The
Academy
NEWSLETTER

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OF
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SPRING 2015

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2015 Annual Meeting

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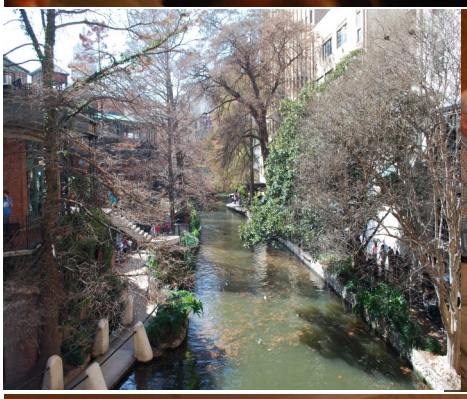





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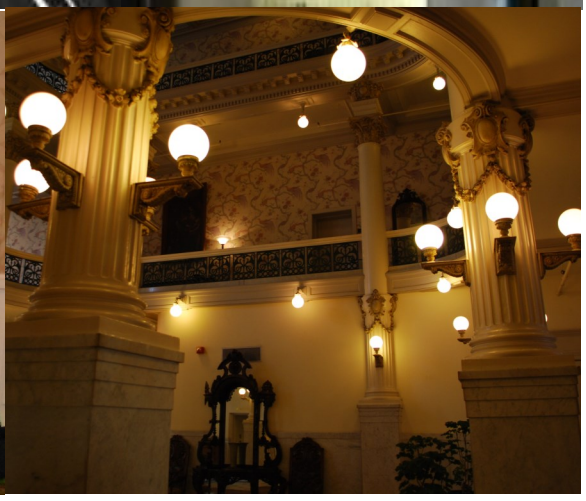

Welcome to New Members

The American Academy of Cardiovascular Perfusion would like to welcome the following individuals whom were voted into membership at the Closing Business Meeting of our annual meeting in San Antonio.

Fellows

Warren Goodwin

Members

Banjac, Igor
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Herrmann, Katelyn
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Jarjees, Dina
Jeck, Dean
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Johnson, Evan
Johnston, Luke
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Lamontagne, Alain
Lee, Min-Ho
Lieberman, Briana
Liu, Yiming Mike
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Manor, Kellen
Marchuk, Brooke
Mastela, Alexis
McCarty, Matthew
McMahon, Marcus
Melendez, Ashley
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Nokleby, Kevin
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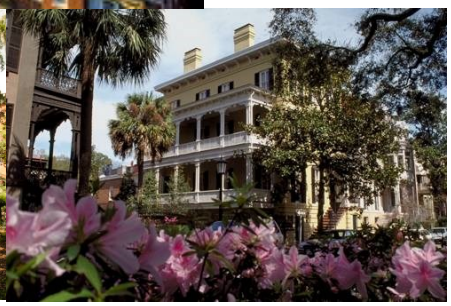
Risso, Ashley
Rodgers, Berkeley
Rodriquez, Krystal
Rowe, Justin
Schuldes, Matthew
Siegferth, Andrew
Silverman, Morgan
Simos, Krystal
Sims, Catherine
Staffaroni, Jenna
Starita, Daniel
Stephens, Rodney
Sydow, Olivia
Tran, Phat
Treadway, Anna
Trebs, Chelsea
Zahid, Zubaidah

2016 Annual Academy Meeting



Savannah, Georgia
February 4-7, 2016

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Awards Committee Selects Winning Paper Presentations

Three students received **Lawrence Awards** for their paper presentations at the Annual Seminar in San Antonio.

