K	31, 55
Topjian, A	8, 11, 31, 42
Türkoğlu, H	22, 23, 31, 93, 94, 95, 96, 97
Tweddell, JS	8, 11, 31, 39

U

Uluer, MC	31, 105
Ündar, A	2, 8, 15, 21, 22, 23, 24, 27, 31, 61, 62, 75, 86, 89, 90, 91, 92, 93, 95, 96, 98, 101, 103, 105, 117

V

Varano, C	20, 31, 80
Vasavada, R	22, 31, 90
Vorkamp, T	31, 109

W

Wagner, G	31, 51
Wang, SG	20, 25, 31, 78, 101, 111
Wang, SL	14, 31, 57
Weaver, BL	8, 16, 31, 62, 105
Wellner, H	21, 31, 83
Wernovsky, G	2, 8, 17, 31
Wise, R	31, 101, 105
Woitas, K	31, 101, 105

Wu, SJ	21, 31, 84
Wu, Y	19, 31, 73

Y

Yamada, A	12, 31, 50
Yamagishi, M	12, 31, 50
Yamazaki, A	12, 31, 48
Yambe, T	12, 31, 50
Yang, S	8, 18, 31, 69

Z

Zahn, JD	8, 15, 24, 31, 61, 92, 103
Zhou, C	14, 31, 57



The concept for the logo of the International Society for Pediatric Mechanical Cardiopulmonary Support originated from Jutta Arens, co-chair of the Young Investigator Committee. Graphic design and layout were completed by Martha Hansell, graphic designer for the Penn State Milton S. Hershey Medical Center, Onur Dur, co-chair of the Young Investigator Committee, and Karen Lu, member of the Young Investigator Committee. Final editing was performed by Dr. Feng Qiu, post-doctoral fellow at the Penn State Hershey Pediatric Cardiovascular Research Center.