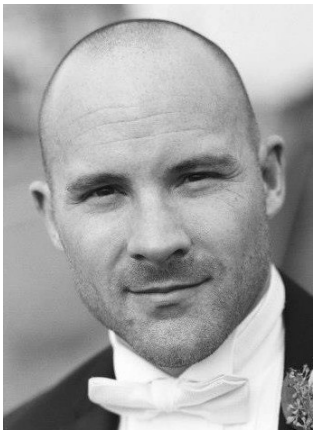
Sean Clingan - In Vitro Elimination Of Gaseous Microemboli Utilizing Hypobaric Oxygenation In The Terumo® Fx15 Oxygenator

Jessika Iwanski - Transmyocardial Revascularization And The Use Of Surgical And/Or Cell Therapy To Remodel Infarcted Hearts

Phat Tran - Red Blood Cell Hemolysis: Is It A Risk Factor Or A Risk Marker For Ventricular Assist Device Thrombosis?

The Lawrence Award is a $500 cash award for the best student papers presentations.

In addition, *Michael Colligan* was awarded the **Best Paper of the Conference -** a $750 cash award funded by the journal *Perfusion* for his presentation entitled, “The Optimal Number To Use When Estimating Patient Blood Volume For Cardiopulmonary Bypass.”



The C. N. Lee Pediatric Presentation Award was given to *Brandon Shade* for his paper entitled, “A Single Center’s Conversion From Roller Pump To Centrifugal Pump Technology In Extracorporeal Membrane Oxygenation .” This $500 award is supported by a generous grant from the New Foundation For Perfusion Education.

2015 *Perfusion* Liaison Report

Mark Kurusz and
John M. Toomasian

Perfusion
Section Editors

In calendar year 2014 there were 229 total submissions to *Perfusion,* including 20 submissions from the Academy. In June, the journal's impact factor was released and it had increased to 1.08, which was the fourth consecutive year of an increase. This signifies the growing respect the journal holds for readers and authors in the field. The overall manuscript acceptance rate is approximately 55-60%, but for Academy papers the acceptance rate in 2014 was 62%, which attests to the high quality of papers submitted from the AACP.

Beginning in 2015, *Perfusion* will publish eight issues each year. Last year, the AACP and SAGE Publications signed 5-year agreement whereby all papers presented at the Academy's annual meeting will be submitted to *Perfusion.* SAGE has also committed an annual $750 cash award given to the author of the best paper presented at the annual AACP meeting that is published in *Perfusion*. Congratulations to James R. Beck for his paper entitled, "Real-time data acquisition and alerts may reduce reaction time and improve perfusionist performance during cardiopulmonary bypass", which appeared in Volume 30, Number 1, January 2015.

As Section Editors for the journal, we maintain close contact with the *Perfusion* journal offices in London. In fact, we are responsible for overseeing reviewer assignments for all AACP papers submitted to the journal, and by prior agreement, one invited reviewer for every AACP submission is an Academy member. Three is the minimum number of reviewers for all papers undergoing peer review for *Perfusion*, and sometimes it may involve up to six reviewers before a recommendation is made to the Editor-in-Chief. Authors and reviewers for a given paper are sent the de-identified reviews, regardless of the reviewers' recommendations.

The Editorial Board composition is currently being reassessed since its last evaluation and changes three years ago. Decisions as to the composition of the Editorial Board are made by Editor-in-Chief with input from Section Editors. Additions or subtractions are based on contributions as an author and track records as reviewers. The Editor-in-Chief welcomes recommendations and/or volunteers. New reviewers are always welcome.

In summary, the affiliation between the Academy and *Perfusion* has been a mutually beneficial relationship. For the last two decades, all papers presented at the Academy meeting, whether in an oral or poster session, are afforded the opportunity for dissemination to an international audience. Another benefit can be found in the edited Commentaries accompanying many AACP papers that add additional perspectives to published papers. All Academy authors, and in particular students who often are first-time presenters, are to be congratulated on their scholarly contributions.

ON BYPASS

Transmyocardial Laser Revascularization and Stem Cell Therapy to Remodel an Infarcted Heart

Jessika Iwanski[1,2*], Raymond K Wong[1], Douglas F Larson[2], Alice S Ferng[2,3], Raymond B Runyan[4], Steven Goldstein[5], Zain Khalpey[2,3]

[1]University of Arizona College of Medicine, Department of Pharmacology [2] University of Arizona College of Medicine, Department of Surgery, Division of Cardiothoracic Surgery [3] University of Arizona College of Medicine, Department of Physiological Sciences [4] University of Arizona College of Medicine, Department of Cellular and Molecular Medicine
[5] Cryolife,Inc. Research and Development

A significant number of patients currently suffering from coronary artery disease (CAD) experience severe ischemia due to multi-vessel atherosclerotic obstruction, leading to heart failure and impaired myocardial function. Patients suffering from diffuse CAD, who present with refractory angina pectoris, are not amenable to percutaneous or conventional surgical interventions due to widespread coronary occlusion. For this patient population the extent of CAD is widespread therefore traditional revascularization alone is not sufficient to reinstate adequate flow through the coronary vessels. Transmyocardial revascularization (TMR) has emerged as an additional therapeutic option for this subset of patients, providing immediate angina relief (usually 2 or more class reduction) with improved quality of life, decreased cardiac events, decreased cardiac re-hospitalizations and decreased repeat revascularizations. Recent studies indicate that the volume of surgical cases being performed with TMR have been steadily rising, predominantly utilizing TMR as an adjunctive therapy to surgical interventions such as coronary artery bypass grafting (CABG). With the increase in case volumes and continued rise of cardiovascular disease, the evolution of this treatment modality continues to grow. Formerly, this laser treatment was proposed to create patent conduits within the myocardium, cause denervation, and redistribution of ventricular wall stress, in an attempt to increase perfusion and meet the aerobic demands of the heart. However present findings argue for an increased angiogenic response, leading to angina relief. The current potential of this therapy focuses on the implementation of stem cells with laser therapy, in order to create a synergistic angiogenic effect while simultaneously increasing myocardial repair and regeneration. Although TMR procedures provide increased vascularization within the myocardium, patients suffering from ischemic cardiomyopathy with depressed ventricular function may not benefit from angiogenesis alone. Therefore, the goal of introducing stem cells is to restore the functional state of a failing heart by providing these cells with a favorable microenvironment that will enhance stem cell engraftment and retention rates within an infarcted myocardium.

This was presented at the 36th Annual Seminar of The American Academy of Cardiovascular Perfusion in San Antonio, Texas. The full manuscript has been submitted to the journal Perfusion for possible publication.

ON BYPASS

HEMOLYSATE-MEDIATED PLATELET AGGREGATION: AN ADDITIONAL RISK MECHANISM RESULTING IN VAD THROMBOSIS

Phat L. Tran

Sarver Heart Center
University of Arizona
Tucson, AZ

This was presented at the 36th Annual Seminar of The American Academy of Cardiovascular Perfusion in San Antonio, Texas. The full manuscript has been submitted to the journal Perfusion for possible publication.

Despite rapid innovation in contemporary interventional medicine, the prognosis for advanced heart failure remains poor, often resulting in multiple hospitalizations, diminished quality of life, and death. Mechanical circulatory support devices are increasingly accepted as the standard of care for heart failure. More particularly, Continuous flow ventricular assist devices (cfVADs) have emerged as effective devices, restoring hemodynamics for advanced heart failure patients, becoming standard-of-care as bridge-to transplant or destination (long-term) therapy. Despite their success cfVADs remain plagued by thrombosis and hemolysis resulting in pump malfunction, recurrent heart failure, and embolic complications including stroke, pump stop and possible death. Recently a dramatic increase in cfVAD thrombosis was reported (NEJM 370:33, 2014), emphasizing the association of hemolysis and a rise in LDH presaging thrombotic events. Furthermore, the role of non-physiological flow and elevated shear stresses as to their contribution to platelet activation has recently been defined (PLoS one 7:e32463, 2012). These perturbed flows may lead to hemolysis and release of red blood cell (RBC) contents. What remain unknown is the link between cfVAD mediated hemolysis and thrombosis. We hypothesized that RBC fragments and released contents will potentiate platelet aggregation and activation. Herein, we specifically examined the effect of RBC hemolysate (RBC-h), plasma free hemoglobin (pHb) and lactate dehydrogenase (LDH), on platelet activation via impedance aggregometry (Multiplate Analyzer, MA). Basically, fresh human blood (normal volunteers, IRB approved) was obtained via venipuncture. Platelet-rich plasma (PRP) and RBCs were isolated via centrifugation. RBC were subjected to multiple PBS washings and hemolysate were prepared via sonication. A wide range of concentrations of RBC-h, pHb and LDH were used as agonist to investigate the platelet aggregation. Interestingly, platelets were found to be significantly aggregated when subjected to high level of pHb (120 mg/dL, 3X higher the threshold of hemolysis reported by INTERMACS), and RBC-h ($5e^6$ RBC-h/µl, $n = 4$, $p < 0.05$); but not LDH. SEM analysis of platelets induced by RBC-h showed platelet activation with dramatic filopodia extension and shape changes in contrast to washed RBC or platelets alone. It appears that RBC hemolysis and its released contents can contribute to platelet activation and the thrombotic process – i.e. risk factors, not just risk markers. In contrast LDH appears to be solely a risk marker. Further understanding the mechanism of platelet activation via RBC hemolytic mechanisms may provide an additional pathway to limit VAD (shear) mediated platelet activation, and reduce the thrombotic risk for VAD patients.

ON BYPASS

VENTRICULAR ASSIST DEVICE ALLOGRAFT SENSITIZATION: THEN TO NOW

Ashley Q. Risso
Raymond K. Wong, PhD, CCP
Douglas F. Larson, PhD

Department of Pharmacology,
University of Arizona
College of Medicine
Tucson, Arizona

Finding suitable hearts for transplant candidates is no easy task. In addition to blood-typing, organ size matching, and donor health, prior exposure to various non-self antigens can affect a candidate's likelihood of being selected for an available organ. A history of pregnancy, infection, and blood product transfusion can increase the risk for allograft sensitization. A host (candidate) exposure to foreign antigen can result in sensitization or polyclonal antibody formation. The host's immune system effectively primes itself against highly variable antigens that are introduced to the body and recognized as "non-self" in preparation for future antigen exposure. In terms of transplantation, preformed antibody burden against human leukocyte antigens (HLA) may be a precursor for organ rejection.

Left ventricular assist devices (LVADs) are increasing in popularity as bridge-to-transplant (BTT) therapy for heart transplant candidates. With growing transplant needs and donor organ scarcity, LVADs provide support for advanced heart failure patients who seldom survive the transplant wait list with medical management alone. Evidence suggests that LVAD-bridged patients are at increased risk for sensitization, a phenomenon that limits a candidate's success at being matched to a donor heart. Although the mechanism is not fully understood, LVAD-bridged candidates have a higher incidence of anti-HLA antibody burden than medically managed heart candidates. This phenomenon is due, in part, to confounding risk factors in the LVAD population. For example, device patients are often at higher risk for hemorrhage requiring supplementation with blood products. Likewise, the risk for infection is generally higher after LVAD implantation. Additionally, biomaterials and inert device components have been seen to cause dysregulation of inflammatory and immune processes.

In thirty years, LVAD technology has rapidly evolved. Compact continuous-flow pumps capable of long-term circulatory support have replaced their less durable pulsatile-flow predecessors. A qualitative review of high quality literature was conducted to compare whether device-type evolution has lessened the incidence of HLA sensitization in heart transplant candidates. While the issue of LVAD-induced sensitization persists today, the incidence associated with modern continuous-flow devices appears to be less than that of past pulsatile-flow devices. Thanks in part to immunosuppressive therapy, rejection and mortality outcomes were similar across all populations, whether the patient was medically managed or bridged with a device; similarly, device-type was not a factor in outcomes. However, LVAD-bridged candidates do appear to experience longer wait times to transplantation than medically managed patients and sensitization can certainly affect that wait.

Regarding perfusion practice, it is possible to reduce the risk of sensitization and subsequent wait times for LVAD heart candidates. Product transfusion should be conservative. Platelets are reported as being especially sensitizing. Leukofiltration of all blood products is best practice; even unfil-

tered non-cellular fresh frozen plasma (FFP) can introduce foreign HLA. If hemorrhage is a concern, autotransfusion and recombinant factors are preferred to banked blood product transfusion. Of note, both cardiopulmonary bypass and LVAD implantation are precursors for immune dysregulation - with an overlapping increase in proinflammatory cytokines and complement. Are these processes synergistic to one another? Is off-pump device implant of benefit for transplant candidates?

This was presented at the 36th Annual Seminar of The American Academy of Cardiovascular Perfusion in San Antonio, Texas. The full manuscript has been submitted to the journal Perfusion for possible publication.

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The Student Section

Off-Label Use

Kacie Baumgartner
University of Iowa Hospitals and Clinics
Perfusion Technology Education Program
Iowa City, IA

Off-label. Unintended use of. Not rated for. These are terms a perfusionist has likely come across in his or her career, and if not, will at some point. Some clinical situations require using perfusion disposables, equipment and drugs in a manner not recommended by the manufacturer because often there is no other FDA approved option or therapy available. It is because of this perfusionists, as patient advocates, have to be problem solvers and make due with what is available and to do right by the patient regardless of the approval status. I will explore off-label use in perfusion on three avenues – drugs, equipment, and technique. This, however, is not an all-inclusive list but more of a generalized exploration.

Drugs

Heparin-induced thrombocytopenia (HIT) and heparin-induced thrombocytopenia and thrombosis (HITT) both require alternative anticoagulation therapies. In HIT, patients have a decreased number of platelets due to removal by splenic macrophages (1). HITT patients also have thrombocytopenia with additional activation of platelets, which leads to platelet release, platelet aggregation, and lastly thrombosis. Instead of using heparin to anti-coagulate patients needing cardiopulmonary bypass (CPB) or extracorporeal membrane oxygenation (ECMO), several direct thrombin inhibiting (DTI) drugs have been utilized. Bivalirudin has been used as an alternative anticoagulation therapy if such patients are in need of extracorporeal life support. It is a direct thrombin inhibitor that does not require a cofactor for desired effect (2). It exhibits a half-life of 25 minutes for which approximately 80% is cleared by circulating proteases and approximately 20% is excreted by the renal system (2). Bivalirudin is FDA approved for patients with unstable angina undergoing percutaneous transluminal coronary angioplasty (3). However, the administration of bivalirudin for use as an anticoagulant during CPB is not FDA approved and therefore using it in such manner is off-label.

Recombinant factor VIIa (rFVIIa) is another example of a pharmacologic therapy not cleared for use by the FDA, yet is often used while on ECMO and after the termination of CPB. It can be utilized to attenuate post-operative bleeding and has been demonstrated in a retrospective study at the University of Iowa, Hospitals and Clinics that rFVIIa may be more beneficial in pediatric patients under 30kg. Infants also under six months of age have greater risk of hemorrhage due to immature coagulation factors (II, V, VII, X, XI, and XII) (4). It should be noted that administration of rFVIIa was given after all other bleeding protocols were exhausted, as this drug is an expensive off-label alternative. As rFVIIa is a clotting factor, one would be apprehensive to give a dose to a patient on any type of extracorporeal life support system. Even as a first year perfusion student, I understand the risk of unwanted thrombus that can result when giving this drug while on ECMO. One must weigh the potential risk of thrombus formation against the potential benefits the administration could have for your patient. A case report from Nationwide Children's Hospital reviewed the off-label administration to a 6-week old on ECMO. With a back-up circuit primed and ready, the team on two separate occasions gave the clotting factor with successful cessation of undesirable chest tube bleeding (5). Recombinant

factor VIIa is FDA approved for patients suffering from acquired hemophilia (6). It is not approved for use on an extracorporeal life support system or for recovery from a CPB procedure; therefore, using it in this way is also off-label.

Perfusion Disposables – Instructions For Use

A distinction needs to be made between technique and equipment. Equipment will be in the form of disposables and technique will be how one intends to use the equipment versus intention of use.

One example of using a disposable off-label is inserting an intra-aortic balloon (IAB) catheter through the left brachial artery. A case report out of Ontario, Canada demonstrates the unconventional off-label use of the IAB, performed in their catheterization lab, and how a perfusionist used experience to assess the critical situation (7). It states the instruction-for-use manual recommends a percutaneous insertion through the femoral artery or direct insertion into the aorta in the operating room. The patient suffered from extensive peripheral vascular disease and had previously undergone aortobifemoral graphs which resulted in a failed femoral approach (7). Threading the catheter through the left brachial artery positioned the IAB tip proximal to the renal arteries whereas the traditional approach would have placed the IAB tip just distal to the left subclavian artery. This off-label use is a prime example of a perfusionist's ingenuity and how resourceful one can be when presented with challenging circumstances.

One disposable of continued off-label use is the oxygenator. Hollow fiber and polymethylpentene (PMP) oxygenators are rated for six hours of use; therefore, using an oxygenator past hour six is off-label and not covered by the manufacturer (8). PMP oxygenators appear to be the gas transfer choice for long term devices like ECMO. However, it is not uncommon for a complex CPB procedure to exceed the six hour mark. The addition of an oxygenator to a ventricular assist device (VAD) is not off-label as you are using the oxygenator for its intended purpose – to oxygenate blood. But a VAD is a long term device making the addition greatly unconventional. Essentially, splicing an oxygenator into a VAD mimics an ECMO circuit, albeit simplified. This technique was done for a patient who first was unable to wean from bypass and ECMO support was also exhausted. The patient received a bi-VAD for both left and right heart support. Once the patient developed acute respiratory distress syndrome, the decision to add an oxygenator to the RVAD (right VAD) was made. The oxygenator was utilized for more than six hours resulting in off-label use of the disposable (9).

Perfusionists are constantly under pressure to reduce prime volume and surface area of our circuits. Reasons for this pressure include decreasing patient hemodilution, reducing the need to administer blood products, and overall cost (10). Some institutes are attempting to adopt a prescriptive patient extracorporeal circuit and oxygenator sizing protocol (10). Their first step was to decrease prime volume by simply combining the oxygenator and integrated arterial filter (10). Another option, while not recommended and off label, may be to undersize the oxygenator per the patient size resulting in pushing the rated gas transfer limits of the disposable. This is an extreme example of off-label use and may be exposing the patient to additional risks including malperfusion.

Myers gives several alternatives to using an oxygenator off-label and to decrease priming volumes in the CPB circuit (11). One technique is autologous priming. By retrograde autologous priming (RAP) and venous autologous priming (VAP), you can reduce prime volumes by 400-900mL for which he compares using a smaller oxygenator will only grant you 100mL (11). RAP comes with disadvantages of its own. Arterial cannulae are built for forward flow, so for sake of the topic, this would be considered an off-label use of the cannula. Improper technique can result in air being pulled across the aortic cannula purse-strings which would be delivered immediately back to your patient at initiation of bypass.

As perfusionists, while a great deal of our career is under direction of the surgeon at the table, our opinions and decisions also dictate outcomes for the patients we treat. It can be said that off-label prescribing is an integral part of contemporary medicine but that off-label prescribing can also harm patients and that the potential for harm is greatest when the off-label use lacks a solid evidence basis (11). Whether it be drugs, equipment or techniques, benefits must outweigh the possible misfortune from each decision made.

Continued on Page 15

Student Experiences From The Annual Meeting

The 2015 American Academy of Cardiovascular Perfusion Conference in San Antonio, Texas saw 40 students in attendance, which continues to bring a new dynamic to the Academy.

Let me just start by saying the perfect liaisons were chosen for the student society and from the moment I arrived at the airport, I felt welcomed and right at home. Everyone was very friendly and filled with information not just for the conference, but also for our future endeavors. They made us realize not only how important we were to the conference, but also to the field. The ambassador program in particular gave us students an opportunity to get to know one another and establish relationships that helped us set up flight, room, fundraiser, and fireside chat arrangements. The fundraiser gave us a chance to be creative but also a chance to communicate with everyone who acknowledged our efforts. The parts I enjoyed the most were the fireside chats! Being able to pick topics we were passionate about allowed us freely speak our minds among incredibly influential and experienced perfusionists. I left extremely enlightened and determined to return and make my mark on the Academy and in perfusion.

Thank you all for giving us this opportunity! It was a real pleasure!

Ashley Melendez

I am so grateful to have been a part of the AACP's student ambassador program this year. The ambassador program allowed students from 12 perfusion programs from all over the country to meet and collaborate together in a unique way. We all worked together to help support and encourage student attendance and participation in the annual symposium. Students brainstormed and planned their portion of the event over several months, providing a framework of collaboration and teamwork which they will then hopefully carry with them into their careers.

The symposium itself was such an amazing educational opportunity for students. Not only were we able to attend student-only fireside chats that were specifically directed toward our questions and concerns as we progress through school, but we were also able to attend the additional fireside chats that were of particular interest to us. In these fireside chats, we were able to discuss with practicing perfusionists and program chiefs our questions and concerns that we have in our current clinical rotations and learn other theories and methods of practice. In addition, the research and case presentations provided important knowledge to supplement our program education and clinical rotation experience, and introduced to us some of the most invaluable aspects of the perfusion community, knowledge sharing, research, and evidence based practice.

Thank you so much for the opportunity and privilege to be a student ambassador. It was an honor to attend and participate in such a great educational program as the AACP annual symposium.

Angela Hedman

Prior to attending, I was a little skeptical about how beneficial the meeting would be - especially considering a student's budget. I had attended state perfusion meetings before, but I just wasn't sure what the student's role would be at a larger, national meeting. However, immediately upon arrival I was pleasantly surprised by how accommodating all CCP's, vendors, and everyone else were to students. Many people took a genuine interest in our needs, and were more than welcoming to our input in all aspects of the meeting. Overall, the meeting was a fantastic environment to learn about our profession, network, and just have fun! The welcoming atmosphere of the AACP speaks wonders to the perfusion community - it is filled with great people and I'm so thrilled to have become a part of it!

Thanks again to Rich, Rich, and Bill for everything during and leading up to the meeting! It was a great experience and I hope to see you again at a meeting in the future!

Kate Herrmann

This was my first AACP meeting and I thoroughly enjoyed it! From the inspiring and innovative presentations to the fireside chats, I was able to get something out of everything during this meeting. I'm definitely looking forward to attending again, hopefully sometime in the very near future!

Mike Liu

Off-Label Use

Continued from Page 13

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Website: www.spectrummedical.com

TERUMO CARDIOVASCULAR SYSTEMS
Phone: 734-663-4145 or 800-521-2818
Fax: 734-663-7981
Website: terumo-cvs.com

Important Academy Dates

The ACADEMY ANNUAL MEETING DEADLINES

ABSTRACT DEADLINE	**October 30, 2015**
MEMBERSHIP DEADLINE	**December 4, 2015**
PRE-REGISTRATION	**January 8, 2016**
HOTEL REGISTRATION	**January 8, 2016**
2015 ANNUAL MEETING	**February 4—7, 2016**

Others Meetings

11th International Conference on Pediatric Mechanical Circulatory Support Systems & Pediatric Cardiopulmonary Perfusion
University of Verona
Verona, Italy
June 10-13, 2015.
Website: http://www.pennstatehershey.org/web/pedscpb

New England Perfusion Symposium
Brigham and Women's Hospital
Boston, MA
June 13, 2015
Phone: 617-638-6234
Website: http://massperfusion.com

Pennsylvania State Perfusion Society Fall Meeting
Crowne Plaza - Valley Forge
King of Prussia, PA
October 3-4, 2015
Phone: 610-265-7500
Website: http://www.cpvalleyforge.com